8638249

THE UNITED STATES OF AMERICA

TO ALL TO WHOM THESE PRESENTS SHALL COME:

UNITED STATES DEPARTMENT OF COMMERCE

United States Patent and Trademark Office

September 23, 2025

THIS IS TO CERTIFY THAT ANNEXED IS A TRUE COPY FROM THE RECORDS OF THIS OFFICE OF THE FILE WRAPPER AND CONTENTS OF:

APPLICATION NUMBER: ***18/113,710***
FILING DATE: ***February 24, 2023***
PATENT NUMBER: ***11832944***
ISSUE DATE: ***December 05, 2023***

Certified by

DIRECTOR OF THE UNITED STATES PATENT AND TRADEMARK OFFICE

Doc Code: TRACK1.REQ
Document Description: TrackOne Request

PTO/AIA/424 (04-14)

CERTIFICATION AND REQUEST FOR PRIORITIZED EXAMINATION UNDER 37 CFR 1.102(e) (Page 1 of 1)

First Named Inventor:	Bobby E. ROGERS	Nonprovisional Application Number (if known):	
Title of Invention:	BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE AND METHOD		

APPLICANT HEREBY CERTIFIES THE FOLLOWING AND REQUESTS PRIORITIZED EXAMINATION FOR THE ABOVE-IDENTIFIED APPLICATION.

1. The processing fee set forth in 37 CFR 1.17(i)(1) and the prioritized examination fee set forth in 37 CFR 1.17(c) have been filed with the request. The publication fee requirement is met because that fee, set forth in 37 CFR 1.18(d), is currently $0. The basic filing fee, search fee, and examination fee are filed with the request or have been already been paid. I understand that any required excess claims fees or application size fee must be paid for the application.

2. I understand that the application may not contain, or be amended to contain, more than four independent claims, more than thirty total claims, or any multiple dependent claims, and that any request for an extension of time will cause an outstanding Track I request to be dismissed.

3. The applicable box is checked below:

I. ☑ Original Application (Track One) - Prioritized Examination under § 1.102(e)(1)

i. (a) The application is an original nonprovisional utility application filed under 35 U.S.C. 111(a). This certification and request is being filed with the utility application via EFS-Web.

---OR---

(b) The application is an original nonprovisional plant application filed under 35 U.S.C. 111(a). This certification and request is being filed with the plant application in paper.

ii. An executed inventor's oath or declaration under 37 CFR 1.63 or 37 CFR 1.64 for each inventor, **or** the application data sheet meeting the conditions specified in 37 CFR 1.53(f)(3)(i) is filed with the application.

II. ☐ Request for Continued Examination - Prioritized Examination under § 1.102(e)(2)

i. A request for continued examination has been filed with, or prior to, this form.
ii. If the application is a utility application, this certification and request is being filed via EFS-Web.
iii. The application is an original nonprovisional utility application filed under 35 U.S.C. 111(a), or is a national stage entry under 35 U.S.C. 371.
iv. This certification and request is being filed prior to the mailing of a first Office action responsive to the request for continued examination.
v. No prior request for continued examination has been granted prioritized examination status under 37 CFR 1.102(e)(2).

Signature /Ben Hudson/	Date 02/24/2023
Name (Print/Typed) Benjamin F. Hudson	Practitioner Registration Number 71474

Note: *This form must be signed in accordance with 37 CFR 1.33. See 37 CFR 1.4(d) for signature requirements and certifications. Submit multiple forms if more than one signature is required.**

☑ *Total of 1 forms are submitted.

Privacy Act Statement

The **Privacy Act of 1974 (P.L. 93-579)** requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether disclosure of these records is required by the Freedom of Information Act.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (*i.e.*, GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspection or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

PTO/AIA/14 (02-18)
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Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Application Data Sheet 37 CFR 1.76	Attorney Docket Number	069366-0574153_KUR2C04US
	Application Number	
Title of Invention	BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE AND METHOD	

The application data sheet is part of the provisional or nonprovisional application for which it is being submitted. The following form contains the bibliographic data arranged in a format specified by the United States Patent and Trademark Office as outlined in 37 CFR 1.76.
This document may be completed electronically and submitted to the Office in electronic format using the Electronic Filing System (EFS) or the document may be printed and included in a paper filed application.

Secrecy Order 37 CFR 5.2:

☐ Portions or all of the application associated with this Application Data Sheet may fall under a Secrecy Order pursuant to 37 CFR 5.2 (Paper filers only. Applications that fall under Secrecy Order may not be filed electronically.)

Inventor Information:

Inventor 1 Remove

Legal Name

Prefix	Given Name	Middle Name	Family Name	Suffix
	Bobby	E.	ROGERS	

Residence Information (Select One) ● US Residency Non US Residency Active US Military Service

City	Park City	State/Province	UT	Country of Residence	US

Mailing Address of Inventor:

Address 1	10755 Scripps Poway, Parkway No. 257		
Address 2			
City	San Diego	State/Province	CA
Postal Code	92131	Country	US

Inventor 2 Remove

Legal Name

Prefix	Given Name	Middle Name	Family Name	Suffix
	Gino		KANG	

Residence Information (Select One) ◉ US Residency Non US Residency Active US Military Service

City	Irvine	State/Province	CA	Country of Residence	US

Mailing Address of Inventor:

Address 1	10755 Scripps Poway, Parkway No. 257		
Address 2			
City	San Diego	State/Province	CA
Postal Code	92131	Country	US

Inventor 3 Remove

Legal Name

Prefix	Given Name	Middle Name	Family Name	Suffix
	John		DETLOFF	

Residence Information (Select One) ◉ US Residency Non US Residency Active US Military Service

PTO/AIA/14 (02-18)
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	Application Number	
Title of Invention	BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE AND METHOD	

City	San Diego	State/Province	CA	Country of Residence	US

Mailing Address of Inventor:

Address 1	10755 Scripps Poway, Parkway No. 257		
Address 2	c/o Kurin, Inc.		
City	San Diego	**State/Province**	CA
Postal Code	92131	**Country**	US

All Inventors Must Be Listed - Additional Inventor Information blocks may be generated within this form by selecting the **Add** button. Add

Correspondence Information:

Enter either Customer Number or complete the Correspondence Information section below.
For further information see 37 CFR 1.33(a).

☐ **An Address is being provided for the correspondence Information of this application.**

Customer Number	27500		
Email Address	docket_ip@pillsburylaw.com	Add Email	Remove Email

Application Information:

Title of the Invention	BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE AND METHOD		
Attorney Docket Number	069366-0574153_KUR2C04US	**Small Entity Status Claimed**	☒
Application Type	Nonprovisional		
Subject Matter	Utility		
Total Number of Drawing Sheets (if any)	50	**Suggested Figure for Publication (if any)**	

Filing By Reference:

Only complete this section when filing an application by reference under 35 U.S.C. 111(c) and 37 CFR 1.57(a). Do not complete this section if application papers including a specification and any drawings are being filed. Any domestic benefit or foreign priority information must be provided in the appropriate section(s) below (i.e., "Domestic Benefit/National Stage Information" and "Foreign Priority Information").

For the purposes of a filing date under 37 CFR 1.53(b), the description and any drawings of the present application are replaced by this reference to the previously filed application, subject to conditions and requirements of 37 CFR 1.57(a).

Application number of the previously filed application	Filing date (YYYY-MM-DD)	Intellectual Property Authority or Country

Publication Information:

☐ Request Early Publication (Fee required at time of Request 37 CFR 1.219)

☐ **Request Not to Publish.** I hereby request that the attached application not be published under 35 U.S.C. 122(b) and certify that the invention disclosed in the attached application **has not and will not** be the subject of an application filed in another country, or under a multilateral international agreement, that requires publication at eighteen months after filing.

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Representative Information:

Representative information should be provided for all practitioners having a power of attorney in the application. Providing this information in the Application Data Sheet does not constitute a power of attorney in the application (see 37 CFR 1.32).
Either enter Customer Number or complete the Representative Name section below. If both sections are completed the customer Number will be used for the Representative Information during processing.

Please Select One:	● Customer Number	US Patent Practitioner	◯ Limited Recognition (37 CFR 11.9)
Customer Number	27500		

Domestic Benefit/National Stage Information:

This section allows for the applicant to either claim benefit under 35 U.S.C. 119(e), 120, 121, 365(c), or 386(c) or indicate National Stage entry from a PCT application. Providing benefit claim information in the Application Data Sheet constitutes the specific reference required by 35 U.S.C. 119(e) or 120, and 37 CFR 1.78.
When referring to the current application, please leave the "Application Number" field blank.

Prior Application Status	Pending		Remove
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)
	Continuation of	17538990	2021-11-11

Prior Application Status	Patented				Remove
Application Number	Continuity Type	Prior Application Number	Filing Date (YYYY-MM-DD)	Patent Number	Issue Date (YYYY-MM-DD)
17538990	Continuation of	16208559	2018-12-04	11185266	2021-11-30

Prior Application Status	Patented				Remove
Application Number	Continuity Type	Prior Application Number	Filing Date (YYYY-MM-DD)	Patent Number	Issue Date (YYYY-MM-DD)
16208559	Continuation of	15994559	2018-05-31	10143412	2018-12-04

Prior Application Status	Patented				Remove
Application Number	Continuity Type	Prior Application Number	Filing Date (YYYY-MM-DD)	Patent Number	Issue Date (YYYY-MM-DD)
15994559	Continuation of	15140448	2016-04-27	10010282	2018-07-03

Prior Application Status	Expired		Remove
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)
15140448	Claims benefit of provisional	62318194	2016-04-04

Application Data Sheet 37 CFR 1.76	Attorney Docket Number	069366-0574153_KUR2C04US
	Application Number	
Title of Invention	BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE AND METHOD	

Prior Application Status	Expired		Remove
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)
15140448	Claims benefit of provisional	62238636	2015-10-07
Prior Application Status	Expired		Remove
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)
15140448	Claims benefit of provisional	62196797	2015-07-24
Additional Domestic Benefit/National Stage Data may be generated within this form by selecting the **Add** button.			Add

Foreign Priority Information:

This section allows for the applicant to claim priority to a foreign application. Providing this information in the application data sheet constitutes the claim for priority as required by 35 U.S.C. 119(b) and 37 CFR 1.55. When priority is claimed to a foreign application that is eligible for retrieval under the priority document exchange program (PDX)[i] the information will be used by the Office to automatically attempt retrieval pursuant to 37 CFR 1.55(i)(1) and (2). Under the PDX program, applicant bears the ultimate responsibility for ensuring that a copy of the foreign application is received by the Office from the participating foreign intellectual property office, or a certified copy of the foreign priority application is filed, within the time period specified in 37 CFR 1.55(g)(1).

			Remove
Application Number	Country[i]	Filing Date (YYYY-MM-DD)	Access Code[i] (if applicable)
Additional Foreign Priority Data may be generated within this form by selecting the **Add** button.			Add

Statement under 37 CFR 1.55 or 1.78 for AIA (First Inventor to File) Transition Applications

☐ This application (1) claims priority to or the benefit of an application filed before March 16, 2013 and (2) also contains, or contained at any time, a claim to a claimed invention that has an effective filing date on or after March 16, 2013.
NOTE: By providing this statement under 37 CFR 1.55 or 1.78, this application, with a filing date on or after March 16, 2013, will be examined under the first inventor to file provisions of the AIA.

Application Data Sheet 37 CFR 1.76	Attorney Docket Number	069366-0574153_KUR2C04US
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Authorization or Opt-Out of Authorization to Permit Access:

When this Application Data Sheet is properly signed and filed with the application, applicant has provided written authority to permit a participating foreign intellectual property (IP) office access to the instant application-as-filed (see paragraph A in subsection 1 below) and the European Patent Office (EPO) access to any search results from the instant application (see paragraph B in subsection 1 below).

Should applicant choose not to provide an authorization identified in subsection 1 below, applicant **must opt-out** of the authorization by checking the corresponding box A or B or both in subsection 2 below.

NOTE: This section of the Application Data Sheet is **ONLY** reviewed and processed with the **INITIAL** filing of an application. After the initial filing of an application, an Application Data Sheet cannot be used to provide or rescind authorization for access by a foreign IP office(s). Instead, Form PTO/SB/39 or PTO/SB/69 must be used as appropriate.

1. Authorization to Permit Access by a Foreign Intellectual Property Office(s)

A. Priority Document Exchange (PDX) - Unless box A in subsection 2 (opt-out of authorization) is checked, the undersigned hereby **grants the USPTO authority** to provide the European Patent Office (EPO), the Japan Patent Office (JPO), the Korean Intellectual Property Office (KIPO), the State Intellectual Property Office of the People's Republic of China (SIPO), the World Intellectual Property Organization (WIPO), and any other foreign intellectual property office participating with the USPTO in a bilateral or multilateral priority document exchange agreement in which a foreign application claiming priority to the instant patent application is filed, access to: (1) the instant patent application-as-filed and its related bibliographic data, (2) any foreign or domestic application to which priority or benefit is claimed by the instant application and its related bibliographic data, and (3) the date of filing of this Authorization. See 37 CFR 1.14(h)(1).

B. Search Results from U.S. Application to EPO - Unless box B in subsection 2 (opt-out of authorization) is checked, the undersigned hereby **grants the USPTO authority** to provide the EPO access to the bibliographic data and search results from the instant patent application when a European patent application claiming priority to the instant patent application is filed. See 37 CFR 1.14(h)(2).

The applicant is reminded that the EPO's Rule 141(1) EPC (European Patent Convention) requires applicants to submit a copy of search results from the instant application without delay in a European patent application that claims priority to the instant application.

2. Opt-Out of Authorizations to Permit Access by a Foreign Intellectual Property Office(s)

☐ A. Applicant **DOES NOT** authorize the USPTO to permit a participating foreign IP office access to the instant application-as-filed. If this box is checked, the USPTO will not be providing a participating foreign IP office with any documents and information identified in subsection 1A above.

☐ B. Applicant **DOES NOT** authorize the USPTO to transmit to the EPO any search results from the instant patent application. If this box is checked, the USPTO will not be providing the EPO with search results from the instant application.

NOTE: Once the application has published or is otherwise publicly available, the USPTO may provide access to the application in accordance with 37 CFR 1.14.

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	Application Number	
Title of Invention	BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE AND METHOD	

Applicant Information:

Providing assignment information in this section does not substitute for compliance with any requirement of part 3 of Title 37 of CFR to have an assignment recorded by the Office.

Applicant 1 — Remove

If the applicant is the inventor (or the remaining joint inventor or inventors under 37 CFR 1.45), this section should not be completed. The information to be provided in this section is the name and address of the legal representative who is the applicant under 37 CFR 1.43; or the name and address of the assignee, person to whom the inventor is under an obligation to assign the invention, or person who otherwise shows sufficient proprietary interest in the matter who is the applicant under 37 CFR 1.46. If the applicant is an applicant under 37 CFR 1.46 (assignee, person to whom the inventor is obligated to assign, or person who otherwise shows sufficient proprietary interest) together with one or more joint inventors, then the joint inventor or inventors who are also the applicant should be identified in this section.

Clear

● Assignee	Legal Representative under 35 U.S.C. 117	Joint Inventor
Person to whom the inventor is obligated to assign.	Person who shows sufficient proprietary interest	

If applicant is the legal representative, indicate the authority to file the patent application, the inventor is:

Name of the Deceased or Legally Incapacitated Inventor:

If the Applicant is an Organization check here. ☒

Organization Name	Kurin, Inc.

Mailing Address Information For Applicant:

Address 1	10755 Scripps Poway Parkway, No. 257		
Address 2			
City	San Diego	**State/Province**	CA
Country	US	Postal Code	92131
Phone Number		Fax Number	
Email Address			

Additional Applicant Data may be generated within this form by selecting the Add button. Add

Assignee Information including Non-Applicant Assignee Information:

Providing assignment information in this section does not substitute for compliance with any requirement of part 3 of Title 37 of CFR to have an assignment recorded by the Office.

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Assignee 1

Complete this section if assignee information, including non-applicant assignee information, is desired to be included on the patent application publication. An assignee-applicant identified in the "Applicant Information" section will appear on the patent application publication as an applicant. For an assignee-applicant, complete this section only if identification as an assignee is also desired on the patent application publication.

Remove

If the Assignee or Non-Applicant Assignee is an Organization check here. ☒

Organization Name	Kurin, Inc.

Mailing Address Information For Assignee including Non-Applicant Assignee:

Address 1	10755 Scripps Poway Parkway, No. 257		
Address 2			
City	San Diego	**State/Province**	CA
Country i	US	Postal Code	92131
Phone Number		Fax Number	
Email Address			

Additional Assignee or Non-Applicant Assignee Data may be generated within this form by selecting the Add button. Add

Signature:

Remove

NOTE: This Application Data Sheet must be signed in accordance with 37 CFR 1.33(b). **However, if this Application Data Sheet is submitted with the INITIAL filing of the application and either box A or B is not checked in subsection 2 of the "Authorization or Opt-Out of Authorization to Permit Access" section, then this form must also be signed in accordance with 37 CFR 1.14(c).**

This Application Data Sheet **must** be signed by a patent practitioner if one or more of the applicants is a **juristic entity** (e.g., corporation or association). If the applicant is two or more joint inventors, this form must be signed by a patent practitioner, **all** joint inventors who are the applicant, or one or more joint inventor-applicants who have been given power of attorney (e.g., see USPTO Form PTO/AIA/81) on behalf of **all** joint inventor-applicants.

See 37 CFR 1.4(d) for the manner of making signatures and certifications.

Signature	/Ben Hudson/			Date (YYYY-MM-DD)	2023-02-24
First Name	Benjamin F.	Last Name	Hudson	Registration Number	71,474

Additional Signature may be generated within this form by selecting the Add button. Add

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This collection of information is required by 37 CFR 1.76. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 23 minutes to complete, including gathering, preparing, and submitting the completed application data sheet form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

Privacy Act Statement

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The information provided by you in this form will be subject to the following routine uses:

1 The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether the Freedom of Information Act requires disclosure of these records.

2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.

3 A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.

4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).

5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent CooperationTreaty.

6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).

7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.

8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspections or an issued patent.

9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE AND METHOD

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application is a Continuation of U.S. Application No. 17/538,990 filed November 11, 2021, entitled "BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE AND METHOD," which is a continuation of U.S. Application No. 16/208,559 filed December 4, 2018, entitled "BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE AND METHOD," now U.S. Patent 11,185,266, issued November 30, 2021, which is a Continuation of U.S. Application No. 15/994,559, filed on May 31, 2018 and titled "BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT EQUESTRATION DEVICE AND METHOD," now U.S. Patent 10,143,412, issued December 4, 2018; which is a Continuation of U.S. Application No. 15/140,448, filed on April 27, 2016, now U.S. Patent 10,010,282 issued July 3, 2018, which claims the benefit of U.S. Provisional Application Serial No. 62/196,797, filed on July 24, 2015 and titled "BLOOD CULTURE IMPROVEMENT SYSTEM AND METHOD"; U.S. Provisional Application Serial No. 62/238,636, filed on October 7, 2015 and titled "BLOOD SEQUESTRATION SYSTEM FOR NON-CONTAMINATED BLOOD SAMPLING"; and U.S. Provisional Application Serial No. 62/318,194, filed on April 4, 2016 and titled "BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE AND METHOD," the disclosures of which are incorporated by reference in their entirety.

BACKGROUND

[0002] Bacteraemia is the presence of microorganisms in the blood. Sepsis, on the other hand, is bacteraemia in the presence of clinical symptoms and signs such as fever, tachycardia, tachypnea and hypotension. Bacteraemia and sepsis are associated with a high mortality and an increased incidence and duration of hospital stay and associated costs.

Many bacteraemias, sepsis, fungaemias and other pathogens actually occur within a hospital or other healthcare settings with catheters and venipunctures being a source of contamination as potential carriers of these pathogens.

[0003] Blood cultures are the standard test used to detect microbial pathogens related to bacteraemia and sepsis in a patient's blood. The term blood culture refers to a single venipuncture, either from a peripheral site or central or arterial line, with the blood inoculated into one or more blood culture bottles or containers. One bottle is considered a blood culture where two or more are considered a set. Multiple sets may be obtained from multiple venipunctures and are associated with different sites on the patient.

[0004] These methods allow for microbial identification and susceptibility testing to be performed, which is a critical component to managing sepsis, however the lack of rapid results and decreased sensitivity for fastidious pathogens has led to the development of improved systems and adjunctive molecular or proteomic testing.

[0005] Collection of blood samples for conducting blood cultures is a critical component of modern patient care and can either positively affect the patient outcome by providing an accurate diagnosis, or can adversely affect the outcome by prolonging unnecessary antimicrobial therapy, the length of hospital stays, and increasing costs.

[0006] One outcome of collection of blood cultures is contamination. Blood culture contamination can lead to a false positive culture result and/or significant increase in healthcare related costs. Sources of blood culture contamination include improper skin antisepsis, improper collection tube disinfection, and contamination of the initial blood draw which may then skew results.

[0007] Blood culture collection kits generally consist of a "butterfly" set, infusion set, or other type of venipuncture device as offered by companies like BD, Smiths, B. Braun and others, and aerobic and anaerobic blood culture bottles. Various different bottles are also available depending on the test requirements. These bottles are specifically designed to optimize recovery of both aerobic and anaerobic organisms. In conventional kits, a bottle used is known generally as a "Vacutainer," which is a blood collection tube formed of a

sterile glass or plastic tube with a closure that is evacuated to create a vacuum inside the tube to facilitate the draw of a predetermined volume of liquid such as blood.

[0008] False positive blood cultures are typically a result of poor sampling techniques. They cause the use of antibiotics when not needed, increasing hospital costs and patient anxiety. Blood cultures are drawn from a needlestick into the skin, and then a Vacutainer is attached to capture a sample of blood. Contamination may occur from improper or incomplete disinfection of the skin area in and around the puncture site. It may also occur from the coring of the skin by the needle during insertion, with the cored skin cells and any associated contamination being pulled into the sample.

[0009] Blood flow through a hypodermic needle is laminar, and as such, a velocity gradient can be developed over the flow tube as a pressure drop is applied to the hypodermic needle. Either forceful aspiration of blood, or using a very small hypodermic needle, can cause lysis and a release of potassium from the red blood cells, thereby rendering the blood samples abnormal.

[0010] In other instances, some patients have delicate veins that can collapse under a pressure drop or vacuum, particularly as applied by a syringe's plunger that is drawn too quickly for the patient's condition. Since such condition is impossible to know beforehand, such vein collapses are a risk and very difficult to control.

[0011] Various strategies have been implemented to decrease blood culture contamination rates, e.g. training staff with regard to aseptic collection technique, feedback with regard to contamination rates and implementation of blood culture collection kits. Although skin antisepsis can reduce the burden of contamination, 20% or more of skin organisms are located deep within the dermis and are unaffected by antisepsis. Changing needles before bottle inoculation is not advisable as it increases the risk to acquire needle stick injuries without decreasing contamination rates.

[0012] Some conventional systems and techniques for reducing blood culture contamination include discarding the initial aliquot of blood taken from central venous catheters, venipunctures, and other vascular access systems. However, these systems require

the user to mechanically manipulate an intravascular device, or require a complex series of steps that are difficult to ensure being followed.

SUMMARY

[0013] This document presents systems and methods for reducing blood culture contamination, lysing of cells, and vein collapse. In some implementations, a system and method can eliminate user variability in disinfection, and also eliminate the risk of skin cells getting into the blood culture sample. The systems and methods disclosed herein do not require a change in existing clinical processes, other than to potentially indicate when a vacutainer or other blood collection device (i.e., syringe) should be attached for drawing contaminant-free blood samples.

[0014] In some implementations of the systems and methods disclosed herein the withdrawal of blood is accomplished passively by use of the patient's own blood pressure, thereby reducing the risk of vein collapse and eliminating any additional user steps over current practice. The systems and methods can be applied to accommodate short-path direct stick or butterfly venipuncture systems. They can also be used with samples drawn through a catheter.

[0015] In one aspect, a blood sequestration device is presented. The blood sequestration device includes an inlet port and an outlet port. The blood sequestration device further includes a sequestration chamber connected with the inlet port, the sequestration chamber having a vent comprising an air permeable blood barrier. The blood sequestration device further includes a sampling channel having a proximal end connected with the inlet port and a distal end connected with the outlet port.

[0016] In another aspect, a blood sequestration device connected with a blood sampling pathway is described. The blood sampling pathway has a patient needle and a sample collection device. The blood sequestration device includes an inlet port connected with the patient needle, and a sequestration chamber connected with the inlet port, the sequestration chamber having a vent comprising an air permeable blood barrier. The blood sequestration device further includes a sampling channel having a proximal end connected with the inlet

port, and an outlet port connected with a distal end of the sampling channel and with the sample collection device.

[0017] In yet another aspect, a blood sequestration device connected with a blood sampling system is described. The blood sampling system includes a patient needle for accessing a blood sample from a patient, and a sample needle that is sealed and adapted for receiving an evacuated blood collection tube. The blood sequestration device includes an inlet port connected with the patient needle to receive the blood sample from the patient. The blood sequestration device further includes a sequestration chamber connected with the inlet port and having a vent comprising an air permeable blood barrier, the sequestration chamber for receiving and sequestering a first portion of the blood sample prior to the sample needle being unsealed by the evacuated blood collection tube. The blood sequestration device further includes a sampling channel having a proximal end connected with the inlet port, the sampling channel for conveying a subsequent portion of the blood sample once the sample needle is unsealed by the evacuated blood collection tube. The blood sequestration device further includes an outlet port connected with a distal end of the sampling channel for conveying the subsequent portion of the blood sample to the sample needle.

[0018] In yet another aspect, a blood sample optimization system is disclosed and described. The blood sample optimization system includes a blood sampling system for accessing and acquiring one or more samples of a patient's blood, and a blood sequestration device for receiving and sequestering a first portion of the one or more samples of the patient's blood which might be contaminated by a venipuncture process and which could result in a false positive identification of a pathogen in the patient's blood.

[0019] The blood sampling system includes a patient needle configured for a venipuncture of a patient to access a sample of blood of a patient, a blood sampling pathway connected with the patient needle for conveying the sample of blood, and a sample needle configured for receiving an evacuated blood collection container to collect and contain a subsequent portion of the sample of blood.

[0020] In yet another aspect, a blood sequestration device is disclosed and described. In some implementations, the blood sequestration device can include an inlet port, an outlet port

connected with the inlet port, and a sequestration chamber connected with the inlet port. The sequestration chamber can have a vent comprising an air permeable blood barrier.

[0021] The blood sequestration device is connected along the blood sampling pathway between the patient needle and the sample needle, and includes an inlet port for receiving the sample of blood. The blood sequestration device further includes a sequestration chamber connected with the inlet port for receiving a first amount of the sample of blood, the sequestration chamber having a vent comprising an air permeable blood barrier for sequestering at least a first portion of the first amount of the sample of blood. The blood sequestration device may further include a sampling channel having a proximal end connected with the inlet port, the sampling channel conveying a subsequent amount of the sample of blood to the evacuated blood collection container upon the sequestration chamber sequestering at least the first portion of the first amount of the sample of blood. The blood sequestration device further includes an outlet port connected with a distal end of the sampling channel, the outlet port for outputting the subsequent amount of the sample of blood.

[0022] The details of one or more embodiments are set forth in the accompanying drawings and the description below. Other features and advantages will be apparent from the description and drawings, and from the claims.

BRIEF DESCRIPTION OF THE DRAWINGS

[0023] These and other aspects will now be described in detail with reference to the following drawings.

[0024] FIG. 1 illustrates a blood sample optimization system.

[0025] FIG. 2 illustrates a blood sample optimization system in accordance with an alternative implementation.

[0026] FIG. 3 illustrates a blood sample optimization system in accordance with another alternative implementation.

[0027] FIG. 4 illustrates a blood sample optimization system in accordance with another alternative implementation.

[0028] FIG. 5 illustrates a blood sample optimization system in accordance with another alternative implementation.

[0029] FIG. 6 illustrates a blood sample optimization system in accordance with an alternative implementation.

[0030] FIG. 7 is a flowchart of a method for optimizing a quality of a blood culture.

[0031] FIGS. 8A – 8E illustrate a blood sequestration system for non-contaminated blood sampling, in accordance with some implementations.

[0032] FIG. 9 illustrates a pathway splitter for use in a blood sequestrations system.

[0033] FIGS. 10A – 10D illustrate a blood sequestration system for non-contaminated blood sampling, in accordance with alternative implementations.

[0034] FIGS. 11A – 11E illustrate a blood sequestration system for non-contaminated blood sampling, in accordance with other alternative implementations.

[0035] FIGS. 12A-12D illustrate a blood sample optimization system including a blood sequestration device in accordance with yet other alternative implementations.

[0036] FIGS. 13A-13D illustrate a blood sample optimization system 1300 in accordance with yet another alternative implementations.

[0037] FIGS. 14A-14E illustrate yet another implementation of a blood sampling system to sequester contaminates of an initial aliquot or sample to reduce false positives in blood cultures or tests performed on a patient's blood sample.

[0038] FIGS. 15A-15G illustrate a blood sequestration device and method of using the same, in accordance with yet another implementation.

[0039] FIGS. 16A-16D illustrate a blood sequestration device in accordance with yet another implementation.

[0040] FIGS. 17A – 17E illustrate a bottom member of a housing for a blood sequestration device.

[0041] FIGS. 18A – 18F illustrate a top member of a housing for a blood sequestration device.

[0042] FIGS. 19A and 19B illustrate a blood sequestration device having a top member mated with a bottom member.

[0043] FIG. 20 shows a blood sample optimization system including a blood sequestration device.

[0044] FIG. 21 illustrates a non-vented blood sequestration device using a wicking material chamber.

[0045] FIGS. 22A and 22B illustrate a material makeup of a filter for sequestering blood in a sequestration chamber of a blood sequestration device.

[0046] FIGS. 23A and 23B illustrate another implementation of a blood sequestration device that uses a vacuum force from a blood collection device.

[0047] Like reference symbols in the various drawings indicate like elements.

DETAILED DESCRIPTION

[0048] This document describes blood sample optimization systems and methods for reducing or eliminating contaminates in collected blood samples, which in turn reduces or eliminates false positive readings in blood cultures or other testing of collected blood samples. In some implementations, a blood sample optimization system includes a patient needle for vascular access to a patient's bloodstream, a sample needle for providing a blood sample to a blood collection container, such as an evacuated blood collection container or tube like a Vacutainer™ or the like, or other sampling device, and a blood sequestration device located between the patient needle and the sample needle. The blood sequestration device includes a sequestration chamber for sequestering an initial, potentially contaminated aliquot of blood, and may further include a sampling channel that bypasses the sequestration

chamber to convey likely uncontaminated blood between the patient needle and the sample needle after the initial aliquot of blood is sequestered in the sequestration chamber.

[0049] FIG. 1 illustrates a blood sample optimization system in accordance with some implementations. The system includes a patient needle 1 to puncture the skin of a patient to access the patient's vein and blood therein. The system further includes a sample needle (i.e., a resealably closed needle for use with Vacutainers™ or the like) 5, which may be contained within and initially sealed by a resealable boot 10, a Luer activated valve, or another collection interface or device. The resealable boot 10 can be pushed aside or around the sample needle 5 by application of a Vacutainer™ bottle (not shown) for drawing the patient's blood. The system can further include a low volume chamber 30 that leads to the sample needle 5, but also includes an orifice or one or more channels 45 that lead to a sequestration chamber 55 formed by a housing 50.

[0050] The sequestration chamber 55 is a chamber, channel, pathway, lock, or other structure for receiving and holding a first aliquot of the patient's blood, which may be in a predetermined or measured amount, depending on a volume of the sequestration chamber 55. The first draw of blood typically contains or is more susceptible to containing organisms that cause bacteraemia and sepsis or other pathogens than subsequent blood draws. The sequestration chamber 55 can be a vessel encased in a solid housing, formed in or defined by the housing itself, or can be implemented as tubing or a lumen. The sequestration chamber 55, regardless how formed and implemented, may have a predetermined volume. In some implementations, the predetermined volume may be based on a volume of the patient needle, i.e. ranging from less than the volume of the patient needle to any volume up to or greater than 20 times or more of the volume of the patient needle. The predetermined volume of the sequestration chamber 55 may also be established to economize or minimize an amount of blood to be sequestered and disposed of.

[0051] The sequestration chamber 55 can be formed, contained or housed in a chamber housing 50, and can be made of plastic, rubber, steel, aluminum or other suitable material. For example, the sequestration chamber 55 could be formed of flexible tubing or other elastomeric materials. The sequestration chamber 55 further includes an air permeable blood barrier 20 that allows air to exit the sequestration chamber 55. As used herein the term

"air permeable blood barrier" means an air permeable but substantially blood impermeable substance, material, or structure. Examples may include hydrophobic membranes and coatings, a hydrophilic membrane or coating combined with a hydrophobic membrane or coating, mesh, a filter, a mechanical valve, antimicrobial material, or any other means of allowing air to be displaced from the sequestration chamber 55 as it is filled with blood. In various exemplary embodiments, an air permeable blood barrier may be formed by one or more materials that allow air to pass through until contacted by a liquid, such material then becomes completely or partially sealed to prevent or inhibit the passage of air and/or liquid. In other words, prior to contact with liquid, the material forms a barrier that is air permeable. After contact with a liquid, the material substantially or completely prevents the further passage of air and/or liquid.

[0052] The orifice or channel 45 can be any desired length, cross-sectional shape or size, and/or can be formed to depart from the low volume chamber 30 at any desired angle or orientation. The orifice or channel 45 may also include a one-way flap or valve 60 that maintains an initial aliquot of blood sample within the sequestration chamber 55. In some specific implementations, the orifice or channel 45 can include a "duck bill" or flapper valve 60, or the like, for one-way flow of blood from low volume chamber 30 to the sequestration chamber 55. The air permeable blood barrier 20 can also be constructed of a material that allows air to exit but then seals upon contact with blood, thereby not allowing external air to enter sequestration chamber 55. This sealing would eliminate the need for a valve.

[0053] Valve 60 can be any type of valve or closing mechanism. Chamber 30 is designed to hold virtually no residual blood, and can be designed to be adapted to hold or allow pass-through of a particular volume or rate of blood into sequestration chamber 55. Likewise, sequestration chamber 55 may also include any type of coating, such as an anti-microbial coating, or a coating that aids identification and/or diagnosis of components of the first, sequestered blood draw.

[0054] Housing 50 and 40 can be formed of any suitable material, including plastic, such as acrylonitrile butadiene styrene (ABS) or other thermoplastic or polymeric material, rubber, steel, or aluminum. The air permeable blood barrier 20 can include a color-providing substance, or other signaling mechanism, that is activated upon contact with blood from the

initial blood draw, or when air displacement is stopped, or any combination of events with blood in the sequestration chamber 55. The air permeable barrier may also include an outer layer such as a hydrophobic membrane or cover that inhibits or prevents the inadvertent or premature sealing of the filter by an external fluid source, splash etc. Sequestration chamber 55 can also be translucent or clear to enable a user to visually confirm the chamber is filled.

[0055] FIG. 2 illustrates a blood sample optimization system in accordance with some alternative implementations. In the implementation shown in FIG. 2, a sequestration chamber 55, or waste chamber, surrounds the patient needle 1, with an open-ended cuff or housing connected with the waste chamber and encircling the sample needle housing base and housing. The patient needle 1 and sample needle 5 are connected together by a boot 56, which forms a continuous blood draw channel therethrough. The boot 56 includes a single orifice or channel leading from the blood draw channel into sequestration chamber 55. The device can include more than one single orifice or channel, in other implementations. Each orifice or channel can include a one-way valve, and can be sized and adapted for predetermined amount of blood flow.

[0056] The sequestration chamber 55 includes an air permeable blood barrier. The filter can further include a sensor or indicator to sense and/or indicate, respectively, when a predetermined volume of blood has been collected in the sequestration chamber 55. That indication will alert a user to attach an evacuated blood collection tube or bottle, such as a Vacutainer™ to the sample needle 5. The housing for the sequestration chamber 55 can be any size or shape, and can include any type of material to define an interior space or volume therein. The interior space is initially filled only with air, but can also be coated with an agent or substance, such as a decontaminate, solidifying agent, or the like. Once evacuated blood collection tube is attached to the sample needle 5, blood will flow automatically into the patient needle 1, through the blood draw channel and sample needle 5, and into the bottle. The sample needle 5 is covered by a resealable boot, coating or membrane that seals the sample needle when a blood collection bottle is not attached thereon or thereto.

[0057] FIG. 3 illustrates a blood sample optimization system in accordance with some alternative implementations. In the implementation shown, a sample needle 5 is surrounded by a resealable boot or membrane, and is further connected with a patient needle 1. A blood

flow channel is formed through the sample needle and the patient needle. The connection between the sample needle and patient needle includes a "T" or "Y" connector 102, which includes a channel, port or aperture leading out from the main blood flow channel to a sequestration chamber 104.

[0058] The T or Y connector 102 may include a flap or one-way valve, and have an opening that is sized and adapted for a predetermined rate of flow of blood. The sequestration chamber 104 can be formed from tubing, or be formed by a solid housing, and is initially filled with air. The sequestration chamber 104 will receive blood that flows out of a patient automatically, i.e. under pressure from the patient's own blood pressure. The sequestration chamber 104 includes an air permeable blood barrier 106, preferably at the distal end of tubing that forms the sequestration chamber 104, and which is connected at the proximal end to the T or Y connector 102. The T or Y connector 102 can branch off at any desired angle for most efficient blood flow, and can be formed so as to minimize an interface between the aperture and channel and the main blood flow channel, so as to minimize or eliminate mixing of the initial aliquot of blood with main blood draw samples.

[0059] In some alternative implementations, the sample needle may be affixed to a tubing of any length, as shown in FIG. 4, connecting at its opposite end to the T or Y connector 102. The sequestration chamber 104 can be any shape or volume so long as it will contain a predetermined amount of blood sample in the initial aliquot. The T or Y connector 102 may also include an opening or channel that is parallel to the main blood flow channel. The air permeable blood barrier may further include an indicator 107 or other mechanism to indicate when a predetermined amount of blood has been collected in the sequestration chamber, or when air being expelled reaches a certain threshold, i.e. to zero. The tubing can also include a clip 109 that can be used to pinch off and prevent fluid flow therethrough.

[0060] Once the air permeable blood barrier and primary chamber are sealed the initial aliquot of blood is trapped in the sequestration chamber 104, an evacuated blood collection tube, such as a Vacutainer™ bottle may be attached to the sample needle 5 to obtain the sample. The blood collection tube can be removed, and the sample needle 5 will be resealed. Any number of follow-on blood collection tubes can then be attached for further blood draws

or samples. Upon completion of all blood draws, the system can be discarded, with the initial aliquot of blood remaining trapped in the sequestration chamber 104.

[0061] FIG. 5 illustrates a blood sample optimization system in accordance with some alternative implementations. In the implementation shown, a sample needle 5 is connected with a patient needle by tubing. A "T" or "Y" connector 120 is added along the tubing at any desired location, and includes an aperture, port or channel leading to a sequestration chamber 204, substantially as described above.

[0062] FIG. 6 illustrates a blood sample optimization system in accordance with some alternative implementations, in which a sequestration chamber 304, formed as a primary collection channel, receives an initial aliquot of blood, and is provided adjacent to the blood sampling channel. The sequestration chamber 304 can encircle the blood sampling channel, the patient needle 1, and/or the sample needle 5. The primary collection channel can include a T or Y connector 120, or other type of aperture or channel. The sequestration chamber 304 includes an air permeable blood barrier, which can also include an indicator of being contacted by a fluid such as blood, as described above.

[0063] In some implementations, either the patient needle 1 or the sample needle 5, or both, can be replaced by a Luer lock male or female connector. However, in various implementations, the connector at a sample needle end of the blood sample optimization system is initially sealed to permit the diversion of the initial aliquot of blood to the sequestration chamber, which is pressured at ambient air pressure and includes the air outlet of the air permeable blood barrier. In this way, the system passively and automatically uses a patient's own blood pressure to overcome the ambient air pressure of the sequestration chamber to push out air through the air permeable blood barrier and displace air in the sequestration chamber with blood.

[0064] FIG. 7 is a flowchart of an exemplary method for optimizing the quality of a blood culture. At 702, a clinician places a needle into a patient's vein. At 704, blood then flows into a sequestration chamber, pushing the air in the sequestration chamber out of the sequestration chamber through an air permeable blood barrier. In some implementations, the volume of the sequestration chamber is less than 0.1 to more than 5 cubic centimeters (cc's), or more. The sequestration chamber is sized and adapted to collect a first portion of a blood

sample, which is more prone to contamination than secondary and other subsequent portion of the blood sample or subsequent draws. Since the sequestration chamber has an air-permeable blood barrier through which air can be displaced by blood pushed from the patient's vein, such blood will naturally and automatically flow into the sequestration chamber before it is drawn into or otherwise enters into a Vacutainer or other bottle for receiving and storing a blood sample.

[0065] When the sequestration chamber fills, the blood will gather at or otherwise make contact with the air permeable blood barrier, which will inhibit or prevent blood from passing therethrough. At 706, when the blood comes into contact with the entire internal surface area of the air permeable blood barrier, the air permeable blood barrier is then closed and air no longer flows out or in. At 708, the clinician may be provided an indictor or can see the full chamber, to indicate the evacuated blood collection tube, such as a Vacutainer™ can be attached. The indicator can include visibility into the primary chamber to see whether it is full, the blood barrier changing color, for example, or other indicator. The fill time of the sequestration chamber may be substantially instantaneous, so such indicator, if present, may be only that the sequestration chamber is filled.

[0066] Prior to an evacuated blood collection tube being attached, communication between the needle, sampling channel, and the sequestration chamber is restricted by the sealing of the sequestration chamber blood barrier thereby not permitting air to reenter the system through the sequestration. Sealing the communication path could also be accomplished with a mechanical twist or other movement, a small orifice or tortuous pathway, eliminating the need for a separate valve or mechanical movement or operation by the clinician. At 710, once the evacuated blood collection tube is removed, the self-sealing membrane closes the sample needle, and at 712, additional subsequent evacuated blood collection tubes may be attached. Once samples have been taken, at 714 the device is removed from the patient and discarded.

[0067] FIGS. 8A – 8E illustrate an exemplary blood sample optimization system 800 for non-contaminated blood sampling, in accordance with some implementations. The blood sample optimization system 800 includes an inlet port 802 that can be connected to tubing, a patient needle (or both), or other vascular or venous access device, and a pathway splitter 804

having a first outlet to a sequestration chamber tubing 806 and a second outlet to sample collection tubing 808. One or both of the sequestration chamber tubing 806 and the sample collection tubing 808 can be formed of tubing. In some implementations, the sequestration chamber tubing 806 is sized so as to contain a particular volume of initial blood sample. The sample collection tubing 808 will receive a blood sample once the sequestration chamber tubing 806 is filled. The sample collection tubing 808 can be connected to a Vacutainer™ base or housing 810, or other blood sample collection device.

[0068] The blood sequestration system 800 further includes a blood sequestration device 812 which, as shown in more detail in FIGS. 8B – 8D, includes a housing 818 that includes a sampling channel 820 defining a pathway for the non-contaminated sample collection tubing 808 or connected at either end to the non-contaminated sample collection tubing 808. The sampling channel 820 can be curved through the housing 818 so as to better affix and stabilize the housing 818 at a location along the non-contaminated sample collection tubing 808.

[0069] The blood sequestration device 812 further includes a sequestration chamber 822 connected with the sequestration chamber tubing 806 or other chamber. The sequestration chamber 822 terminates at an air permeable blood barrier 824. The air permeable blood barrier 824 can also include a coloring agent that turns a different color upon full contact with blood, as an indicator that the regular collection of blood samples (i.e. the non-contaminated blood samples) can be initiated. Other indicators may be used, such as a small light, a sound generation mechanism, or the like. In some implementations, the air permeable blood barrier is positioned at a right angle from the direction of sequestration chamber 822, but can be positioned at any distance or orientation in order to conserve space and materials used for the housing 818. The housing 818 and its contents can be formed of any rigid or semi-rigid material or set of materials.

[0070] FIG. 9 illustrates a pathway splitter 900 for use in a blood sequestrations system, such as those shown in FIGS. 8A – 8E, for example. The pathway splitter 900 includes an inlet port 902, a main line outlet port 904, and a sequestration channel outlet port 906. The inlet port 902 can be connected to main tubing that is in turn connected to a patient needle system, or directly to a patient needle. The main line outlet port 904 can be connected to

main line tubing to a blood sampling system, such as a vacutainer base or housing, or directly to such blood sampling system. The sequestration channel outlet port 906 can be connected to sequestration tubing for receiving and sequestering a first sample of blood, up to a measured amount or predetermined threshold. Alternatively, the sequestration channel outlet port 906 can be connected to a sequestration chamber. The sequestration channel outlet port 906 is preferably 20-70 degrees angled from the main line outlet port 904, which in turn is preferably in-line with the inlet port 902. Once the predetermined amount of initial blood sample is sequestered in the sequestration tubing or chamber, in accordance with mechanisms and techniques described herein, follow-on blood samples will flow into the inlet port 902 and directly out the main line outlet port 904, without impedance.

[0071] FIGS. 10A – 10D illustrate a blood sequestration device 1000 in accordance with alternative implementations. The blood sequestration device 1000 includes an inlet port 1002, a main outlet port 1004, and a sequestration channel port 1006. The inlet port 1002 can be connected to a patient needle or related tubing. The main outlet port 1004 can be connected to a blood sample collection device such as a Vacutainer, associated tubing, or a Luer activated valve, or the like. The sequestration channel port 1006 splits off from the main outlet port 1004 to a sequestration chamber 1008. In some implementations, the sequestration chamber 1008 is formed as a helical channel within a housing or other container 1001.

[0072] The sequestration chamber 1008 is connected at the distal end to an air permeable blood barrier 1010, substantially as described above. Air in the sequestration chamber 1008 is displaced through the air permeable blood barrier 1010 by an initial aliquot of blood that is guided into the sequestration channel port 1006. Once the sequestration chamber 1008 is filled, further blood draws through the main outlet port 1004 can be accomplished, where these samples will be non-contaminated.

[0073] FIGS. 11A – 11E illustrate a blood sequestration device 1100 in accordance with other alternative implementations. The blood sequestration device 1100 includes an inlet port 1102, similar to the inlet ports described above, a main outlet port 1104, and a sequestration channel port 1106 that splits off from the main outlet port 1104 and inlet port 1102. The sequestration channel port is connected to a sequestration chamber 1108. In the

implementation shown in FIGS. 11A – 11E, the blood sequestration device includes a base member 1101 having a channel therein, which functions as the sequestration chamber 1108. The channel can be formed as a tortuous path through the base member 1101, which is in turn shaped and formed to rest on a limb of a patient.

[0074] A portion of the sequestration chamber 1108 can protrude from the base member or near a top surface of the base member, just before exiting to an air permeable blood barrier 1110, to serve as a blood sequestration indicator 1109. The indicator 1109 can be formed of a clear material, or a material that changes color when in contact with blood.

[0075] In some implementations, the blood sequestration device 1100 can include a blood sampling device 1120 such as a normally closed needle, Vacutainer™ shield or other collection device. The blood sampling device 1120 can be manufactured and sold with the blood sequestration device 1100 for efficiency and convenience, so that a first aliquot of blood that may be contaminated by a patient needle insertion process can be sequestered. Thereafter, the blood sampling device 1120 can draw non-contaminated blood samples to reduce the risk of false positive testing and ensure a non-contaminated sample.

[0076] FIGS. 12A-12D illustrate a blood sample optimization system 1200 in accordance with yet other alternative implementations. The system 1200 includes a blood sequestration device 1202 for attaching to a blood sampling device 1204, such as a Vacutainer™ or other collection and sampling device. The blood sequestration device 1202 is configured and arranged to receive, prior to a Vacutainer™ container or vial being attached to a collection needle of the blood sampling device 1204, a first aliquot or amount of blood, and sequester that first aliquot or amount in a sequestration channel of the blood sequestration device 1202.

[0077] In some implementations, the blood sequestration device 1202 can include an inlet port 1212, a main outlet port, and a sequestration channel port. The inlet port 1212 can be connected to a patient needle or related tubing. The main outlet port 1214 can be connected to a normally closed needle or device to enable connection with an evacuated blood collection container or other collection device such as a Vacutainer™, associated tubing, luer connectors, syringe, a Luer activated valve, or the like. The sequestration channel port splits off from the main outlet port to a sequestration chamber 1218.

[0078] In some implementations, the sequestration chamber 1218 is formed as a channel within the body of a sequestration device 1202. The sequestration chamber 1218 can be a winding channel, such as a U-shaped channel, an S-shaped channel, a helical channel, or any other winding channel. The sequestration device 1202 can include a housing or other containing body, and one or more channels formed therein. As shown in FIGS. 12A and 12B, the sequestration device 1202 includes a main body 1206 and a cap 1208. The main body 1206 is formed with one or more cavities or channels, which are further formed with one or more arms 1210 that extend from the cap 1208, and which abut the cavities or channels in the main body 1206 to form the primary collection port and main outlet port.

[0079] FIGS. 13A-13D illustrate a blood sample optimization system 1300 in accordance with yet other alternative implementations. The system 1300 includes a blood sequestration device 1302 for attaching to a blood sampling device 1304, such as a Vacutainer or other bodily fluid collection and sampling device. The blood sequestration device 1302 is configured and arranged to receive, prior to a Vacutainer container or vial being attached to a collection needle of the blood sampling device 1304, a first aliquot or amount of blood, and to sequester that first aliquot or amount of blood or other bodily fluid in a sequestration channel of the blood sequestration device 1302.

[0080] The blood sequestration device 1302 includes a housing 1301 having an inlet port 1314, a main outlet port 1312, and a sequestration channel port 1316. The inlet port 1314 can be connected to a patient needle or associated tubing. The main outlet port 1312 can be connected to a normally closed needle or device to enable connection with an evacuated blood collection container or other collection device such as a Vacutainer™, associated tubing, luer connectors, syringe, a Luer activated valve, or the like. The sequestration channel port 1316 splits off from the main inlet port 1314 to a sequestration chamber 1318.

[0081] In the implementation shown in FIGS. 13A-D, the sequestration chamber 1318 is formed as a cavity or chamber within housing 1301 or formed by walls that define housing 1301. The sequestration chamber 1318 can be a winding channel, such as a U-shaped channel, an S-shaped channel, a helical channel, or any other winding channel, that is defined by the cooperation and connection of housing 1301 with cap 1307 which cap 1307 can include a protrusion 1305 that provides one or more walls or directors for the winding

channel in the sequestration chamber 1318. The protrusion 1305 from the cap 1307 can be straight or curved, and may have various channels, apertures or grooves embedded therein, and can extend from the cap 1307 any angle or orientation. When the cap 1307 is connected with the housing 1301 to complete the formation of the sequestration chamber 1318, the protrusion 1305 forms at least part of the winding channel to sequester a first aliquot or amount of blood or other bodily fluid in a sequestration channel formed in the sequestration chamber 1318 and by the winding channel.

[0082] The sequestration chamber 1318 includes an air permeable blood barrier 1310, substantially as described above. Air in the sequestration chamber 1318 is displaced through the air permeable blood barrier 1310 by an initial aliquot of blood that is provided into the sequestration chamber 1318 by the blood pressure of the patient. Once the sequestration chamber 1318 is filled and the air in the sequestration chamber 1318 displaced, the blood pressure of the patient will be insufficient to drive or provide further blood into the blood sequestration device 1302, and in particular the outlet port 1312, until a force such as a vacuum or other pressure, such as provided by the blood sample collection device like Vacutainer is provided to draw out a next aliquot or amount of blood or bodily fluid. Further blood draws through the main outlet port 1312 can be accomplished, where these samples will be non-contaminated since any contaminants would be sequestered in the sequestration chamber 1318 with the first aliquot of blood.

[0083] FIGS. 14A-14E illustrate yet another implementation of a blood sampling system 1400 to sequester contaminates of an initial aliquot or sample to reduce false positives in blood cultures or tests performed on a patient's blood sample. The blood sampling system 1400 includes a blood sequestration device 1401 that can be connected between a blood sample collection device 1403 and a patient needle (not shown). The blood sample collection device 1403 can be a Vacutainer or the like. The blood sequestration device 1401 includes an inlet port 1402 that can be connected with a patient needle that is inserted into a patient's vascular system for access to and withdrawing of a blood sample. The inlet port 1402 may also be connected with tubing or other conduit that is in turn connected with the patient needle.

[0084] The inlet port 1402 defines an opening into the blood sequestration device 1401, which opening can be the same cross sectional dimensions as tubing or other conduit connected with the patient needle or the patient needle itself. For instance, the opening can be circular with a diameter of approximately 0.045 inches, but can have a diameter of between 0.01 inches or less to 0.2 inches or more. The blood sequestration device 1401 further includes an outlet port 1404, which defines an opening out of the blood sequestration device 1401 and to the blood sample collection device 1403. The outlet port 1404 may also be connected with tubing or other conduit that is in turn connected with the blood sequestration device 1403. The outlet port 1404 can further include a connector device such as a threaded cap, a Luer connector (male or female), a non threaded interference or glue joint fitting for attachment of various devices including but not limited to tubing, or the like.

[0085] The blood sequestration device 1401 further includes a sampling channel 1406 between the inlet port 1402 and the outlet port 1404, and which functions as a blood sample pathway once a first aliquot of blood has been sequestered. The sampling channel 1406 can be any sized, shaped or configured channel, or conduit. In some implementations, the sampling channel 1406 has a substantially similar cross sectional area as the opening of the inlet port 1402. In other implementations, the sampling channel 1406 can gradually widen from the inlet port 1402 to the outlet port 1404.

[0086] The blood sequestration device 1401 further includes a sequestration chamber 1408 that is connected to and split off or diverted from the sampling channel 1406 at any point between the inlet port 1402 and the outlet port 1404, but preferably from a proximal end of the sampling channel 1406 near the inlet port 1402. The sequestration chamber 1408 is at first maintained at atmospheric pressure, and includes an air outlet 1412 at or near a distal end of the sequestration chamber 1408 opposite the diversion point from the sampling channel 1406. The air outlet 1412 includes an air permeable blood barrier 1412. As shown in FIG. 14B, the air permeable blood barrier 1412 can be overlaid with a protective cover 1416. The protective cover 1416 can be sized and configured to inhibit a user from touching the air permeable blood barrier 1412 with their finger or other external implement, while still allowing air to exit the air permeable blood barrier 1412 as the air is displaced from the sequestration chamber 1408 by blood being forced into the sequestration chamber 1408 by a patient's own blood pressure. In addition the protective cover 1416 can be constructed to

inhibit or prevent accidental exposure of the air permeable blood barrier to environmental fluids or splashes. This can be accomplished in a variety of mechanical ways including but not limited to the addition of a hydrophobic membrane to the protective cover.

[0087] As shown in FIGS. 14C and 14D, the sampling channel 1406 can be cylindrical or frusto-conical in shape, going from a smaller diameter to a larger diameter, to minimize a potential to lyse red blood cells. Likewise, the sampling channel 1406 is formed with a minimal amount of or no sharp turns or edges, which can also lyse red blood cells. The sampling channel 1406 splits off to the sequestration chamber 1408 near the inlet port 1402 via a diversion pathway 1409. The diversion pathway 1409 can have any cross-sectional shape or size, but is preferably similar to the cross-sectional shape of at least part of the inlet port 1402.

[0088] In some implementations, the sampling channel 1406 and the sequestration chamber 1408 are formed by grooves, channels, locks or other pathways formed in housing 1414. The housing 1414 can be made of plastic, metal or other rigid or semi-rigid material. The housing 1414 can have a bottom member that sealably mates with a top member. One or both of the bottom member and the top member can include the sampling channel 1406 and the sequestration chamber 1408, as well as the diversion pathway 1409, the inlet port 1402, and the outlet port 1404. In some other implementations, one or more of the diversion pathway 1409, the inlet port 1402, and/or the outlet port 1404 can be at least partially formed by a cap member that is connected to either end of the housing 1414. In some implementations, the top member and the bottom member, as well as the cap member(s), can be coupled together by laser welding, heat sealing, gluing, snapping, screwing, bolting, or the like. In other implementations, some or all of the interior surface of the diversion pathway 1409 and/or sequestration chamber 1408 can be coated or loaded with an agent or substance, such as a decontaminate, solidifying agent, or the like. For instance, a solidifying agent can be provided at the diversion pathway 1409 such that when the sequestration chamber 1408 is filled and the initial aliquot of blood backs up to the diversion pathway 1409, that last amount of sequestered blood could solidify, creating a barrier between the sequestration chamber 1408 and the sampling channel 1406.

[0089] FIGS. 15A-15G illustrate a blood sequestration device 1500. The blood sequestration device 1500 can be connected to a normally closed needle or device to enable connection with an evacuated blood collection container or other collection device such as a Vacutainer™, associated tubing, luer connectors, syringe, a Luer activated valve, or the like.

[0090] The blood sequestration device 1500 includes an inlet port 1502 that can be connected with a patient needle that is inserted into a patient's vascular system for access to and withdrawing of a blood sample. The inlet port 1502 may also be connected with tubing or other conduit that is in turn connected with the patient needle. The inlet port 1502 defines an opening into the blood sequestration device 1500, which opening may be the same cross sectional dimensions as tubing or other conduit connected with the patient needle or the patient needle itself. For instance, the opening can be circular with a diameter of approximately 0.045 inches, but can have a diameter of between 0.01 inches or less to 0.2 inches or more.

[0091] The inlet port 1502 can also include a sealing or fluid-tight connector or connection, such as threading or Luer fitting, or the like. In some implementations, tubing or other conduit associated with the patient needle can be integral with the inlet port 1502, such as by co-molding, gluing, laser weld, or thermally bonding the parts together. In this manner, the blood sequestration device 1500 can be fabricated and sold with the patient needle as a single unit, eliminating the need for connecting the patient needle to the blood sequestration device 1500 at the time of blood draw or sampling.

[0092] The blood sequestration device 1500 further includes an outlet port 1504, which defines an opening out of the blood sequestration device 1500 and to the blood sample collection device. The outlet port 1504 may also be connected with tubing or other conduit that is in turn connected with the blood sequestration device, and may also include a sealing or fluid-tight connector or connection, such as threading or Luer fitting, or the like. Accordingly, as discussed above, the blood sequestration device 1500 can be fabricated and sold with the patient needle and/or tubing and the blood sample collection device as a single unit, eliminating the need for connecting the patient needle and the blood sample collection device to the blood sequestration device 1500 at the time of blood draw or sampling.

[0093] The blood sequestration device 1500 further includes a sampling channel 1506 between the inlet port 1502 and the outlet port 1504, and which functions as a blood sample pathway once a first aliquot of blood has been sequestered. The sampling channel 1506 can be any sized, shaped or configured channel or conduit. In some implementations, the sampling channel 1506 has a substantially similar cross sectional area as the opening of the inlet port 1502. In other implementations, the sampling channel 1506 can gradually widen from the inlet port 1502 to the outlet port 1504.

[0094] The blood sequestration device 1500 further includes a sequestration chamber 1508 that is connected to and split off or diverted from the sampling channel 1506 at any point between the inlet port 1502 and the outlet port 1504, but preferably from a proximal end of the sampling channel 1506 near the inlet port 1502. In some implementations, the diversion includes a Y-shaped junction. The sequestration chamber 1508 is preferably maintained at atmospheric pressure, and includes a vent 1510 at or near a distal end of the sequestration chamber 1508. The vent 1510 includes an air permeable blood barrier 1512. FIG. 15C illustrates the blood sequestration device 1500 with the sequestration chamber 1508 filled with a first aliquot or sample of blood from the patient.

[0095] The air permeable blood barrier 1512 can be covered with a protective cover 1516. The protective cover 1516 can be sized and configured to inhibit a user from touching the air permeable blood barrier 1512 with their finger or other external implement, while still allowing air to exit the air permeable blood barrier 1512 as the air is displaced from the sequestration chamber 1508 by blood being forced into the sequestration chamber 1508 by a patient's own blood pressure. The protective cover 1516 can be constructed to inhibit or prevent accidental exposure of the filter to environmental fluids or splashes. This can be accomplished in a variety of mechanical ways including but not limited to the addition of a hydrophobic membrane to the protective cover.

[0096] FIG. 15B is a perspective view of the blood sequestration device 1500 from the outlet port 1504 and top side of a housing 1501 of the blood sequestration device 1500 that includes the vent 1510, and illustrating an initial aliquot of blood filling sequestration chamber 1508 while the sampling channel 1506 is empty, before a sample collection device is activated. FIG. 15G is a perspective view of the blood sequestration device 1500 from the

outlet port 1504 and bottom side of the housing 1501 of the blood sequestration device 1500, and illustrating the initial aliquot of blood filling sequestration chamber 1508 while the sampling channel 1506 is empty, before the sample collection device is activated. FIG. 15C is another perspective view of the blood sequestration device 1500 from the inlet port 1502 and top side of a housing 1501 of the blood sequestration device 1500 that includes the vent 1510, and illustrating blood now being drawn through sampling channel 1506 while the sequestered blood remains substantially in the sequestration chamber 1508.

[0097] FIG. 15D is a cross section of the blood sequestration device 1500 in accordance with some implementations, showing the housing 1501 that defines the sampling channel 1506 and the sequestration chamber 1508. FIGS. 15E and 15F illustrate various form factors of a housing for a blood sequestration device, in accordance with one or more implementations described herein.

[0098] The sequestration chamber 1508 can have a larger cross-sectional area than the sampling channel 1506, and the cross-sectional area and length can be configured for a predetermined or specific volume of blood to be sequestered or locked. The sampling channel 1506 can be sized to be compatible with tubing for either or both of the patient needle tubing or the blood collection device tubing.

[0099] The housing 1501 can be formed of multiple parts or a single, unitary part. In some implementations, and as illustrated in FIG. 15D, the housing 1501 includes a top member 1520 and a bottom member 1522 that are mated together, one or both of which having grooves, channels, locks, conduits or other pathways pre-formed therein, such as by an injection molding process or by etching, cutting, drilling, etc. The top member 1520 can be connected with the bottom member 1522 by any mating or connection mechanism, such as by laser welding, thermal bonding, ultrasonic welding, gluing, using screws, rivets, bolts, or the like, or by other mating mechanisms such as latches, grooves, tongues, pins, flanges, or the like.

[00100] In some implementations, such as shown in FIG. 15D, the top member 1520 can include the grooves, channels, locks, conduits or other pathways, while the bottom member 1522 can include a protrusion 1524 that is sized and adapted to fit into at least one of the grooves, channels, locks or other pathways of the top member 1520. The protrusion 1524

can provide a surface feature, such as a partial groove or channel, for instance, to complete the formation of either the sampling channel 1506 and/or the sequestration chamber 1508. In some implementations, the protrusion 1524 can be formed with one or more angled sides or surfaces for a tighter fit within the corresponding groove, channel, lock or other pathway. In yet other implementations, both the top member 1520 and the bottom member can include grooves, channels, locks or other pathways, as well as one or more protrusions 1524.

[00101] In some implementations, the sampling channel 1506 and the sequestration chamber 1508 are formed by grooves, channels, locks or other pathways formed in housing 1501. The housing 1501 can be made of any suitable material, including rubber, plastic, metal or other material. The housing 1501 can be formed of a clear or translucent material, or of an opaque or non-translucent material. In other implementations, the housing 1501 can be mostly opaque or non-translucent, while the housing surface directly adjacent to the sampling channel 1506 and/or the sequestration chamber 1508 is clear or translucent, giving a practitioner a visual cue or sign that the sequestration chamber 1508 is first filled to the extent necessary or desired, and/or then a visual cue or sign that the sequestered blood remains sequestered while a clean sample of blood is drawn through the sampling channel 1506. Other visual cues or signs of the sequestration can include, without limitation: the air permeable blood barrier 1512 turning a different color upon contact, saturation, or partial saturation with blood; a color-coded tab or indicator at any point along or adjacent to the sequestration chamber; an audible signal; a vibratory signal; or other signal.

[00102] After a venipuncture by a patient needle of a patient (not shown), which could gather a number of pathogens from the patient's skin, a first amount of the patient's blood with those pathogens will make its way into the input port 1502 blood sequestration device 1500 and flow into the sequestration chamber 1508 by following the path of least resistance, as the patient's own blood pressure overcomes the atmospheric pressure in the sequestration chamber 1508 to displace air therein through the air permeable blood barrier 1512. The patient's blood pressure will not be sufficient to overcome the air pressure that builds up in the sealed sampling channel 1506. Eventually, the sequestration chamber 1508, which has a predetermined volume, is filled with blood that displaces air through the air permeable blood barrier 1512. Once the blood hits the air permeable blood barrier, the blood interacts with the air permeable blood barrier 1512 material to completely or partially seal the vent 1510. A

signal or indication may be provided that the practitioner can now utilize the Vacutainer capsule or other blood sample collection device to acquire a next amount of the patient's blood for sampling. The blood in the sequestration chamber 1508 is now effectively sequestered in the sequestration chamber.

[00103] Upon filling the blood sequestration pathway 1508 but prior to use of the Vacutainer or other blood sample collection device, the patient's blood pressure may drive compression of the air in the sampling channel 1506, possibly resulting in a small amount of blood moving past the diversion point to the sequestration chamber 1508 and into the sampling channel 1506, queuing up the uncontaminated blood to be drawn through the sampling channel 1506.

[00104] FIGS. 16-19 illustrate yet another implementation of a blood sequestration device. FIGS. 16A-16D illustrate a blood sequestration device 1600 that can be connected between a blood sample collection device, such as an evacuated blood collection container like a Vacutainer™ (not shown), and a patient needle (not shown) and/or associated tubing. FIG. 17 illustrates a bottom member of the blood sequestration device, and FIG. 18 illustrates a top member of the blood sequestration device, which top member and bottom member can be mated together to form an input port, and output port, a sequestration chamber and a sampling channel, as explained more fully below. FIGS. 19A and B show the top member and bottom member mated together. It should be understood that FIGS. 16-19 illustrate one exemplary manner of constructing a blood sequestration device as described herein, and other forms of construction are possible.

[00105] Referring to FIGS. 16A – D, the blood sequestration device 1600 includes an inlet port 1602 that can be connected with a patient needle that is inserted into a patient's vascular system for access to and withdrawing of a blood sample. The inlet port 1602 may also be connected with tubing or other conduit that is in turn connected with the patient needle. The inlet port 1602 defines an opening into the blood sequestration device 1600, which opening can be the same cross sectional dimensions as tubing or other conduit connected with the patient needle or the patient needle itself. For instance, the opening can be circular with a diameter of approximately 0.045 inches, but can have a diameter of between 0.01 inches or less to 0.2 inches or more.

[00106] The inlet port 1602 can also include a sealing or fluid-tight connector or connection, such as threading or Luer fitting, or the like. In some implementations, tubing or other conduit associated with the patient needle can be integral with the inlet port 1602, such as by co-molding, gluing, laser weld, or thermally bonding the parts together. In this manner, the blood sequestration device 1600 can be fabricated and sold with the patient needle and/or tubing as a single unit, eliminating the need for connecting the patient needle to the blood sequestration device 1600 at the time of blood draw or sampling.

[00107] The blood sequestration device 1600 further includes an outlet port 1604, which defines an opening out of the blood sequestration device 1600 and to the blood sample collection device. The outlet port 1604 may also be connected with tubing or other conduit that is in turn connected with the blood sequestration device, and may also include a sealing or fluid-tight connector or connection, such as threading or Luer fitting, or the like. Accordingly, as discussed above, the blood sequestration device 1600 can be fabricated and sold with the patient needle and/or tubing and the blood sample collection device as a single unit, eliminating the need for connecting the patient needle and the blood sample collection device to the blood sequestration device 1600 at the time of blood draw or sampling.

[00108] The blood sequestration device 1600 further includes a sampling channel 1606 between the inlet port 1602 and the outlet port 1604, and a sequestration chamber 1608 that is connected to and split off or diverted from the sampling channel 1606 at any point between the inlet port 1602 and the outlet port 1604. The sampling channel 1606 functions as a blood sampling pathway once a first aliquot of blood has been sequestered in the sequestration chamber 1608. The sampling channel 1606 can be any sized, shaped or configured channel, or conduit. In some implementations, the sampling channel 1606 has a substantially similar cross sectional area as the opening of the inlet port 1602. In other implementations, the sampling channel 1606 can gradually widen from the inlet port 1602 to the outlet port 1604. The sequestration chamber 1608 may have a larger cross section to form a big reservoir toward the sequestration channel path so that the blood will want to enter the reservoir first versus entering a smaller diameter on the sampling channel 1606, as is shown more fully in FIGS. 17 and 19.

[00109] In some exemplary implementations, the diversion between the sampling channel 1606 and the sequestration chamber 1608 is by diverter junction 1607. Diverter junction 1607 may be a substantially Y-shaped, T-shaped, or U-shaped. In some preferred exemplary implementations, and as shown in FIG. 17A – 17B, the diverter junction 1607 is configured such that the flow out of the inlet port 1602 is preferentially directed toward the sequestration chamber 1608. The sequestration chamber 1608 may also include or form a curve or ramp to direct the initial blood flow toward and into the sequestration chamber 1608.

[00110] The sequestration chamber 1608 is preferably maintained at atmospheric pressure, and includes a vent 1610 at or near a distal end of the sequestration chamber 1608. The vent 1610 may include an air permeable blood barrier 1612 as described above.

[00111] The blood sequestration device 1600 can include a housing 1601 that can be formed of multiple parts or a single, unitary part. In some implementations, and as illustrated in FIGS. 17A – 17E and FIGS. 18A – 18F, the housing 1601 includes a top member 1620 and a bottom member 1622 that are mated together. The blood sequestration device 1600 can also include a gasket or other sealing member (not shown) so that when the top member 1620 is mechanically attached with the bottom member 1622, the interface between the two is sealed by the gasket or sealing member. The FIGS. 17A – 17E illustrate a bottom member 1622 of a housing for a blood sequestration device 1600. The bottom member 1622 can include grooves, channels, locks, conduits or other pathways pre-formed therein, such as by an injection molding process or by etching, cutting, drilling, etc., to form the sampling channel 1606, the sequestration chamber 1608, and diverter junction 1607.

[00112] The sequestration chamber 1608 may have a larger cross section than the sampling channel 1606 so that the blood will preferentially move into the sequestration chamber first versus entering a smaller diameter on the sampling channel 1606.

[00113] FIGS. 18A – 18F illustrate the top member 1620, which can be connected with the bottom member 1622 by any mating or connection mechanism, such as by laser welding, thermal bonding, gluing, using screws, rivets, bolts, or the like, or by other mating mechanisms such as latches, grooves, tongues, pins, flanges, or the like. The top member 1620 can include some or all of the grooves, channels, locks, conduits or other pathways to form the sampling channel 1606, the sequestration chamber 1608, and the diverter junction

1607. In yet other implementations, both the top member 1620 and the bottom member 1622 can include the grooves, channels, locks or other pathways.

[00114] In some implementations, the sampling channel 1606 and the sequestration chamber 1608 are formed by grooves, channels, locks or other pathways formed in housing 1601. The housing 1601 can be made of rubber, plastic, metal or any other suitable material. The housing 1601 can be formed of a clear or translucent material, or of an opaque or non-translucent material. In other implementations, the housing 1601 can be mostly opaque or non-translucent, while the housing surface directly adjacent to the sampling channel 1606 and/or the sequestration chamber 1608 may be clear or translucent, giving a practitioner a visual cue or sign that the sequestration chamber 1608 is first filled to the extent necessary or desired, and/or then a visual cue or sign that the sequestered blood remains sequestered while a clean sample of blood is drawn through the sampling channel 1606. Other visual cues or signs of the sequestration can include, without limitation: the air permeable blood barrier 1612 turning a different color upon contact, saturation, or partial saturation with blood; a color-coded tab or indicator at any point along or adjacent to the sequestration chamber; an audible signal; a vibratory signal; or other signal.

[00115] As shown in FIGS. 18A – 18F, the air permeable blood barrier 1612 can be covered with, or surrounded by, a protective member 1616. The protective member 1616 can be sized and configured to inhibit a user from touching the air permeable blood barrier 1612 with their finger or other external implement, while still allowing air to exit the air permeable blood barrier 1612 as the air is displaced from the sequestration chamber 1608. In some implementations, the protective member 1616 includes a protrusion that extends up from a top surface of the top member 1620 and around the air permeable blood barrier 1612. The protective cover 1616 can be constructed to inhibit or prevent accidental exposure of the filter to environmental fluids or splashes. This can be accomplished in a variety of mechanical ways including but not limited to the addition of a hydrophobic membrane to the protective cover.

[00116] In use, the blood sequestration device 1600 includes a sampling channel 1606 and a sequestration chamber 1608. Both pathways are initially air-filled at atmospheric pressure, but the sampling channel 1606 is directed to an output port 1604 that will be initially sealed

by a Vacutainer or other such sealed blood sampling device, and the sequestration chamber 1608 terminates at a vent 1610 to atmosphere that includes an air permeable blood barrier 1612.

[00117] After a venipuncture by a patient needle of a patient (not shown), which could gather a number of pathogens from the patient's skin, a first amount of the patient's blood with those pathogens will pass through input port 1602 of blood sequestration device 1600. This initial volume of potentially contaminated blood will preferentially flow into the sequestration chamber 1608 by finding the path of least resistance. The patient's own blood pressure overcomes the atmospheric pressure in the vented sequestration chamber 1608 to displace air therein through the air permeable blood barrier 1612, but is not sufficient to overcome the air pressure that builds up in the sealed sampling channel 1606. In various exemplary embodiments, the sequestration chamber 1608 and sampling channel 1606 can be configured such that the force generated by the patient's blood pressure is sufficient to overcome any effect of gravity, regardless of the blood sequestration device's orientation.

[00118] Eventually, the sequestration chamber 1608 fills with blood that displaces air through the air permeable blood barrier 1612. Once the blood contacts the air permeable blood barrier, the blood interacts with the air permeable blood barrier 1612 material to completely or partially seal the vent 1610. A signal or indication may be provided that the practitioner can now utilize the Vacutainer or other blood sampling device.

[00119] Upon filling the blood sequestration pathway 1608 but prior to use of the Vacutainer or other blood sample collection device, the patient's blood pressure may drive compression of the air in the sampling channel 1606, possibly resulting in a small amount of blood moving past the diversion point into the sampling channel 1606, queuing up the uncontaminated blood to be drawn through the sampling channel 1606.

[00120] FIG. 19A is a side view, and FIG. 19B is a cross-sectional view, of the blood sequestration device 1600, illustrating the top member 1620 mated with the bottom member 1622.

[00121] FIG. 20 shows a blood sample optimization system 2000 that includes a patient needle 2002 for vascular access to a patient's bloodstream, a blood sample collection device

2004 to facilitate the collecting of one or more blood samples, and a conduit 2006 providing a fluid connection between the patient needle 2002 and the blood sample collection device 2004. In some implementations, the blood sample collection device 2004 includes a protective shield that includes a sealed collection needle on which a sealed vacuum-loaded container is placed, which, once pierced by the collection needle, draws in a blood sample under vacuum pressure or force through the conduit 2006 from the patient needle 2002.

[00122] The blood sample optimization system 2000 further includes a blood sequestration device 2008, located at any point on the conduit 2006 between the patient needle 2002 and the blood sample collection device 2004 as described herein.

[00123] FIG. 21 illustrates a non-vented blood sequestration device 2100 using a wicking material chamber. The blood sequestration device 2100 includes a housing 2101 that has a sampling channel 2104 that is at least partially surrounded or abutted by a sequestration chamber 2102 that is filled with a wicking material. An initial aliquot of blood is drawn in from the patient needle into the sampling channel 2104 where it is immediately wicked into the wicking material of the sequestration chamber 2102. The wicking material and/or sequestration chamber 2102 is sized and adapted to receive and hold a predetermined amount of blood, such that follow-on or later blood draws pass by the wicking material and flow straight through the sampling channel 2104 to a sampling device such as a Vacutainer. The wicking material can include a substance such as a solidifier, a decontaminate, or other additive.

[00124] As described herein, an air permeable blood barrier may be created using a wide variety of different structures and materials. As shown in FIGS. 22A and B, an air permeable blood barrier 2202 of a blood sequestration device 2200 can include a polymer bead matrix 2204, in which at least some beads are treated to make them hydrophilic. The air permeable blood barrier 2202 further includes a self-sealing material 2206, such as carboxymethyl cellulose (CMC) or cellulose gum, or other sealing material. The air permeable blood barrier 2202 can further include voids 2208 that permit air flow before contact or during partial contact with a fluid such as blood. As shown in FIG. 22B, contact with a fluid causes the self-sealing material 2206 to swell and close off the voids 2208, occluding air flow through the voids 2208 and creating a complete or partial seal.

[00125] FIGS. 23A and B illustrate yet another implementation of a blood sequestration device 2300, having an inlet port 2302 to connect with a patient needle, an outlet port 2304 to connect with a blood sample collection device, a sequestration chamber 2306, and a sampling channel 2308 that bypasses the sequestration chamber 2306 once the sequestration chamber is filled to an initial aliquot of potentially contaminated blood to be sequestered. The sequestration chamber 2306 includes a hydrophobic plug 2312 at a distal end of the sequestration chamber 2306 that is farthest from the inlet port 2302. A vacuum or other drawing force applied from the outlet port 2304, such as from a Vacutainer or the like, draws in blood into the inlet port 2302 and directly into the sequestration chamber 2306, where the initial aliquot of blood will contact the hydrophobic plug 2312 and cause the initial aliquot of blood to back up into the sequestration chamber 2306 and be sequestered there. A small amount of blood may make its way into the sampling channel 2308, which is initially closed off by valve 2308. Upon release of the valve 2308, and under further force of the vacuum or other force, follow-on amounts of blood will flow into inlet port 2302, bypass the sequestration chamber 2306, and flow into and through sampling channel 2308 toward the outlet port 2304 and to the collection device.

[00126] The sampling channel 2308 can have any suitable geometry and can be formed of plastic tubing or any other suitable material. Valve 2308 can be a clip or other enclosing device to pinch, shunt, bend or otherwise close off the sampling channel before the initial aliquot of blood is sequestered in the sequestration chamber 2306.

[00127] Although a variety of embodiments have been described in detail above, other modifications are possible. Other embodiments may be within the scope of the following claims.

CLAIMS

1. A device comprising:

an inlet port;

an outlet port;

a chamber connected with the inlet port and configured to receive a first portion of blood, the chamber including an air permeable material that seals at least partially upon contact with a portion of the first portion of blood; and

a sampling channel having a proximal end connected with the inlet port and a distal end connected with the outlet port.

2. The device in accordance with claim 1, wherein the device is configured such that, when a drawing force is applied at the outlet port, blood is drawn into the inlet port and into the chamber.

3. The device in accordance with claim 2, wherein the device is further configured such that an initial aliquot of blood will contact the air permeable material and back up into the chamber.

4. The device in accordance with claim 3, wherein the device is further configured such that follow-on amounts of blood will flow through the sampling channel towards the outlet port.

5. The device in accordance with claim 1, wherein the air permeable material is located at a distal end of the chamber.

6. The device in accordance with claim 1, wherein the air permeable material is a hydrophobic plug.

7. The device in accordance with claim 1, wherein the air permeable material is a hydrophobic membrane.

8. The device in accordance with claim 1, wherein the air permeable material is a hydrophilic membrane.

9. The device in accordance with claim 1, wherein the sampling channel further comprises a valve configured to close off the sampling channel.

10. The device in accordance with claim 9, wherein the valve is a clip.

11. The device in accordance with claim 1, further comprising a junction configured to direct an initial blood flow into the chamber.

12. The device in accordance with claim 1, further comprising a junction configured such that flow out of the inlet port is preferentially directed toward the chamber.

13. The device in accordance with claim 1, wherein the chamber has a larger cross-sectional area than the sampling channel.

14. The device in accordance with claim 1, further comprising a housing that defines the chamber and the sampling channel.

15. The device in accordance with claim 14, wherein the housing comprises a bottom member mated with a top member, each of the bottom member and the top member defining a part of each of the inlet port, the outlet port, the chamber, and the sampling channel.

16. The device in accordance with claim 1, further comprising a patient needle and a sample collection device.

ABSTRACT

Blood sample optimization systems and methods are described that reduce or eliminate contaminates in collected blood samples, which in turn reduces or eliminates false positive readings in blood cultures or other testing of collected blood samples. A blood sample optimization system can include a blood sequestration device located between a patient needle and a sample needle. The blood sequestration device can include a sequestration chamber for sequestering an initial, potentially contaminated aliquot of blood, and may further include a sampling channel that bypasses the sequestration chamber to convey likely uncontaminated blood between the patient needle and the sample needle after the initial aliquot of blood is sequestered in the sequestration chamber.

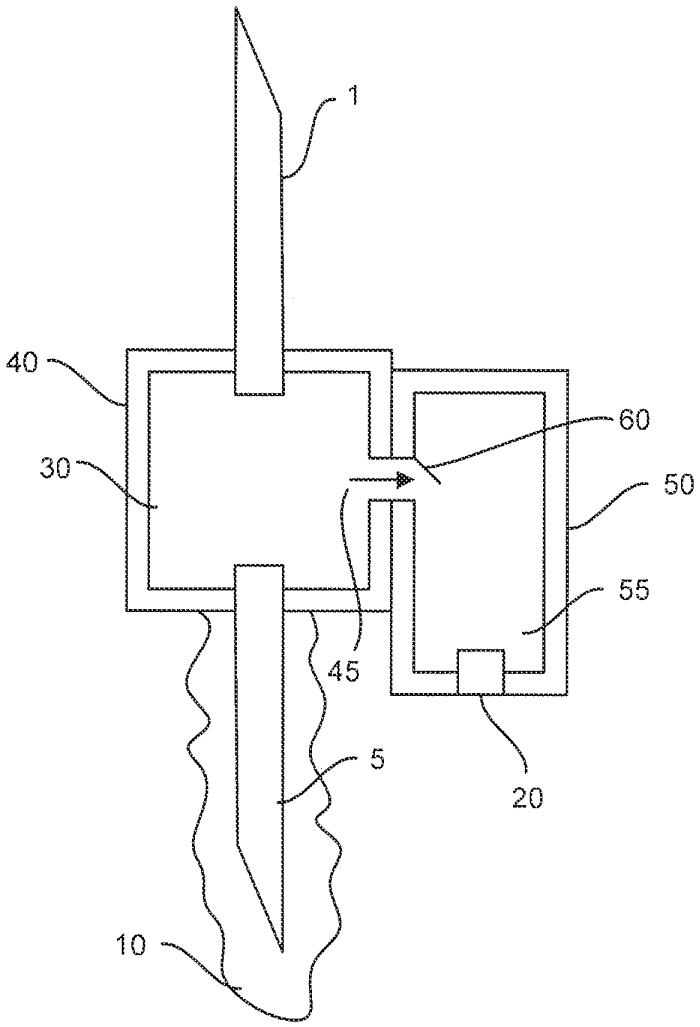


FIG. 1

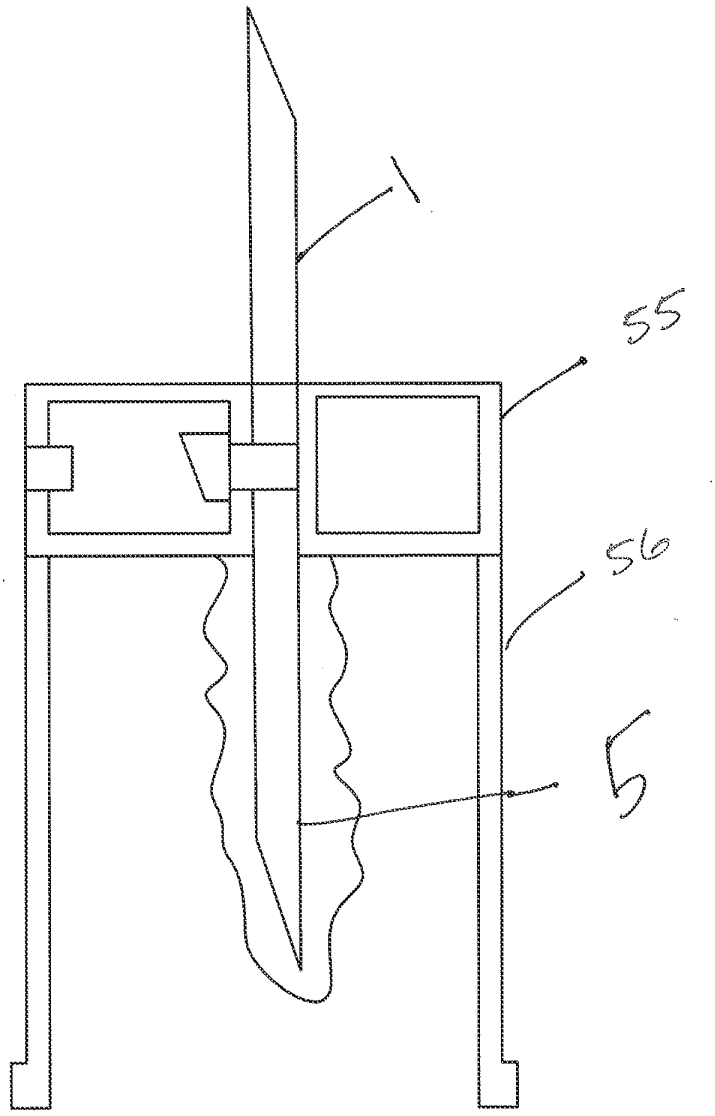


FIG. 2

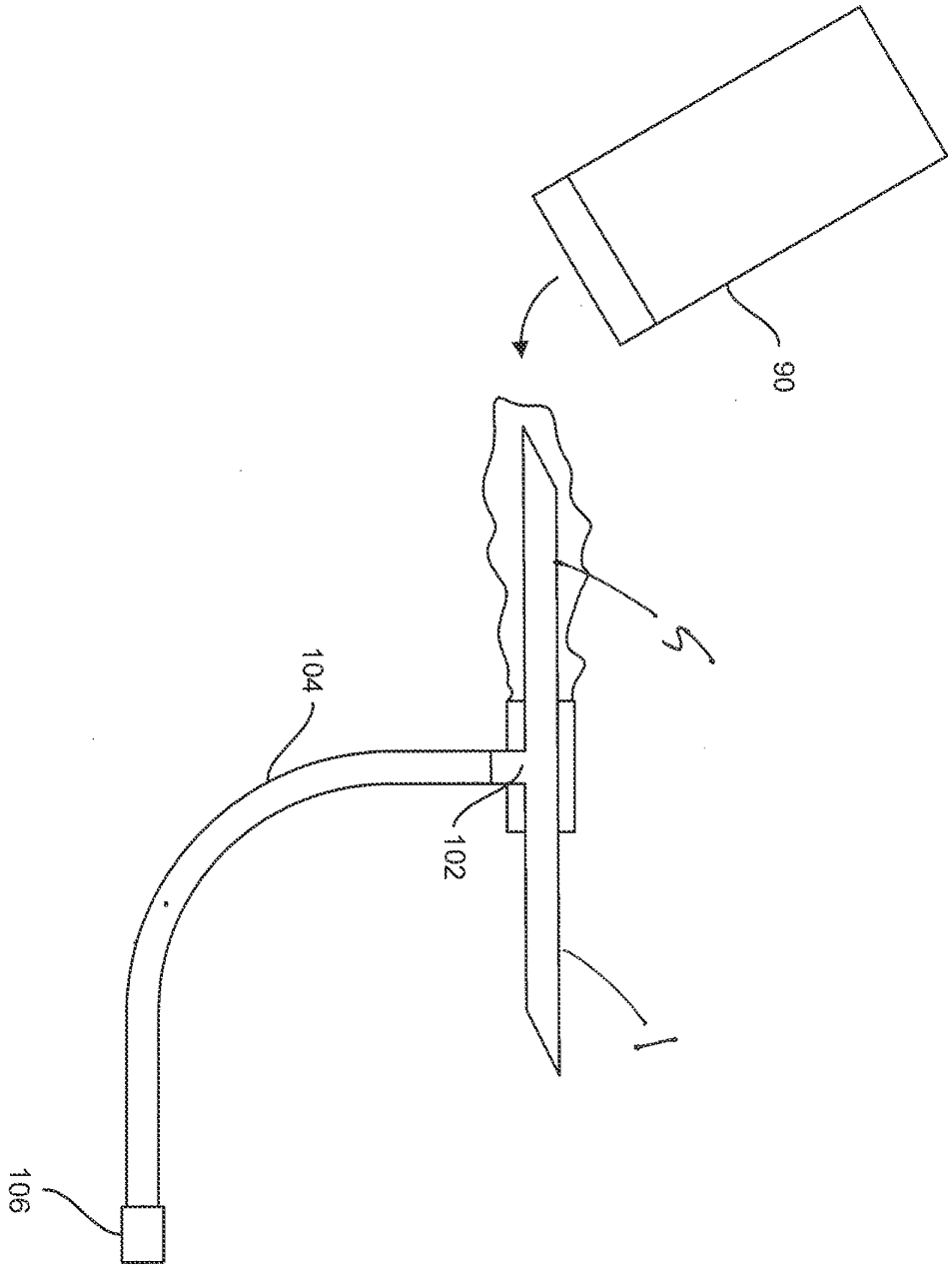


FIG. 3

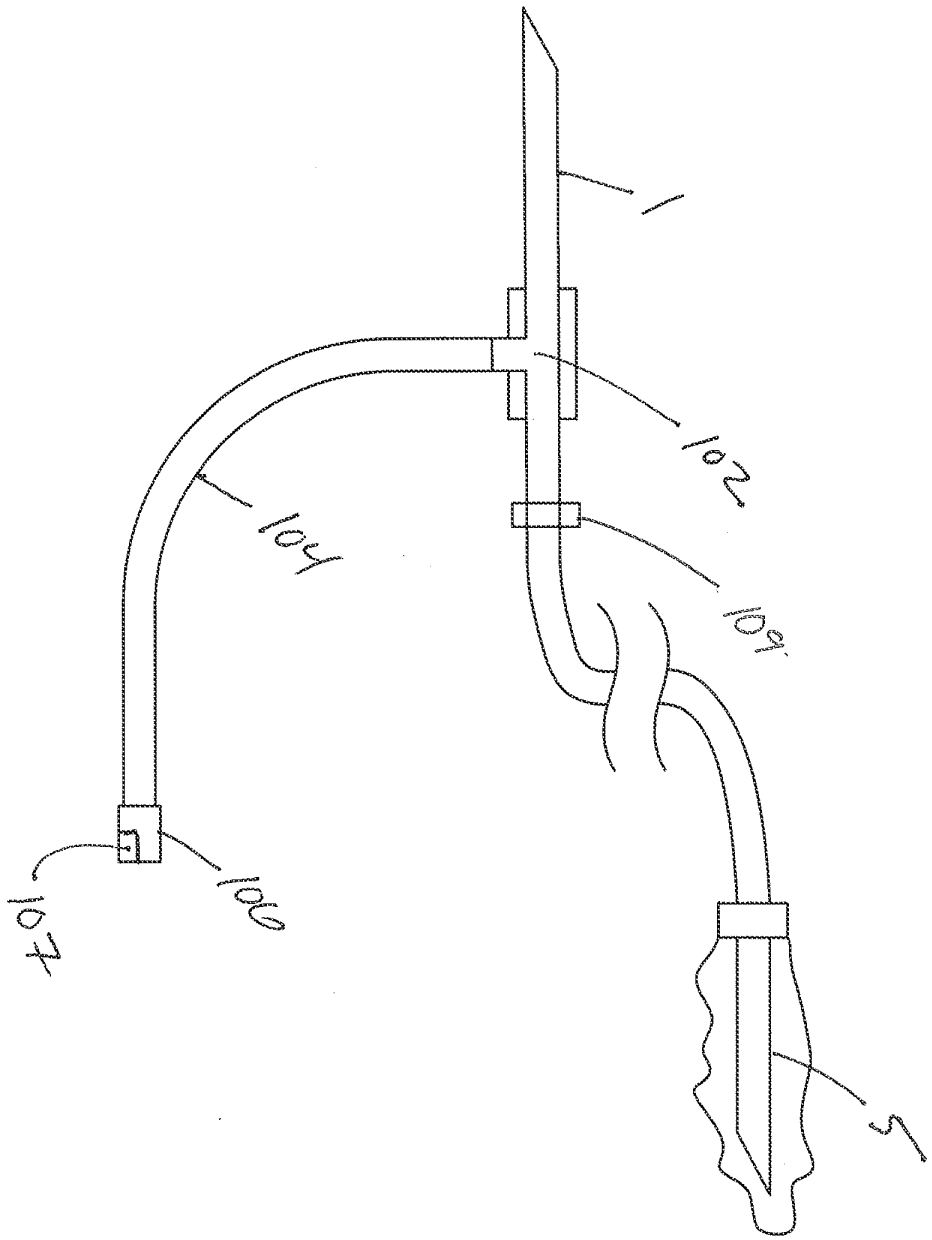


FIG. 4

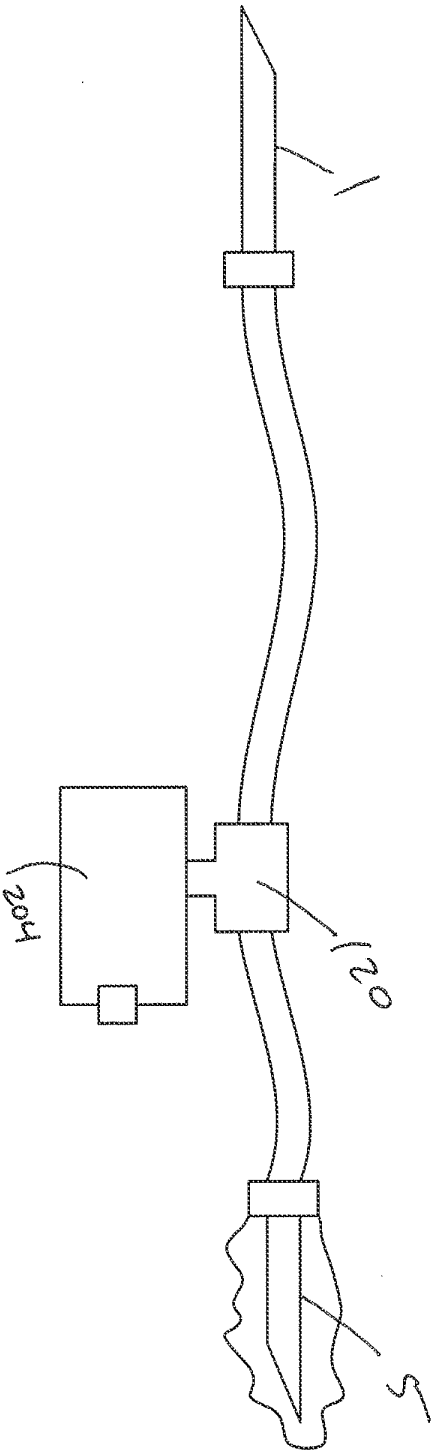
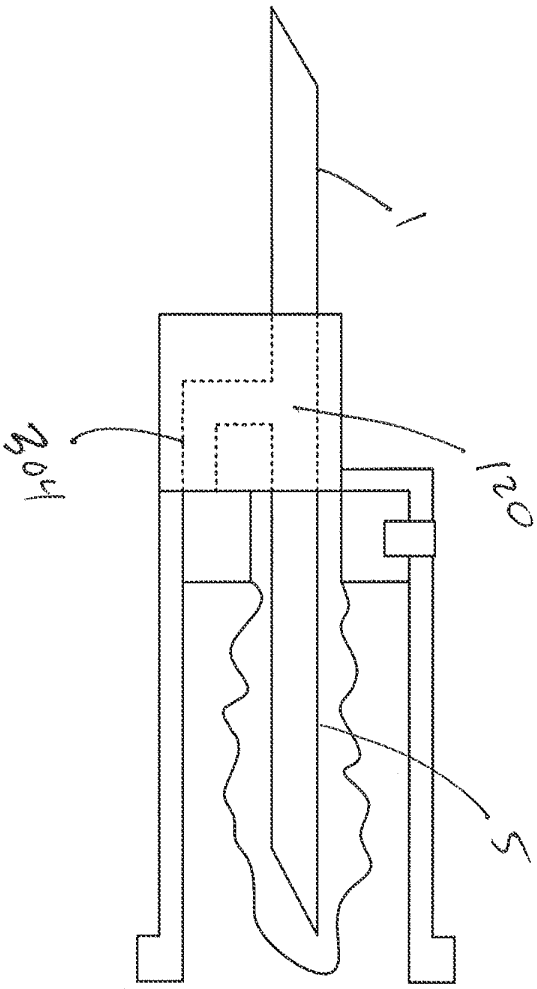


FIG. 5

FIG. 6



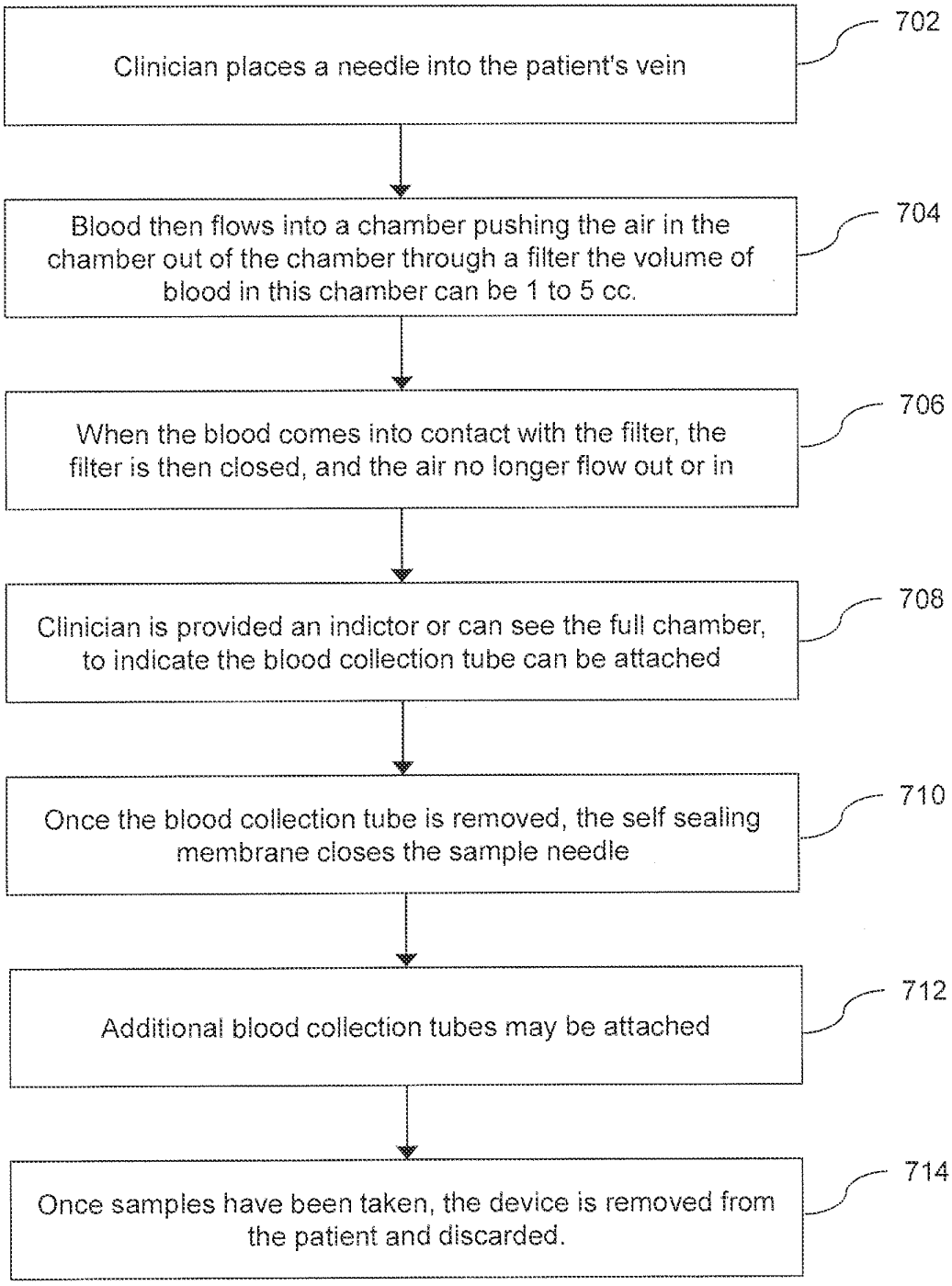

Clinician places a needle into the patient's vein
702
Blood then flows into a chamber pushing the air in the chamber out of the chamber through a filter the volume of blood in this chamber can be 1 to 5 cc.
704
When the blood comes into contact with the filter, the filter is then closed, and the air no longer flow out or in
706
Clinician is provided an indictor or can see the full chamber, to indicate the blood collection tube can be attached
708
Once the blood collection tube is removed, the self sealing membrane closes the sample needle
710
Additional blood collection tubes may be attached
712
Once samples have been taken, the device is removed from the patient and discarded.
714

FIG. 7

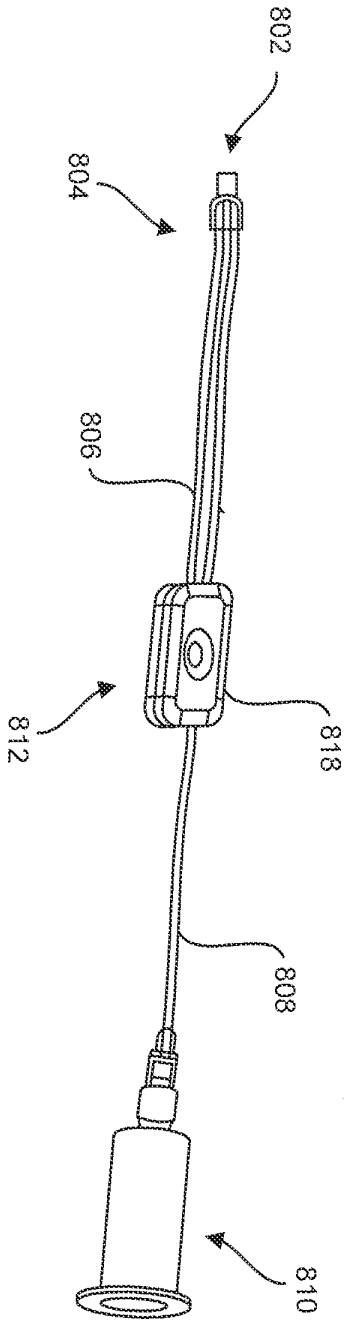


FIG. 8A

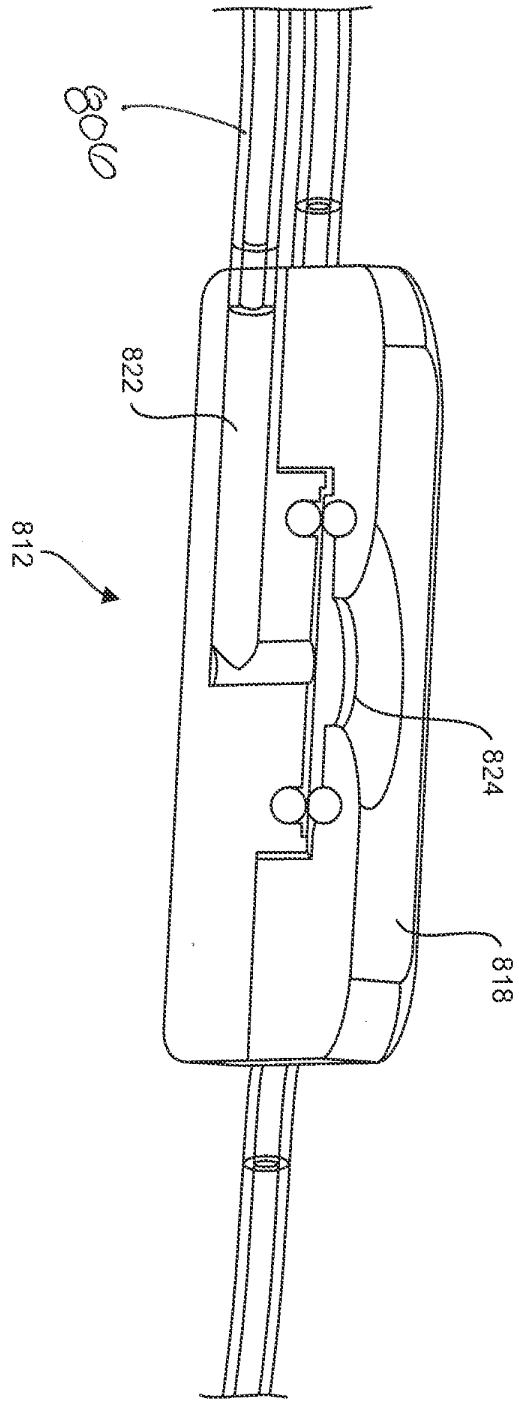


FIG. 8B

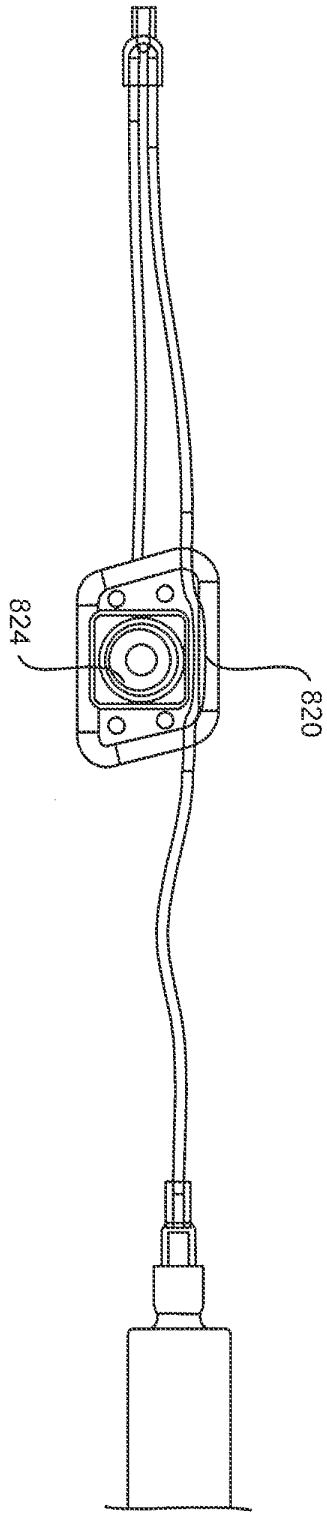


FIG. 8C

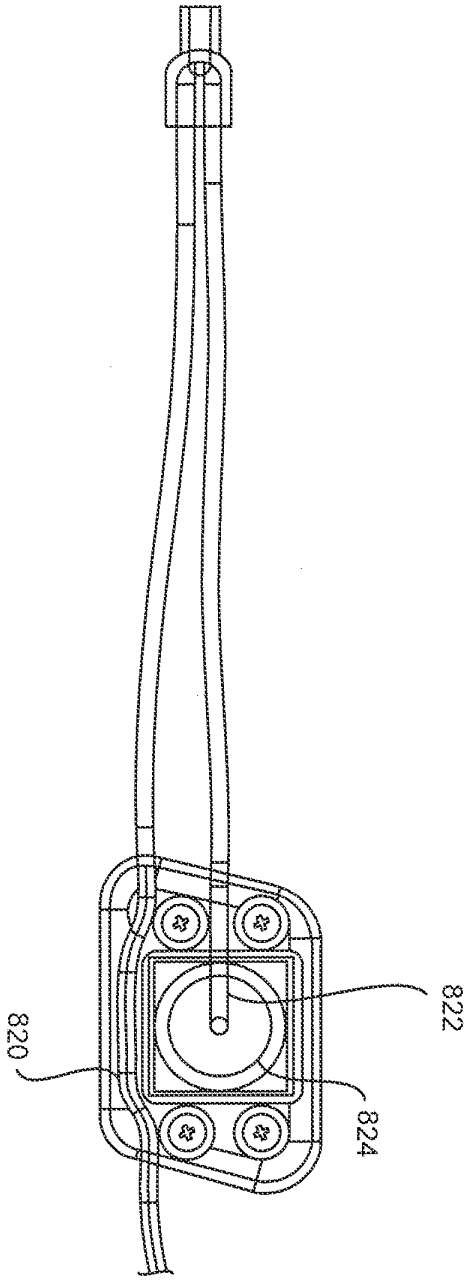


FIG. 8D

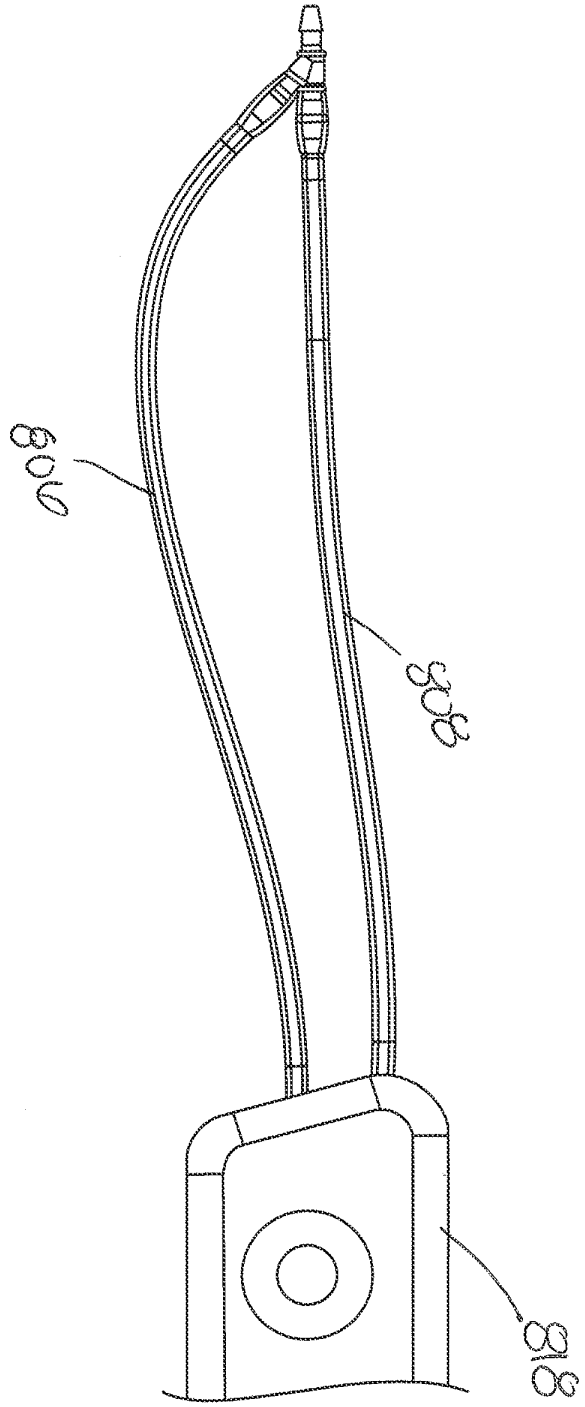
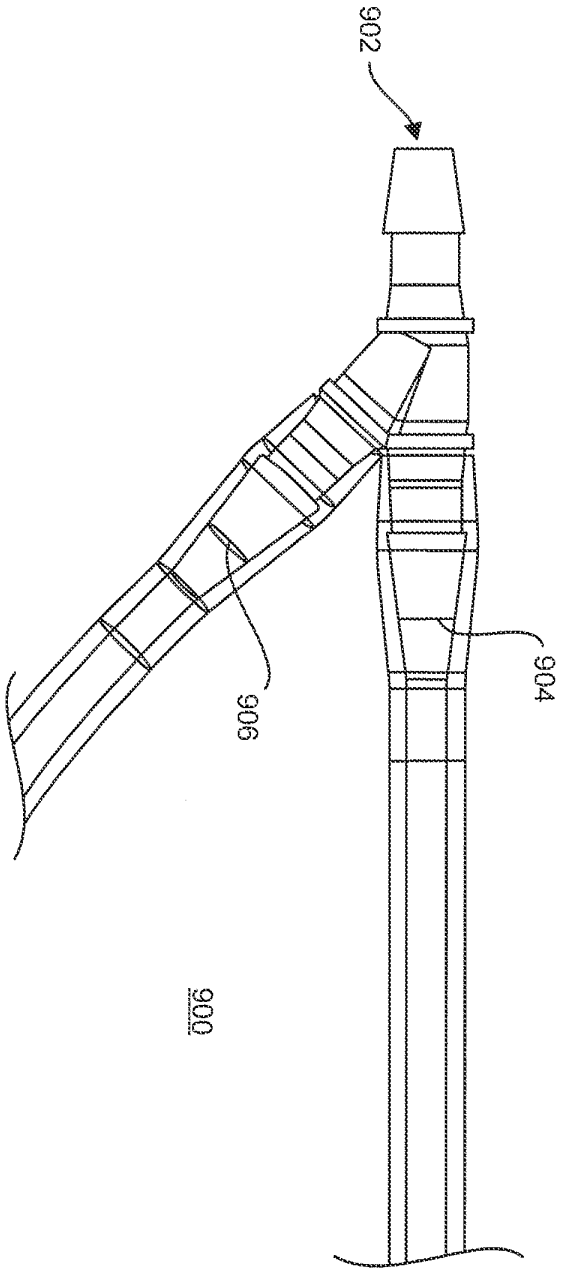


FIG. 8E

FIG. 9



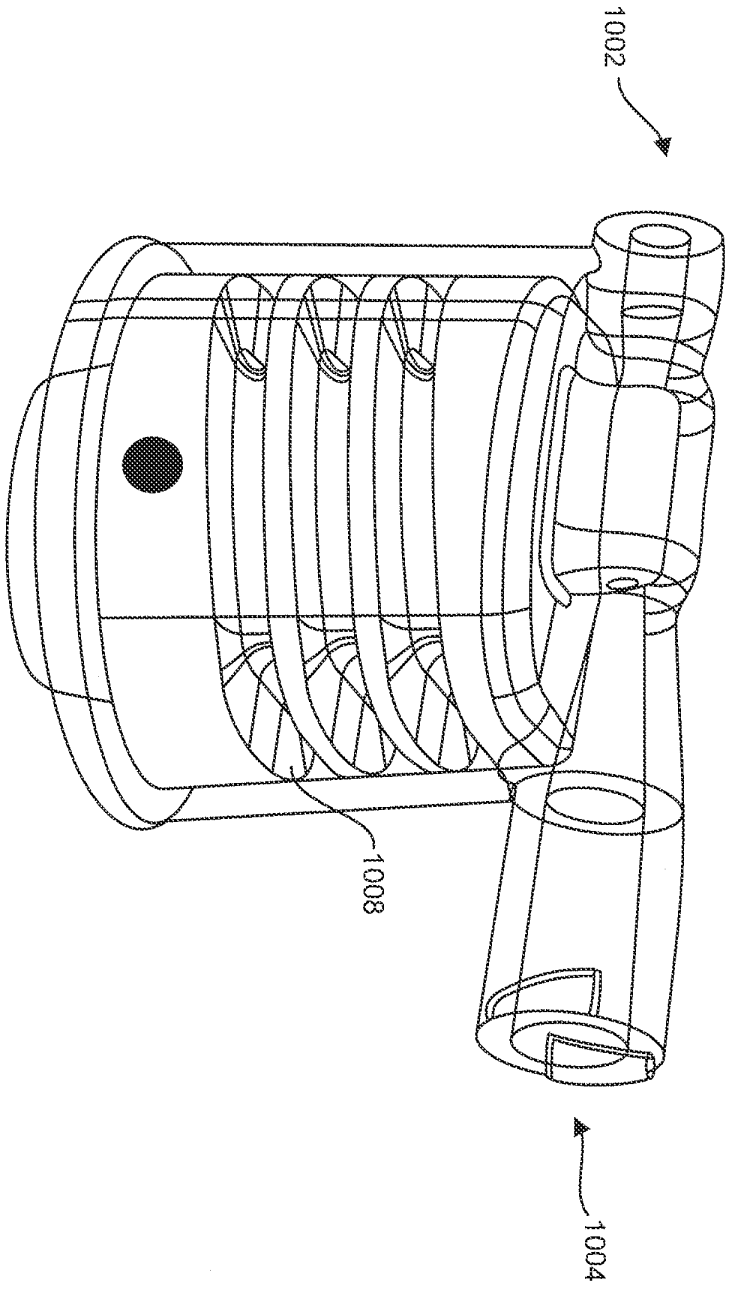


FIG. 10A

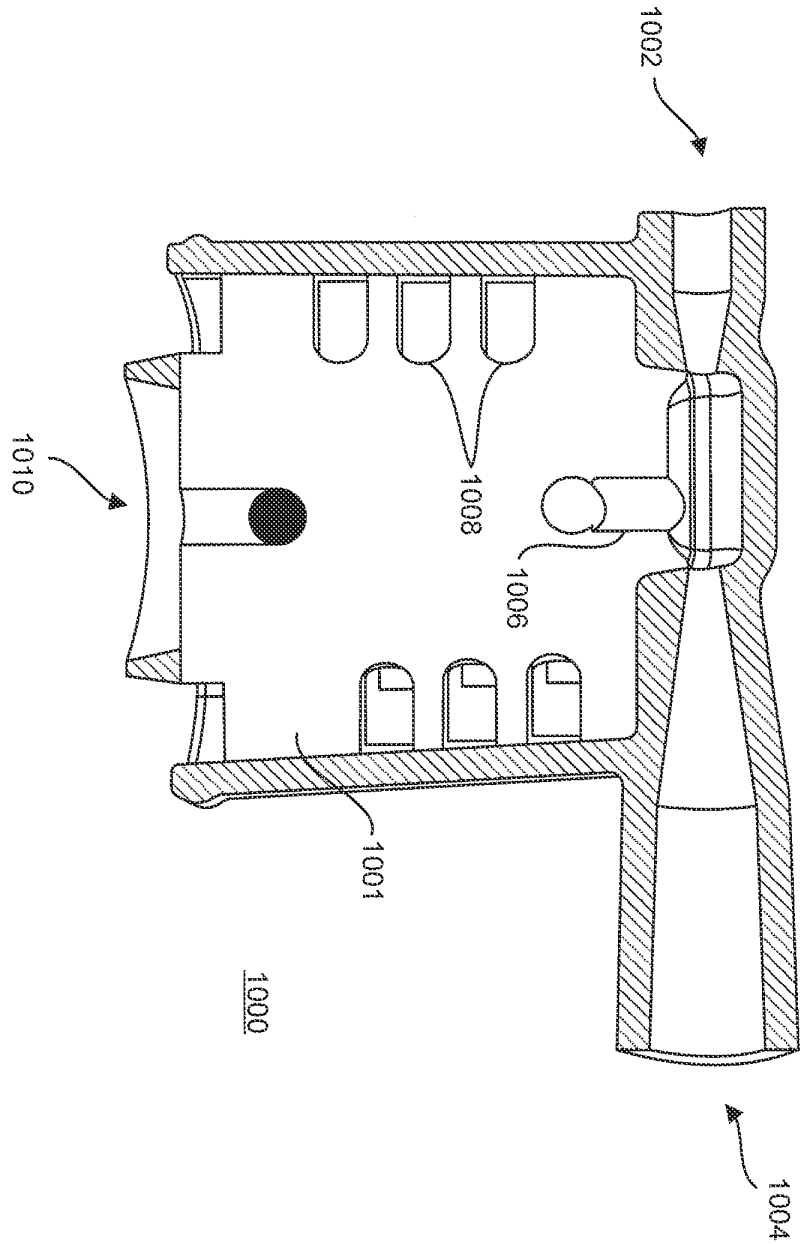


FIG. 10B

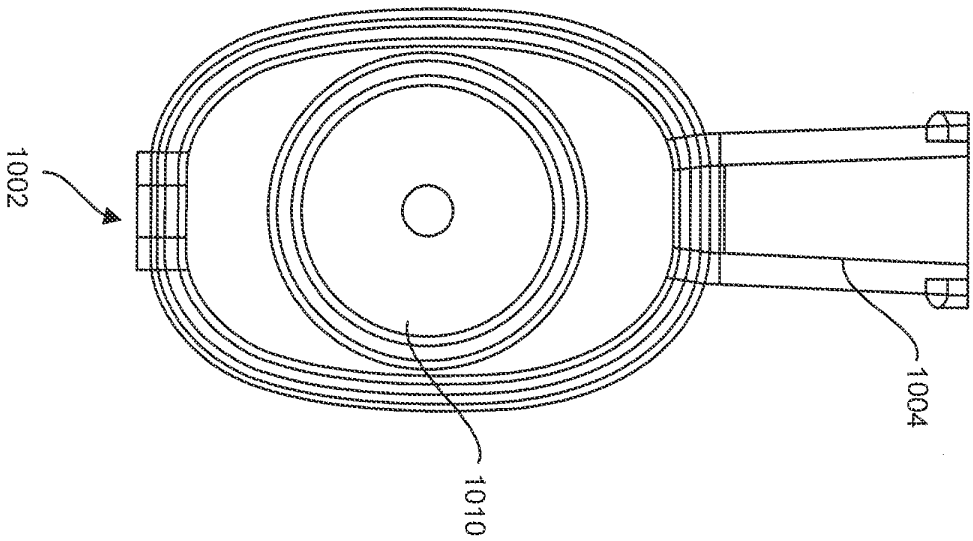


FIG. 10C

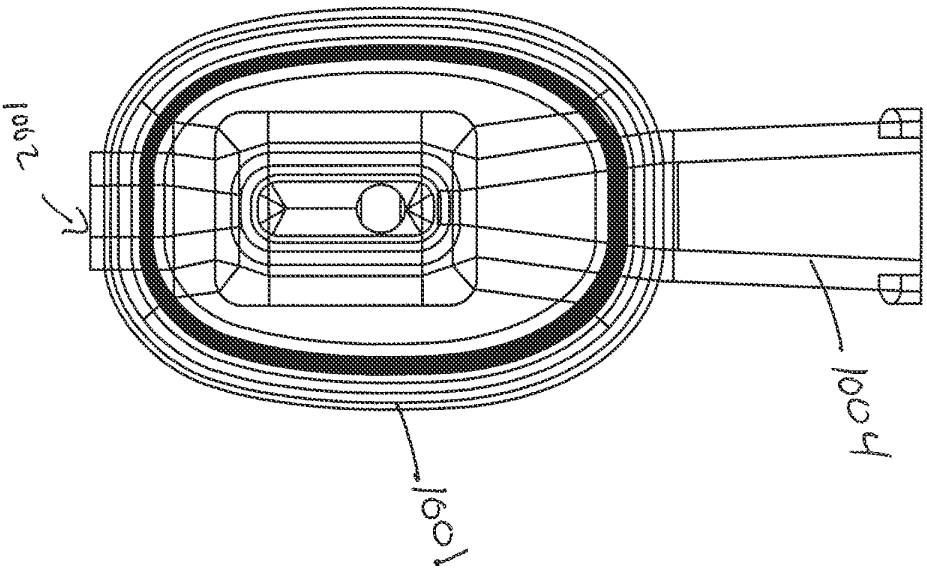


FIG. 10D

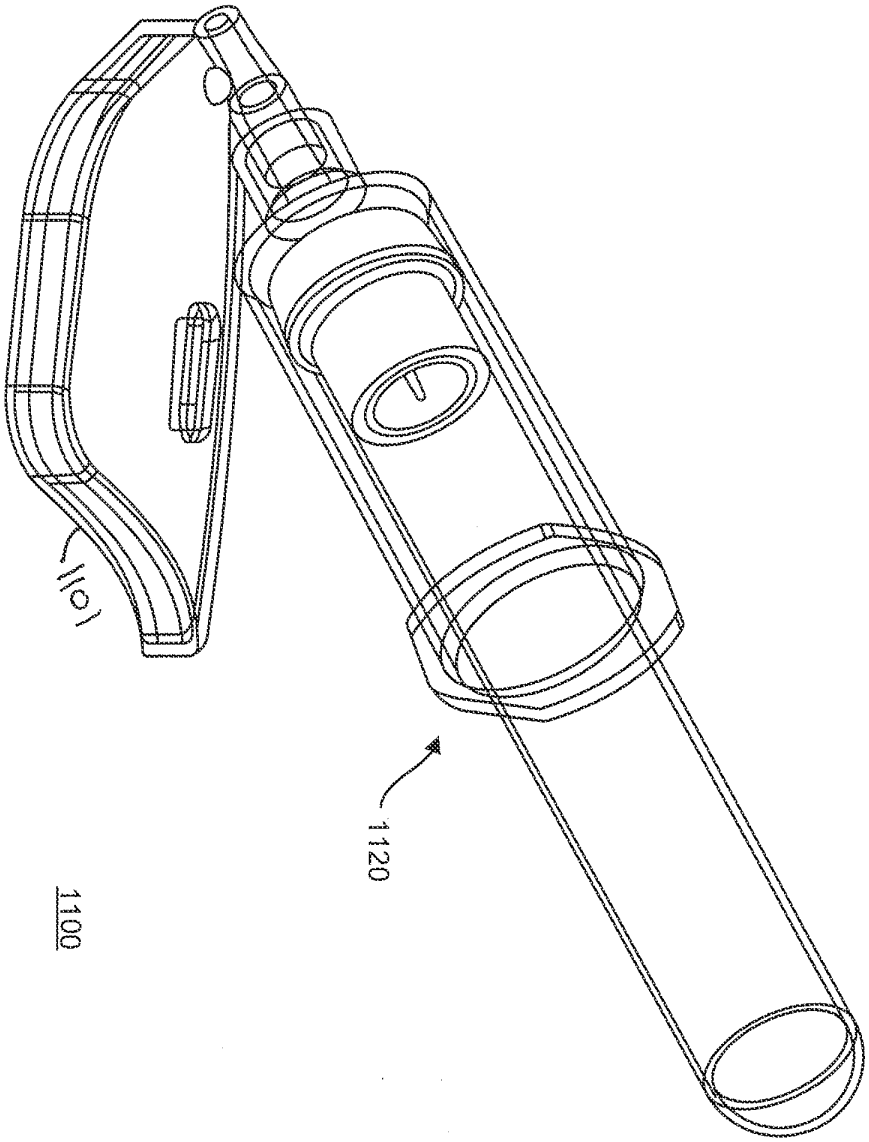


FIG. 11A

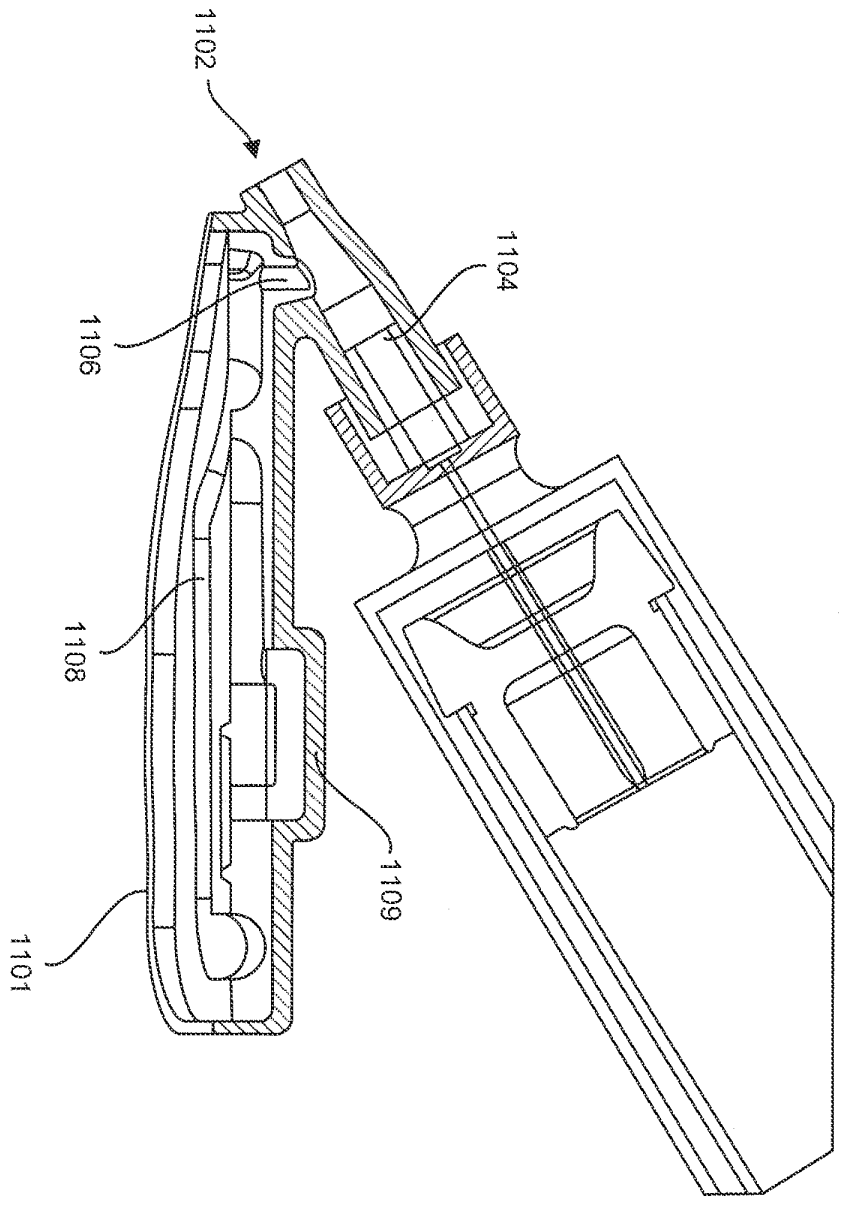


FIG. 11B

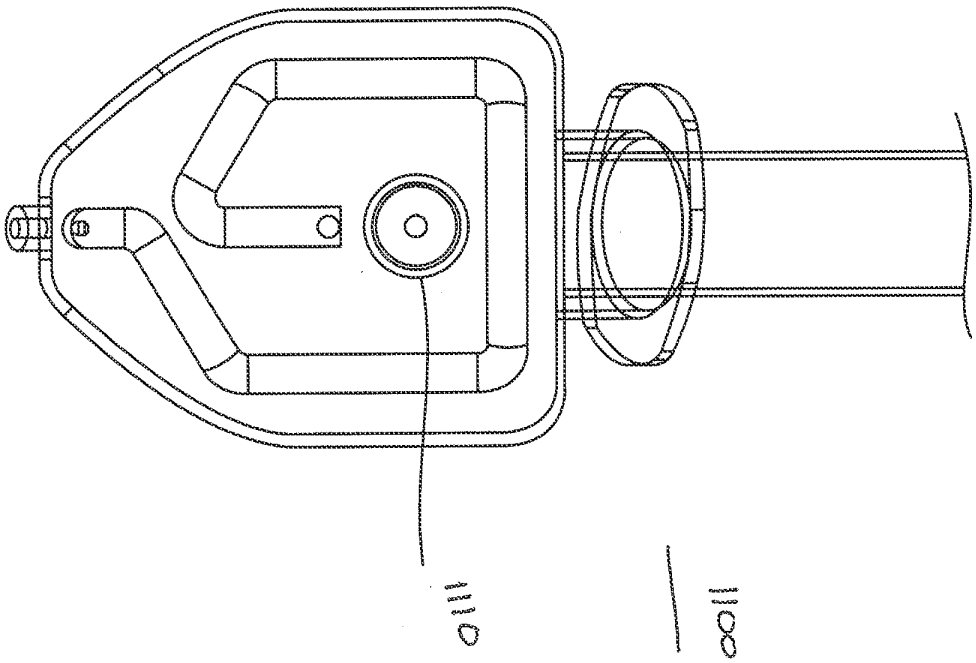


FIG. 11C

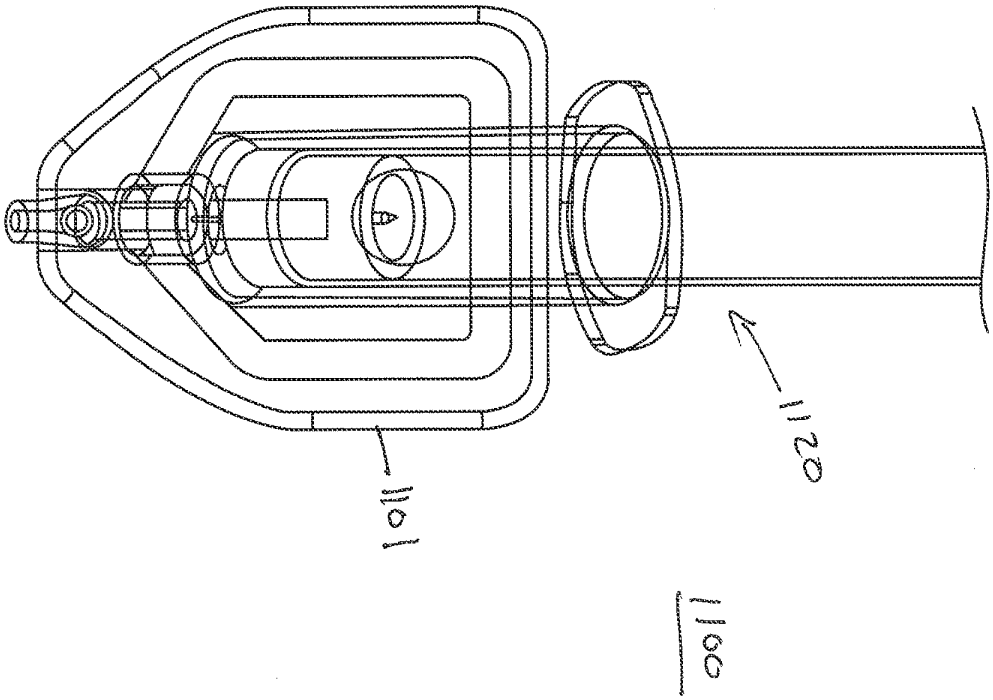


FIG. 11D

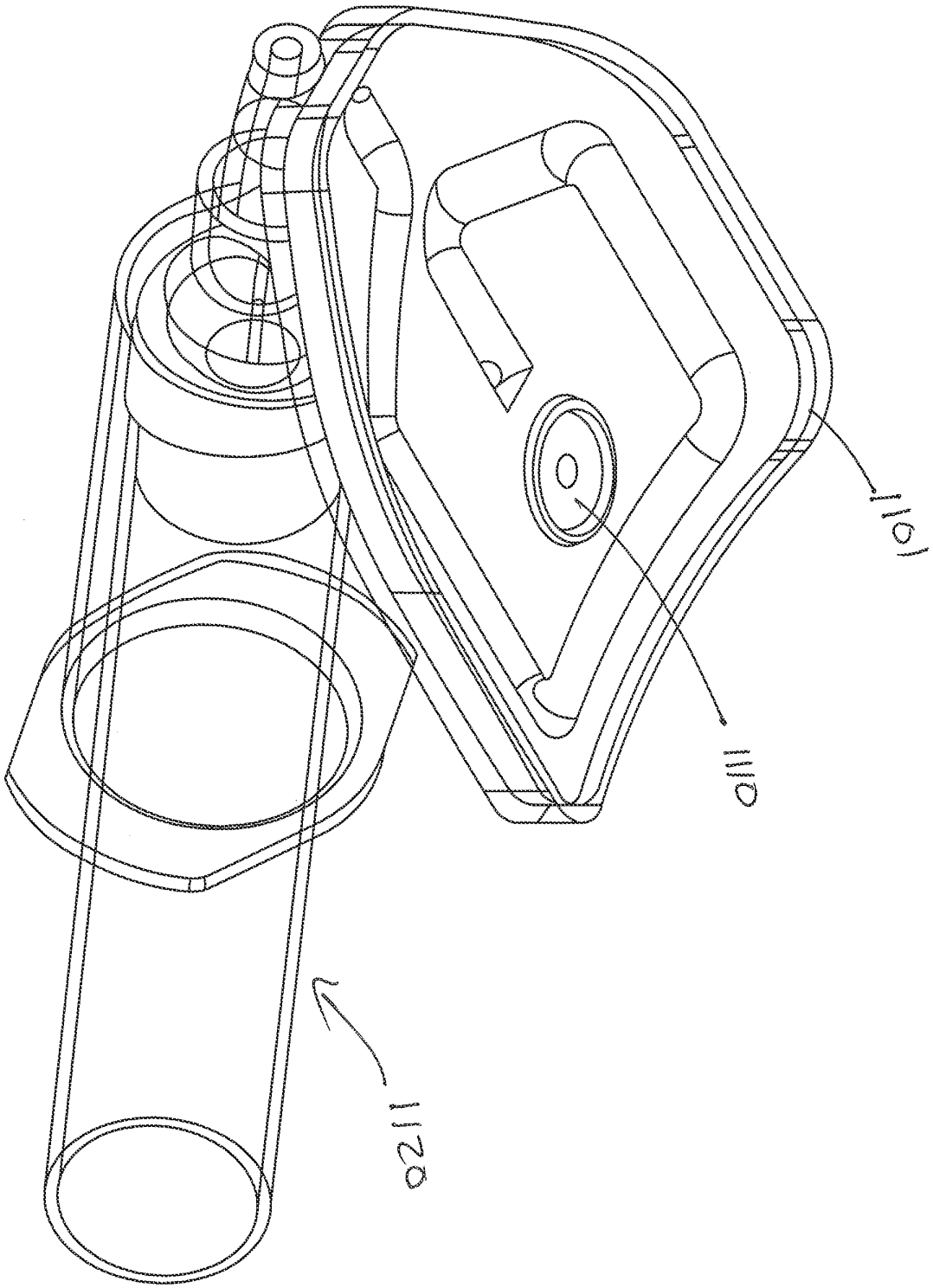


FIG. 11E

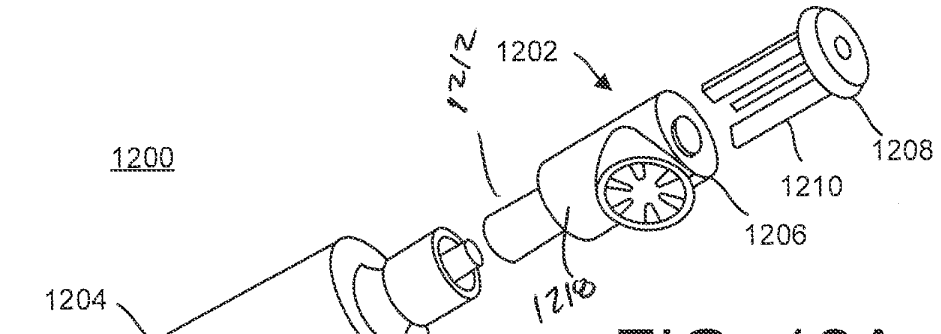


FIG. 12A

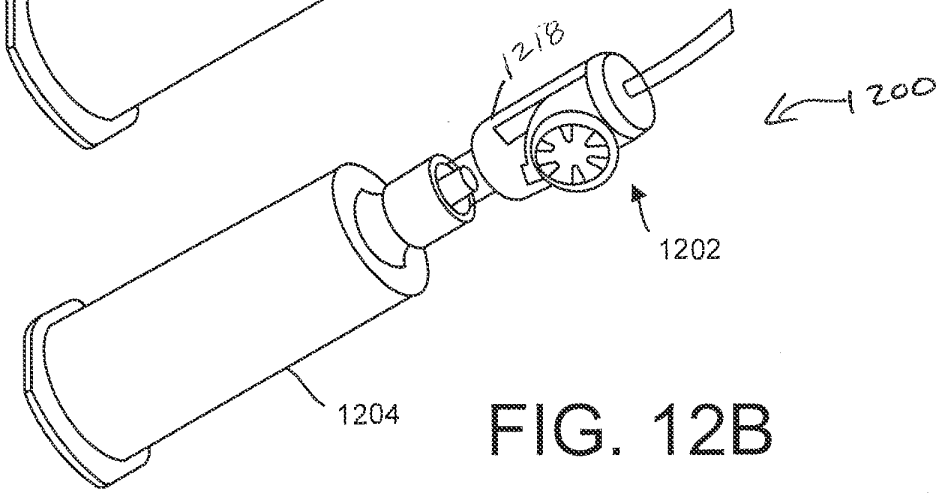


FIG. 12B

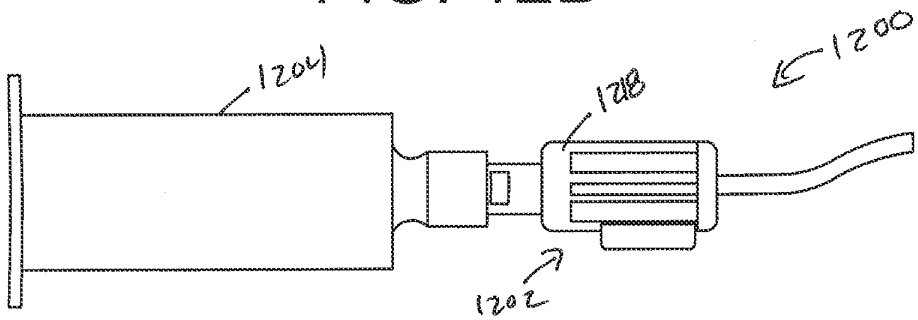


FIG. 12C

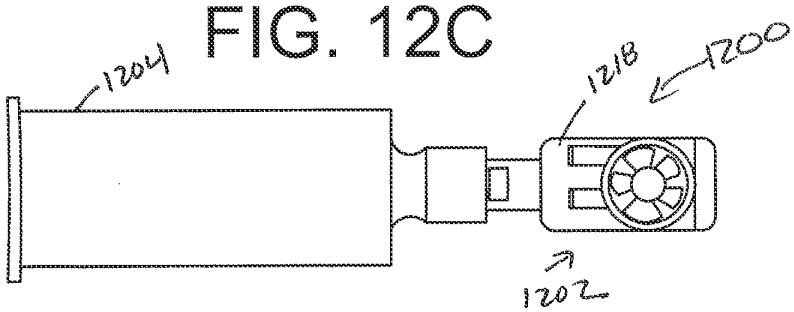


FIG. 12D

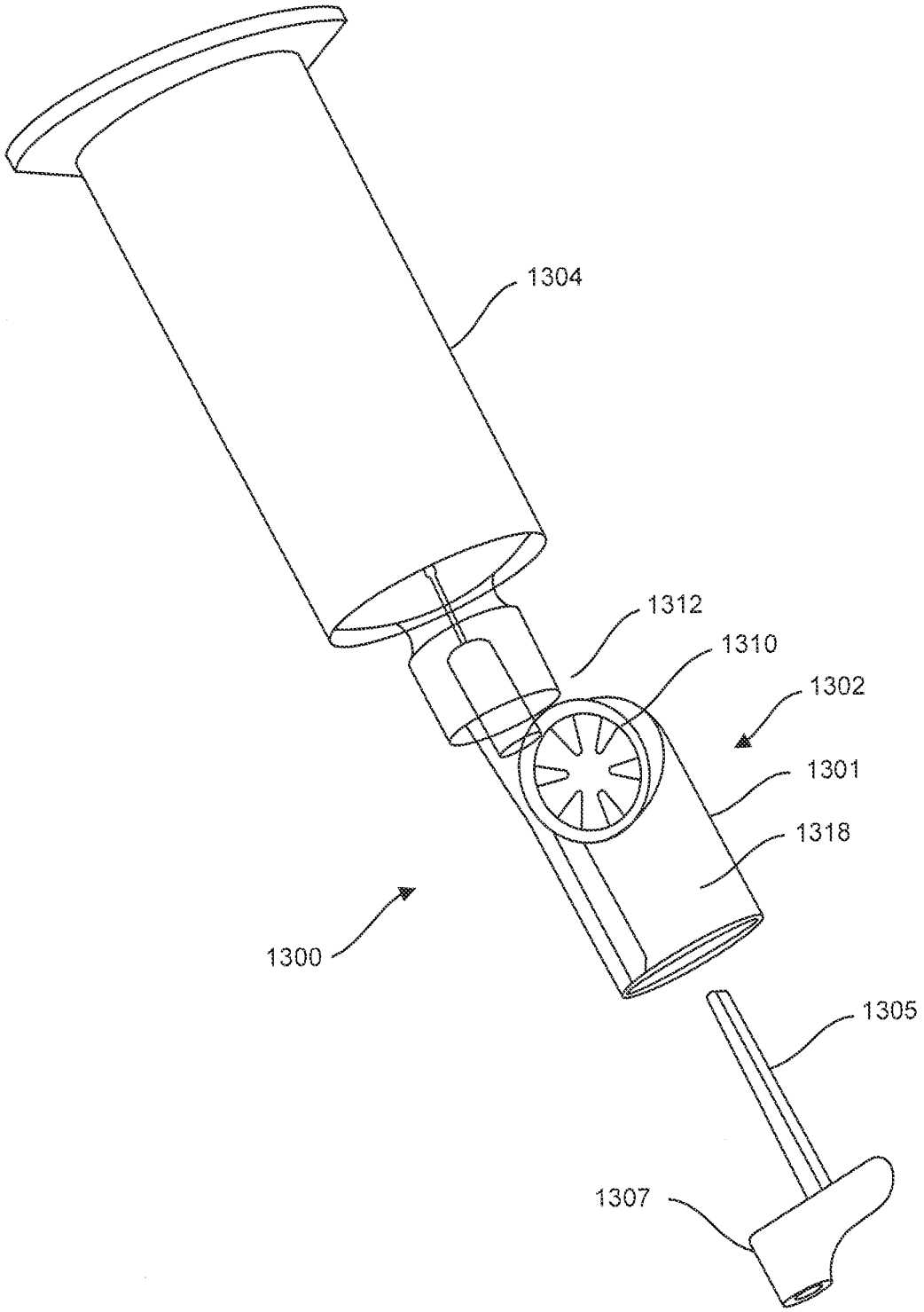


FIG. 13A

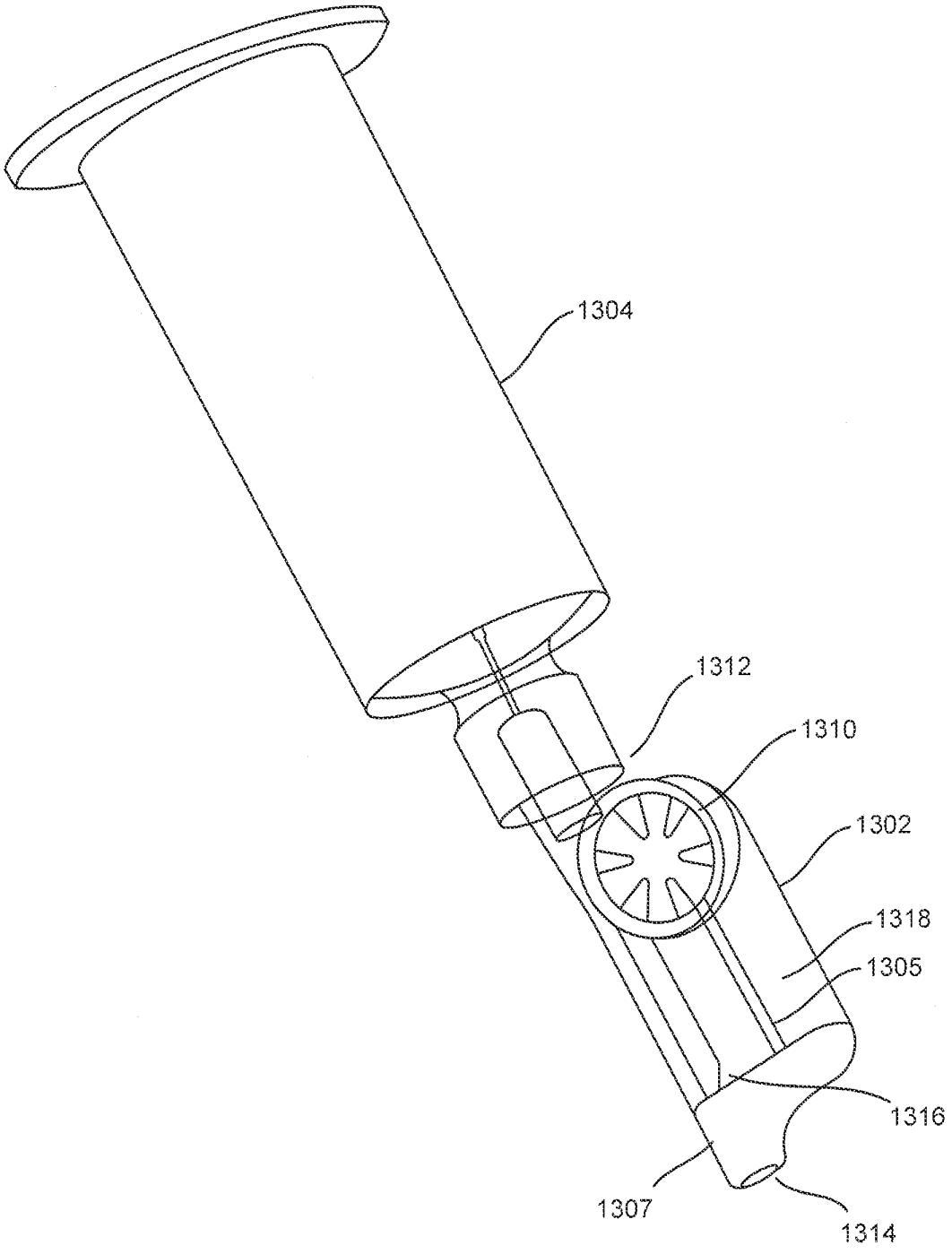


FIG. 13B

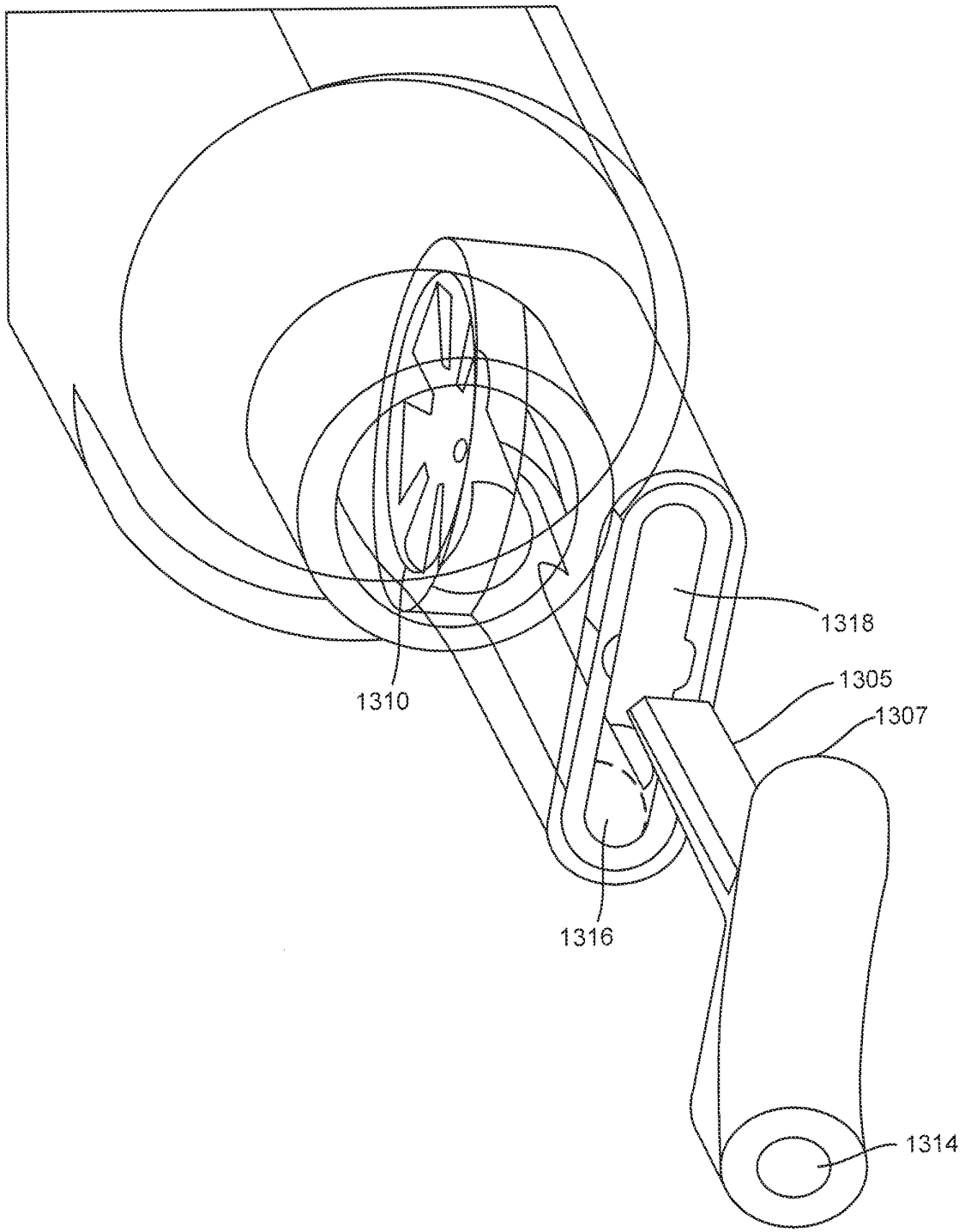


FIG. 13C

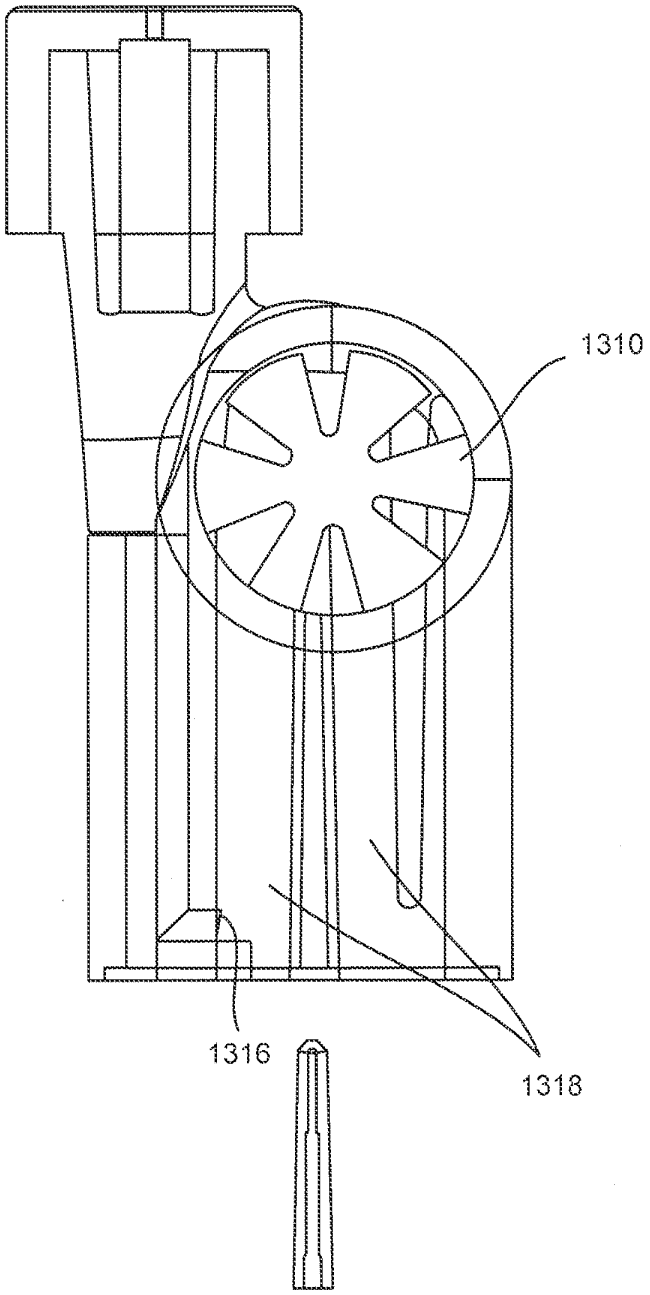


FIG. 13D

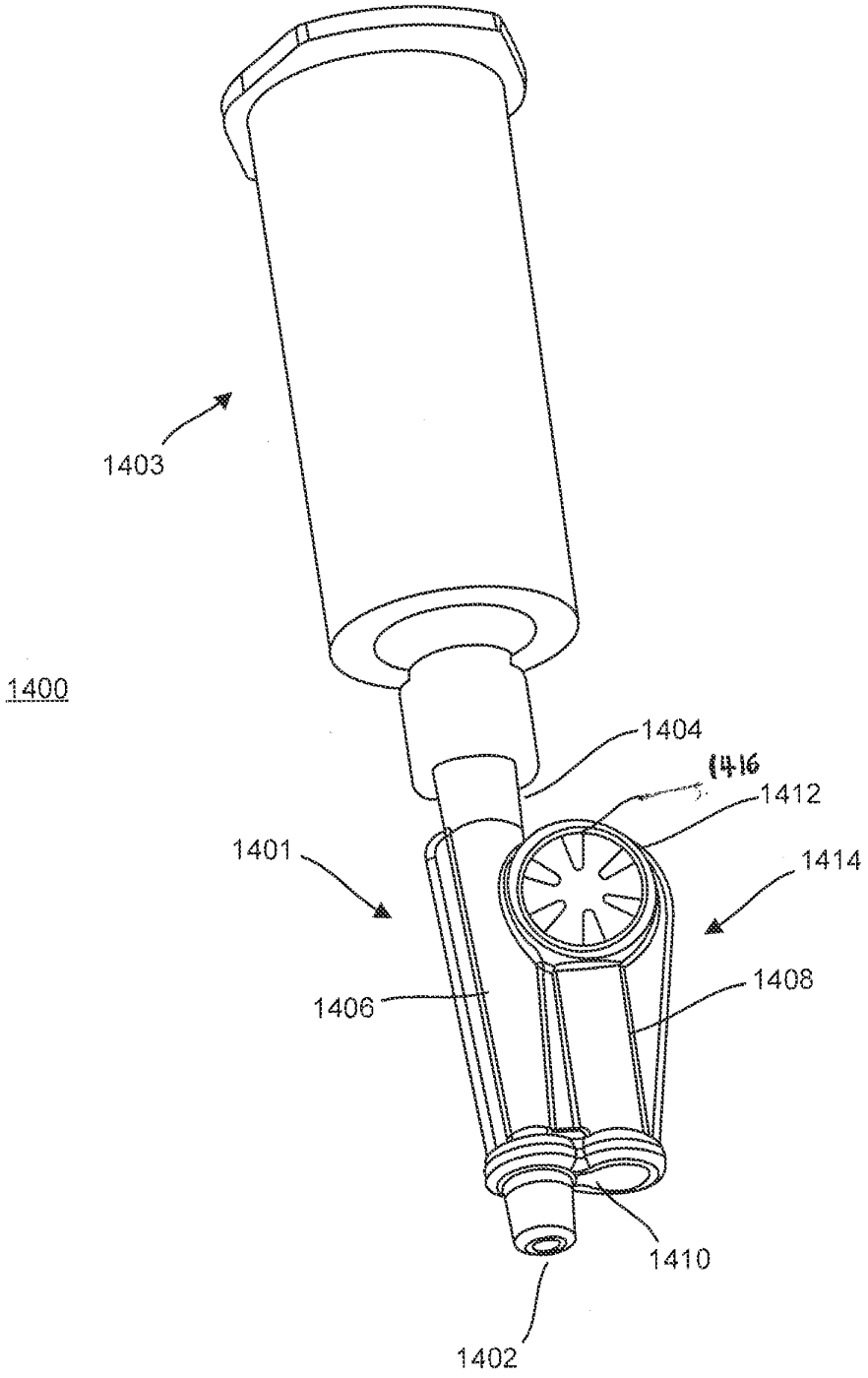


FIG. 14A

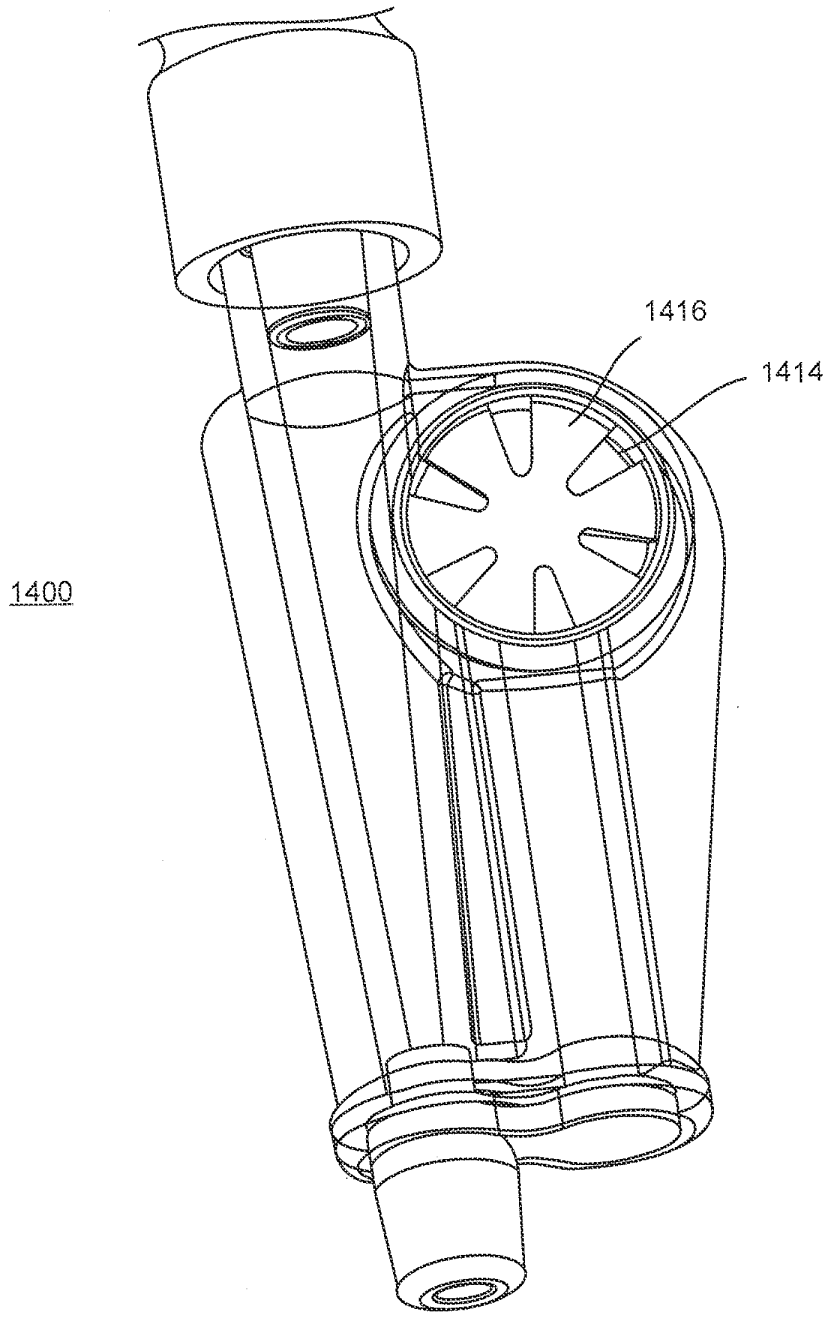


FIG. 14B

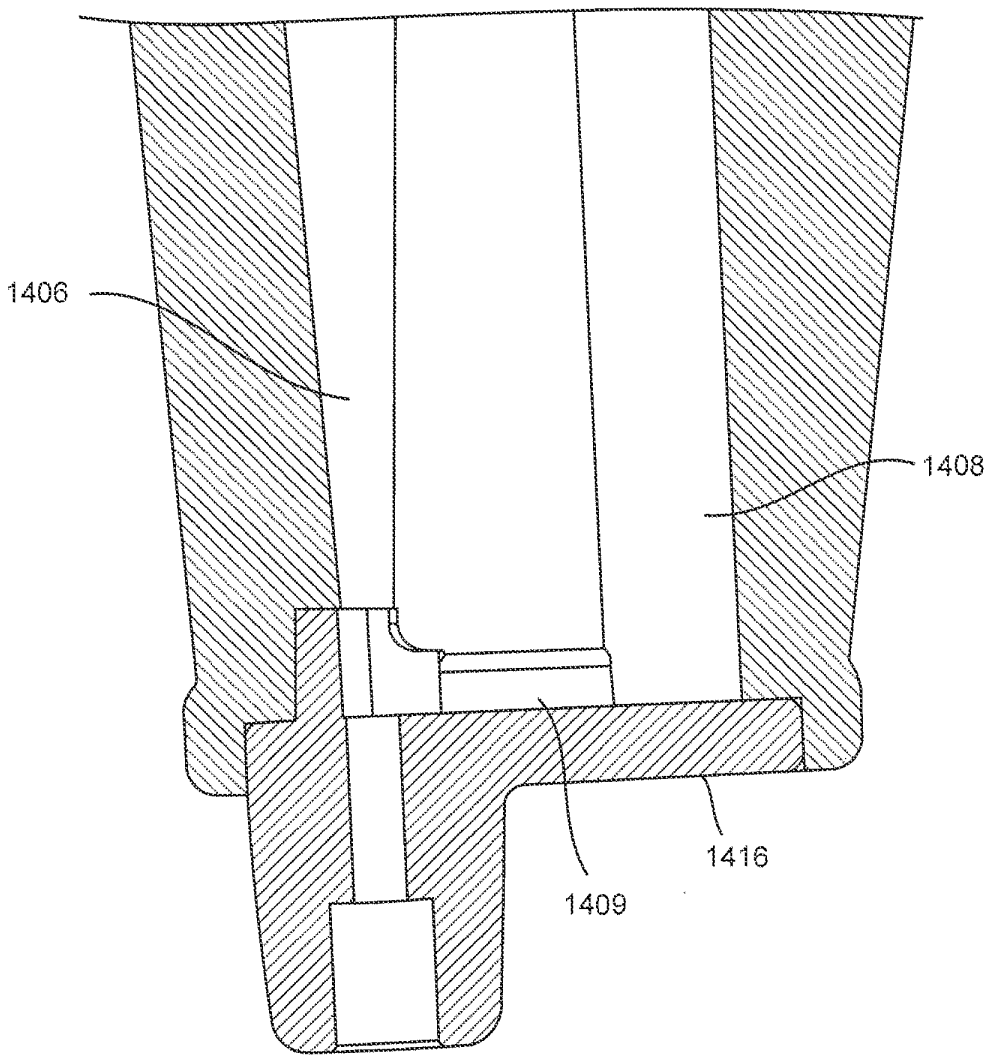


FIG. 14C

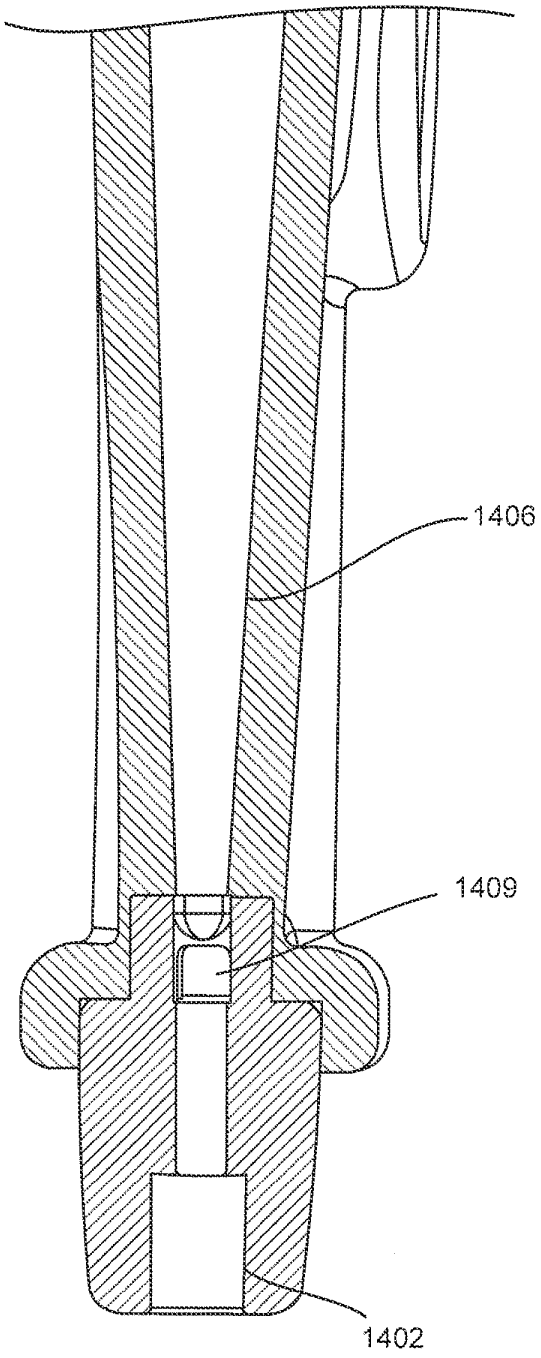


FIG. 14D

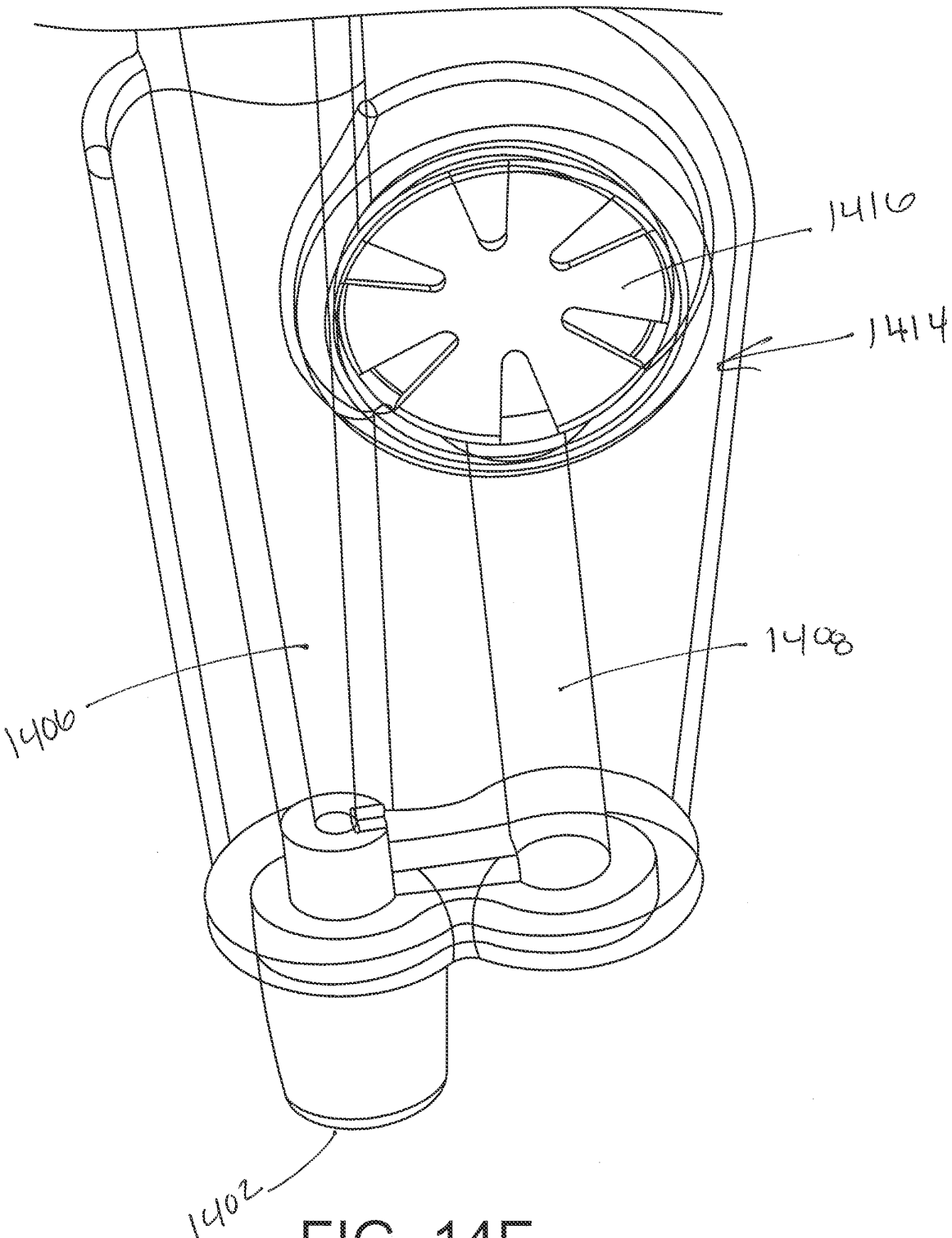


FIG. 14E

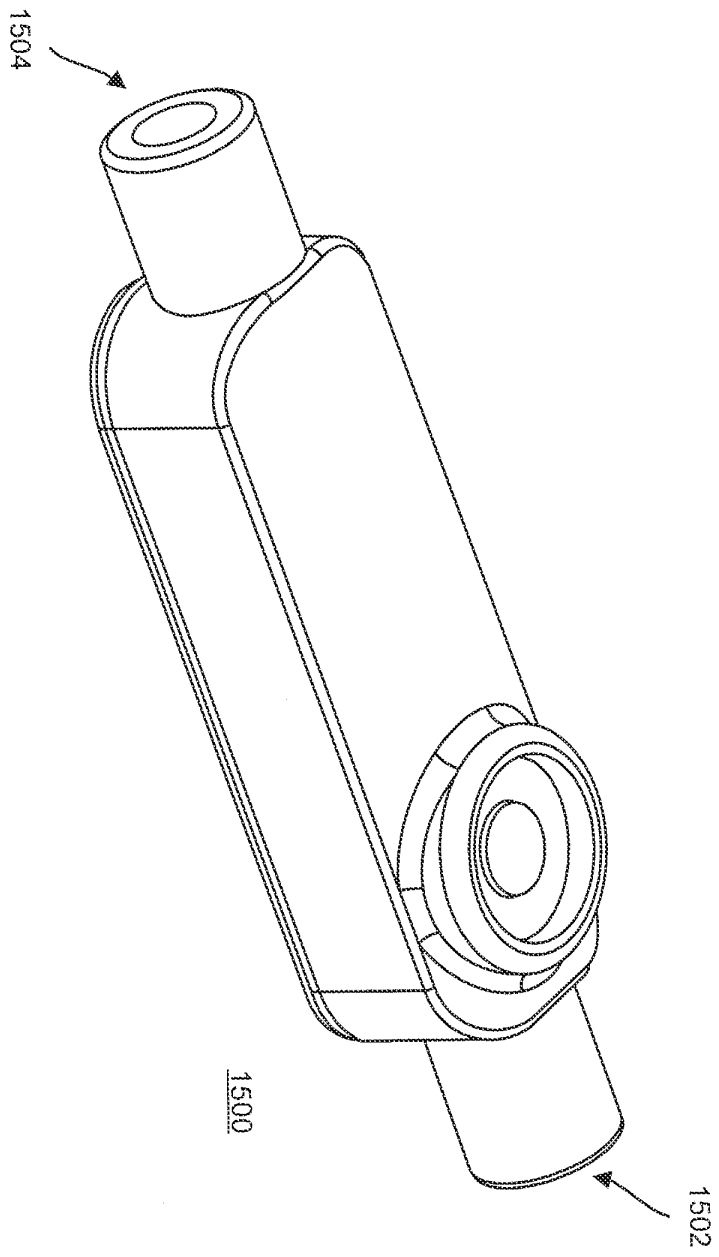


FIG. 15A

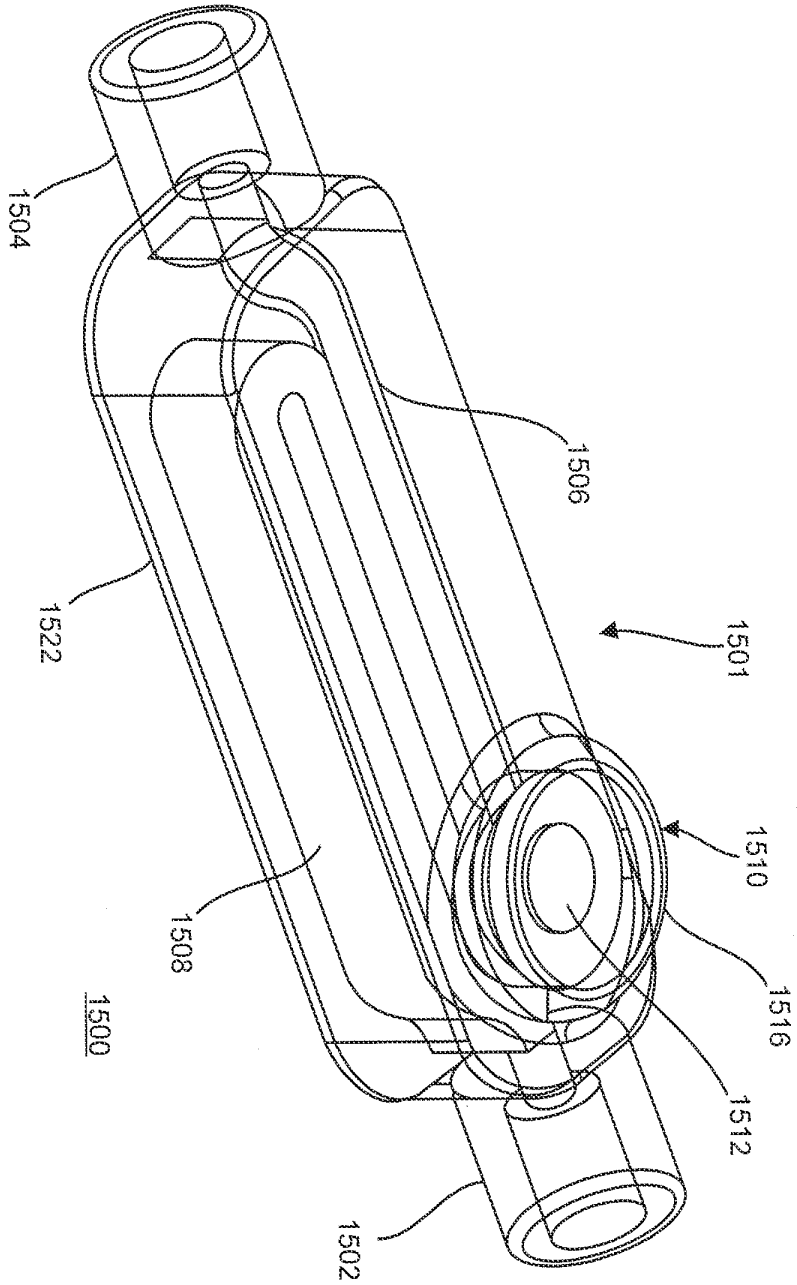


FIG. 15B

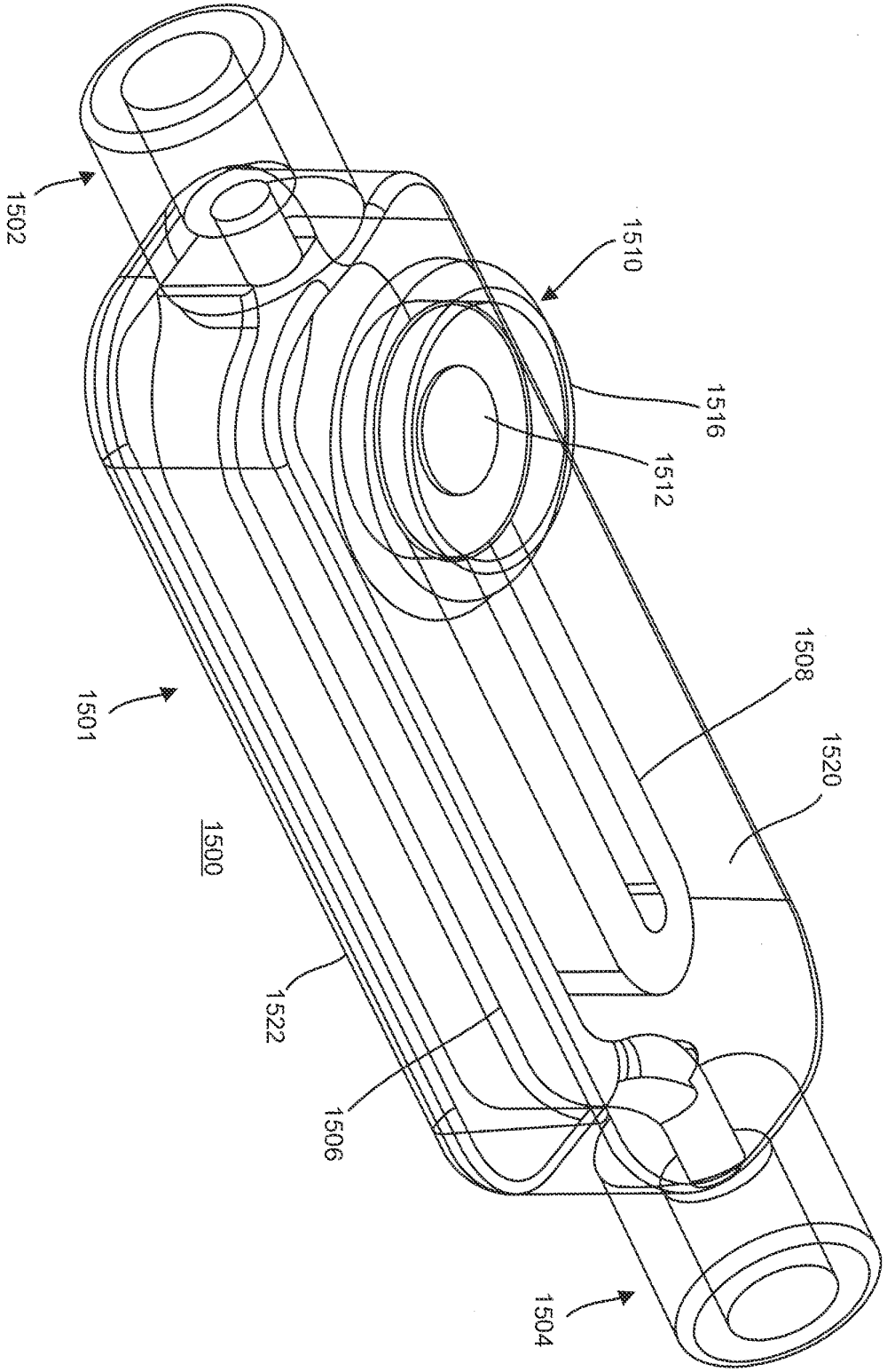


FIG. 15C

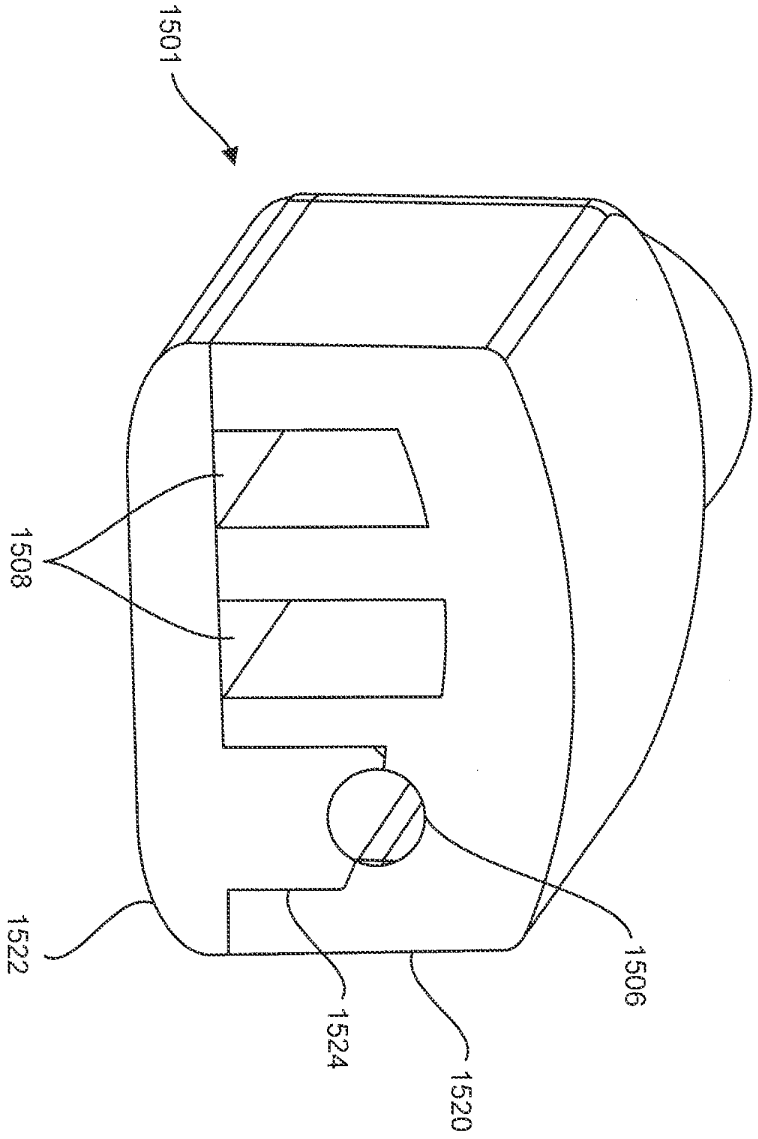


FIG. 15D

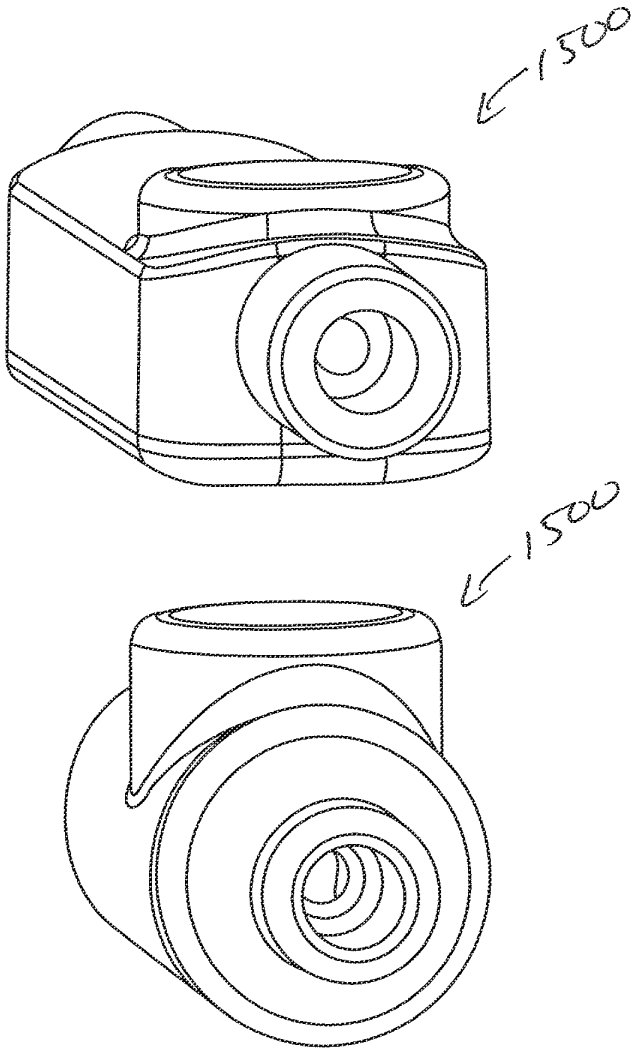


FIG. 15E

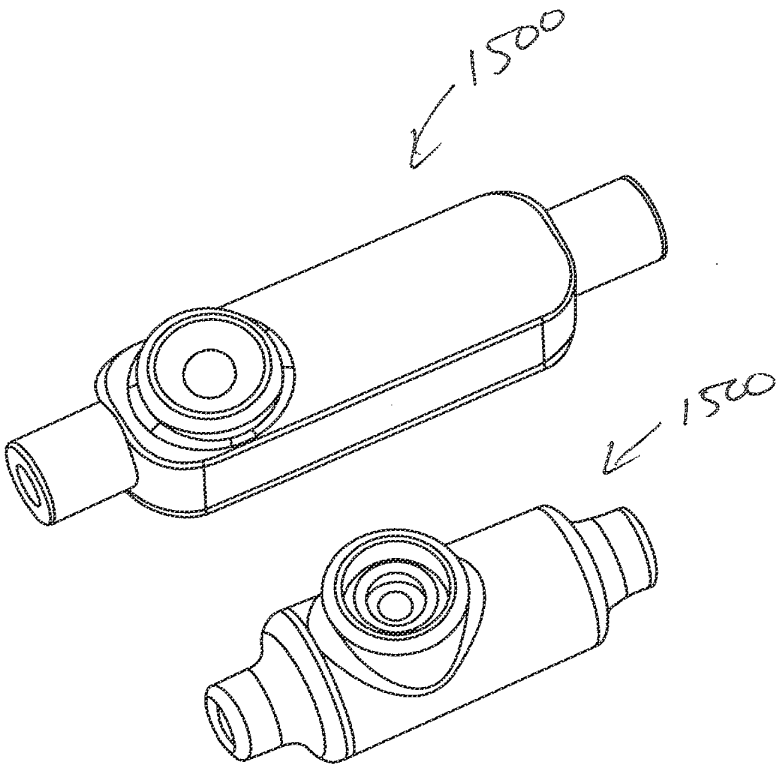


FIG. 15F

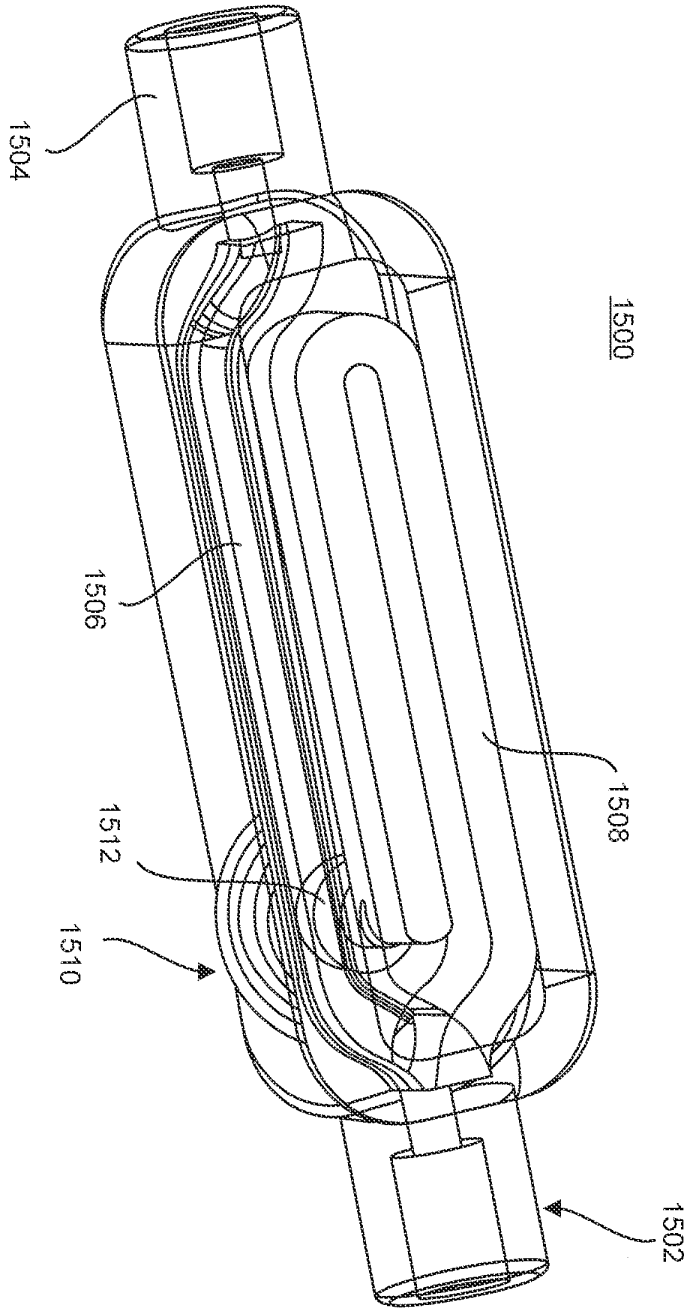


FIG. 15G

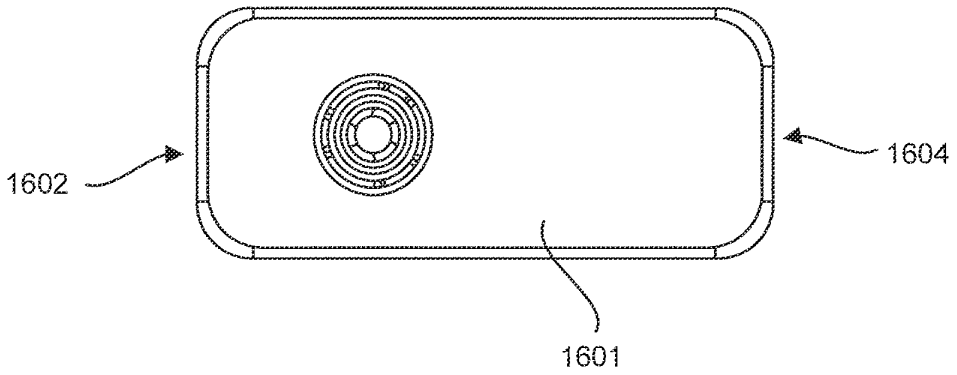


FIG. 16A

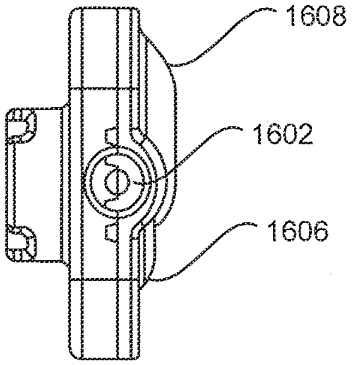


FIG. 16C

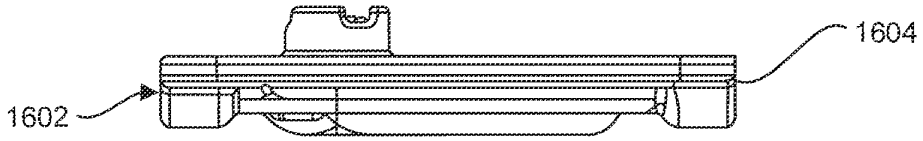


FIG. 16B

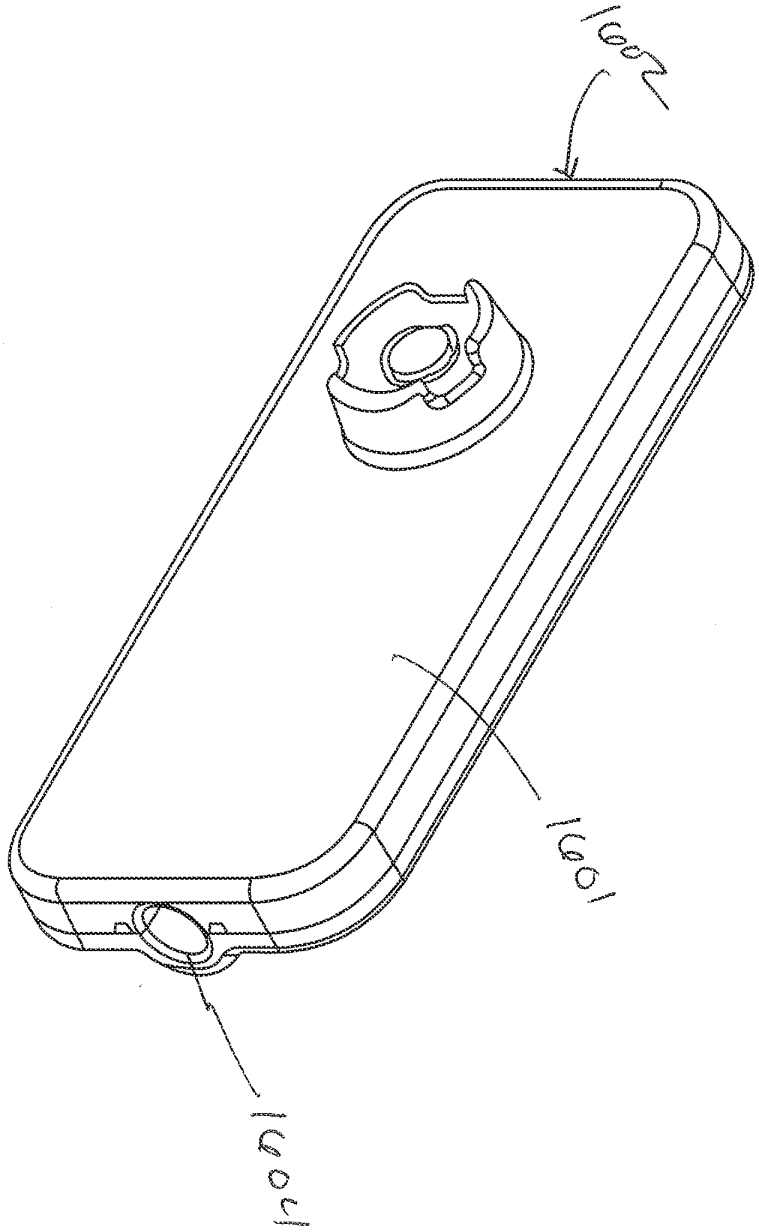


FIG. 16D

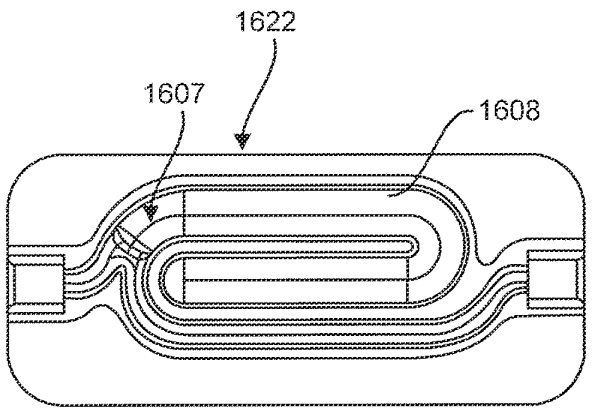


FIG. 17A

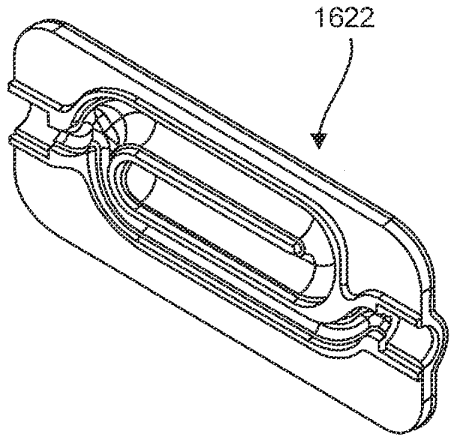


FIG. 17B

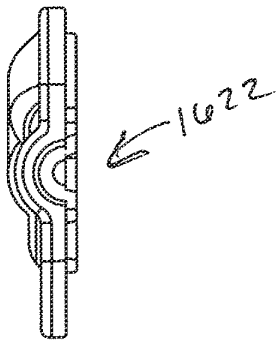


FIG. 17C

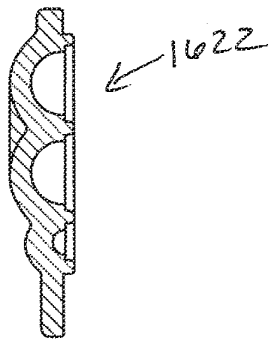


FIG. 17D

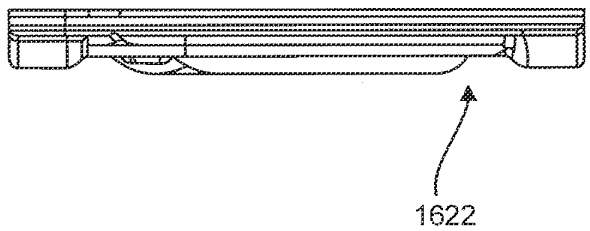


FIG. 17E

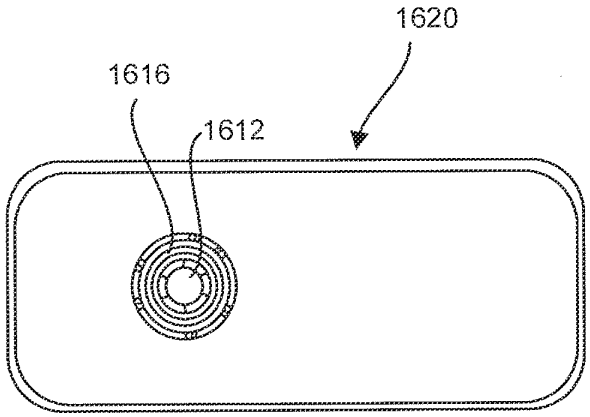


FIG. 18A

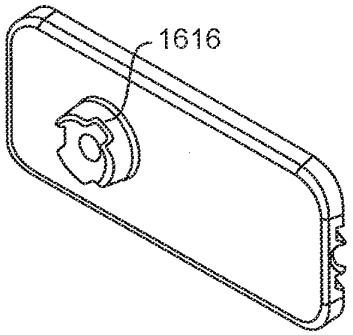


FIG. 18B

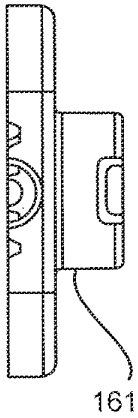


FIG. 18C

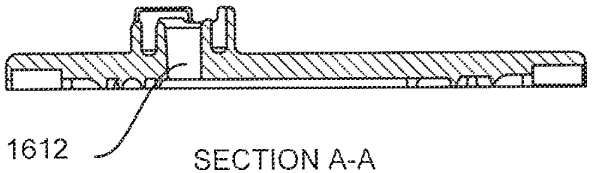


FIG. 18D

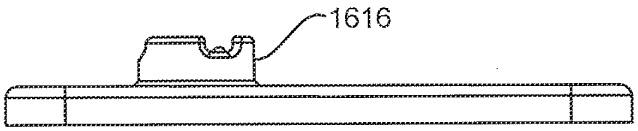


FIG. 18E

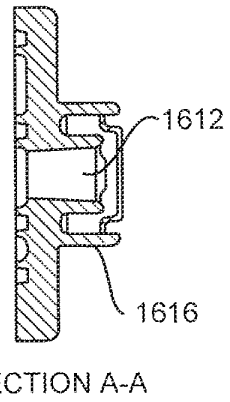


FIG. 18F

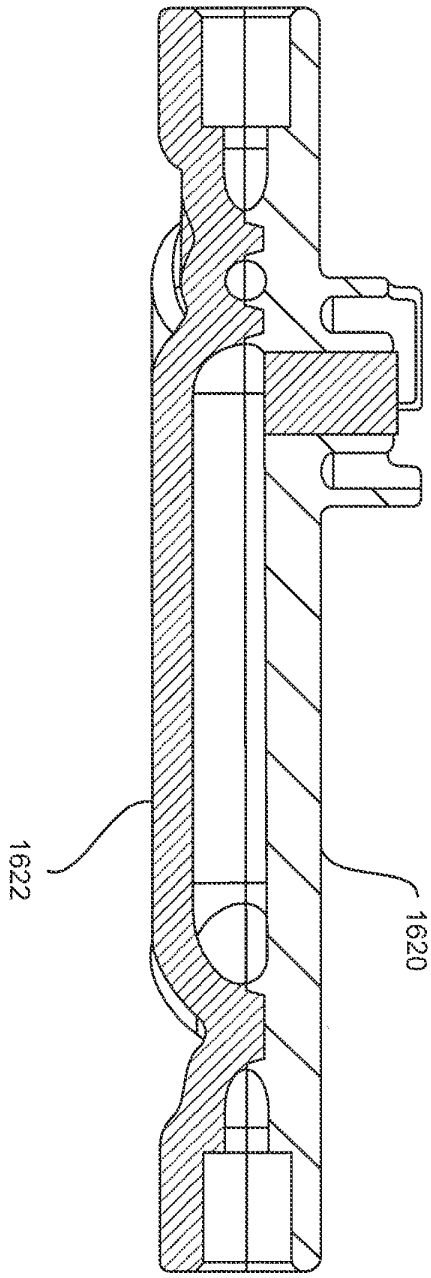


FIG. 19A

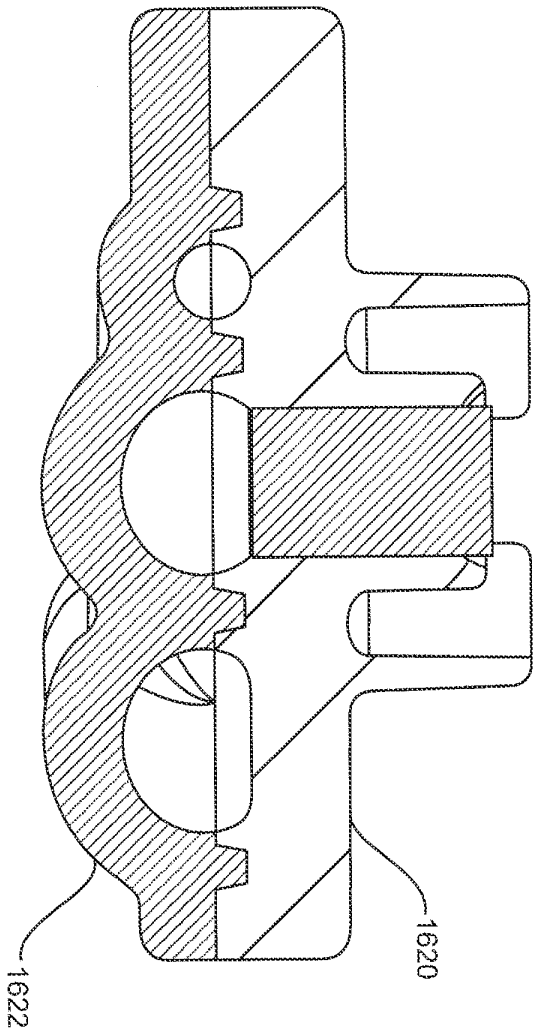


FIG. 16B

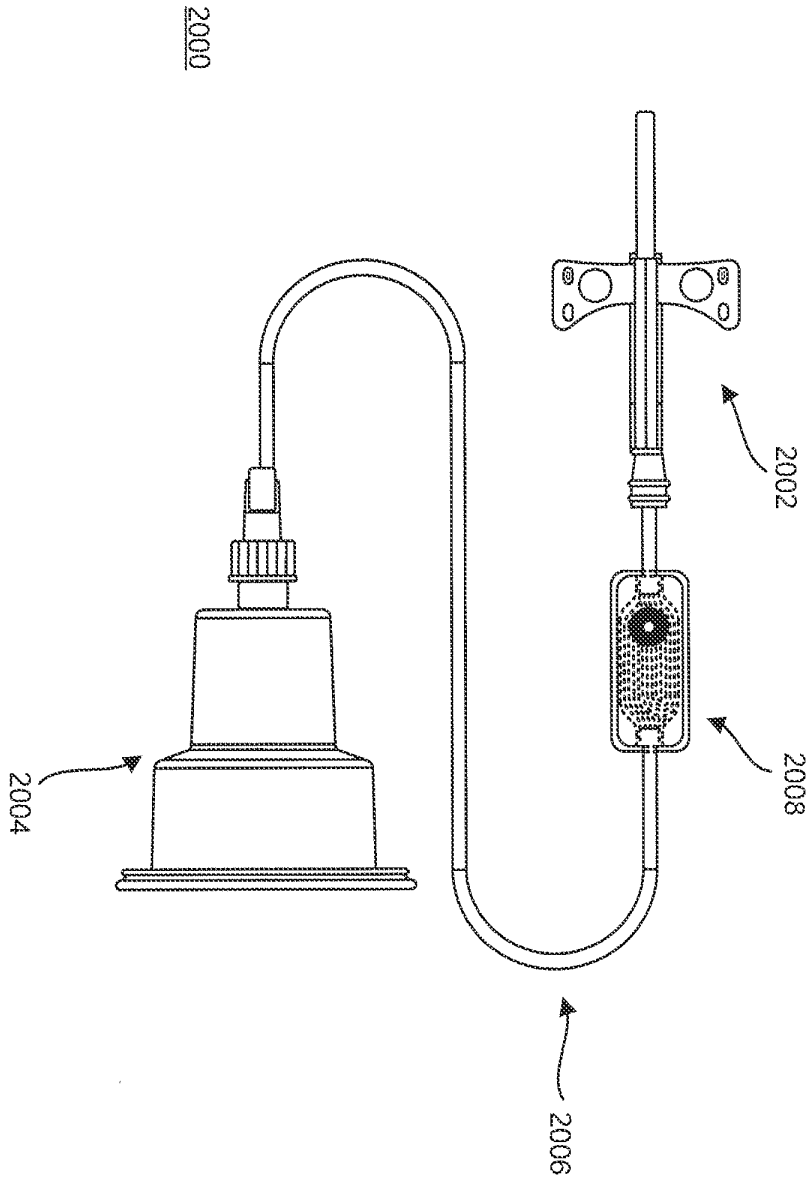


FIG. 20

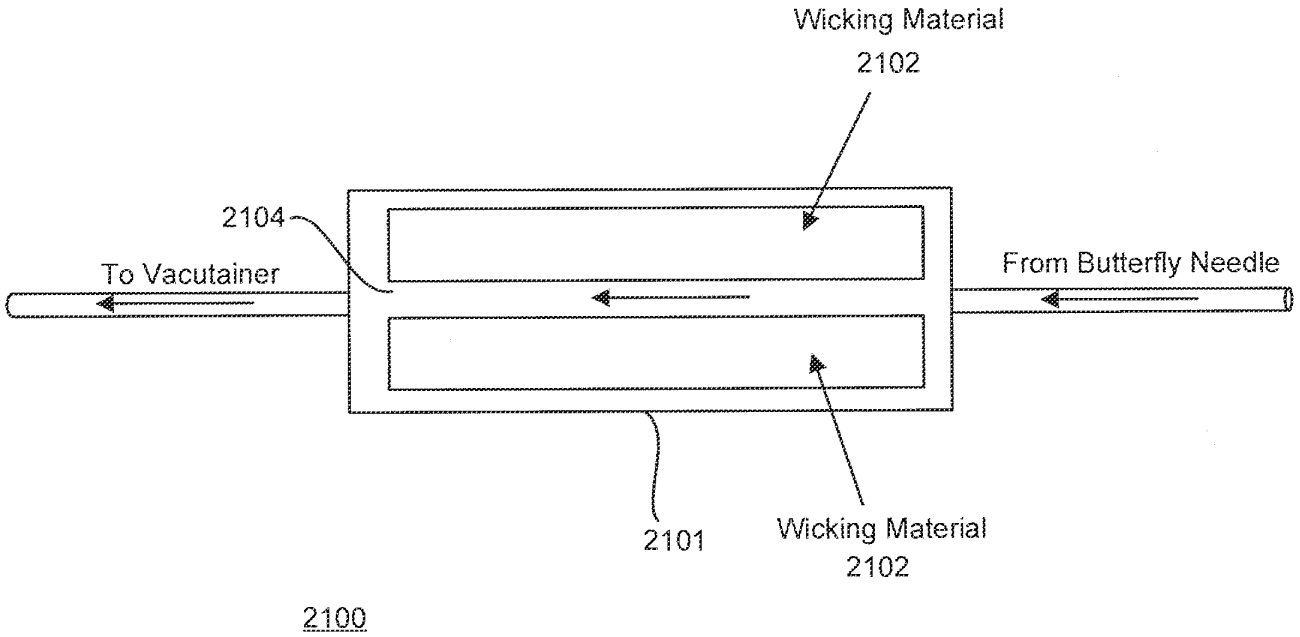

Wicking Material
2102
2104
To Vacutainer
From Butterfly Needle
2101
Wicking Material
2102
2100

FIG. 21

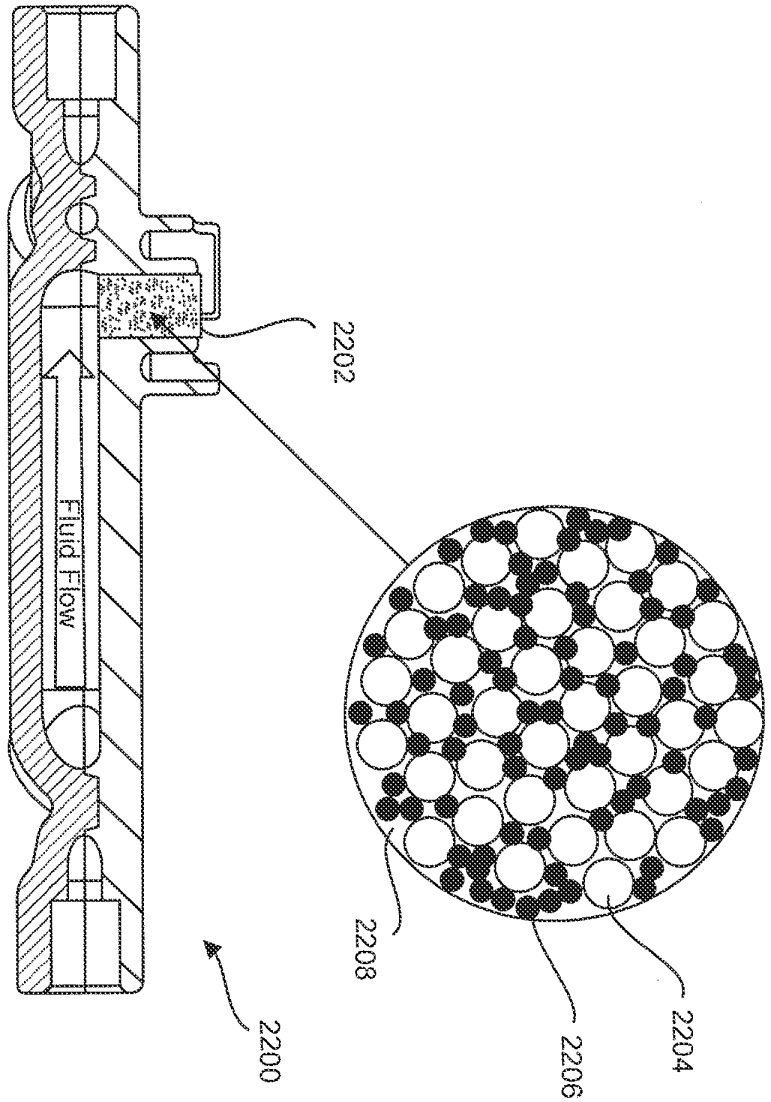


FIG. 22A

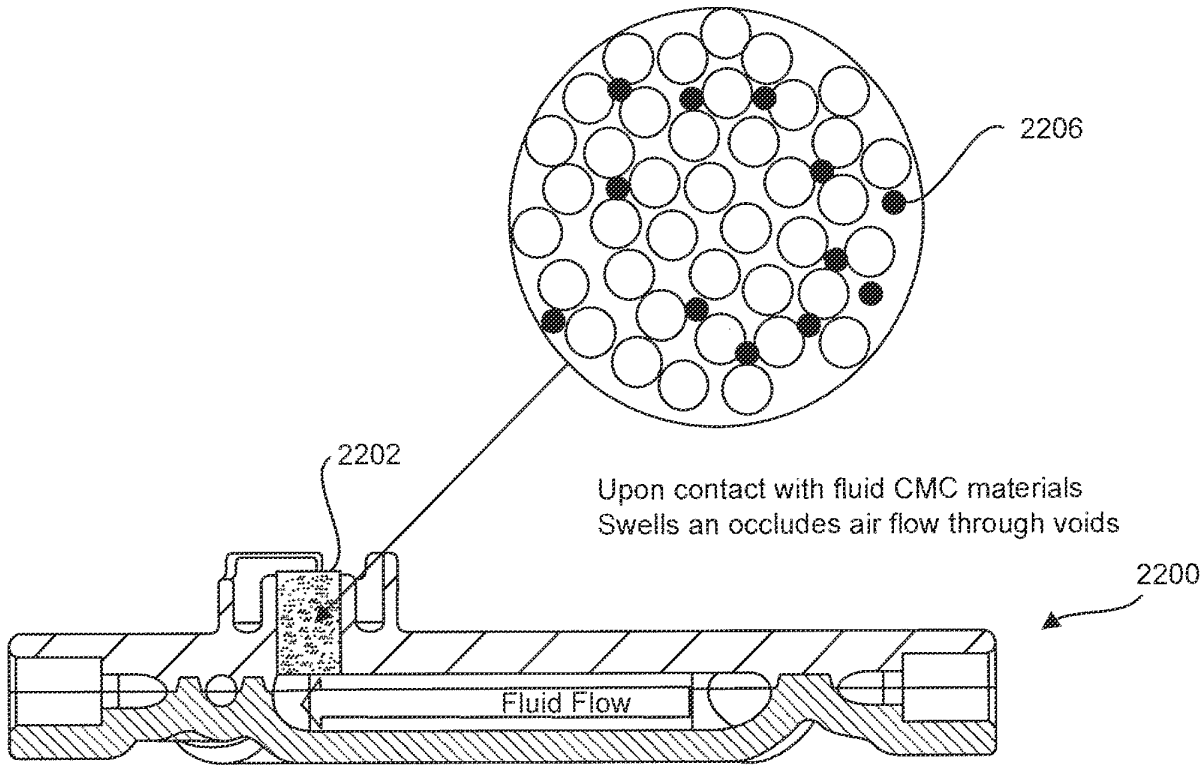

2206
2202
Upon contact with fluid CMC materials
Swells an occludes air flow through voids
2200
Fluid Flow

FIG. 22B

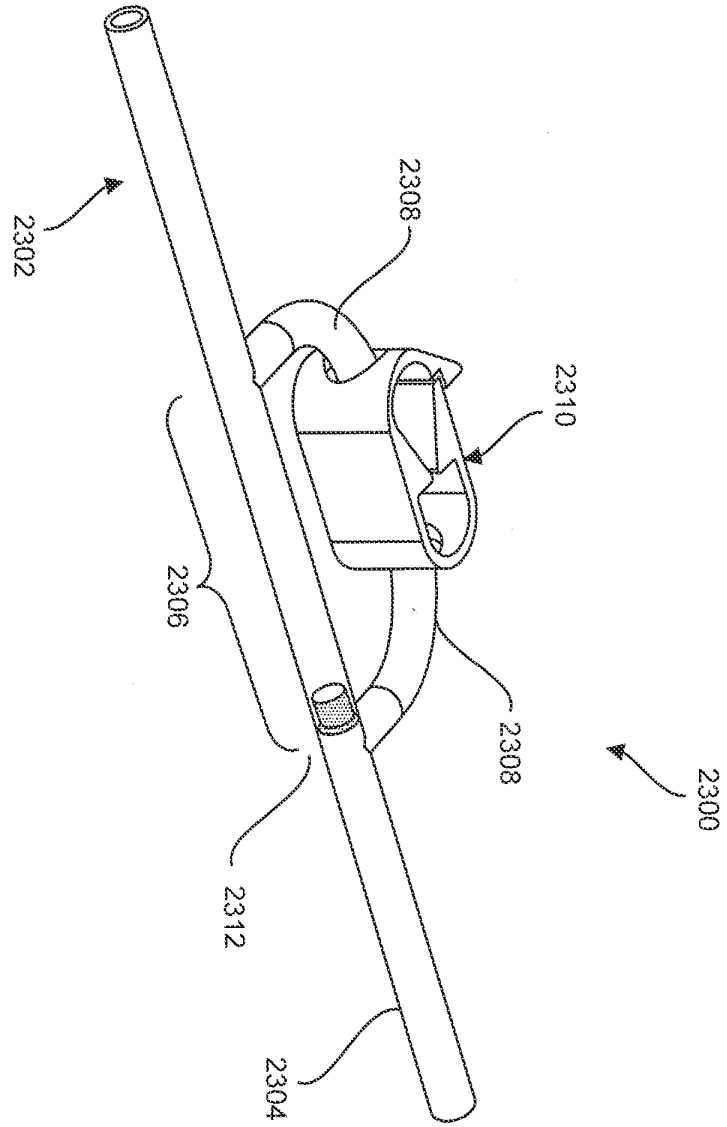


FIG. 23A

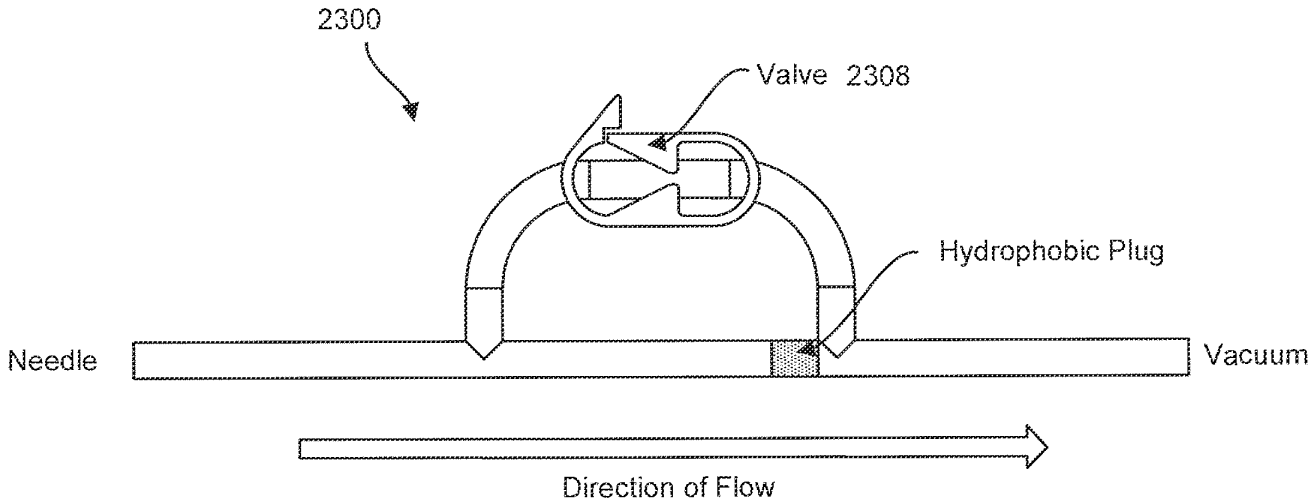

2300
Valve 2308
Hydrophobic Plug
Needle
Vacuum
Direction of Flow

FIG. 23B

Doc Code: PA..
Document Description: Power of Attorney

PTO/AIA/82A (07-13)
Approved for use through 03/31/2021. OMB 0651-0035
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
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TRANSMITTAL FOR POWER OF ATTORNEY TO ONE OR MORE REGISTERED PRACTITIONERS

NOTE: This form is to be submitted with the Power of Attorney by Applicant form (PTO/AIA/82B) to identify the application to which the Power of Attorney is directed, in accordance with 37 CFR 1.5, unless the application number and filing date are identified in the Power of Attorney by Applicant form. If neither form PTO/AIA/82A nor form PTO/AIA82B identifies the application to which the Power of Attorney is directed, the Power of Attorney will not be recognized in the application.

Application Number	New
Filing Date	February 24, 2023
First Named Inventor	Bobby E. ROGERS
Title	BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE AND METHOD
Art Unit	Not Yet Assigned
Examiner Name	Not Yet Assigned
Attorney Docket Number	069366-0574153_KUR2C04US

SIGNATURE of Applicant or Patent Practitioner

Signature	/Ben Hudson	Date (Optional)	02-24-2023
Name	Benjamin F. Hudson	Registration Number	71,474
Title (if Applicant is a juristic entity)	Appointed Practitioner		
Applicant Name (if Applicant is a juristic entity)			

NOTE: This form must be signed in accordance with 37 CFR 1.33. See 37 CFR 1.4(d) for signature requirements and certifications. If more than one applicant, use multiple forms.

☑ *Total of 1 forms are submitted.

This collection of information is required by 37 CFR 1.131, 1.32, and 1.33. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 3 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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Doc Code: PA.
Document Description: Power of Attorney

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POWER OF ATTORNEY BY APPLICANT

I hereby revoke all previous powers of attorney given in the application identified in either the attached transmittal letter or the boxes below.

Application Number	Filing Date

(Note: The boxes above may be left blank if information is provided on form PTO/AIA/82A.)

☑ I hereby appoint the Patent Practitioner(s) associated with the following Customer Number as my/our attorney(s) or agent(s), and to transact all business in the United States Patent and Trademark Office connected therewith for the application referenced in the attached transmittal letter (form PTO/AIA/82A) or identified above: 27500

OR

☐ I hereby appoint Practitioner(s) named in the attached list (form PTO/AIA/82C) as my/our attorney(s) or agent(s), and to transact all business in the United States Patent and Trademark Office connected therewith for the patent application referenced in the attached transmittal letter (form PTO/AIA/82A) or identified above. (Note: Complete form PTO/AIA/82C.)

Please recognize or change the correspondence address for the application identified in the attached transmittal letter or the boxes above to:

☑ The address associated with the above-mentioned Customer Number

OR

☐ The address associated with Customer Number:

OR

☐ Firm or Individual Name					
Address					
City		State		Zip	
Country					
Telephone		Email			

I am the Applicant (if the Applicant is a juristic entity, list the Applicant name in the box):

Kurin, Inc.

☐ Inventor or Joint Inventor (title not required below)

☐ Legal Representative of a Deceased or Legally Incapacitated Inventor (title not required below)

☑ Assignee or Person to Whom the Inventor is Under an Obligation to Assign (provide signer's title if applicant is a juristic entity)

☐ Person Who Otherwise Shows Sufficient Proprietary Interest (e.g., a petition under 37 CFR 1.46(b)(2) was granted in the application or is concurrently being filed with this document) (provide signer's title if applicant is a juristic entity)

SIGNATURE of Applicant for Patent

The undersigned (whose title is supplied below) is authorized to act on behalf of the applicant (e.g., where the applicant is a juristic entity).

Signature		Date (Optional)	
Name	Bobby E. Rogers		
Title	CEO		

NOTE: Signature - This form must be signed by the applicant in accordance with 37 CFR 1.33. See 37 CFR 1.4 for signature requirements and certifications. If more than one applicant, use multiple forms.

☐ Total of forms are submitted.

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DECLARATION (37 CFR 1.63) FOR UTILITY OR DESIGN APPLICATION USING AN APPLICATION DATA SHEET (37 CFR 1.76)

Title of Invention	BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE AND METHOD

As the below named inventor, I hereby declare that:

This declaration is directed to:

☐ The attached application, or

☒ United States application or PCT international application number 15/140,448 filed on April 27, 2016.

The above-identified application was made or authorized to be made by me.

I believe that I am the original inventor or an original joint inventor of a claimed invention in the application.

I hereby acknowledge that any willful false statement made in this declaration is punishable under 18 U.S.C. 1001 by fine or imprisonment of not more than five (5) years, or both.

WARNING:

Petitioner/applicant is cautioned to avoid submitting personal information in documents filed in a patent application that may contribute to identity theft. Personal information such as social security numbers, bank account numbers, or credit card numbers (other than a check or credit card authorization form PTO-2038 submitted for payment purposes) is never required by the USPTO to support a petition or an application. If this type of personal information is included in documents submitted to the USPTO, petitioners/applicants should consider redacting such personal information from the documents before submitting them to the USPTO. Petitioner/applicant is advised that the record of a patent application is available to the public after publication of the application (unless a non-publication request in compliance with 37 CFR 1.213(a) is made in the application) or issuance of a patent. Furthermore, the record from an abandoned application may also be available to the public if the application is referenced in a published application or an issued patent (see 37 CFR 1.14). Checks and credit card authorization forms PTO-2038 submitted for payment purposes are not retained in the application file and therefore are not publicly available.

LEGAL NAME OF INVENTOR

Inventor: Bobby E. Rogers Date (Optional): _____

Signature: Bobby E. Rogers

Note: An application data sheet (PTO/SB/14 or equivalent), including naming the entire inventive entity, must accompany this form or must have been previously filed. Use an additional PTO/AIA/01 form for each additional inventor.

This collection of information is required by 35 U.S.C. 115 and 37 CFR 1.63. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 1 minute to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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DECLARATION (37 CFR 1.63) FOR UTILITY OR DESIGN APPLICATION USING AN APPLICATION DATA SHEET (37 CFR 1.76)

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- ☐ The attached application, or
- ■ United States application or PCT international application number 15/140,448 filed on April 27, 2016.

The above-identified application was made or authorized to be made by me.

I believe that I am the original inventor or an original joint inventor of a claimed invention in the application.

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LEGAL NAME OF INVENTOR

Inventor: Gino Kang Date (Optional): 1/22/2018

Signature: _____

Note: An application data sheet (PTO/SB/14 or equivalent), including naming the entire inventive entity, must accompany this form or must have been previously filed. Use an additional PTO/AIA/01 form for each additional inventor.

This collection of information is required by 35 U.S.C. 115 and 37 CFR 1.63. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 1 minute to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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WARNING:

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LEGAL NAME OF INVENTOR

Inventor: John Detloff Date (Optional): 1-23-18

Signature: John C. Detloff

Note: An application data sheet (PTO/SB/14 or equivalent), including naming the entire inventive entity, must accompany this form or must have been previously filed. Use an additional PTO/AIA/01 form for each additional inventor.

This collection of information is required by 35 U.S.C. 115 and 37 CFR 1.63. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 1 minute to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

Electronic Patent Application Fee Transmittal

Application Number:	
Filing Date:	
Title of Invention:	BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE AND METHOD
First Named Inventor/Applicant Name:	Bobby E. ROGERS
Filer:	Benjamin F. Hudson/Sandra Edge
Attorney Docket Number:	069366-0574153_KUR2C04US

Filed as Small Entity

Filing Fees for Track I Prioritized Examination - Nonprovisional Application under 35 USC 111(a)

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
UTILITY FILING FEE (ELECTRONIC FILING)	4011	1	64	64
UTILITY SEARCH FEE	2111	1	280	280
UTILITY EXAMINATION FEE	2311	1	320	320
REQUEST FOR PRIORITIZED EXAMINATION	2817	1	1680	1680
Pages:				
Claims:				
Miscellaneous-Filing:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
PUBL. FEE- EARLY, VOLUNTARY, OR NORMAL	1504	1	0	0
PROCESSING FEE, EXCEPT PROV. APPLS.	2830	1	56	56
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				
Miscellaneous:				
		Total in USD ($)		**2400**

Electronic Acknowledgement Receipt	
EFS ID:	47585172
Application Number:	18113710
International Application Number:	
Confirmation Number:	2715
Title of Invention:	BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE AND METHOD
First Named Inventor/Applicant Name:	Bobby E. ROGERS
Customer Number:	27500
Filer:	Benjamin F. Hudson/Sandra Edge
Filer Authorized By:	Benjamin F. Hudson
Attorney Docket Number:	069366-0574153_KUR2C04US
Receipt Date:	24-FEB-2023
Filing Date:	
Time Stamp:	11:35:16
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	DA
Payment was successfully received in RAM	$2400
RAM confirmation Number	E20232NB35539919
Deposit Account	
Authorized User	
The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:	

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Track One Request	069366-0574153_KUR2C04US_TRACK1_REQUEST.pdf	114487 4f21a6647106241c789064b2bbb8c31f4e769e5a	no	2
Warnings:					
Information:					
2	Application Data Sheet	069366-0574153_ADS.pdf	1308501 756174fa8bf8c4dc0a05c7e57cf5fa419a3b1d5b	no	9
Warnings:					
Information:					
3		069366-0574153_KUR2C04US_Specification.pdf	189555 432cc8eb0db0a9fbef3ead67647971b16ab3f6d1	yes	36

Multipart Description/PDF files in .zip description

Document Description	Start	End
Specification	1	32
Claims	33	35
Abstract	36	36

Warnings:					
Information:					
4	Drawings-only black and white line drawings	069366-0574153_KUR2C04US_Drawings.pdf	2933047 99bd507eec06fff934d811e994235dc4d3918df0	no	50
Warnings:					
Information:					
5	Power of Attorney	069366-0574153_KUR2C04US_Power_of_Attorney.pdf	1133508 714e0c82e1fe36b45e6cb22b455a689acd63b1a9	no	2

Warnings:					
Information:					
6	Oath or Declaration filed	069366-0574153_KUR2C04US_Declarations.pdf	779382 adf2f9262e19932b55b8cc483fae531c11c332e6	no	3
Warnings:					
Information:					
7	Fee Worksheet (SB06)	fee-info.pdf	51227 17bc14efe69882e11c548de0c5a5031bbb876ff6	no	2
Warnings:					
Information:					
		Total Files Size (in bytes):	6509707		

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NUMBER	FILING or 371(c) DATE	GRP ART UNIT	FIL FEE REC'D	ATTY.DOCKET.NO	TOT CLAIMS	IND CLAIMS
18/113,710	02/24/2023		664	069366-0574153_KUR2C04US	16	1

CONFIRMATION NO. 2715

FILING RECEIPT

27500
PILLSBURY WINTHROP SHAW PITTMAN LLP (CV)
ATTENTION: DOCKETING DEPARTMENT
P.O BOX 10500
McLean, VA 22102

OC000000055406030

Date Mailed: 03/29/2023

Receipt is acknowledged of this non-provisional utility patent application. The application will be taken up for examination in due course. Applicant will be notified as to the results of the examination. Any correspondence concerning the application must include the following identification information: the U.S. APPLICATION NUMBER, FILING DATE, NAME OF FIRST INVENTOR, and TITLE OF INVENTION. Fees transmitted by check or draft are subject to collection.

Please verify the accuracy of the data presented on this receipt. If an error is noted on this Filing Receipt, please submit a written request for a corrected Filing Receipt, including a properly marked-up ADS showing the changes with strike-through for deletions and underlining for additions. If you received a "Notice to File Missing Parts" or other Notice requiring a response for this application, please submit any request for correction to this Filing Receipt with your reply to the Notice. When the USPTO processes the reply to the Notice, the USPTO will generate another Filing Receipt incorporating the requested corrections provided that the request is grantable.

Inventor(s)

Bobby E. ROGERS, Park City, UT;
Gino KANG, Irvine, CA;
John DETLOFF, San Diego, CA;

Applicant(s)

Kurin, Inc., San Diego, CA;

Assignment For Published Patent Application

Kurin, Inc., San Diego, CA

Power of Attorney: The patent practitioners associated with Customer Number 27500

Domestic Priority data as claimed by applicant

This application is a CON of 17/538,990 11/30/2021 *
which is a CON of 16/208,559 12/04/2018 PAT 11,185,266
which is a CON of 15/994,559 05/31/2018 PAT 10,143,412
which is a CON of 15/140,448 04/27/2016 PAT 10,010,282
which claims benefit of 62/318,194 04/04/2016
and claims benefit of 62/238,636 10/07/2015
and claims benefit of 62/196,797 07/24/2015

(*) Data provided by applicant is not consistent with PTO records.

Foreign Applications for which priority is claimed (You may be eligible to benefit from the **Patent Prosecution Highway** program at the USPTO. Please see http://www.uspto.gov for more information.) - None.

Foreign application information must be provided in an Application Data Sheet in order to constitute a claim to foreign priority. See 37 CFR 1.55 and 1.76.

Permission to Access Application via Priority Document Exchange: Yes

Permission to Access Search Results: Yes

Applicant may provide or rescind an authorization for access using Form PTO/SB/39 or Form PTO/SB/69 as appropriate.

If Required, Foreign Filing License Granted: 03/28/2023
The country code and number of your priority application, to be used for filing abroad under the Paris Convention, is **US 18/113,710**
Projected Publication Date: 07/06/2023
Non-Publication Request: No
Early Publication Request: No
**** SMALL ENTITY ****
Title

BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE AND METHOD

Preliminary Class

Statement under 37 CFR 1.55 or 1.78 for AIA (First Inventor to File) Transition Applications: No

PROTECTING YOUR INVENTION OUTSIDE THE UNITED STATES

Since the rights granted by a U.S. patent extend only throughout the territory of the United States and have no effect in a foreign country, an inventor who wishes patent protection in another country must apply for a patent in a specific country or in regional patent offices. Applicants may wish to consider the filing of an international application under the Patent Cooperation Treaty (PCT). An international (PCT) application generally has the same effect as a regular national patent application in each PCT-member country. The PCT process **simplifies** the filing of patent applications on the same invention in member countries, but **does not result** in a grant of "an international patent" and does not eliminate the need of applicants to file additional documents and fees in countries where patent protection is desired.

Almost every country has its own patent law, and a person desiring a patent in a particular country must make an application for patent in that country in accordance with its particular laws. Since the laws of many countries differ in various respects from the patent law of the United States, applicants are advised to seek guidance from specific foreign countries to ensure that patent rights are not lost prematurely.

Applicants also are advised that in the case of inventions made in the United States, the Director of the USPTO must issue a license before applicants can apply for a patent in a foreign country. The filing of a U.S. patent application serves as a request for a foreign filing license. The application's filing receipt contains further information and guidance as to the status of applicant's license for foreign filing.

Applicants may wish to consult the USPTO booklet, "General Information Concerning Patents" (specifically, the section entitled "Treaties and Foreign Patents") for more information on timeframes and deadlines for filing foreign

patent applications. The guide is available either by contacting the USPTO Contact Center at 800-786-9199, or it can be viewed on the USPTO website at http://www.uspto.gov/web/offices/pac/doc/general/index.html.

For information on preventing theft of your intellectual property (patents, trademarks and copyrights), you may wish to consult the U.S. Government website, http://www.stopfakes.gov. Part of a Department of Commerce initiative, this website includes self-help "toolkits" giving innovators guidance on how to protect intellectual property in specific countries such as China, Korea and Mexico. For questions regarding patent enforcement issues, applicants may call the U.S. Government hotline at 1-866-999-HALT (1-866-999-4258).

LICENSE FOR FOREIGN FILING UNDER

Title 35, United States Code, Section 184

Title 37, Code of Federal Regulations, 5.11 & 5.15

GRANTED

The applicant has been granted a license under 35 U.S.C. 184, if the phrase "IF REQUIRED, FOREIGN FILING LICENSE GRANTED" followed by a date appears on this form. Such licenses are issued in all applications where the conditions for issuance of a license have been met, regardless of whether or not a license may be required as set forth in 37 CFR 5.15. The scope and limitations of this license are set forth in 37 CFR 5.15(a) unless an earlier license has been issued under 37 CFR 5.15(b). The license is subject to revocation upon written notification. The date indicated is the effective date of the license, unless an earlier license of similar scope has been granted under 37 CFR 5.13 or 5.14.

This license is to be retained by the licensee and may be used at any time on or after the effective date thereof unless it is revoked. This license is automatically transferred to any related applications(s) filed under 37 CFR 1.53(d). This license is not retroactive.

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NOT GRANTED

No license under 35 U.S.C. 184 has been granted at this time, if the phrase "IF REQUIRED, FOREIGN FILING LICENSE GRANTED" DOES NOT appear on this form. Applicant may still petition for a license under 37 CFR 5.12, if a license is desired before the expiration of 6 months from the filing date of the application. If 6 months has lapsed from the filing date of this application and the licensee has not received any indication of a secrecy order under 35 U.S.C. 181, the licensee may foreign file the application pursuant to 37 CFR 5.15(b).

SelectUSA

The United States represents the largest, most dynamic marketplace in the world and is an unparalleled location for business investment, innovation, and commercialization of new technologies. The U.S. offers tremendous resources and advantages for those who invest and manufacture goods here. Through SelectUSA, our nation works to promote and facilitate business investment. SelectUSA provides information assistance to the international investor community; serves as an ombudsman for existing and potential investors; advocates on behalf of U.S. cities, states, and regions competing for global investment; and counsels U.S. economic development organizations on investment attraction best practices. To learn more about why the United States is the best country in the world to develop technology, manufacture products, deliver services, and grow your business, visit http://www.SelectUSA.gov or call +1-202-482-6800.

PATENT APPLICATION FEE DETERMINATION RECORD

Substitute for Form PTO-875

Application or Docket Number: 18/113,710

APPLICATION AS FILED - PART I

FOR	(Column 1) NUMBER FILED	(Column 2) NUMBER EXTRA	SMALL ENTITY RATE($)	SMALL ENTITY FEE($)	OR	OTHER THAN SMALL ENTITY RATE($)	OTHER THAN SMALL ENTITY FEE($)
BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A	N/A	64		N/A	
SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A	N/A	280		N/A	
EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A	320		N/A	
TOTAL CLAIMS (37 CFR 1.16(i))	16 minus 20 =	* 0	x =	0	OR		
INDEPENDENT CLAIMS (37 CFR 1.16(h))	1 minus 3 =	*	x =	0			
APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is $310 ($155 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).			0			
MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))				0			
* If the difference in column 1 is less than zero, enter "0" in column 2.			TOTAL	664		TOTAL	

APPLICATION AS AMENDED - PART II

		(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	SMALL ENTITY RATE($)	SMALL ENTITY ADDITIONAL FEE($)	OR	OTHER THAN SMALL ENTITY RATE($)	OTHER THAN SMALL ENTITY ADDITIONAL FEE($)
AMENDMENT A	Total (37 CFR 1.16(i))	*	Minus	**	=	x =		OR	x =	
	Independent (37 CFR 1.16(h))	*	Minus	***	=	x =		OR	x =	
	Application Size Fee (37 CFR 1.16(s))									
	FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							OR		
						TOTAL ADD'L FEE		OR	TOTAL ADD'L FEE	

		(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	RATE($)	ADDITIONAL FEE($)	OR	RATE($)	ADDITIONAL FEE($)
AMENDMENT B	Total (37 CFR 1.16(i))	*	Minus	**	=	x =		OR	x =	
	Independent (37 CFR 1.16(h))	*	Minus	***	=	x =		OR	x =	
	Application Size Fee (37 CFR 1.16(s))									
	FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							OR		
						TOTAL ADD'L FEE		OR	TOTAL ADD'L FEE	

* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.
** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".
*** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3".
The "Highest Number Previously Paid For" (Total or Independent) is the highest found in the appropriate box in column 1.

To: Docket_IP@pillsburylaw.com,,
From: PAIR_eOfficeAction@uspto.gov
Cc: PAIR_eOfficeAction@uspto.gov
Subject: Private PAIR Correspondence Notification for Customer Number 27500

Mar 29, 2023 03:22:05 AM

Dear PAIR Customer:

PILLSBURY WINTHROP SHAW PITTMAN LLP (CV)
ATTENTION: DOCKETING DEPARTMENT
P.O BOX 10500
McLean, VA 22102
UNITED STATES

The following USPTO patent application(s) associated with your Customer Number, 27500 , have new outgoing correspondence. This correspondence is now available for viewing in Private PAIR.

The official date of notification of the outgoing correspondence will be indicated on the form PTOL-90 accompanying the correspondence.

Disclaimer:
The list of documents shown below is provided as a courtesy and is not part of the official file wrapper. The content of the images shown in PAIR is the official record.

Application	Document	Mailroom Date	Attorney Docket No.
18113710	APP.FILE.REC	03/29/2023	069366-0574153_KUR2C04US

To view your correspondence online or update your email addresses, please visit us anytime at https://sportal.uspto.gov/secure/myportal/privatepair.

If you have any questions, please email the Electronic Business Center (EBC) at EBC@uspto.gov with 'e-Office Action' on the subject line or call 1-866-217-9197 during the following hours:

Monday - Friday 6:00 a.m. to 12:00 a.m.

Thank you for prompt attention to this notice,

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PATENT APPLICATION INFORMATION RETRIEVAL SYSTEM

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CORRECTED Application Data Sheet 37 CFR 1.76	Attorney Docket Number	069366-0574153_KUR2C04US
	Application Number	16/113,710
Title of Invention	BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE AND METHOD	

The application data sheet is part of the provisional or nonprovisional application for which it is being submitted. The following form contains the bibliographic data arranged in a format specified by the United States Patent and Trademark Office as outlined in 37 CFR 1.76.
This document may be completed electronically and submitted to the Office in electronic format using the Electronic Filing System (EFS) or the document may be printed and included in a paper filed application.

Secrecy Order 37 CFR 5.2:

☐ Portions or all of the application associated with this Application Data Sheet may fall under a Secrecy Order pursuant to 37 CFR 5.2 (Paper filers only. Applications that fall under Secrecy Order may not be filed electronically.)

Inventor Information:

Inventor 1 Remove

Legal Name

Prefix	Given Name	Middle Name	Family Name	Suffix
	Bobby	E.	ROGERS	

Residence Information (Select One) ● US Residency ○ Non US Residency ○ Active US Military Service

City	Park City	State/Province	UT	Country of Residence	US

Mailing Address of Inventor:

Address 1	10755 Scripps Poway, Parkway No. 257		
Address 2			
City	San Diego	State/Province	CA
Postal Code	92131	Country	US

Inventor 2 Remove

Legal Name

Prefix	Given Name	Middle Name	Family Name	Suffix
	Gino		KANG	

Residence Information (Select One) ◉ US Residency ○ Non US Residency ○ Active US Military Service

City	Irvine	State/Province	CA	Country of Residence	US

Mailing Address of Inventor:

Address 1	10755 Scripps Poway, Parkway No. 257		
Address 2			
City	San Diego	State/Province	CA
Postal Code	92131	Country	US

Inventor 3 Remove

Legal Name

Prefix	Given Name	Middle Name	Family Name	Suffix
	John		DETLOFF	

Residence Information (Select One) ◉ US Residency ○ Non US Residency ○ Active US Military Service

PTO/AIA/14 (02-18)
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Application Data Sheet 37 CFR 1.76	Attorney Docket Number	069366-0574153_KUR2C04US
	Application Number	16/113,710
Title of Invention	BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE AND METHOD	

City	San Diego	State/Province	CA	Country of Residence	US

Mailing Address of Inventor:

Address 1	10755 Scripps Poway, Parkway No. 257		
Address 2	c/o Kurin, Inc.		
City	San Diego	**State/Province**	CA
Postal Code	92131	**Country**	US

All Inventors Must Be Listed - Additional Inventor Information blocks may be generated within this form by selecting the **Add** button. Add

Correspondence Information:

Enter either Customer Number or complete the Correspondence Information section below. For further information see 37 CFR 1.33(a).

☐ **An Address is being provided for the correspondence Information of this application.**

Customer Number	27500		
Email Address	docket_ip@pillsburylaw.com	Add Email	Remove Email

Application Information:

Title of the Invention	BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE AND METHOD		
Attorney Docket Number	069366-0574153_KUR2C04US	**Small Entity Status Claimed**	☒
Application Type	Nonprovisional		
Subject Matter	Utility		
Total Number of Drawing Sheets (if any)	50	**Suggested Figure for Publication (if any)**	

Filing By Reference:

Only complete this section when filing an application by reference under 35 U.S.C. 111(c) and 37 CFR 1.57(a). Do not complete this section if application papers including a specification and any drawings are being filed. Any domestic benefit or foreign priority information must be provided in the appropriate section(s) below (i.e., "Domestic Benefit/National Stage Information" and "Foreign Priority Information").

For the purposes of a filing date under 37 CFR 1.53(b), the description and any drawings of the present application are replaced by this reference to the previously filed application, subject to conditions and requirements of 37 CFR 1.57(a).

Application number of the previously filed application	Filing date (YYYY-MM-DD)	Intellectual Property Authority or Country

Publication Information:

☐ Request Early Publication (Fee required at time of Request 37 CFR 1.219)

☐ **Request Not to Publish.** I hereby request that the attached application not be published under 35 U.S.C. 122(b) and certify that the invention disclosed in the attached application **has not and will not** be the subject of an application filed in another country, or under a multilateral international agreement, that requires publication at eighteen months after filing.

PTO/AIA/14 (02-18)
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Application Data Sheet 37 CFR 1.76	Attorney Docket Number	069366-0574153_KUR2C04US
	Application Number	18/113,710
Title of Invention	BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE AND METHOD	

Representative Information:

Representative information should be provided for all practitioners having a power of attorney in the application. Providing this information in the Application Data Sheet does not constitute a power of attorney in the application (see 37 CFR 1.32).
Either enter Customer Number or complete the Representative Name section below. If both sections are completed the customer Number will be used for the Representative Information during processing.

Please Select One:	● Customer Number	US Patent Practitioner	○ Limited Recognition (37 CFR 11.9)
Customer Number	27500		

Domestic Benefit/National Stage Information:

This section allows for the applicant to either claim benefit under 35 U.S.C. 119(e), 120, 121, 365(c), or 386(c) or indicate National Stage entry from a PCT application. Providing benefit claim information in the Application Data Sheet constitutes the specific reference required by 35 U.S.C. 119(e) or 120, and 37 CFR 1.78.
When referring to the current application, please leave the "Application Number" field blank.

Prior Application Status	Pending		Remove
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)
	Continuation of	17538990	~~2021-11-11~~ 2021-11-30

Prior Application Status	Patented				Remove
Application Number	Continuity Type	Prior Application Number	Filing Date (YYYY-MM-DD)	Patent Number	Issue Date (YYYY-MM-DD)
17538990	Continuation of	16208559	2018-12-04	11185266	2021-11-30

Prior Application Status	Patented				Remove
Application Number	Continuity Type	Prior Application Number	Filing Date (YYYY-MM-DD)	Patent Number	Issue Date (YYYY-MM-DD)
16208559	Continuation of	15994559	2018-05-31	10143412	2018-12-04

Prior Application Status	Patented				Remove
Application Number	Continuity Type	Prior Application Number	Filing Date (YYYY-MM-DD)	Patent Number	Issue Date (YYYY-MM-DD)
15994559	Continuation of	15140448	2016-04-27	10010282	2018-07-03

Prior Application Status	Expired		Remove
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)
15140448	Claims benefit of provisional	62318194	2016-04-04

Application Data Sheet 37 CFR 1.76	Attorney Docket Number	069366-0574153_KUR2C04US
	Application Number	16/113,710
Title of Invention	BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE AND METHOD	

Prior Application Status	Expired		Remove
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)
15140448	Claims benefit of provisional	62238636	2015-10-07
Prior Application Status	Expired		Remove
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)
15140448	Claims benefit of provisional	62196797	2015-07-24
Additional Domestic Benefit/National Stage Data may be generated within this form by selecting the **Add** button.			Add

Foreign Priority Information:

This section allows for the applicant to claim priority to a foreign application. Providing this information in the application data sheet constitutes the claim for priority as required by 35 U.S.C. 119(b) and 37 CFR 1.55. When priority is claimed to a foreign application that is eligible for retrieval under the priority document exchange program (PDX)[i] the information will be used by the Office to automatically attempt retrieval pursuant to 37 CFR 1.55(i)(1) and (2). Under the PDX program, applicant bears the ultimate responsibility for ensuring that a copy of the foreign application is received by the Office from the participating foreign intellectual property office, or a certified copy of the foreign priority application is filed, within the time period specified in 37 CFR 1.55(g)(1).

Remove

Application Number	Country[i]	Filing Date (YYYY-MM-DD)	Access Code[i] (if applicable)

Additional Foreign Priority Data may be generated within this form by selecting the **Add** button. Add

Statement under 37 CFR 1.55 or 1.78 for AIA (First Inventor to File) Transition Applications

☐ This application (1) claims priority to or the benefit of an application filed before March 16, 2013 and (2) also contains, or contained at any time, a claim to a claimed invention that has an effective filing date on or after March 16, 2013.
NOTE: By providing this statement under 37 CFR 1.55 or 1.78, this application, with a filing date on or after March 16, 2013, will be examined under the first inventor to file provisions of the AIA.

PTO/AIA/14 (02-18)
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Application Data Sheet 37 CFR 1.76	Attorney Docket Number	069366-0574153_KUR2C04US
	Application Number	18/113,710
Title of Invention	BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE AND METHOD	

Authorization or Opt-Out of Authorization to Permit Access:

When this Application Data Sheet is properly signed and filed with the application, applicant has provided written authority to permit a participating foreign intellectual property (IP) office access to the instant application-as-filed (see paragraph A in subsection 1 below) and the European Patent Office (EPO) access to any search results from the instant application (see paragraph B in subsection 1 below).

Should applicant choose not to provide an authorization identified in subsection 1 below, applicant **must opt-out** of the authorization by checking the corresponding box A or B or both in subsection 2 below.

NOTE: This section of the Application Data Sheet is **ONLY** reviewed and processed with the **INITIAL** filing of an application. After the initial filing of an application, an Application Data Sheet cannot be used to provide or rescind authorization for access by a foreign IP office(s). Instead, Form PTO/SB/39 or PTO/SB/69 must be used as appropriate.

1. Authorization to Permit Access by a Foreign Intellectual Property Office(s)

A. Priority Document Exchange (PDX) - Unless box A in subsection 2 (opt-out of authorization) is checked, the undersigned hereby **grants the USPTO authority** to provide the European Patent Office (EPO), the Japan Patent Office (JPO), the Korean Intellectual Property Office (KIPO), the State Intellectual Property Office of the People's Republic of China (SIPO), the World Intellectual Property Organization (WIPO), and any other foreign intellectual property office participating with the USPTO in a bilateral or multilateral priority document exchange agreement in which a foreign application claiming priority to the instant patent application is filed, access to: (1) the instant patent application-as-filed and its related bibliographic data, (2) any foreign or domestic application to which priority or benefit is claimed by the instant application and its related bibliographic data, and (3) the date of filing of this Authorization. See 37 CFR 1.14(h)(1).

B. Search Results from U.S. Application to EPO - Unless box B in subsection 2 (opt-out of authorization) is checked, the undersigned hereby **grants the USPTO authority** to provide the EPO access to the bibliographic data and search results from the instant patent application when a European patent application claiming priority to the instant patent application is filed. See 37 CFR 1.14(h)(2).

The applicant is reminded that the EPO's Rule 141(1) EPC (European Patent Convention) requires applicants to submit a copy of search results from the instant application without delay in a European patent application that claims priority to the instant application.

2. Opt-Out of Authorizations to Permit Access by a Foreign Intellectual Property Office(s)

☐ A. Applicant **DOES NOT** authorize the USPTO to permit a participating foreign IP office access to the instant application-as-filed. If this box is checked, the USPTO will not be providing a participating foreign IP office with any documents and information identified in subsection 1A above.

☐ B. Applicant **DOES NOT** authorize the USPTO to transmit to the EPO any search results from the instant patent application. If this box is checked, the USPTO will not be providing the EPO with search results from the instant application.

NOTE: Once the application has published or is otherwise publicly available, the USPTO may provide access to the application in accordance with 37 CFR 1.14.

PTO/AIA/14 (02-18)
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Application Data Sheet 37 CFR 1.76	Attorney Docket Number	069366-0574153_KUR2C04US
	Application Number	16/113,710
Title of Invention	BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE AND METHOD	

Applicant Information:

Providing assignment information in this section does not substitute for compliance with any requirement of part 3 of Title 37 of CFR to have an assignment recorded by the Office.

Applicant 1 — Remove

If the applicant is the inventor (or the remaining joint inventor or inventors under 37 CFR 1.45), this section should not be completed. The information to be provided in this section is the name and address of the legal representative who is the applicant under 37 CFR 1.43; or the name and address of the assignee, person to whom the inventor is under an obligation to assign the invention, or person who otherwise shows sufficient proprietary interest in the matter who is the applicant under 37 CFR 1.46. If the applicant is an applicant under 37 CFR 1.46 (assignee, person to whom the inventor is obligated to assign, or person who otherwise shows sufficient proprietary interest) together with one or more joint inventors, then the joint inventor or inventors who are also the applicant should be identified in this section.

Clear

● Assignee	Legal Representative under 35 U.S.C. 117	Joint Inventor
Person to whom the inventor is obligated to assign.	Person who shows sufficient proprietary interest	

If applicant is the legal representative, indicate the authority to file the patent application, the inventor is:

Name of the Deceased or Legally Incapacitated Inventor:

If the Applicant is an Organization check here. ☒

Organization Name	Kurin, Inc.		
Mailing Address Information For Applicant:			
Address 1	10755 Scripps Poway Parkway, No. 257		
Address 2			
City	San Diego	**State/Province**	CA
Country	US	Postal Code	92131
Phone Number		Fax Number	
Email Address			

Additional Applicant Data may be generated within this form by selecting the Add button. Add

Assignee Information including Non-Applicant Assignee Information:

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Application Data Sheet 37 CFR 1.76	Attorney Docket Number	069366-0574153_KUR2C04US
	Application Number	18/113,710
Title of Invention	BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE AND METHOD	

Assignee 1

Complete this section if assignee information, including non-applicant assignee information, is desired to be included on the patent application publication. An assignee-applicant identified in the "Applicant Information" section will appear on the patent application publication as an applicant. For an assignee-applicant, complete this section only if identification as an assignee is also desired on the patent application publication.

Remove

If the Assignee or Non-Applicant Assignee is an Organization check here. ☒

Organization Name	Kurin, Inc.

Mailing Address Information For Assignee including Non-Applicant Assignee:

Address 1	10755 Scripps Poway Parkway, No. 257		
Address 2			
City	San Diego	**State/Province**	CA
Country i	US	Postal Code	92131
Phone Number		Fax Number	
Email Address			

Additional Assignee or Non-Applicant Assignee Data may be generated within this form by selecting the Add button. Add

Signature:

Remove

NOTE: This Application Data Sheet must be signed in accordance with 37 CFR 1.33(b). **However, if this Application Data Sheet is submitted with the INITIAL filing of the application and either box A or B is not checked in subsection 2 of the "Authorization or Opt-Out of Authorization to Permit Access" section, then this form must also be signed in accordance with 37 CFR 1.14(c).**

This Application Data Sheet **must** be signed by a patent practitioner if one or more of the applicants is a **juristic entity** (e.g., corporation or association). If the applicant is two or more joint inventors, this form must be signed by a patent practitioner, **all** joint inventors who are the applicant, or one or more joint inventor-applicants who have been given power of attorney (e.g., see USPTO Form PTO/AIA/81) on behalf of **all** joint inventor-applicants.

See 37 CFR 1.4(d) for the manner of making signatures and certifications.

Signature	/Ben Hudson/			Date (YYYY-MM-DD)	2023-04-13
First Name	Benjamin F.	Last Name	Hudson	Registration Number	71,474

Additional Signature may be generated within this form by selecting the Add button. Add

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Application Data Sheet 37 CFR 1.76	Attorney Docket Number	069366-0574153_KUR2C04US
	Application Number	18/113,710
Title of Invention	BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE AND METHOD	

This collection of information is required by 37 CFR 1.76. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 23 minutes to complete, including gathering, preparing, and submitting the completed application data sheet form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1 The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether the Freedom of Information Act requires disclosure of these records.

2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.

3 A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.

4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).

5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent CooperationTreaty.

6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).

7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.

8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspections or an issued patent.

9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

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ELECTRONIC ACKNOWLEDGEMENT RECEIPT

APPLICATION #	RECEIPT DATE / TIME	ATTORNEY DOCKET #
18/113,710	**04/13/2023 06:38:20 PM ET**	**069366-0574153_KUR2C04US**

Title of Invention

BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE AND METHOD

Application Information

APPLICATION TYPE	Utility - Nonprovisional Application under 35 USC 111(a)	PATENT #	-
CONFIRMATION #	2715	FILED BY	Trent Tercenio
PATENT CENTER #	61919473	FILING DATE	02/24/2023
CUSTOMER #	27500	FIRST NAMED INVENTOR	Bobby E. ROGERS
CORRESPONDENCE ADDRESS	-	AUTHORIZED BY	Benjamin Hudson

Documents

TOTAL DOCUMENTS: 1

DOCUMENT	PAGES	DESCRIPTION	SIZE (KB)
069366-0574153_KUR2C04US_Corrected_ADS.pdf	9	Application Data Sheet	2883 KB

Warning: This is not a USPTO supplied ADS fillable form. Data in the form cannot be automatically loaded to other USPTO systems.

Digest

DOCUMENT	MESSAGE DIGEST(SHA-512)
069366-	321259FC37AD58E00D2A03FE7CE1A36D2F7D0B0414097C329

0574153_KUR2C04US_Corrected_ADS.pdf	88F7DE099BA81CCE9364DE4285FC4E194265C46BDEA61BAC3862E81DD31508C32B027771B6470B5

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
18/113,710	02/24/2023	Bobby E. ROGERS	069366-0574153_KUR2C04US	2715

27500 7590 04/26/2023

PILLSBURY WINTHROP SHAW PITTMAN LLP (CV)
ATTENTION: DOCKETING DEPARTMENT
P.O BOX 10500
McLean, VA 22102

EXAMINER	
CENTRAL, DOCKET	

ART UNIT	PAPER NUMBER
3791	

NOTIFICATION DATE	DELIVERY MODE
04/26/2023	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

Docket_IP@pillsburylaw.com

Decision Granting Request for Prioritized Examination (Track I)	**Application No.** 18/113,710	**Applicant(s)** ROGERS et al.	
	Examiner FIKIRTE A GEREMEW	**Art Unit** OMBL	**AIA (FITF) Status** Yes

1. THE REQUEST FILED 24 February 2023 IS **GRANTED** .

The above-identified application has met the requirements for prioritized examination

A. ☑ for an original nonprovisional application (Track I).
B. ☐ for an application undergoing continued examination (RCE).

2. **The above-identified application will undergo prioritized examination**. The application will be accorded special status throughout its entire course of prosecution until one of the following occurs:

A. filing a **petition for extension of time** to extend the time period for filing a reply;

B. filing an **amendment to amend the application to contain more than four independent claims, more than thirty total claims** , or a multiple dependent claim;

C. filing a **request for continued examination** ;

D. filing a notice of appeal;

E. filing a request for suspension of action;

F. mailing of a notice of allowance;

G. mailing of a final Office action;

H. completion of examination as defined in 37 CFR 41.102; or

I. abandonment of the application.

Telephone inquiries with regard to this decision should be directed to FIKIRTE GEREMEW at (703) 756-1930. In his/her absence, calls may be directed to Petition Help Desk at (571) 272-3282.

/FIKIRTE A GEREMEW/ PROGRAM SUPPORT ASSISTANT, OMBL	

TO: Docket_IP@pillsburylaw.com
FROM: noreply@uspto.gov
CC: PatentCenter_eOfficeAction@uspto.gov
SUBJECT: USPTO: Patent Electronic System - Correspondence Notification for Customer Number 27500

Thu Apr 27 05:21:40 EDT 2023

Dear Patent Center Customer:

Correspondence Address:

PILLSBURY WINTHROP SHAW PITTMAN LLP (CV)
ATTENTION: DOCKETING DEPARTMENT
P.O BOX 10500
McLean,VIRGINIA,22102
UNITED STATES

This is a courtesy notification regarding the following USPTO patent application(s) associated with your Customer Number, 27500, that have new outgoing correspondence. This correspondence is now available for viewing in Patent Center.

The official date of notification of the outgoing correspondence will be indicated on the form (e.g., PTOL-90) accompanying the correspondence.

Disclaimer:
The list of documents shown below are provided as a courtesy and is not part of the official file wrapper. The content of the images shown in the Image File Wrapper is the official record.

Application	Document	Mailroom Date	Attorney Docket No.
18113710	TRACK1.GRANT	04/26/2023	069366-0574153_KUR2C04US

To view your correspondence online, please sign in to Patent Center and then select Workbench/View correspondence. To update your email address(es), select Manage/Manage customer numbers.

If you have any questions, please contact the Patent Electronic Business Center (EBC) at ebc@uspto.gov or 866-217-9197 Monday – Friday, 6 a.m. to midnight ET.

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Sincerely,

The Patent Center Team

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
18/113,710	02/24/2023	Bobby E. ROGERS	069366-0574153_KUR2C04US	2715

27500 7590 05/12/2023

PILLSBURY WINTHROP SHAW PITTMAN LLP (CV)
ATTENTION: DOCKETING DEPARTMENT
P.O BOX 10500
McLean, VA 22102

EXAMINER	
ABOUELELA, MAY A	

ART UNIT	PAPER NUMBER
3791	

NOTIFICATION DATE	DELIVERY MODE
05/12/2023	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

Docket_IP@pillsburylaw.com

Office Action Summary	Application No. 18/113,710	Applicant(s) ROGERS et al.	
	Examiner MAY A ABOUELELA	Art Unit 3791	AIA (FITF) Status Yes

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTHS FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☑ Responsive to communication(s) filed on 02/24/2023.

☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on _____.

2a)☐ This action is **FINAL.** 2b) ☑ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims*

5) ☑ Claim(s) 1-16 is/are pending in the application.

5a) Of the above claim(s) _____ is/are withdrawn from consideration.

6) ☐ Claim(s) _____ is/are allowed.

7) ☑ Claim(s) 1-16 is/are rejected.

8) ☐ Claim(s) _____ is/are objected to.

9) ☐ Claim(s) _____ are subject to restriction and/or election requirement

* If any claims have been determined allowable, you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see http://www.uspto.gov/patents/init_events/pph/index.jsp or send an inquiry to **PPHfeedback@uspto.gov.**

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☑ The drawing(s) filed on 02/24/2023 is/are: a)☑ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

Certified copies:

a)☐ All b)☐ Some** c)☐ None of the:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

** See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☑ Notice of References Cited (PTO-892)

2) ☐ Information Disclosure Statement(s) (PTO/SB/08a and/or PTO/SB/08b) Paper No(s)/Mail Date _____.

3) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date _____.

4) ☐ Other: _____.

Notice of Pre-AIA or AIA Status

1. The present application, filed on or after March 16, 2013, is being examined under the first inventor to file provisions of the AIA.

Claim Interpretation

2. The following is a quotation of 35 U.S.C. 112(f):

> (f) Element in Claim for a Combination. – An element in a claim for a combination may be expressed as a means or step for performing a specified function without the recital of structure, material, or acts in support thereof, and such claim shall be construed to cover the corresponding structure, material, or acts described in the specification and equivalents thereof.

The following is a quotation of pre-AIA 35 U.S.C. 112, sixth paragraph:

> An element in a claim for a combination may be expressed as a means or step for performing a specified function without the recital of structure, material, or acts in support thereof, and such claim shall be construed to cover the corresponding structure, material, or acts described in the specification and equivalents thereof.

The claims in this application are given their broadest reasonable interpretation using the plain meaning of the claim language in light of the specification as it would be understood by one of ordinary skill in the art. The broadest reasonable interpretation of a claim element (also commonly referred to as a claim limitation) is limited by the description in the specification when 35 U.S.C. 112(f) or pre-AIA 35 U.S.C. 112, sixth paragraph, is invoked.

As explained in MPEP § 2181, subsection I, claim limitations that meet the following three-prong test will be interpreted under 35 U.S.C. 112(f) or pre-AIA 35 U.S.C. 112, sixth paragraph:

(A) the claim limitation uses the term “means” or “step” or a term used as a substitute for “means” that is a generic placeholder (also called a nonce term or a non-

structural term having no specific structural meaning) for performing the claimed function;

(B) the term "means" or "step" or the generic placeholder is modified by functional language, typically, but not always linked by the transition word "for" (e.g., "means for") or another linking word or phrase, such as "configured to" or "so that"; and

(C) the term "means" or "step" or the generic placeholder is not modified by sufficient structure, material, or acts for performing the claimed function.

Use of the word "means" (or "step") in a claim with functional language creates a rebuttable presumption that the claim limitation is to be treated in accordance with 35 U.S.C. 112(f) or pre-AIA 35 U.S.C. 112, sixth paragraph. The presumption that the claim limitation is interpreted under 35 U.S.C. 112(f) or pre-AIA 35 U.S.C. 112, sixth paragraph, is rebutted when the claim limitation recites sufficient structure, material, or acts to entirely perform the recited function.

Absence of the word "means" (or "step") in a claim creates a rebuttable presumption that the claim limitation is not to be treated in accordance with 35 U.S.C. 112(f) or pre-AIA 35 U.S.C. 112, sixth paragraph. The presumption that the claim limitation is not interpreted under 35 U.S.C. 112(f) or pre-AIA 35 U.S.C. 112, sixth paragraph, is rebutted when the claim limitation recites function without reciting sufficient structure, material or acts to entirely perform the recited function.

Claim limitations in this application that use the word "means" (or "step") are being interpreted under 35 U.S.C. 112(f) or pre-AIA 35 U.S.C. 112, sixth paragraph, except as otherwise indicated in an Office action. Conversely, claim limitations in this

application that do not use the word “means” (or “step”) are not being interpreted under 35 U.S.C. 112(f) or pre-AIA 35 U.S.C. 112, sixth paragraph, except as otherwise indicated in an Office action.

This application includes one or more claim limitations that do not use the word “means,” but are nonetheless being interpreted under 35 U.S.C. 112(f) or pre-AIA 35 U.S.C. 112, sixth paragraph, because the claim limitation(s) uses a generic placeholder that is coupled with functional language without reciting sufficient structure to perform the recited function and the generic placeholder is not preceded by a structural modifier. Such claim limitation(s) is/are:

Limitation “junction” in claims11 and 12, the claims does not recite enough structure that corresponds to the claimed “junction” to perform the claimed function of direct an initial blood flow into the chamber, the specification disclose (Diverter junction 1607 may be a substantially Y-shaped, T-shaped, or U-shaped, par.00109) that can be interpreted as the structure that corresponds to the claimed “junction”.

Because this/these claim limitation(s) is/are being interpreted under 35 U.S.C. 112(f) or pre-AIA 35 U.S.C. 112, sixth paragraph, it/they is/are being interpreted to cover the corresponding structure described in the specification as performing the claimed function, and equivalents thereof.

If applicant does not intend to have this/these limitation(s) interpreted under 35 U.S.C. 112(f) or pre-AIA 35 U.S.C. 112, sixth paragraph, applicant may: (1) amend the claim limitation(s) to avoid it/them being interpreted under 35 U.S.C. 112(f) or pre-AIA 35 U.S.C. 112, sixth paragraph (e.g., by reciting sufficient structure to perform the claimed function); or (2) present a sufficient showing that the claim limitation(s) recite(s)

sufficient structure to perform the claimed function so as to avoid it/them being interpreted under 35 U.S.C. 112(f) or pre-AIA 35 U.S.C. 112, sixth paragraph.

Claim Rejections - 35 USC § 112

3. The following is a quotation of 35 U.S.C. 112(b):
(b) CONCLUSION.—The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the inventor or a joint inventor regards as the invention.

The following is a quotation of 35 U.S.C. 112 (pre-AIA), second paragraph:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 12 is rejected under 35 U.S.C. 112(b) or 35 U.S.C. 112 (pre-AIA), second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the inventor or a joint inventor (or for applications subject to pre-AIA 35 U.S.C. 112, the applicant), regards as the invention.

Claim 12 recite the limitation “flow out” in line 2, this limitation is not defined by the claim, which renders the claims indefinite. One with ordinary skill in the art would not be able to know the flow of which parameter. As broadly as claimed the scope of the claim is indeterminate with respect to the claimed “flow”.
For the purpose of examination, the above limitation will be interpreted as the flow of blood.

Still, claim 12 recite the limitation “preferentially” in line 2, this limitation is not defined by the claim, which renders the claims indefinite. One with ordinary skill in the art would not be able to know if it is just preferred to direct the flow to the chamber, or the junction

actually/positively directs the flow toward the chamber. The scope of the claim remains indeterminate because of the claimed "preferentially".

For the purpose of examination, the above limitation will be interpreted as it is only preferred to direct the flow toward the chamber.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a)(1) the claimed invention was patented, described in a printed publication, or in public use, on sale, or otherwise available to the public before the effective filing date of the claimed invention.

Claim(s) 1, 5, 8-14 and 16 is/are rejected under 35 U.S.C. 102(1)(a) as being anticipated by Christensen et al (US 20100057004).

As to claim 1, Christensen discloses a device comprising:

an inlet port (catheter 14 and the frontal inlet port of device 10 where catheter 14 is connected/inserted therein, par.41-43 and par.47, fig.1-4);

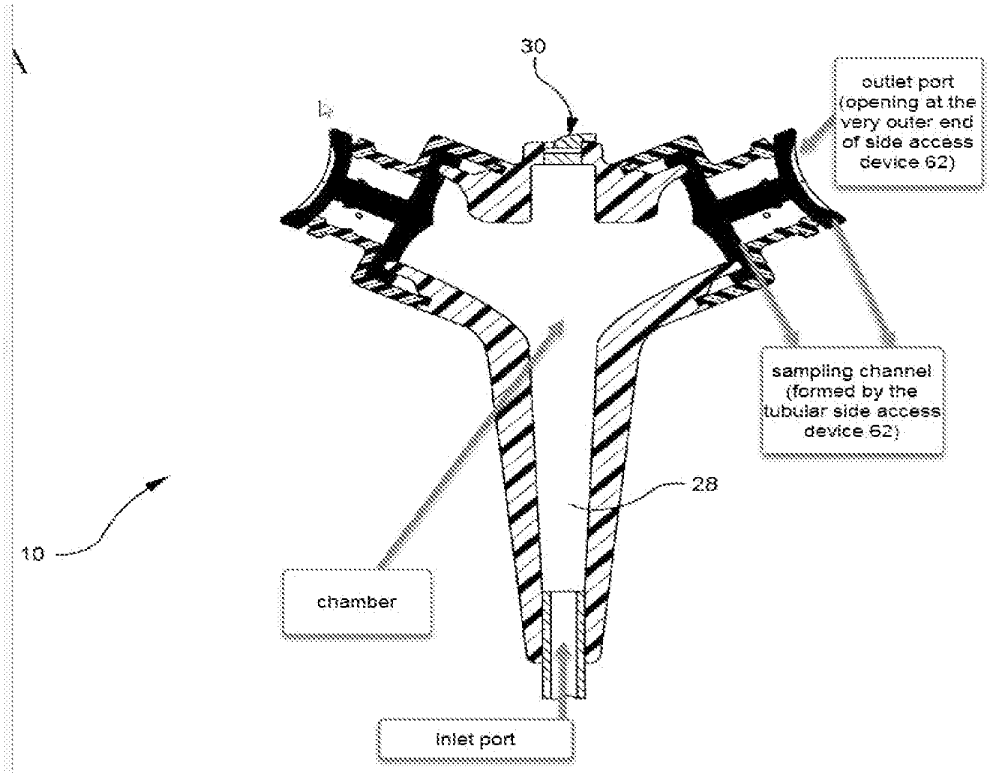
an outlet port (outlet opening at the very outer end of side access device 62 of device 10 where tube 16 is connected to and/or outlet port at the end of tube 16 connected to Y-adapter 18, par.41-43, par.53, fig.1-5);

a chamber (a fluid path 28 filling the interior of the extravascular system 10, par.47, fig.1-4) connected with the inlet port (fluid path 28 within the interior of device 10 is connected to catheter 14 and the frontal inlet port of device 10, fig.1-5) and configured

to receive a first portion of blood (operator will insert the needle 12 into the vasculature of a patient and wait for flashback of blood to travel into the system 10 to confirm that the needle 12 is properly located within the vasculature of the patient, par.43)(The Examiner respectfully notes that flashback of blood, is considered the initial portion of blood),

the chamber including an air permeable material (venting material in vent 30, par.48-50, a removable filter plug 50 and a re-seal elastomer 52 in vent 30, par.51-53, or 114 in the vent, par.71, fig.1-16) that seals at least partially upon contact with a portion of the first portion of blood (par.48-53); and

a sampling channel (tubular channel formed by side access device 62 of device 10 and integrated extension tube 16, par.41-42, fig.1-6) having a proximal end connected with the inlet port and a distal end connected with the outlet port (tubular channel formed by side access device 62 of device 10 having proximal end connected to frontal inlet port of device 10 at catheter 14, and having a distal end connected to the outlet opening at the very outer end of side access device 62 of device 10, as best seen in fig.1-6).



As to claim 5, Christensen discloses the device, wherein the air permeable material is located at a distal end of the chamber (a vent may be placed at or near the start of the fluid path, or the vent may be placed at any point in between the start or end of the fluid path of the extravascular system, par.45, as best seen in fig.1-3).

As to claim 8, Christensen discloses the device, wherein the air permeable material is a hydrophilic membrane (vent 30 includes an expandable vent material 114 that is hydrophilic, par.71, fig.16).

As to claim 9, Christensen discloses the device, wherein the sampling channel further comprises a valve configured to close off the sampling channel (side clamp 20, par.41, slide clamp 20 on the integrated extension tubing 16 is provided to eliminate blood exposure when the vent plug 22 is replaced with another vascular access device, par.42, fig.1).

As to claim 10, Christensen discloses the device, wherein the valve is a clip (clamp 20, par.41, fig.1)

As to claim 11, Christensen discloses the device, further comprising a junction configured to direct an initial blood flow into the chamber (the longitudinal shape at the beginning of fluid path 28 formed in the interior of device 10 forces the flashback blood to enter the interior of device 10, par.43-48, and/or vent 30, vent 30 may be placed at or near the terminus of the system 10 in order to allow fluid, including gas, blood, saline, and water, to fill the internal chamber of the fluid path directly adjacent any vascular access devices of the system 10, par.51-52, fig.1-6).

As to claim 12, Christensen discloses the device, further comprising a junction configured such that flow out of the inlet port is preferentially directed toward the chamber (the longitudinal shape at the beginning of fluid path 28 formed in the interior of device 10 forces the flashback blood to enter the interior of device 10, par.43-48, and/or vent 30, vent 30 may be placed at or near the terminus of the system 10 in order to allow fluid, including gas, blood, saline, and water, to fill the internal chamber of the

fluid path directly adjacent any vascular access devices of the system 10, par.51-52, fig.1-6).

As to claim 13, Christensen discloses the device, wherein the chamber has a larger cross- sectional area than the sampling channel (the cross-sectional area of fluid path 28 of the interior of device 10 is larger than the side tubular channel and tube 16, as best seen in fig.1-3).

As to claim 14, Christensen discloses the device, further comprising a housing that defines the chamber and the sampling channel (housing of device 10 defines fluid path 28 formed at the interior of device 10 and defines the side tubular channel fromed by access device 62 and a portion of integrated tube 16, as best seen in fig.1-3).

As to claim 16, Christensen discloses the device, further comprising a patient needle (needle 12, par.41-43, fig.1) and a sample collection device (Luer access device or port 24, par.41)(Examiner respectfully notes that the luer access device is a device that is connected to obtain blood sample in a sampling container, see link: https://www.medline.com/product/Blood-Transfer-and-Luer-Lock-Access-Device/Z05-PF253812#:~:text=Luer%20lock%20access%20devices%20%28LLAD%20and%20ACSD%29%20are,reduce%20the%20risk%20of%20transfer-related%20injuries%20and%20infections).

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent for a claimed invention may not be obtained, notwithstanding that the claimed invention is not identically disclosed as set forth in section 102, if the differences between the claimed invention and the prior art are such that the claimed invention as a whole would have been obvious before the effective filing date of the claimed invention to a person having ordinary skill in the art to which the claimed invention pertains. Patentability shall not be negated by the manner in which the invention was made.

Claim(s) 2-4, 6 and 7 is/are rejected under 35 U.S.C. 103 as being obvious over Christensen et al (US 20100057004), in view of Weilbacher et al (US 2008/0167577).

As to claims 2-4, 6 and 7, Christensen discloses the device, wherein the device is further configured such that an initial aliquot of blood will contact the air permeable material and back up into the chamber (operator will insert the needle 12 into the vasculature of a patient and wait for flashback of blood to travel into the system 10 to confirm that the needle 12 is properly located within the vasculature of the patient. The blood travels into and along the catheter 14 and extension tubing 16 because a vent plug 22 permits air to escape the system 10 as blood enters the system 10, par.43, and a fluid path 28 within the interior of the extravascular system 10. The fluid path 28 is in communication with a vent 30, and the vent 30 is capable of venting gas from the fluid path 28 of the system 10, par.47 and par.53), wherein the device is further configured such that follow-on amounts of blood will flow through the sampling channel towards the outlet port (blood travels into and along the catheter 14 and extension tubing 16 because a vent plug 22 permits air to escape the system 10 as blood enters the system 10, par.43).

Christensen discloses the invention substantially as above, but failed to explicitly teach wherein the device is configured such that, when a drawing force is applied at the outlet port, blood is drawn into the inlet port and into the chamber, and wherein the air permeable material is a hydrophobic plug/membrane.

However Weilbacher discloses an analogous vascular access needle assembly (abstract, fig.1-3), when a drawing force is applied at the outlet port, blood is drawn into the inlet port and into the chamber (collection tube 17 is maintained at a vacuum such that when distal needle portion 20 is properly positioned in a vein 38 of a patient and collection tube 17 is positioned within cavity 34 OF BODY 30, blood will flow through needle 10 into blood collection tube 17, par.33, fig.1)(the Examiner respectfully notes the vacuum applies blood drawing force), and wherein the air permeable material is a hydrophobic plug/membrane (filter material 116 disposed in chamber 112, wherein material includes a hydrophobic material. In an alternate embodiment, the material includes a hydrophilic wicking material. In yet another embodiment, the material includes a hydrophobic plug, par.11 and par.35, fig.2).

As these types of blood drawing force are well-known in the art, so it would have been obvious to one having an ordinary skill in the art before the effective filing date of the invention to maintain blood collection devices and/or luer accesses devices connected to port 24 taught by Christensen's invention under vacuum, as tube 17 taught by Weilbacher's invention, to facilitated blood sampling and prevent unwanted blood exposure/spilling, as taught by Weilbacher's invention (par.33).

Still, as the hydrophobic air permeable filter/material are well known in the art to vent air, so it would have been obvious to one having an ordinary skill in the art before the effective filing date of the invention to substitute the hydrophilic material taught by Christensen's invention, with the hydrophobic material taught by Weilbacher's invention, for the same reason of venting air from sampling chamber, as taught by Weilbacher's invention (par.11 and par.35-36).

6. Claim(s) 15 is/are rejected under 35 U.S.C. 103 as being obvious over Christensen et al (US 20100057004).

As to claim 15, Christensen disclose the device wherein the housing the top and bottom surface of the housing 10 defines a part of each the inlet port, the outlet port, the chamber, and the sampling channel (housing/body of device 10 have upper and lower surface that define and enclose inlet port, outlet port, chamber and sampling channel, as best seen in fig.1-2 and explained in claims 1 above).
However, Christensen failed to teach the housing comprises a bottom member mated with a top member, since housing/body of device 10 is made from integrated top and bottom surfaces, but it since has been held that the term "integral" is sufficiently broad to embrace constructions united by such means as fastening and welding. In re Hotte, 177 USPQ 326, 328 (CCPA 1973). So, it would have been obvious to one having an ordinary skill in the art before the effective filing date of the invention to make housing of device 10 from top and bottom members that can mate as one integral housing to house all different component of the device.

Also, it would have been prima facie obvious to modify housing 10 to obtain the invention as specified in Claim 15 to be formed/designed of top and bottom mating surafces because such a modification would have been considered a mere design consideration which fails to patentably distinguish over the prior art of Christensen's invention. In re Rose, 105 USPQ 237 (CCPA 1955).

Double Patenting

7. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory double patenting rejection is appropriate where the claims at issue are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).
A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the reference application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of

activities undertaken within the scope of a joint research agreement. A terminal disclaimer must be signed in compliance with 37 CFR 1.321(b).

The USPTO internet Web site contains terminal disclaimer forms which may be used. Please visit http://www.uspto.gov/forms/. The filing date of the application will determine what form should be used. A web-based eTerminal Disclaimer may be filled out completely online using web-screens. An eTerminal Disclaimer that meets all requirements is auto-processed and approved immediately upon submission. For more information about eTerminal Disclaimers, refer to http://www.uspto.gov/patents/process/file/efs/guidance/eTD-info-I.jsp.

Claims 1-16 are non-provisionally rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-16 of U.S Patent Application No.10010282, over claims 1-16 of U.S Patent Application No.9820682, over claims 1-23 of U.S Patent Application No.10143412, over claims 1-26 of U.S Patent Application No.11185266 and over claims 1-20 of U.S Patent Application No.11311219. Although the claims at issue are not identical, they are not patentably distinct from each other because the U.S Patent Application and the instance application are claiming a common subject matter including: a device comprising: an inlet port, an outlet port; a chamber configured to receive a first portion of blood, the chamber including an air permeable material that seals at least partially upon contact with a portion of the first portion of blood; and a sampling channel connected with the outlet port.

Also claims 1-16 are provisionally rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-20 of pending Applications No. 17/730118 and 17/538990. Although the claims at issue are not identical, they are not patentably distinct from each other because the pending Application and the instance application are claiming a common subject matter including: a device comprising: an inlet port, an outlet port; a chamber configured to receive a first portion of blood, the chamber including an air permeable material that seals at least partially upon contact with a portion of the first portion of blood; and a sampling channel connected with the outlet port.

This is a provisional nonstatutory double patenting rejection because the patentably indistinct claims have not in fact been patented.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MAY A ABOUELELA whose telephone number is (571)270-7917. The examiner can normally be reached 8-5.

Examiner interviews are available via telephone, in-person, and video conferencing using a USPTO supplied web-based collaboration tool. To schedule an interview, applicant is encouraged to use the USPTO Automated Interview Request (AIR) at http://www.uspto.gov/interviewpractice.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, JACQUELINE CHENG can be reached on 5712725596. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of published or unpublished applications may be obtained from Patent Center. Unpublished application information in Patent Center is available to registered users. To file and manage patent submissions in Patent Center, visit: https://patentcenter.uspto.gov. Visit https://www.uspto.gov/patents/apply/patent-center for more information about Patent Center and https://www.uspto.gov/patents/docx for information about filing in DOCX format. For additional questions, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/MAY A ABOUELELA/
Primary Examiner, Art Unit 3791

Notice of References Cited	Application/Control No. 18/113,710	Applicant(s)/Patent Under Reexamination ROGERS et al.	
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Index of Claims	Application/Control No.	Applicant(s)/Patent Under Reexamination
	18/113,710	ROGERS et al.
	Examiner	**Art Unit**
	MAY A ABOUELELA	3791

✓	Rejected	-	Cancelled	N	Non-Elected	A	Appeal
=	Allowed	÷	Restricted	I	Interference	O	Objected

CLAIMS

☐ Claims renumbered in the same order as presented by applicant ☐ CPA ☐ T.D. ☐ R.1.47

CLAIM		DATE								
Final	Original	05/08/2023								
	1	✓								
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	4	✓								
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	12	✓								
	13	✓								
	14	✓								
	15	✓								
	16	✓								

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	18/113,710	ROGERS et al.
	Examiner	Art Unit
	MAY A ABOUELELA	3791

CPC - Searched*		
Symbol	Date	Examiner
A61B5/150992 OR A61B5/15003 OR A61B5/150213 OR A61B5/150221 OR A61B5/150389 OR A61B5/150473 OR A61B5/150572 OR A61B5/153 OR A61B5/154 OR A61M39/04 OR A61M39/0693 OR A61M2039/0202 OR A61M2039/0633 OR A61M2039/068	05/08/2023	MA

CPC Combination Sets - Searched*		
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US Classification - Searched*			
Class	Subclass	Date	Examiner

* See search history printout included with this form or the SEARCH NOTES box below to determine the scope of the search.

Search Notes		
Search Notes	Date	Examiner
text search, class/subclass search, inventor name search	05/08/2023	MA

Interference Search			
US Class/CPC Symbol	US Subclass/CPC Group	Date	Examiner

/MAY A ABOUELELA/ Primary Examiner, Art Unit 3791	

Bibliographic Data

Application No: 18/113,710

Foreign Priority claimed: ○ Yes ◉ No

35 USC 119 (a-d) conditions met: ☐ Yes ☑ No ☐ Met After Allowance

Verified and Acknowledged: /MAY A ABOUELELA/ Examiner's Signature | Initials

Title: BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE AND METHOD

FILING or 371(c) DATE	CLASS	GROUP ART UNIT	ATTORNEY DOCKET NO.
02/24/2023	600	3791	069366-0574153_KUR2C04US
RULE			

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Gino KANG, Irvine, CA, UNITED STATES

John DETLOFF, San Diego, CA, UNITED STATES

CONTINUING DATA

This application is a CON of 17538990 11/30/2021

17538990 is a CON of 16208559 12/04/2018 PAT 11185266

16208559 is a CON of 15994559 05/31/2018 PAT 10143412

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PE2E SEARCH - Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	British Equivalents	Time Stamp
L1	0	("15140443").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2016/12/20 11:05 PM
L2	1	("20020099309").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2016/12/21 11:38 AM
L3	1	("14055232").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2016/12/21 11:39 AM
L4	1763	(600/573).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2016/12/21 05:18 PM
L5	63	(("ROGERS") near3 ("Bobby")).INV.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2016/12/21 05:19 PM
L6	28	("2004/0073171").URPN.	(USPAT)	OR	OFF	OFF	2016/12/21 05:36 PM
L7	0	("1and(bloodnear4sequest$5)").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2016/12/21 05:41 PM
L8	5225	1and (blood near4 sequest$5)	(US-PGPUB; USPAT)	OR	OFF	OFF	2016/12/21 05:42 PM
L9	7	L4 and (blood near4 sequest$5)	(US-PGPUB; USPAT)	OR	OFF	OFF	2016/12/21 05:42 PM
L10	73	("20020002349" | "20020183651" | "20030055381" | "20040010228" | "20040054333" | "20040147855" | "20050004524" | "20050240161" | "20050245885" | "20050281713" | "20060287639" | "2707953" | "3013557" | "3098016" | "3382865" | "3405706" | "3494351" | "3577980" | "3648684" | "3848579" | "3937211" | "4057050" | "4133863" | "4166450" | "4340067" | "4370987" | "4444203" | "4459997" | "4509534" | "4676256" | "4865583" | "4890627" | "4988339" | "5009847" | "5097842" | "5108927" | "5122129" | "5269317" | "5360011" | "5429610" | "5450856" | "5507299" | "5577513" | "5762633" | "5882318" | "5922551" | "6016712" | "6057105" | "6159164" | "6210909" | "6364890" | "6387086" | "6403381" |	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2016/12/21 05:43 PM

		"6692479" | "6746420" | "6913580" | "7044941" | "7087047").PN. OR ("8197420").URPN.					
L11	2	L10 and (blood near4 sequest$5)	(US-PGPUB; USPAT)	OR	OFF	OFF	2016/12/21 05:44 PM
L12	77	("0453322" | "0577682" | "0729011" | "1074965" | "1110189" | "1450016" | "1521890" | "2218899" | "2688325" | "2895773" | "3176595" | "3214069" | "3236268" | "3263874" | "3486503" | "3577980" | "3754644" | "3794221" | "3834387" | "3855997" | "3937211" | "3958570").PN. OR ("4057050").URPN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2016/12/21 05:47 PM
L13	852	L4 and (blood near4 (sequest$5 or sampl$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2016/12/21 05:47 PM
L14	46	L10 and (blood near4 (sequest$5 or sampl$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2016/12/21 05:47 PM
L15	1	("8197420").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2016/12/21 06:29 PM
L16	1	("20130317391").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2016/12/21 06:42 PM
L17	1254	(600/583).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2016/12/21 06:43 PM
L18	1070	L17 and (blood near4 (sequest$5 or sampl$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2016/12/21 06:43 PM
L19	265030	(blood near4 (sequest$5 or sampl$4))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2016/12/21 07:09 PM
L20	5653	L19 AND ((A61B10/0096 OR A61B5/150022).CPC.)	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2016/12/21 07:10 PM
L21	207	L20 and (seal near4 air)	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2016/12/21 07:10 PM
L22	23	"2004087258"	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2016/12/21 08:59 PM
L23	1	("20050004524").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/11 08:23 PM
L24	1	("20030105414").PN.	(US-PGPUB; USPAT;	OR	ON	ON	2017/04/11

			USOCR)				08:24 PM
L25	1	("5749857").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/11 08:26 PM
L26	13	("20040073171"|"20040147855"|"20050240161"|"20130317391"|"20160174888"|"4057050"|"8197420"|"8523826"|"8535241"|"8540663"|"8568371"|"8864684"|"9138572").PN.	(US-PGPUB; USPAT)	OR	OFF	OFF	2017/04/11 08:39 PM
L27	1	("15140443").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/11 09:43 PM
L28	0	("4and(bloodnear4air)").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/11 10:01 PM
L29	3	L26 and (blood near4 air)	(US-PGPUB; USPAT)	OR	OFF	OFF	2017/04/11 10:01 PM
L30	6	L26 and vent$4	(US-PGPUB; USPAT)	OR	OFF	OFF	2017/04/11 10:02 PM
L31	5	("2013/0317391").URPN.	(USPAT)	OR	OFF	OFF	2017/04/11 10:06 PM
L32	48	("2005/0004524").URPN.	(USPAT)	OR	OFF	OFF	2017/04/11 10:17 PM
L33	1	("20120170037").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/12 04:11 PM
L34	1	("6139540").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/13 12:52 PM
L35	1	("20040116878").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/13 12:54 PM
L36	1	("20100152752").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/13 01:16 PM
L37	1	("6395003").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/13 01:20 PM
L38	5	("2013/0317391").URPN.	(USPAT)	OR	OFF	OFF	2017/04/13 01:43 PM
L39	1	("4444203").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/13 01:44 PM
L40	1	("20020004647").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/13 01:48 PM
L41	1	("3817240").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/13 01:57 PM
L42	1	("3874367").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/13 01:57 PM
L43	1	("3886930").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/13 01:58 PM
L44	1	("4106497").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/13 01:59 PM
L45	1	("4154229").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/13 01:59 PM
L46	1	("4207870").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/13 02:00 PM

L47	292	("2913000" | "3817240" | "3859998" | "3864979" | "4016879" | "4046144").PN. OR ("4207870").URPN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2017/04/13 02:01 PM
L48	1	("4412548").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/13 02:04 PM
L49	1	("5222502").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/13 02:11 PM
L50	1	("5520193").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/13 02:15 PM
L51	1	("20100057004").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/13 02:16 PM
L52	1	("20070088279").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/13 02:29 PM
L53	1733	(600/573).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2017/04/13 03:29 PM
L54	13	L53 and ((vent$4 near4 air) and flash$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2017/04/13 03:52 PM
L55	1255	(600/583).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/13 04:23 PM
L56	4	L55 and ((vent$4 near4 air) and flash$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2017/04/13 04:23 PM
L57	272301	(blood near4 (sequest$5 or sampl$4))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2017/04/13 04:29 PM
L58	5898	L57 AND ((A61B10/0096 OR A61B5/150022).CPC.)	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2017/04/13 04:29 PM
L59	114	L58 and ((vent$4 near4 air) and flash$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2017/04/13 04:29 PM
L60	2	("2007/0088279").URPN.	(USPAT)	OR	OFF	OFF	2017/04/13 05:58 PM
L61	1	("6358217").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/21 02:02 PM
L62	6	("2002/0004647").URPN.	(USPAT)	OR	OFF	OFF	2017/09/27 12:48 PM
L63	2	("14493796").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/09/27 01:21 PM
L64	2	("14494208").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/09/27 01:23 PM
L65	1	("15140443").PN.	(US-PGPUB; USPAT)	OR	ON	ON	2017/09/27 01:28 PM
L66	1	("20080145933").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/09/27 01:51 PM
L67	9	("2008/0145933").URPN.	(USPAT)	OR	OFF	OFF	2017/09/27 01:55 PM
L68	1	("20040054333").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/09/27 01:59 PM

L69	1	("20120109034").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/09/27 02:37 PM
L70	1	("20100228206").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/09/27 02:39 PM
L71	3	("2010/0228206").URPN.	(USPAT)	OR	OFF	OFF	2017/09/27 02:47 PM
L72	66	(("ROGERS") near3 ("Bobby")).INV.	(US-PGPUB; USPAT)	OR	OFF	OFF	2017/09/28 01:41 PM
L73	4	L72 and (blood near4 (sequest$5 or sampl$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2017/09/28 01:42 PM
L74	1733	(600/573).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2017/09/28 01:58 PM
L75	845	L74 and (blood near4 (sequest$5 or sampl$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2017/09/28 01:58 PM
L76	9	L75 and ((vent$4 near4 air) and flash$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2017/09/28 01:59 PM
L77	86	("2007/0083162").URPN.	(USPAT)	OR	OFF	OFF	2017/09/28 01:59 PM
L78	1	("15140443").PN.	(US-PGPUB; USPAT)	OR	ON	ON	2017/09/28 01:59 PM
L79	9	("2008/0145933").URPN.	(USPAT)	OR	OFF	OFF	2017/09/28 02:04 PM
L80	1258	(600/583).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2017/09/28 02:20 PM
L81	1071	L80 and (blood near4 (sequest$5 or sampl$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2017/09/28 02:20 PM
L82	78	L81 and (vent$4 near4 air)	(US-PGPUB; USPAT)	OR	OFF	OFF	2017/09/28 02:21 PM
L83	282596	(blood near4 (sequest$5 or sampl$4))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2017/09/28 04:01 PM
L84	6183	L83 AND ((A61B10/0096 OR A61B5/150022).CPC.)	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2017/09/28 04:01 PM
L85	387	L84 and (vent$4 near4 air)	(US-PGPUB; USPAT)	OR	OFF	OFF	2017/09/28 04:01 PM
L86	362	L85 and @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2017/09/28 04:02 PM
L87	12	("2005/0010189").URPN.	(USPAT)	OR	OFF	OFF	2017/09/28 04:03 PM
L88	1363	(604/164.01).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/09/28 04:04 PM
L89	74	L88 and (blood near4 (sequest$5 or sampl$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2017/09/28 04:05 PM
L90	21	("3965910" | "3996923"	(US-PGPUB; USPAT;	OR	OFF	OFF	2017/09/28

		| "4131127" | "4301811" | "4450854" | "4506691" | "4819684" | "5147333" | "5393035" | "5636975").PN. OR ("6569117").URPN.	USOCR)				04:09 PM
L91	499	(435/294.1).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/09/28 04:12 PM
L92	18	L91 and (blood near4 (sequest$5 or sampl$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2017/09/28 04:12 PM
L93	9	("2008/0145933").URPN.	(USPAT)	OR	OFF	OFF	2017/09/28 04:13 PM
L95	67	(("ROGERS") near3 ("Bobby")).INV.	(US-PGPUB; USPAT)	OR	OFF	OFF	2018/01/09 04:23 PM
L96	1258	(600/583).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2018/01/09 04:25 PM
L97	4	L96 and ((vent$4 near4 air) and flash$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2018/01/09 04:25 PM
L98	3	L97 and (blood near4 (sequest$5 or sampl$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2018/01/09 04:26 PM
L99	1733	(600/573).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2018/01/09 04:50 PM
L100	13	L99 and ((vent$4 near4 air) and flash$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2018/01/09 04:50 PM
L101	255	("1779451" | "2004050" | "2700385" | "2836942" | "2854976" | "2953243" | "3021942" | "3073307" | "3074542" | "3255873" | "3294231" | "3323523" | "3329146" | "3333682" | "3367488" | "3382865" | "3485239" | "3537452" | "3585984" | "3610240" | "3658061" | "3664879" | "3817240" | "3828775" | "3859998" | "3874367" | "3886930" | "3890971" | "3904033" | "3934722" | "3968876" | "4106497" | "4108175" | "4113090" | "4139009" | "4154229" | "4166450" | "4175008" | "4193400" | "4207870" | "4269186" | "4300678" | "4312362" | "4317445" | "4340068" | "4375849" | "4398544" | "4409990" | "4412548" | "4416290" | "4416291" | "4418703" | "4430082" | "4436098" | "4444203" | "4592744"	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2018/01/09 04:51 PM

		| "4634428" | "4643722" | "4659330" | "4664249" | "4664654" | "4671408" | "4679571" | "4681567" | "4695274" | "4702738" | "4723943" | "4728320" | "4728321" | "4731059" | "4735311" | "4735618" | "4737144" | "4738663" | "4743233" | "4746008" | "4747836" | "4747837" | "4772272" | "4778453" | "4781697" | "4782841" | "4788986" | "4790828" | "4793484" | "4795432" | "4795443" | "4801295" | "4804372" | "4813426" | "4816022" | "4816024" | "4819659" | "4820277" | "4826490" | "4826491" | "4838871" | "4842587" | "4844089" | "4846796" | "4850968" | "4850976" | "4850977" | "4850978" | "4850994" | "4850996" | "4858607" | "4863434" | "4863435" | "4863436" | "4865592" | "4867746" | "4872552" | "4874383" | "4874384" | "4883469" | "4886072" | "4886503" | "4888001" | "4892107" | "4892521" | "4894052" | "4900309" | "4909791" | "4909792").PN. OR ("4921096" | "4927018" | "4944397" | "4966591" | "4971068" | "4976699" | "4982842" | "5011475" | "5011479" | "5030207" | "5032116" | "5033476" | "5055102" | "5069225" | "5078693" | "5078698" | "5092845" | "5112327" | "5116325" | "5120319" | "5122121" | "5135509" | "5137518" | "5139489" | "5151089" | "5154285" | "5181523" | "5188611" | "5197954" | "5201794" | "5207653" | "5217025" | "5222502" | "5232454" | "5232455" | "5242411" | "5242417" | "5277311" | "5290246" | "5295969" | "5303713" | "5306259" | "5312369" | "5401251" | "5405332" | "5423765"					

		| "5450856" | "5462534" | "5485854" | "5486163" | "5490841" | "5496281" | "5509907" | "5520193" | "5533984" | "5542932" | "5584816" | "5599313" | "5599318" | "5603699" | "5632732" | "5643219" | "5662617" | "5665075" | "5669889" | "5693022" | "5697914" | "5702369" | "5733265" | "5755701" | "5807351" | "5830190" | "5836920" | "5885249" | "5893844" | "5913846" | "5984895" | "5993426" | "6059737" | "6077244" | "6077253" | "6080137" | "6096006" | "6110160" | "6120482" | "6156010" | "6190370" | "6261263" | "6511439" | "6533760" | "6964658" | "7160267" | "RE31086").PN. OR ("7615033").URPN.					
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L103	1347	(604/164.01).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2018/01/09 05:11 PM
L104	17	L103 and ((vent$4 near4 air) and flash$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2018/01/09 05:11 PM
L105	19	("2009/0312711").URPN.	(USPAT)	OR	OFF	OFF	2018/01/09 05:11 PM
L106	11	("2007/0106220").URPN.	(USPAT)	OR	OFF	OFF	2018/01/09 05:11 PM
L107	288967	(blood near4 (sequest$5 or sampl$4))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2018/01/09 05:16 PM
L108	6321	L107 AND ((A61B10/0096 OR A61B5/150022).CPC.)	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2018/01/09 05:16 PM
L109	121	L108 and ((vent$4 near4 air) and flash$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2018/01/09 05:17 PM
L110	448	(435/294.1).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2018/01/09 05:31 PM
L111	6	L110 and ((vent$4 near4 air) and flash$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2018/01/09 05:31 PM
L113	71	(("ROGERS") near3 ("Bobby")).INV.	(US-PGPUB; USPAT)	OR	OFF	OFF	2018/07/24 01:31 PM
L114	0	("15140443").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2018/07/24 01:38 PM

L115	2	(15/140443).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2018/07/24 01:38 PM
L116	2	(15/140448).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2018/07/24 01:40 PM
L117	1735	(600/573).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2018/07/24 01:56 PM
L118	854	L117 and (blood near4 (sequest$5 or sampl$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2018/07/24 01:56 PM
L119	91	L118 and (vent$4 near4 air)	(US-PGPUB; USPAT)	OR	OFF	OFF	2018/07/24 01:57 PM
L120	1258	(600/583).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2018/07/24 02:06 PM
L121	1074	L120 and (blood near4 (sequest$5 or sampl$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2018/07/24 02:06 PM
L122	80	L121 and (vent$4 near4 air)	(US-PGPUB; USPAT)	OR	OFF	OFF	2018/07/24 02:06 PM
L123	301210	(blood near4 (sequest$5 or sampl$4))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2018/07/24 02:11 PM
L124	6556	L123 AND ((A61B10/0096 OR A61B5/150022).CPC.)	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2018/07/24 02:11 PM
L125	3664	L124 and @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2018/07/24 02:12 PM
L126	12749	"19" and ((vent$4 near4 air) and flash$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2018/07/24 02:12 PM
L127	117	L125 and ((vent$4 near4 air) and flash$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2018/07/24 02:12 PM
L128	1348	(604/164.01).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2018/07/24 02:16 PM
L129	75	L128 and (blood near4 (sequest$5 or sampl$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2018/07/24 02:17 PM
L130	1	("20120291564").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2018/07/24 02:21 PM
L131	448	(435/294.1).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2018/07/24 02:25 PM
L132	18	L131 and (blood near4 (sequest$5 or sampl$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2018/07/24 02:25 PM
L133	98	("20020002349" | "20020183651" | "20030055381" | "20030208151" | "20040010228" | "20040054333" | "20040147855" | "20050004524" |	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2018/07/24 02:44 PM

		"20050240161" | "20050245885" | "20050281713" | "20060287639" | "20080108954" | "20080145933" | "2707953" | "3013557" | "3098016" | "3382865" | "3405706" | "3494351" | "3577980" | "3648684" | "3848579" | "3937211" | "4057050" | "4133863" | "4166450" | "4340067" | "4370987" | "4444203" | "4459997" | "4509534" | "4657160" | "4676256" | "4865583" | "4890627" | "4988339" | "5009847" | "5097842" | "5108927" | "5122129" | "5269317" | "5330464" | "5360011" | "5429610" | "5450856" | "5507299" | "5577513" | "5762633" | "5865812" | "5882318" | "5922551" | "6016712" | "6057105" | "6159164" | "6210909" | "6364890" | "6387086" | "6403381" | "6626884" | "6692479" | "6746420" | "6913580" | "7044941" | "7087047" | "7335188" | "7744573" | "8197420" | "8231546" | "8337418").PN. OR ("8535241").URPN.					
L134	307	("2913000" | "3817240" | "3859998" | "3864979" | "4016879" | "4046144").PN. OR ("4207870").URPN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2018/07/24 02:47 PM
L135	23	("4166450").PN. OR ("4412548").URPN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2018/07/24 02:48 PM
L136	307	("2913000" | "3817240" | "3859998" | "3864979" | "4016879" | "4046144").PN. OR ("4207870").URPN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2018/07/24 02:48 PM
L137	4	("2007/0088279").URPN.	(USPAT)	OR	ON	ON	2018/07/24 02:48 PM
L138	1	(14/990763).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2018/07/24 02:58 PM
L139	9	(blood and sequest$5 and junction and first and portion and sampl$4).clm.	(US-PGPUB; USPAT)	OR	ON	ON	2018/07/24 03:07 PM

L140	1	(15/287421).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2018/07/25 09:39 PM
L141	2	(14/055232).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2018/07/26 11:56 AM
L142	2	(15/140443).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2019/11/07 03:24 PM
L143	1	(15/893518).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2019/11/07 03:25 PM
L144	34	("20020004647"|"20030105414"|"20040054333"|"20040073171"|"20040147855"|"20050004524"|"20050240161"|"20070088279"|"20080145933"|"20100057004"|"20130317391"|"20160174888"|"3817240"|"3874367"|"3886930"|"4057050"|"4106497"|"4154229"|"4207870"|"4412548"|"5222502"|"5520193"|"5749857"|"6569117"|"8197420"|"8523826"|"8535241"|"8540663"|"8568371"|"8864684"|"9022951"|"9060724"|"9138572"|"9204864").PN.	(US-PGPUB; USPAT)	OR	ON	ON	2019/11/07 05:53 PM
L145	272	((("ROGERS") near3 ("Bobby")) OR (("KANG") near3 ("Gino")) OR (("STROUP") near3 ("David")) OR (("COCHRAN") near3 ("Jonas")) OR (("DEPTALA") near3 ("Arthur")) OR (("DETLOFF") near3 ("John")) OR (("POGUE") near3 ("Lonnie")) OR (("MACOWSKI") near3 ("Brian")) OR (("GARRETT") near3 ("Chad"))).INV.	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2019/11/07 05:57 PM
L146	9	L145 and (blood near4 sequest$5)	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/11/07 05:58 PM
L147	34	("20020004647"|"20030105414"|"20040054333"|"20040073171"|"20040147855"|"20050004524"|"20050240161"|"20070088279"|"20080145933"|"20100057004"|"20130317391"|"20160174888"|"3817240"|"38743	(US-PGPUB; USPAT)	OR	ON	ON	2019/11/07 06:26 PM

		67"|"3886930"|"4057050"|"4106497"|"4154229"|"4207870"|"4412548"|"5222502"|"5520193"|"5749857"|"6569117"|"8197420"|"8523826"|"8535241"|"8540663"|"8568371"|"8864684"|"9022951"|"9060724"|"9138572"|"9204864").PN.					
L148	5	L147 and ((vent$4 near4 air) and flash$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/11/07 06:29 PM
L149	6	("2010/0057004").URPN.	(USPAT)	OR	ON	ON	2019/11/07 06:40 PM
L150	0	L149 and ((vent$4 near4 air) and flash$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/11/07 07:20 PM
L151	1258	(600/583).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2019/11/07 07:21 PM
L152	4	L151 and ((vent$4 near4 air) and flash$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/11/07 07:21 PM
L153	1766	(600/573).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2019/11/07 07:21 PM
L154	13	L153 and ((vent$4 near4 air) and flash$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/11/07 07:21 PM
L155	811	(600/576).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2019/11/07 07:22 PM
L156	48	L155 and ((vent$4 near4 air) and flash$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/11/07 07:22 PM
L157	1351	(604/164.01).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2019/11/07 07:43 PM
L158	17	L157 and ((vent$4 near4 air) and flash$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/11/07 07:43 PM
L159	448	(435/294.1).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2019/11/07 07:43 PM
L160	6	L159 and ((vent$4 near4 air) and flash$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/11/07 07:44 PM
L161	333030	(blood near4 (sequest$5 or sampl$4))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2019/11/07 07:44 PM
L162	6981	L161 AND ((A61B10/0096 OR A61B5/150022).CPC.)	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2019/11/07 07:44 PM
L163	139	L162 and ((vent$4 near4 air) and flash$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/11/07 07:44 PM
L164	117	L163 and @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/11/07 07:45 PM
L165	1	L146 and (enclos$3 near4 mechanism)	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/11/07 07:51 PM
L166	1	("7637875").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2019/11/08 04:57 PM

L167	1	(15/139716).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2019/11/11 12:09 PM
L168	1	(15/520430).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2019/11/12 11:02 AM
L169	1	("7637875").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2019/11/12 12:11 PM
L170	1	("20120253321").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2019/11/12 12:13 PM
L171	1	(15/861959).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2019/11/12 12:14 PM
L172	1	("4207870").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2019/12/09 02:17 PM
L173	1	("5749857").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2019/12/09 03:14 PM
L174	1	("20080167577").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2019/12/09 03:19 PM
L175	4	("2008/0167577").URPN.	(USPAT)	OR	ON	ON	2019/12/09 03:30 PM
L176	1	("8197420").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2019/12/09 03:31 PM
L177	39	(US-20040073171-$ or US-20160174888-$ or US-20050240161-$ or US-20040147855-$ or US-20130317391-$ or US-20050004524-$ or US-20030105414-$ or US-20020004647-$ or US-20100057004-$ or US-20070088279-$ or US-20080145933-$ or US-20040054333-$ or US-20100010372-$ or US-20080319346-$ or US-20080167577-$).did. or (US-9138572-$ or US-8568371-$ or US-8540663-$ or US-8523826-$ or US-8197420-$ or US-4057050-$ or US-8864684-$ or US-8535241-$ or US-5749857-$ or US-9060724-$ or US-9204864-$ or US-3817240-$ or US-3874367-$ or US-3886930-$ or US-4106497-$ or US-4154229-$ or US-4207870-$ or US-4412548-$ or US-5222502-$ or US-5520193-$ or US-	(US-PGPUB; USPAT)	OR	ON	ON	2019/12/09 03:37 PM

		9022951-$ or US-6569117-$ or US-3741197-$ or US-8603009-$).did.					
L178	8	("20040054333"|"8197420"|"9855001"|"9861306"|"10045724"|"10028687"|"8337418"|"10028689").PN.	(US-PGPUB; USPAT)	OR	ON	ON	2019/12/09 03:42 PM
L179	100	("20020002349" | "20020183651" | "20030055381" | "20040010228" | "20040054333" | "20040147855" | "20050004524" | "20050240161" | "20050245885" | "20050281713" | "20060287639" | "2707953" | "3013557" | "3098016" | "3382865" | "3405706" | "3494351" | "3577980" | "3648684" | "3848579" | "3937211" | "4057050" | "4133863" | "4166450" | "4340067" | "4370987" | "4444203" | "4459997" | "4509534" | "4676256" | "4865583" | "4890627" | "4988339" | "5009847" | "5097842" | "5108927" | "5122129" | "5269317" | "5360011" | "5429610" | "5450856" | "5507299" | "5577513" | "5762633" | "5882318" | "5922551" | "6016712" | "6057105" | "6159164" | "6210909" | "6364890" | "6387086" | "6403381" | "6692479" | "6746420" | "6913580" | "7044941" | "7087047").PN. OR ("8197420").URPN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2019/12/09 03:43 PM
L180	70	L179 and (blood near4 (sequest$5 or sampl$4 or flash$4))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2019/12/09 03:43 PM
L181	43	L180 and @ad<"20120530"	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/12/09 03:44 PM
L182	270	((("BULLINGTON") near3 ("Gregory")) OR (("PATTON") near3 ("Richard")) OR (("MIAZGA") near3	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2019/12/09 04:13 PM

		("Jay")) OR (("GAW") near3 ("Shan"))).INV.					
L183	335813	(blood near4 (sequest$5 or sampl$4))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2019/12/09 04:22 PM
L184	7259	L183 AND ((A61B10/0096 OR A61B5/150022).CPC.)	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2019/12/09 04:22 PM
L185	325	("2913000" | "3817240" | "3859998" | "3864979" | "4016879" | "4046144").PN. OR ("4207870").URPN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2019/12/09 04:33 PM
L186	594	L184 and (flash$6 and seal$4)	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/12/09 04:40 PM
L187	476	L186 and @ad<"20120530"	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/12/09 04:40 PM
L188	1735	(600/573).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2019/12/09 05:14 PM
L189	1123	L188 and ((blood or fluid$4) near4 (sequest$5 or sampl$4 or flash$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/12/09 05:15 PM
L190	1013	L189 and @ad<"20120530"	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/12/09 05:15 PM
L191	10	L190 and ((vent$4 near4 air) and flash$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/12/09 05:16 PM
L192	1259	(600/583).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2019/12/09 05:23 PM
L193	1143	L192 and ((blood or fluid$4) near4 (sequest$5 or sampl$4 or flash$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/12/09 05:23 PM
L194	1038	L193 and @ad<"20120530"	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/12/09 05:23 PM
L195	3	L194 and ((vent$4 near4 air) and flash$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/12/09 05:23 PM
L196	811	(600/576).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2019/12/09 05:24 PM
L197	618	L196 and ((blood or fluid$4) near4 (sequest$5 or sampl$4 or flash$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/12/09 05:24 PM
L198	557	L197 and @ad<"20120530"	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/12/09 05:24 PM
L199	1	(15/854273).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2019/12/09 05:25 PM
L200	1351	(604/164.01).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2019/12/09 05:31 PM
L201	219	L200 and ((blood or	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/12/09

		fluid$4) near4 (sequest$5 or sampl$4 or flash$4))					05:33 PM
L202	199	L201 and @ad<"20120530"	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/12/09 05:33 PM
L203	448	(435/294.1).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2019/12/09 05:36 PM
L204	44	L203 and ((blood or fluid$4) near4 (sequest$5 or sampl$4 or flash$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/12/09 05:37 PM
L205	1	(15/508871).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2019/12/10 11:58 AM
L206	342199	(blood near4 (sequest$5 or sampl$4))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2020/03/16 12:53 PM
L207	4239	L206 AND ((A61B10/0096 OR A61B5/150022).CPC.)	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 12:53 PM
L208	146	L207 and ((vent$4 near4 air) and flash$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 12:54 PM
L209	101	L208 and @ad<"20120530"	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 12:55 PM
L210	1735	(600/573).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2020/03/16 01:38 PM
L211	1123	L210 and ((blood or fluid$4) near4 (sequest$5 or sampl$4 or flash$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 01:38 PM
L212	1013	L211 and @ad<"20120530"	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 01:39 PM
L213	22	L212 and (((vent$4 or open$5 or hole or aperture) near4 air) and flash$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 01:39 PM
L214	108	("20020193748" | "20030093009" | "20030105414" | "20030220614" | "20030229315" | "20040059302" | "20040092872" | "20040193120" | "20050004524" | "20050065482" | "20050124944" | "20050187493" | "20050245868" | "20050245869" | "20050245870" | "20050245879" | "20050245885" |	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2020/03/16 01:46 PM

		"20060036219" | "20060224122" | "20070106220" | "20070106224" | "20070167914" | "20080086085" | "20080177202" | "20080319345" | "20080319346" | "20090204026" | "20100262038" | "4106497" | "4207870" | "4305406" | "4572210" | "4573976" | "4641663" | "4795443" | "4840619" | "4894055" | "4900307" | "4994046" | "5015241" | "5195985" | "5215534" | "5222502" | "5242417" | "5246428" | "5256153" | "5295970" | "5303713" | "5312372" | "5336199" | "5348544" | "5356392" | "5411492" | "5439449" | "5466223" | "5501675" | "5542932" | "5599313" | "5662617" | "5665075" | "5672161" | "5676658" | "5702369" | "5704920" | "5733265" | "5755522" | "5957892" | "5984899" | "6149629" | "6224576" | "6254575" | "6261263" | "6298541" | "6344032" | "6436086" | "6440104" | "6524277" | "6533760" | "6592556" | "6623456" | "6635032" | "6648855" | "6695819" | "6699217" | "6712792" | "6780169" | "6837877" | "6869415" | "6984223" | "7001363" | "7128726" | "7147624" | "7160267" | "7163526" | "7223258" | "7226432" | "7396343" | "7428773" | "7537581" | "7766879" | "D422700" | "D442280" | "D604836" | "D604837" | "D604838" | "D604839" | "D605287").PN. OR ("8603009").URPN.					
L215	26	L214 and (((vent$4 or open$5 or hole or aperture) near4 air) and flash$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 01:47 PM

L216	27	("2008/0319346").URPN.	(USPAT)	OR	ON	ON	2020/03/16 01:47 PM
L217	23	("2003/0105414").URPN.	(USPAT)	OR	ON	ON	2020/03/16 01:48 PM
L218	1258	(600/583).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2020/03/16 01:52 PM
L219	1143	L218 and ((blood or fluid$4) near4 (sequest$5 or sampl$4 or flash$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 01:52 PM
L220	25	L219 and (((vent$4 or open$5 or hole or aperture) near4 air) and flash$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 01:52 PM
L221	353695	((blood or fluid$4) near4 (sequest$5 or sampl$4 or flash$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 01:54 PM
L222	3643	L221 and (((vent$4 or open$5 or hole or aperture) near4 air) and flash$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 01:55 PM
L223	1926	L222 and @ad<"20120530"	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 01:55 PM
L224	785	L223 and ((blood or fluid$4) near4 (sequest$5 or flash$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 01:56 PM
L225	7046	(600/300).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2020/03/16 02:32 PM
L226	14	L225 and ((blood or fluid$4) near4 (sequest$5 or flash$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 02:35 PM
L227	1352	(604/164.01).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2020/03/16 02:36 PM
L228	135	L227 and ((blood or fluid$4) near4 (sequest$5 or flash$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 02:36 PM
L229	19	L228 and (((vent$4 or open$5 or hole or aperture) near4 air) and flash$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 02:36 PM
L230	448	(435/294.1).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2020/03/16 02:47 PM
L231	3	L230 and ((blood or fluid$4) near4 (sequest$5 or flash$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 02:47 PM
L232	19	("2008/0145933").URPN.	(USPAT)	OR	ON	ON	2020/03/16 02:48 PM
L233	795	(600/576).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2020/03/16 02:58 PM
L234	71	L233 and ((blood or fluid$4) near4 (sequest$5 or flash$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 02:58 PM

L235	57	L234 and @ad<"20120530"	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 02:59 PM
L236	371	(600/577).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2020/03/16 03:12 PM
L237	11	L236 and ((blood or fluid$4) near4 (sequest$5 or flash$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 03:12 PM
L238	45	("20040054333"|"20050240161"|"4412548"|"5749857"|"8197420"|"9855001"|"9861306"|"20020004647"|"20100057004"|"3741197"|"20040073171"|"3874367"|"4057050"|"4106497"|"8197420"|"8535241"|"8540663"|"8603009"|"8864684"|"10045724"|"3817240"|"10028687"|"20030105414"|"5222502"|"5520193"|"6569117"|"8568371"|"20040147855"|"20070088279"|"20080145933"|"20100010372"|"3886930"|"8523826"|"9060724"|"9204864"|"8337418"|"20050004524"|"20080167577"|"20080319346"|"20130317391"|"4154229"|"9022951"|"10028689"|"20160174888"|"4207870"|"9138572").PN.	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 03:13 PM
L239	6	("2008/0167577").URPN.	(USPAT)	OR	ON	ON	2020/03/16 03:13 PM
L240	118	("3500828" | "3670729" | "3714945" | "3977400" | "3994293" | "3995619" | "4106491" | "4200096" | "4468224" | "4531987" | "4549554" | "4735215" | "4828548" | "4874373" | "4893635" | "4894052" | "4907599" | "4944308" | "4994042" | "5129884" | "5400798").PN. OR ("5749857").URPN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2020/03/16 03:15 PM
L241	6	("2008/0167577").URPN.	(US-PGPUB; USPAT)	OR	ON	ON	2020/03/16 03:15 PM
L242	274	((("BULLINGTON") near3 ("Gregory")) OR (("PATTON") near3 ("Richard")) OR (("MIAZGA") near3 ("Jay")) OR (("GAW") near3 ("Shan"))).INV.	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2020/03/16 03:25 PM

L243	61	L242 and ((blood or fluid$4) near4 (sequest$5 or flash$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 03:25 PM
L244	1	(15/854273).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2020/03/16 03:47 PM
L245	0	(14/502498).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2020/03/16 04:11 PM
L246	1	("20110082383").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2020/03/16 04:24 PM
L247	1	("8150506").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2020/03/16 04:24 PM
L252	1	(15/057214).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2020/03/17 11:28 AM
L253	348964	(blood near4 (sequest$5 or sampl$4))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2020/06/10 05:22 PM
L254	7453	L253 AND ((A61B10/0096 OR A61B5/150022).CPC.)	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2020/06/10 05:22 PM
L255	155	L254 and ((vent$4 near4 air) and flash$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/06/10 05:23 PM
L256	77	(("ROGERS") near3 ("Bobby")).INV.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2020/06/10 05:35 PM
L257	343953	(blood same (sequest$5 or sampl$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/06/10 05:40 PM
L258	11	L256 and (blood same (sequest$5 or sampl$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/06/10 05:41 PM
L259	1	("5749857").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2020/06/10 05:50 PM
L260	121	("3500828" | "3670729" | "3714945" | "3977400" | "3994293" | "3995619" | "4106491" | "4200096" | "4468224" | "4531987" | "4549554" | "4735215" | "4828548" | "4874373" | "4893635" | "4894052" | "4907599" | "4944308" | "4994042" | "5129884" | "5400798").PN. OR ("5749857").URPN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2020/06/10 06:19 PM
L261	32	L260 and (blood near4 (sequest$5 or sampl$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/06/10 06:20 PM
L262	1	("3648684").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2020/06/10 06:38 PM
L263	1	("4056101").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2020/06/10 06:38 PM
L264	329	(600/577).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2020/06/10

							06:39 PM
L265	11	L264 and ((blood or fluid$4) near4 (sequest$5 or flash$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/06/10 06:39 PM
L266	29	("2008/0319346").URPN.	(USPAT)	OR	ON	ON	2020/06/10 06:40 PM
L267	812	(600/576).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2020/06/10 06:40 PM
L268	72	L267 and ((blood or fluid$4) near4 (sequest$5 or flash$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/06/10 06:40 PM
L269	1767	(600/573).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2020/06/10 06:44 PM
L270	31	L269 and ((blood or fluid$4) near4 (sequest$5 or flash$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/06/10 06:45 PM
L271	77	("4676249" | "4787891" | "4850960" | "4874382" | "4886067" | "4886500" | "4900307" | "4904242" | "4917102" | "4950252" | "4955862" | "5046508" | "5116353" | "5125718" | "5129884" | "5163911" | "5217435" | "5290244" | "5295974" | "5314503" | "5318585" | "5330432" | "5360410" | "5366441" | "5376075" | "5395337" | "5531692" | "5695475" | "5695479" | "5702367" | "5735813" | "5749857" | "5788654" | "5800395" | "5846226" | "5871470" | "5882342" | "5919172" | "5935108" | "5935113" | "5989220" | "6050976" | "6077244" | "6099504" | "6126641" | "6162195").PN. OR ("6398743").URPN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2020/06/10 06:46 PM
L272	18	L271 and ((blood or fluid$4) near4 (sequest$5 or flash$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/06/10 06:46 PM
L273	1	(15/893518).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2020/06/10 06:48 PM
L274	7050	(600/300).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2020/06/10 06:49 PM
L275	14	L274 and ((blood or fluid$4) near4 (sequest$5 or flash$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/06/10 06:49 PM
L276	1259	(600/583).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2020/06/10 06:51 PM
L277	7	L276 and ((blood or	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/06/10

		fluid$4) near4 (sequest$5 or flash$4))					06:51 PM
L278	1368	(604/164.01).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2020/06/10 06:52 PM
L279	135	L278 and ((blood or fluid$4) near4 (sequest$5 or flash$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/06/10 06:52 PM
L280	499	(435/294.1).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2020/06/10 07:08 PM
L281	3	L280 and ((blood or fluid$4) near4 (sequest$5 or flash$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/06/10 07:08 PM
L282	20	("2008/0145933").URPN.	(USPAT)	OR	ON	ON	2020/06/10 07:08 PM
L286	1	("10045704").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2020/06/10 08:56 PM
L287	1	("10143412").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/03/01 09:16 PM
L288	1	("10010282").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/03/01 09:17 PM
L289	100	((("ROGERS") near3 ("Bobby")) OR (("KANG") near3 ("Gino")) OR (("DETLOFF") near3 ("John"))).INV.	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/01 09:17 PM
L290	2	(15/140443).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/03/01 09:36 PM
L291	1	(15/855439).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/03/01 09:39 PM
L292	180	(("ROGERS") near3 ("Bobby")).INV.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2021/03/02 12:19 PM
L293	11	L292 and (blood near4 sequest$5)	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 12:20 PM
L294	2	(15/140443).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/03/02 12:47 PM
L295	1	(15/855439).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/03/02 12:49 PM
L296	1	("20020048170").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/03/02 01:36 PM
L297	1	("20040174525").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/03/02 01:49 PM
L298	1	("10045704").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/03/02 03:09 PM
L299	27321	(A61B5/150992 or A61B5/15003 or A61B5/150213 or A61B5/150389 or A61B5/150473 or A61B5/150572 or	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2021/03/02 03:17 PM

		A61B5/154 or A61B5/153 or A61M39/0693 or A61M39/04 or A61B5/150221 or A61M2039/0633 or A61M2039/0202 or A61M2039/068).cpc.					
L300	4594	L299 and ((blood or fluid$4) near4 (sequest$5 or sampl$4 or flash$4 or collect$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 03:27 PM
L301	3762	L300 and @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 03:28 PM
L302	257	L301 and (air near4 permeab$4)	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 03:29 PM
L303	420	L301 and ((air or gas$4) near4 permeab$4)	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 03:29 PM
L304	1	("20110167658").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/03/02 03:30 PM
L305	5	("2015/0306288").URPN.	(USPAT)	OR	ON	ON	2021/03/02 04:15 PM
L306	1	(16/208559).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/03/02 04:32 PM
L307	2	("2009/0043225").URPN.	(USPAT)	OR	ON	ON	2021/03/02 04:49 PM
L308	1736	(600/573).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2021/03/02 05:00 PM
L309	1363	L308 and ((blood or fluid$4) near4 (sequest$5 or sampl$4 or flash$4 or collect$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 05:00 PM
L310	73	L309 and ((air or gas$4) near4 permeab$4)	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 05:01 PM
L311	73	L310 and @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 05:01 PM
L312	812	(600/576).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/03/02 05:34 PM
L313	711	L312 and ((blood or fluid$4) near4 (sequest$5 or sampl$4 or flash$4 or collect$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 05:34 PM
L314	58	L313 and ((air or gas$4) near4 permeab$4)	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 05:34 PM
L315	58	L314 and @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 05:34 PM
L316	371	(600/577).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/03/02 05:42 PM
L317	277	L316 and ((blood or fluid$4) near4 (sequest$5 or sampl$4 or flash$4 or collect$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 05:42 PM

L318	20	L317 and ((air or gas$4) near4 permeab$4)	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 05:43 PM
L319	336	("2913000" | "3817240" | "3859998" | "3864979" | "4016879" | "4046144").PN. OR ("4207870").URPN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2021/03/02 05:44 PM
L320	210	L319 and ((blood or fluid$4) near4 (sequest$5 or sampl$4 or flash$4 or collect$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 05:44 PM
L321	196	L320 and @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 05:44 PM
L322	1259	(600/583).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/03/02 05:48 PM
L323	1208	L322 and ((blood or fluid$4) near4 (sequest$5 or sampl$4 or flash$4 or collect$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 05:48 PM
L324	73	L323 and ((air or gas$4) near4 permeab$4)	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 05:48 PM
L325	73	L324 and @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 05:49 PM
L326	1368	(604/164.01).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/03/02 05:59 PM
L327	271	L326 and ((blood or fluid$4) near4 (sequest$5 or sampl$4 or flash$4 or collect$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 06:00 PM
L328	10	L327 and ((air or gas$4) near4 permeab$4)	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 06:00 PM
L329	268	L327 and @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 06:00 PM
L330	182	(("ROGERS") near3 ("Bobby")).INV.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2021/07/08 02:22 PM
L331	27660	(A61B5/150992 or A61B5/15003 or A61B5/150213 or A61B5/150389 or A61B5/150473 or A61B5/150572 or A61B5/154 or A61B5/153 or A61M39/0693 or A61M39/04 or A61B5/150221 or A61M2039/0633 or A61M2039/0202 or A61M2039/068).cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2021/07/08 03:27 PM
L332	4684	L331 and ((blood or fluid$4) near4	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 03:28 PM

		(sequest$5 or sampl$4 or flash$4 or collect$4))					
L333	3769	L332 and @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 03:29 PM
L334	579	L333 and (vent$4 near4 air)	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 03:29 PM
L335	1	("9820682").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/07/08 03:54 PM
L336	1	("4207870").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/07/08 03:56 PM
L337	337	("2913000" | "3817240" | "3859998" | "3864979" | "4016879" | "4046144").PN. OR ("4207870").URPN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2021/07/08 04:19 PM
L338	211	L337 and ((blood or fluid$4) near4 (sequest$5 or sampl$4 or flash$4 or collect$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:19 PM
L339	196	L338 and @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:19 PM
L340	37	L339 and (vent$4 near4 air)	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:19 PM
L341	221	("20010021827" | "20020004650" | "20020055716" | "20020072715" | "20020103464" | "20020103465" | "20020107488" | "20020151856" | "20020193748" | "20030028171" | "20030036730" | "20030050608" | "20030055385" | "20030078544" | "20030093009" | "20030105414" | "20030114797" | "20030120222" | "20030176842" | "20030181873" | "20030191438" | "20030199827" | "20030216687" | "20030220614" | "20030229315" | "20030229316" | "20040024370" | "20040059302" | "20040092872" | "20040102740" | "20040111068" | "20040193120" |	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2021/07/08 04:21 PM

		"20040204681" | "20040210197" | "20050004524" | "20050059936" | "20050065482" | "20050124944" | "20050165353" | "20050187493" | "20050228345" | "20050245868" | "20050245869" | "20050245870" | "20050245879" | "20050245885" | "20050283093" | "20060015073" | "20060036217" | "20060036219" | "20060079847" | "20060129064" | "20060189934" | "20060189936" | "20060224122" | "20060270947" | "20060276756" | "20070021724" | "20070027430" | "20070106220" | "20070106224" | "20070167914" | "20070282275" | "20080015513" | "20080086085" | "20080177202" | "20080221528" | "20080269691" | "20080306452" | "20080319345" | "20080319346" | "20090204026" | "20090227896" | "20100063455" | "20100191189" | "20100262038" | "20110118674" | "4106497" | "4207870" | "4305406" | "4572210" | "4573976" | "4641663" | "4795443" | "4813426" | "4840619" | "4887998" | "4894055" | "4900307" | "4923477" | "4994046" | "5015241" | "5195985" | "5215534" | "5219333" | "5222502" | "5242417" | "5246428" | "5256153").PN. OR ("5295970" | "5295975"					

		| "5303713" | "5312372" | "5318547" | "5336199" | "5344408" | "5348544" | "5356392" | "5389085" | "5403286" | "5411492" | "5439449" | "5466223" | "5501675" | "5542932" | "5549558" | "5595566" | "5599313" | "5607402" | "5662617" | "5665075" | "5669889" | "5672161" | "5676658" | "5681295" | "5685855" | "5687740" | "5688241" | "5695474" | "5702369" | "5704920" | "5718239" | "5733265" | "5755522" | "5769826" | "5795336" | "5879337" | "5893845" | "5910130" | "5921964" | "5957892" | "5984899" | "6149629" | "6171284" | "6183445" | "6224576" | "6254575" | "6261263" | "6261265" | "6298541" | "6344032" | "6419658" | "6436086" | "6440104" | "6471677" | "6475191" | "6485469" | "6524277" | "6533760" | "6554807" | "6575939" | "6592556" | "6623456" | "6623461" | "6635032" | "6641555" | "6648855" | "6648856" | "6659983" | "6695819" | "6699217" | "6712792" | "6716199" | "6761704" | "6773419" | "6780169" | "6805689" | "6811545" | "6835190" | "6837877" | "6846302" | "6860872" | "6869415" | "6905483" | "6918891" | "6958054" | "6974423" | "6984223" | "6997913" | "7001363" | "7083600" | "7101355" | "7128726" | "7147624" | "7160267" | "7163526" | "7201740" | "7211065" | "7223258" | "7226432" | "7361159" | "7396343" | "7428773" | "7524308" | "7537581" | "7670320" | "7727190" | "7766879" | "7938808" | "8066679" | "8282605" | "8795198" | "D422700" | "D442280" | "D604836" | "D604837"					

		| "D604838" | "D604839" | "D605287" | "RE35539" | "RE43473").PN. OR ("9615783").URPN.					
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L343	148	("20020193748" | "20030105414" | "20030229315" | "20040059302" | "20040092872" | "20050004524" | "20050187493" | "20050245868" | "20050245869" | "20050245870" | "20050245885" | "20060036219" | "20070106220" | "20070167914" | "20080086085" | "20080177202" | "4106497" | "4207870" | "4305406" | "4573976" | "4641663" | "4795443" | "4840619" | "4894055" | "4900307" | "4994046" | "5015241" | "5195985" | "5215534" | "5222502" | "5242417" | "5256153" | "5295970" | "5303713" | "5312372" | "5336199" | "5348544" | "5356392" | "5411492" | "5439449" | "5466223" | "5501675" | "5542932" | "5672161" | "5676658" | "5702369" | "5704920" | "5755522" | "5984899" | "6149629" | "6261263" | "6298541" | "6436086" | "6440104" | "6524277" | "6533760" | "6592556" | "6623456" | "6635032" | "6648855" | "6699217" | "6712792" | "6780169" | "6837877" | "6869415" | "6984223" |	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2021/07/08 04:21 PM

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L344	41	("2735430" | "2798487" | "3187749" | "3240209" | "3585984" | "3817240" | "4166450" | "4207870" | "4295477" | "4312362").PN. OR ("4436098").URPN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2021/07/08 04:22 PM
L345	163	L341 and ((blood or fluid$4) near4 (sequest$5 or sampl$4 or flash$4 or collect$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:22 PM
L346	163	L345 and @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:23 PM
L347	22	("2005/0283093").URPN.	(USPAT)	OR	ON	ON	2021/07/08 04:23 PM
L348	163	L345 and ((blood or fluid$4) near4 (sequest$5 or sampl$4 or flash$4 or collect$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:27 PM
L349	163	L348 and @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:27 PM
L350	1736	(600/573).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2021/07/08 04:37 PM
L351	1363	L350 and ((blood or fluid$4) near4 (sequest$5 or sampl$4 or flash$4 or collect$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:37 PM
L352	1346	L351 and @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:38 PM
L353	136	L352 and (vent$4 near4 air)	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:38 PM
L354	812	(600/576).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/07/08 04:41 PM
L355	711	L354 and ((blood or fluid$4) near4 (sequest$5 or sampl$4 or flash$4 or collect$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:41 PM
L356	699	L355 and @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:41 PM
L357	123	L356 and (vent$4 near4 air)	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:41 PM
L358	371	(600/577).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/07/08 04:44 PM
L359	277	L358 and ((blood or fluid$4) near4 (sequest$5 or sampl$4	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:45 PM

		or flash$4 or collect$4))					
L360	260	L359 and @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:45 PM
L361	1259	(600/583).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/07/08 04:46 PM
L362	1208	L361 and ((blood or fluid$4) near4 (sequest$5 or sampl$4 or flash$4 or collect$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:46 PM
L363	1194	L362 and @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:47 PM
L364	1194	L363 and @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:47 PM
L366	1	("9820682").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/02 03:05 PM
L367	319	((("BULLINGTON") near3 ("Gregory")) OR (("PATTON") near3 ("Richard")) OR (("MIAZGA") near3 ("Jay")) OR (("GAW") near3 ("Shan"))).INV.	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2022/02/02 03:14 PM
L368	1	(16/376745).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/02 03:35 PM
L369	190	(("ROGERS") near3 ("Bobby")).INV.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2022/02/02 03:36 PM
L370	2	(15/140448).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/02 03:41 PM
L371	1	("9820682").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/02 03:42 PM
L372	1	("9060725").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/02 03:42 PM
L373	1	("9060724").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/02 03:43 PM
L374	1	("9022950").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/02 03:45 PM
L375	1	("9022951").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/02 03:45 PM
L376	1	("10292633").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/02 03:46 PM
L377	1	("10433779").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/02 03:47 PM
L378	1	("10436554").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/02 03:48 PM
L379	1	("10736554").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/02 03:49 PM
L380	1	("10912506").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/02 03:49 PM
L381	1	("10010282").PN.	(US-PGPUB; USPAT;	OR	OFF	OFF	2022/02/02

			USOCR)				03:49 PM
L382	1	(16/376745).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/02 03:50 PM
L383	1	("9820682").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/02 03:51 PM
L384	276	(600/579).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/02 03:52 PM
L385	204	L384 and @ad<"20120530"	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/02/02 03:53 PM
L386	37427	(A61B5/150221 or A61B5/15003 or A61B5/150236 or A61B5/150244 or A61B5/150251 or A61B5/150389 or A61B5/150503 or A61B5/150992 or A61B5/153 or A61B5/155 or A61B10/0048 or A61B10/0051 or A61B10/007 or A61B2010/0061 or A61B2010/0077 or A61B2010/008).cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2022/02/02 04:35 PM
L387	7279	L386 and ((blood or fluid$4) near4 (sequest$5 or sampl$4 or flash$4 or collect$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/02/02 04:36 PM
L388	4442	L387 and @ad<"20120530"	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/02/02 04:36 PM
L389	874	L388 and (seal$4 near4 (member or mechanism$4 or vent$4 or elastic$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/02/02 04:38 PM
L390	26	("2008/0145933").URPN.	(USPAT)	OR	ON	ON	2022/02/02 04:52 PM
L391	44	("2008/0319346").URPN.	(USPAT)	OR	ON	ON	2022/02/02 04:59 PM
L392	385	L386 and ((blood or fluid) near4 (seal$4 near4 (member or mechanism$4 or vent$4 or elastic$4)))	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/02/02 05:28 PM
L393	171	L392 and @ad<"20120530"	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/02/02 05:28 PM
L394	355	(604/103).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/02 05:52 PM
L395	7	L394 and ((blood or fluid) near4 (seal$4 near4 (member or mechanism$4 or vent$4 or elastic$4)))	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/02/02 05:52 PM

L396	1	(16/328127).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/03 12:00 PM
L397	0	"1020130062845"	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/02/04 04:17 PM
L398	8	"20130062845"	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/02/04 04:17 PM
L399	14	"2013021595"	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/02/04 04:18 PM
L400	2	(14/055232).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/04 07:10 PM
L401	1	(15/746656).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/05 11:48 AM
L402	0	(17/388440).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/07 09:34 AM
L403	1	("20050048465").PN.	(US-PGPUB; USPAT)	OR	ON	ON	2022/02/07 09:34 AM
L404	196	(("ROGERS") near3 ("Bobby")).INV.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2022/05/18 03:08 PM
L405	16	L404 and (blood near4 sequest$5)	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/05/18 03:08 PM
L406	16	L404 and ((blood or chamber) near4 sequest$5)	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/05/18 03:08 PM
L407	16	L406 and (junct$4 or bypass$4)	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/05/18 03:09 PM
L408	16	L406 and junct$4	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/05/18 03:09 PM
L409	22445	(A61B5/150992 or A61B5/15003 or A61B5/150213 or A61B5/150221 or A61B5/150389 or A61B5/150473 or A61B5/150572 or A61B5/154 or A61B5/15074).cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2022/05/18 03:54 PM
L410	4525	L409 and ((blood or fluid$4) near4 (sequest$5 or sampl$4 or flash$4 or collect$4 or flush$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/05/18 03:55 PM
L411	3810	L410 and @ad<"20170210"	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/05/18 03:56 PM
L412	820	L411 and ((vent$4 or	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/05/18

		open$4 or apertur$4) near4 air)					03:57 PM
L413	22445	(A61B5/150992 or A61B5/15003 or A61B5/150213 or A61B5/150221 or A61B5/150389 or A61B5/150473 or A61B5/150572 or A61B5/154 or A61B5/15074).cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2022/05/18 05:51 PM
L414	4603	L413 and ((blood or fluid$4 or chamber) same (sequest$5 or sampl$4 or flash$4 or collect$4 or flush$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/05/18 05:51 PM
L415	511	L414 and ((junct$4 or bypass$4 or divert$4) near4 (blood or fluid))	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/05/18 05:52 PM
L416	355	L415 and @ad<"20170210"	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/05/18 05:53 PM
L417	1	(16/819033).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/05/18 06:10 PM
L418	1	(17/094692).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/05/18 06:25 PM
L419	1	(17/538990).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/05/18 06:25 PM
L420	1	("11311219").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/05/18 06:27 PM
L421	1	("11185266").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/05/18 06:30 PM
L422	1	("10143412").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/05/18 06:31 PM
L423	1	("9820682").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/05/18 06:32 PM
L424	252	(("ROGERS") near3 ("Bobby")).INV.	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2022/10/13 01:41 PM
L425	38	424 AND (closur$4 OR enclos$4)	(US-PGPUB; USPAT)	OR	ON	ON	2022/10/13 01:42 PM

L426	42781	(A61B5/150213 OR A61B5/15003 OR A61B5/150221 OR A61B5/150251 OR A61B5/150732 OR A61B5/15074 OR A61B5/150992 OR A61B5/153 OR A61B5/150389 OR A61B5/150503).cpc.	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/10/13 01:47 PM
L427	5205	426 AND @ad<"20170210"	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/10/13 01:50 PM
L428	4803	427 AND ((blood OR fluid$4) near4 (sequest$5 OR sampl$4 OR flash$4 OR collect$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/10/13 01:51 PM
L429	519	428 AND ((closur$4 OR enclos$4 OR pug$4) near5 (vent OR open$4 OR air))	(US-PGPUB; USPAT)	OR	ON	ON	2022/10/13 01:54 PM
L430	169	"5749857"	(US-PGPUB; USPAT)	OR	ON	ON	2022/10/13 02:14 PM
L431	1	("5749857").pn.	(US-PGPUB; USPAT)	OR	ON	ON	2022/10/13 02:14 PM
L432	346	427 AND ((junct$4 OR bypass$4 OR divert$4) near4 (blood OR fluid))	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/10/13 02:18 PM
L433	186	("3500828" | "3670729" | "3714945" | "3977400" | "3994293" | "3995619" | "4106491" | "4200096" | "4468224" | "4531987" | "4549554" | "4735215" | "4828548" | "4874373" | "4893635" | "4894052" | "4907599" | "4944308" | "4994042" | "5129884" | "5400798").pn. OR ("5749857").urpn. AND (PGPB | USPT | USOC).dbnm.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/10/13 02:32 PM
L434	124	433 AND ((blood OR fluid$4) near4 (sequest$5 OR sampl$4 OR flash$4 OR collect$4 OR optimiz$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/10/13 02:34 PM
L435	1	("5749857").pn.	(US-PGPUB; USPAT)	OR	ON	ON	2022/10/13

							02:34 PM
L436	1	17/138056	(US-PGPUB; USPAT)	OR	ON	ON	2022/10/19 11:35 AM
L437	253	(("ROGERS") near3 ("Bobby")).INV.	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2022/11/16 03:25 PM
L438	39	437 AND (closur$4 OR enclos$4)	(US-PGPUB; USPAT)	OR	ON	ON	2022/11/16 03:25 PM
L439	35391	(A61B5/150992 OR A61B5/15003 OR A61B5/150213 OR A61B5/150221 OR A61B5/150389 OR A61B5/150473 OR A61B5/150572 OR A61B5/154 OR A61B5/15074).cpc.	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2022/11/16 03:46 PM
L440	4100	439 AND @ad<"20170210"	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/11/16 03:48 PM
L441	3875	440 AND ((blood OR fluid$4 OR urine) SAME (sequest$5 OR sampl$4 OR flash$4 OR collect$4 OR optimiz$5))	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/11/16 03:49 PM
L442	368	441 AND ((junct$4 OR bypass$4 OR divert$4) near5 (blood OR fluid OR urine))	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/11/16 03:50 PM
L443	7	"10827964"	(US-PGPUB; USPAT)	OR	ON	ON	2022/11/16 04:13 PM
L444	1	16/819033	(US-PGPUB; USPAT)	OR	ON	ON	2022/11/16 04:48 PM
L445	359	"4207870"	(US-PGPUB; USPAT)	OR	ON	ON	2022/11/16 05:07 PM

L446	1	("4207870").pn.	(US-PGPUB; USPAT)	OR	ON	ON	2022/11/16 05:07 PM
L447	3814	440 AND ((blood OR fluid$4 OR urine) near5(sequest$5 OR sampl$4 OR flash$4 OR collect$4 OR optimiz$5))	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/11/16 05:17 PM
L448	366	447 AND ((junct$4 OR bypass$4 OR divert$4) near5 (blood OR fluid OR urine))	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/11/16 05:17 PM
L449	89	(("ROGERS") near3 ("Bobby")).INV.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2023/04/11 01:13 PM
L450	24	449 AND ((blood OR fluid$4 OR urine) near5(sequest$5 OR sampl$4 OR flush$4 OR collect$4 OR optimiz$5or flash$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/04/11 01:14 PM
L451	24	449 AND ((blood OR fluid$4 OR urine) near5(sequest$5 OR sampl$4 OR flush$4 OR collect$4 OR optimiz$5 OR flash$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/04/11 01:14 PM
L452	6634	(A61B5/150213 OR A61B5/15003 OR A61B5/150221 OR A61B5/150251 OR A61B5/150732 OR A61B5/15074 OR A61B5/150992 OR A61B5/153 OR A61B5/150389 OR A61B5/150503).cpc.	(US-PGPUB; USPAT)	OR	ON	ON	2023/04/11 01:32 PM
L453	5326	452 AND @ad<"20170210"	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/04/11 01:32 PM
L454	4928	453 AND ((blood OR fluid$4 OR urine) near5(sequest$5 OR sampl$4 OR flush$4 OR collect$4 OR optimiz$5 OR flash$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/04/11 01:32 PM
L455	371	454 AND ((junct$4 OR bypass$4 OR divert$4) near5 (blood OR fluid OR urine))	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/04/11 01:33 PM
L456	11	("2016/0361006").urpn. AND (PGPB | USPT | USOC).dbnm.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2023/04/11 03:03 PM
L457	1	17/094692	(US-PGPUB; USPAT)	OR	ON	ON	2023/04/11 03:11 PM
L458	49	("20020004647"|"20030	(US-PGPUB; USPAT)	OR	ON	ON	2023/04/11

		105414"|"20040054333"|"20040073171"|"20040147855"|"20050004524"|"20050240161"|"20070083162"|"20070088279"|"20080086085"|"20080145933"|"20080167577"|"20080319346"|"20100010372"|"20100057004"|"20120016266"|"20130317391"|"20160008579"|"20160174888"|"3741197"|"3817240"|"3874367"|"3886930"|"4057050"|"4106497"|"4154229"|"4207870"|"4412548"|"4436098"|"4444203"|"5222502"|"5520193"|"5749857"|"6398743"|"6569117"|"8197420"|"8523826"|"8535241"|"8540663"|"8568371"|"8603009"|"8864684"|"9022950"|"9022951"|"9060724"|"9138572"|"9155495"|"9204864"|"9877675").PN.					03:18 PM
L459	13	458 AND ((junct$4 OR bypass$4 OR divert$4) near5 (blood OR fluid OR urine))	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/04/11 03:18 PM
L460	155	("2707953" | "2992974" | "3013557" | "3098016" | "3382865" | "3405706" | "3494351" | "3577980" | "3635798" | "3648684" | "3848579" | "3890203" | "3937211" | "4057050" | "4133863" | "4166450" | "4340067" | "4370987" | "4425235" | "4444203" | "4459997" | "4509534" | "4657160" | "4676256" | "4865583" | "4890627" | "4988339" | "5009847" | "5097842" | "5108927" | "5122129" | "5269317" | "5330464" | "5360011" | "5429610" | "5450856" | "5454786" | "5485854" | "5507299" | "5577513" | "5762633" | "5865812" | "5882318" | "5922551" | "6016712" | "6057105" | "6159164" | "6210909" | "6328726" | "6364890" | "6387086" | "6403381"	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2023/04/11 03:21 PM

		| "6520948" | "6626884" | "6692479" | "6716187" | "6746420" | "6913580" | "7044941" | "7087047" | "7335188" | "7384416" | "7744573" | "8197420" | "8231546" | "8337418" | "8535241" | "8647286" | "8864684" | "8876734" | "20020002349" | "20020183651" | "20030055381" | "20030208151" | "20040010228" | "20040054283" | "20040054333" | "20040147855" | "20050004524" | "20050240161" | "20050245885" | "20050281713" | "20060287639" | "20080108954" | "20080145933" | "20100152681" | "20120095367" | "20120215131" | "20130079604" | "20130116599" | "20130317391" | "20140081172").pn. OR ("9060724").urpn. AND (PGPB | USPT | USOC).dbnm.					
L461	31	("2008/0145933").urpn. AND (PGPB | USPT | USOC).dbnm.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2023/04/11 03:30 PM
L462	1	("5749857").pn.	(US-PGPUB; USPAT)	OR	ON	ON	2023/04/11 03:46 PM
L463	13	459 AND ((junct$4 OR bypass$4 OR divert$4) near5 (blood OR fluid OR urine))	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/04/11 03:47 PM
L464	4994	453 AND ((blood OR fluid$4 OR urine OR semen) SAME (sequest$5 OR sampl$4 OR flush$4 OR collect$4 OR optimiz$5 OR flash$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/04/11 03:58 PM
L465	968	464 AND ((junct$4 OR bypass$4 OR diver$5) SAME (blood OR fluid OR urine OR semen))	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/04/11 03:59 PM
L466	707	465 AND housing	(US-PGPUB; USPAT)	OR	ON	ON	2023/04/11 04:50 PM

L467	2911	464 AND ((blood OR fluid$4 OR urine OR semen) near5 (first OR second OR subsequent$4 OR bypass))	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/04/11 04:52 PM
L468	2954	464 AND ((blood OR fluid$4 OR urine OR semen) near5 (first OR second OR subsequent$4 OR convey$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/04/11 04:52 PM
L469	2891	464 AND ((blood OR fluid$4 OR urine OR semen) near5 (first OR second OR subsequent$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/04/11 04:52 PM
L470	790	469 AND ((junct$4 OR bypass$4 OR diver$5) SAME (blood OR fluid OR urine OR semen))	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/04/11 04:53 PM
L471	1	17/538990	(US-PGPUB; USPAT)	OR	ON	ON	2023/05/08 12:35 PM
L472	164	(("ROGERS") near3 ("Bobby")).INV.	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2023/05/08 02:18 PM
L473	1	("4207870").pn.	(US-PGPUB; USPAT)	OR	ON	ON	2023/05/08 03:23 PM
L474	1	("10827964").pn.	(US-PGPUB; USPAT)	OR	ON	ON	2023/05/08 03:31 PM
L475	1	("11311219").pn.	(US-PGPUB; USPAT)	OR	ON	ON	2023/05/08 03:32 PM
L476	1	"17094692"	(US-PGPUB; USPAT)	OR	ON	ON	2023/05/08 03:34 PM
L477	2	"17730118"	(US-PGPUB; USPAT)	OR	ON	ON	2023/05/08 03:34 PM
L478	1	("10012828").pn.	(US-PGPUB; USPAT)	OR	ON	ON	2023/05/08 03:36 PM
L479	1	("10010282").pn.	(US-PGPUB; USPAT)	OR	ON	ON	2023/05/08 03:36 PM
L480	48138	(A61B5/150992 OR A61B5/15003 OR	(US-PGPUB; USPAT; USOCR; FIT (AU, AP,	OR	ON	ON	2023/05/08 03:59 PM

		A61B5/150213 OR A61B5/150221 OR A61B5/150389 OR A61B5/150473 OR A61B5/150572 OR A61B5/153 OR A61B5/154 OR A61M39/04 OR A61M39/0693 OR A61M2039/0202 OR A61M2039/0633 OR A61M2039/068).cpc.	AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT; IBM_TDB)				
L481	5081	480 AND @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/05/08 04:15 PM
L482	3947	481 AND ((blood OR fluid$4 OR urine) near5(sequest$5 OR sampl$4 OR flush$4 OR collect$4 OR optimiz$5 OR flash$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/05/08 04:17 PM
L483	1	17/538990	(US-PGPUB; USPAT)	OR	ON	ON	2023/05/08 04:17 PM
L484	1069	482 AND (air near5 (filter$4 OR material$4 OR membrane OR permeab$4 OR vent$4))	(US-PGPUB; USPAT)	OR	ON	ON	2023/05/08 04:32 PM
L485	203	("3500828" | "3670729" | "3714945" | "3977400" | "3994293" | "3995619" | "4106491" | "4200096" | "4468224" | "4531987" | "4549554" | "4735215" | "4828548" | "4874373" | "4893635" | "4894052" | "4907599" | "4944308" | "4994042" | "5129884" | "5400798").pn. OR ("5749857").urpn. AND (PGPB | USPT | USOC).dbnm.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2023/05/08 04:51 PM
L486	606	484 AND ((pressure OR vacuum) near5 (draw OR forc$4 OR withdraw OR flow$4)) SAME (blood OR fluid)	(US-PGPUB; USPAT)	OR	ON	ON	2023/05/08 05:32 PM
L487	24	("2010/0057004").urpn. AND (PGPB | USPT | USOC).dbnm.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2023/05/08 05:35 PM
L488	3	487 AND @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/05/08 05:55 PM
L489	49	((US-20080319346-A1 OR US-20100057004-	(US-PGPUB; USPAT; USOCR; FIT (AU, AP,	OR	ON	ON	2023/05/08 06:07 PM

		A1 OR US-20070088279-A1 OR US-20080145933-A1 OR US-20040054333-A1 OR US-20100010372-A1 OR US-20080167577-A1 OR US-20080086085-A1 OR US-20070083162-A1 OR US-20160008579-A1 OR US-20120016266-A1 OR US-20130317391-A1 OR US-20160174888-A1 OR US-20050240161-A1 OR US-20040147855-A1 OR US-20040073171-A1 OR US-20050004524-A1 OR US-20030105414-A1 OR US-20020004647-A1).did. AND PGPB.dbnm.) OR ((US-4412548-A OR US-5222502-A OR US-5520193-A OR US-9022951-B2 OR US-6569117-B1 OR US-3741197-A OR US-8603009-B2 OR US-4207870-A OR US-9877675-B2 OR US-4444203-A OR US-6398743-B1 OR US-9022950-B2 OR US-9155495-B2 OR US-4436098-A OR US-9138572-B2 OR US-8568371-B2 OR US-8540663-B2 OR US-8523826-B2 OR US-8197420-B2 OR US-4057050-A OR US-8864684-B2 OR US-8535241-B2 OR US-5749857-A OR US-9060724-B2 OR US-9204864-B2 OR US-3817240-A OR US-3874367-A OR US-3886930-A OR US-4106497-A OR US-4154229-A).did. AND USPT.dbnm.)	AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT; IBM_TDB)				
L490	25	489 AND (air near5 (filter$4 OR material$4	(US-PGPUB; USPAT)	OR	ON	ON	2023/05/08 06:07 PM

		OR membrane OR permeab$4 OR vent$4))					
L491	204	482 AND (hous$4 SAME (inlet AND outlet AND channel))	(US-PGPUB; USPAT)	OR	ON	ON	2023/05/08 06:29 PM
L492	118	491 AND (hous$4 near5 ((top OR upper) AND (lower OR bottom)))	(US-PGPUB; USPAT)	OR	ON	ON	2023/05/08 06:33 PM
L493	1	489 AND (hous$4 near5 ((top OR upper) AND (lower OR bottom)))	(US-PGPUB; USPAT)	OR	ON	ON	2023/05/08 06:39 PM
L494	0	489 AND (hous$4 near5 ((top OR upper) SAME (lower OR bottom)))	(US-PGPUB; USPAT)	OR	ON	ON	2023/05/08 06:39 PM
L495	27	492 AND (hous$4 near5 ((top OR upper) SAME (lower OR bottom)))	(US-PGPUB; USPAT)	OR	ON	ON	2023/05/08 06:39 PM
L496	172	484 AND (hous$4 near5 ((top OR upper) SAME (lower OR bottom)))	(US-PGPUB; USPAT)	OR	ON	ON	2023/05/08 06:41 PM

PE2E SEARCH - Search History (Interference)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	British Equivalents	Time Stamp
N94	1	(port and sequest$5 and junction and chamber and sampl$4 and vent and barrier).clm.	(US-PGPUB; USPAT)	OR	OFF	OFF	2017/09/28 04:15 PM
N112	3	(port and sequest$5 and chamber and sampl$4 and vent and barrier).clm.	(US-PGPUB; USPAT)	OR	OFF	OFF	2018/01/09 05:39 PM
N248	4	(blood and fluid$4 and inlet and outlet and port and reservoir and allow and initial$4 and sequest$5).clm.	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 03:30 PM
N249	4	(blood and fluid$4 and inlet and outlet and port and reservoir and allow$4 and initial$4 and sequest$5).clm.	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 03:30 PM
N250	495	(blood and fluid$4 and allow$4 and initial$4).clm.	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 03:31 PM
N251	107	(blood and fluid$4 and	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16

		allow$4 and initial$4 and subsequent$4).clm.					03:31 PM
N283	9	((blood or fluid$4) and sequestrat$4 and chamber and sampl$4 and vent$4 and air$4).clm.	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/06/10 06:31 PM
N284	530	((blood or fluid$4) and chamber and sampl$4 and vent$4 and air$4).clm.	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/06/10 06:31 PM
N285	84	((blood or fluid$4) and chamber and cap and sampl$4 and vent$4 and air$4).clm.	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/06/10 06:32 PM
N365	6	(port and sequest$5 and junction and chamber and sampl$4 and vent and barrier).clm.	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:49 PM
N366	9	(blood AND fluid$4 AND inlet AND outlet AND junct$4 AND inhibit$4).clm.	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/11/16 05:31 PM
N367	84	((blood OR fluid$4) AND chamber AND sampl$4 AND junction AND (inhibit$4 OR prevent$4)).clm.	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/11/16 05:36 PM
N368	25	(blood AND chamber AND sampl$4 AND junction AND inlet AND outlet AND port AND first).clm.	(US-PGPUB; USPAT)	OR	ON	ON	2023/04/11 04:48 PM
N369	4	(blood AND chamber AND sampl$4 AND junction AND inlet AND outlet AND port AND first AND hous$4 AND subsequent).clm.	(US-PGPUB; USPAT)	OR	ON	ON	2023/04/11 04:49 PM
N370	64902	"465" AND housing	(US-PGPUB; USPAT)	OR	ON	ON	2023/04/11 04:50 PM

PTO/SB/08a (02-18)
Approved for use through 11/30/2020. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	18113710
Filing Date	2023-02-24
First Named Inventor	Bobby E. ROGERS
Art Unit	-
Examiner Name	
Attorney Docket Number	069366-0574153_KUR2C04US

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Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
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Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2] i	Kind Code[4]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear	T[5]
	1							

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	18113710
	Filing Date	2023-02-24
	First Named Inventor	Bobby E. ROGERS
	Art Unit	-
	Examiner Name	
	Attorney Docket Number	069366-0574153_KUR2C04US

	1	Ziegler, R., et al. "Controlled Clinical Laboratory Comparison of Two Supplemented Aerobic and Anaerobic Media Used in Automated Blood Culture Systems to Detect Bloodstream Infections," Journal of Clinical Microbiology, Mar. 1998, p. 657-661.	
	2	Pall Medical, "Leukotrap Filtration Systems for Whole Blood Derived Platelets, Leukotrap RC PL and Leukotrap PL Systems" literature, (2005) 8 pages.	
	3	Meissner, George F. , et al., "The Standard Clotting Time, A Method Based on the Use of Whole Venous Blood in Capillary Tubes," The American Journal of Clinical Pathology, Vol. 39, No. 3., pp. 321-323, March 1963.	
	4	Mayer, G.A. "A Method for the Reliable Determination of Clotting Time in Whole Blood," Canadian Medical Association Journal, June 15, 1955, Vol. 72, Pages 927-929.	

If you wish to add additional non-patent literature document citation information please click the Add button Add

EXAMINER SIGNATURE

Examiner Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. [2] Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). [3] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [4] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [5] Applicant is to place a check mark here if English language translation is attached.

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	18113710
	Filing Date	2023-02-24
	First Named Inventor	Bobby E. ROGERS
	Art Unit	-
	Examiner Name	
	Attorney Docket Number	069366-0574153_KUR2C04US

CERTIFICATION STATEMENT

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

OR

☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

See attached certification statement.

The fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

☒ A certification statement is not submitted herewith.

SIGNATURE

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

Signature	/Benjamin F. Hudson/	Date (YYYY-MM-DD)	2023-05-10
Name/Print	Benjamin F. Hudson	Registration Number	71,474

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majority of cases this is not necessary and is better not done, for reasons to be mentioned later. In most cases the herniated part of the disc lies medial to the affected nerve root, so the nerve is carefully taken medially over the herniation until the disc is sufficiently exposed. Epidural bleeding, if present, is checked by placing small pieces of wet cotton below and above the disc in the epidural space. After this, the herniated disc is removed by incision and extraction in the usual manner.

DISC REMOVAL

We have the impression that many surgeons try to remove too much disc tissue. We are not in favour of this. It is necessary to remove the extruded part of the ring cartilage, and it is advisable to remove some nuclear tissue as well, but it is not recommended that as much tissue as possible be removed. The nucleus pulposus will dry and shrink rapidly after operation, and ingrowing fibrous tissue will make a recurrence of this part of the disc herniation very unlikely. In the majority of recurrences, the cause of the pain is not a new herniation, but rather the occurrence of scar tissue at the operative site, or nerve damage during operation. Of the ring cartilage, only the herniated part should be removed; the rest cannot be reached adequately, and, unless bony fusion of the spine is performed, it is better to leave as much ring cartilage as possible to give more support. Also, removal of nearly the whole disc is inadvisable without foraminotomy. The same holds true for scraping the cartilage of the vertebral bodies and crushing the intravertebral articulation. None of these procedures should be done unless fusion of the spinal column is performed.

When a definite disc herniation is found and there is no clinical or roentgenological evidence of a rupture at a lower or higher level, we end the operation by apposing the muscles and fascia with interrupted sutures, a running suture being used for the skin. Before closing, however, the patient is asked to move his back and legs, and to cough and strain; when all this causes none of the pain that it did before operation, it may be concluded that the operation has been successful, and that no pressure is left on the freed nerve root or at any other level. In this clinical testing on the operating table lies the third advantage of local anæsthesia.

When no herniation is found, we explore the higher and lower discs as indicated, and if there is no evident herniation we inject one c.c. of absolute alcohol into the suspected disc, to obtain shrinkage of the nucleus.

With the above technique, the great majority of cases can be operated on within thirty minutes. The short time of operation is important because the patient is under local anæsthesia, and also this short period may be significant in preventing infection of the disc, of which several cases have been reported in the recent literature. An intravenous drip or blood transfusion is never necessary.

With this technique we have obtained a complete cure (that is, no complaints, and return to former occupation) in 75% of cases, according to a follow-up study of 125 cases five years after operation.

SUMMARY

A technique for herniated disc removal is described using local anæsthesia. We believe the advantages of this technique are simplicity, less bleeding, a safeguard against nerve root damage, and the possibility of checking the operative result during the operation.

A METHOD FOR THE RELIABLE DETERMINATION OF CLOTTING TIME IN WHOLE BLOOD*

G. A. MAYER, M.D.,† *Kingston, Ont.*

THE INVESTIGATION of the clotting time of whole blood has for a long time been a routine procedure in medical practice. Though clotting-time values in health and in various pathological conditions are recorded in many textbooks and publications, these observations are difficult to interpret because different and not properly standardized techniques are used. Even the well known and widely used Lee-White method[1] has been shown to give varying results due to subjective differences in the performance of the test.[2]

In a preliminary study of the Lee-White method we noted differences up to ±40% in parallel determinations when the test was performed by different interns and technicians following the instructions of different textbooks. In the hands of the author, even under the most rigidly standardized conditions the Lee-White method showed a standard error of ±14%. Since errors and differences in the technique occur easily and frequently, not only in routine work but also in research, we can understand how difficult is the proper interpretation of the clotting-time data in different reports.

A rigorously standardized technique may improve the Lee-White method, but this can be achieved only by long training and a special study of the problem; it is unlikely that in routine

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work this improved accuracy can be attained. In spite of high degrees of skill, the technical error is high.

This indicated to us the necessity of finding a method which has fewer sources of error and can be performed easily with a high degree of accuracy by an average technician. After careful study of all sources of error in the different methods, we adopted the following procedure to obtain reliable and accurate clotting-time values.

MATERIALS

1. 10 ml. all-glass syringe (preferably with Luer-lock).
2. Sharp 21-gauge needle with short bevel.
3. Three-way stop cock (optional). (Items 1 to 3 are autoclaved for each determination.)
4. Glass capillary tubes of 100 mm. length and of 1.6 to 1.8 mm. diameter. One end of each tube is marked with a small piece of adhesive tape.
5. Plasticine.
6. Stop-watch.
7. A large thermos-flask with rubber cork for a water-bath.

Since this type of flask is available only without an insulating and protective case, an aluminium pail of adequate size with a carrying handle should be made by a plumber. This water-bath can be carried easily to the bedside. Some fibre-glass insulating material should be placed between the thermos-flask and its container. The flask is filled with about three litres of water at 21° C. The temperature of the water will be constant for three to five hours when the external environmental temperature is between 15 and 28° C. The temperature of the water should be checked every hour and if necessary should be adjusted with cold or hot water. To prevent sinking of the capillary tubes to the bottom, we constructed a simple rack of hard-rubber tubes, wire, and a foam-rubber plate to fit in the flask. The flat top of the rack is about 2 cm. under the water level. With this arrangement we can take out the tubes easily without immersing our hands in the water-bath.

The temperature of the water-bath should be checked with an accurate mercury thermometer.

METHOD

(1) After application of a tourniquet to the arm a neat venipuncture is made and approximately 5 to 8 ml. of blood drawn slowly into the syringe. This blood washes out from the needle the tissue juice which might have been picked up during the stab. Since the blood in the syringe is not used for the test, the admixture of tissue juice with the tested blood is practically eliminated.

(2) For filling the capillary tubes we have two equally good techniques:

(a) After disconnecting the syringe but leaving the needle *in situ*, the end of a capillary tube is introduced into the butt of the needle and filled with blood. Since for later handling it is important to be sure which end of the capillary tube the blood entered first, we recommend marking the opposite end with adhesive tape.

(b) If we do not wish to discard the blood drawn into the syringe (which may be important in small animal experiments, where a 5 to 8 ml. blood-loss is considerable), we can use the three-way stop-cock between the needle and the syringe. We draw the blood into the syringe, and then switch the stop-cock between the needle and the third side opening, and through this we collect the first blood drops in the capillary tube. By switching back we connect the needle with the syringe and reinject the blood into the vein.

(3) The stop-watch is started when the blood enters the capillary tube.

(4) Both ends of the capillary are sealed immediately with plasticine, and placed horizontally in the water-bath.

(5) After three or four minutes, small pieces should be broken off every 30 seconds from the end which the blood entered first (opposite the tag). After each break the capillary should be resealed and replaced in the water-bath.

The breaking of the capillary tubes needs some skill. A brisk movement may cut the first fragile fibrin thread. To avoid this we suggest holding the capillary tube with the index fingers and thumbs of both hands, keeping these four fingers tightly together and breaking only in this position. This will prevent too brisk a separation of the broken parts and the cutting of the fibrin thread by the sharp glass edges. It is also important to have a clear white background (sheet of white paper) to be able to see the first very thin fibrin strand.

(6) The end-point is marked by the presence of a white thin fibrin thread 2 cm. in length. As the earliest fibrin can be detected at the end of the capillary tube where the blood entered, it is important to start breaking at this end. The first fibrin thread is very fragile and breaks easily. In 20 to 30 seconds its resistance increases and one can draw longer and longer threads. When a 2 cm. thread can be drawn without disruption the arbitrary end-point has been reached. The fibrin thread is first a yellowish translucent filament. After the end-point has been reached, it is covered with little beads of blood, and later the whole blood is clotted and can be pulled out of the tube. The blood droplets on the filament signify that our arbitrary end-point is just passed, while the thick blood clot signifies considerable overtime.

When the clotting time is elevated, fibrin formation is slower. Two to four minutes may elapse between the first sign of fibrin formation and the end-point.

DISCUSSION

(1) In accordance with other workers[1, 3, 4] we have found that the major source of error in the different clotting-time methods is the mixture of tissue juice with the blood. This error in technique occurs frequently and results in erroneous readings. In our procedure this source of error is easily avoided; the first 5 to 8 ml. of blood are not used and the blood passing out of the needle afterwards is relatively free of disturbing tissue juice.

(2) Since the coagulation of blood involves stoichiometric and enzymatic reactions, it is obvious that the environmental temperature must

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significantly influence the speed of the process. Several authors[2, 4-7] have demonstrated clearly the inverse relationship between clotting time and environmental temperature. The temperature to be adopted is a matter of dispute. Most authors recommend body temperature (37° C.), claiming that this is the temperature at which coagulation takes place physiologically.

We had some objections to this proposal and adopted 21° C. temperature. Firstly, 37° C. is not physiological, as the temperature of blood in the body is higher than this. Secondly, for maintaining a 37° C. temperature, one would need an electric water-bath carried to the bedside, while a lower temperature such as 21° C. can be easily maintained in an inexpensive large thermos-flask. Thirdly, at 37° C. the clotting time is too short to detect minor differences. Fowler[8] has noted that 10 minutes after intravenous injection of 25 mgm. heparin the clotting time at room temperature was prolonged, but it was within normal limits when the test was carried out at 37° C. We have noted also that the higher temperature decreases the sensitivity of the test.

(3) The effect of glass surface on the clotting process has been clearly demonstrated.[3] Since the extent of the blood-glass contact in the method with syringe and test tubes cannot be standardized, coating of glassware with different substances was suggested. In spite of the valuable observations obtained with these materials in the research of clotting mechanism, this method is not popular in routine work because of the extremely prolonged clotting time so obtained.

In the method suggested by us the extent of blood-glass surface is standardized by the use of capillary tubes of similar size and by exclusion of the variable effect of syringe and test tubes.

We must mention that Pichotka *et al.*[9] described a method for the estimation of clotting time in animals which resembles ours. These authors recommended sealing a capillary tube into the butt of a needle with paraffin. The needle is introduced into the vein without using a syringe and the first drop of blood collected in the glass capillary tube. The presence of a fibrin thread marks the end-point. This method merely represents a modification of the well-known technique using capillary blood in capillary tubes. It retains the same major source of error—the admixture of tissue juice with the tested blood. This erroneous step occurs in many other suggested methods, in which it is postulated that all the blood drawn from a vein is free of tissue juice. Since not only the first few drops but also the first few ml. of venous blood may contain considerable amounts of tissue juice,[3] with marked influence on the clotting time, the results with the method suggested by Pichotka *et al.*[9] could not have been accurate. In fact, the literature shows no further reports on this technique.

ACCURACY OF THE METHOD

We performed this test on 50 occasions, blood being collected from the same subject through the same needle by several interns and the author. The clotting times were measured under the above-mentioned conditions. The readings exhibited a standard error of the differences of the means of ±6%.

In 30 healthy male adults the test was made on both arms simultaneously by different interns and the author. The pooled data of the investigators showed a standard error of ±7.5%. It it noteworthy that the interns did not have special training in the technique.

NORMAL VALUES

In the 30 healthy male adults in a postabsorptive state, the clotting time measured by the same investigator following our procedure was 9.2 min., the standard error being ±0.41 min. (±4.4%).

SUMMARY

(1) A standardized test for determination of clotting time is described. It is easily performed by untrained workers with inexpensive material, and gives reproducible and accurate results.

(2) The standard error of the technique in normal bloods is ±0.41 min. (±4.4%).

(3) Since the possibility of subjective error is minimal, comparison of results of different workers is possible.

The author wishes to express his thanks to Dr. W. F. Connell, Professor of Medicine and Head of the Department, for his suggestions and aid in the preparation of this paper.

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COMPLICATIONS FOLLOWING CEREBRAL ARTERIOGRAPHY

In a recent article Perese *et al.* comment on the dangers of cerebral arteriography. In a series of 234 consecutive arteriographic studies with 35% iodopyracet there were 37 complications. Three permanent hemiplegias and 19 transient hemipareses were observed; transient sensory changes occurred in six patients, and one patient had a partial occlusion of the retinal artery. One fatality was due to an excessive amount of contrast medium, and the deaths of six patients appeared to be hastened by the procedure.—*A. M. A. Arch. Neurol. & Psychiat.*, 71: 105, 1954.

INFORMATION DISCLOSURE STATEMENT BY APPLICANT		
	Application Number	18113710
	Filing Date	02/24/2023
	First Named Inventor	Bobby E. ROGERS
	Art Unit	-
	Client Number	069366
Page 1 of 1	**Matter Number**	0574153_KUR2C04US

GENERAL

Pursuant to 37 C.F.R. 1.97 and 1.98 and to the duty of disclosure set forth in 37 C.F.R. 1.56, the Examiner in charge of the above-identified application is requested to consider and make of record the references listed herewith. A copy of each listed reference, other than U.S. patents/applications and references cited in a parent application, is enclosed.

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TIMING

In accordance with 37 CFR 1.97(b), this Information Disclosure Statement is being filed within three months of the filing of a national application other than a continued prosecution application under 37 CFR 1.53(d); within three months of the date of entry of the national stage as set forth in 37 CFR 1.491 in an international application; before the mailing of a first Office Action on the merits; or before the mailing of a first Office Action after the filing of a request for continued examination under 37 CFR 1.114.

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No certification statement is required. This Information Disclosure Statement is being filed in accordance with 37 CFR 1.97(b).

FEE

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ADDITIONAL COMMENTS

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APPLICATION #	RECEIPT DATE / TIME	ATTORNEY DOCKET #
18/113,710	**05/10/2023 06:57:54 PM ET**	**069366-0574153_KUR2C04US**

Title of Invention

BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE AND METHOD

Application Information

APPLICATION TYPE	Utility - Nonprovisional Application under 35 USC 111(a)	PATENT #	-
CONFIRMATION #	2715	FILED BY	Trent Tercenio
PATENT CENTER #	62047590	FILING DATE	02/24/2023
CUSTOMER #	27500	FIRST NAMED INVENTOR	Bobby E. ROGERS
CORRESPONDENCE ADDRESS	-	AUTHORIZED BY	Benjamin Hudson

Documents

TOTAL DOCUMENTS: 6

DOCUMENT	PAGES	DESCRIPTION	SIZE (KB)
069366-0574153_KUR2C04US-A-NPL-050.pdf	3	Non Patent Literature	310 KB
069366-0574153_KUR2C04US-B-NPL-002.pdf	8	Non Patent Literature	4918 KB
069366-0574153_KUR2C04US-B-NPL-001.pdf	5	Non Patent Literature	7065 KB
069366-0574153_KUR2C04US-B-	3	Non Patent Literature	225 KB

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069366-0574153_KUR2C04US_PTO_IDS-Form-B.pdf	4	Information Disclosure Statement (IDS) Form (SB08)	1029 KB
069366-0574153_KUR2C04US_Transmittal-Letter.pdf	1	Transmittal Letter	497 KB

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New International Application Filed with the USPTO as a Receiving Office

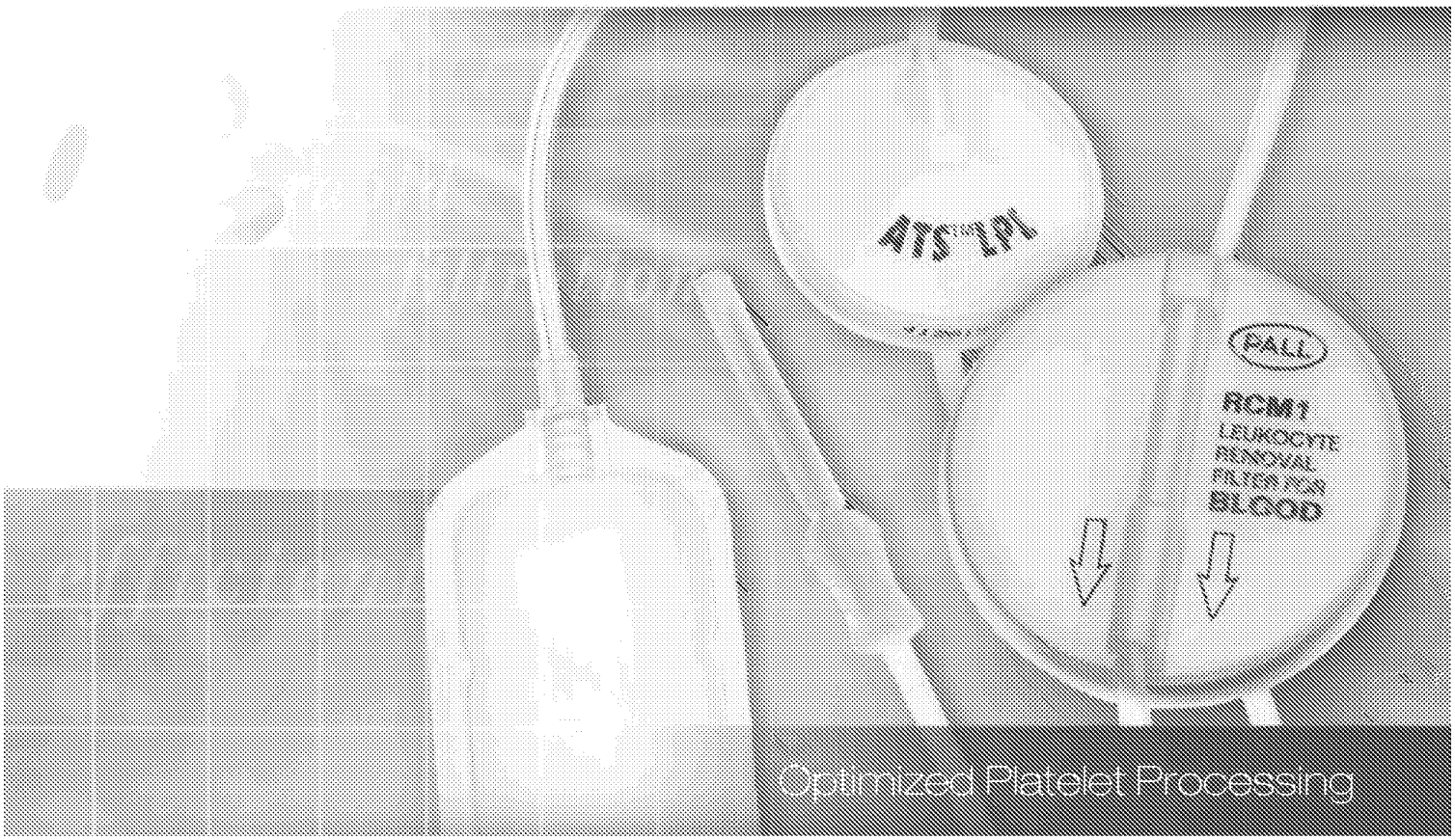
If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

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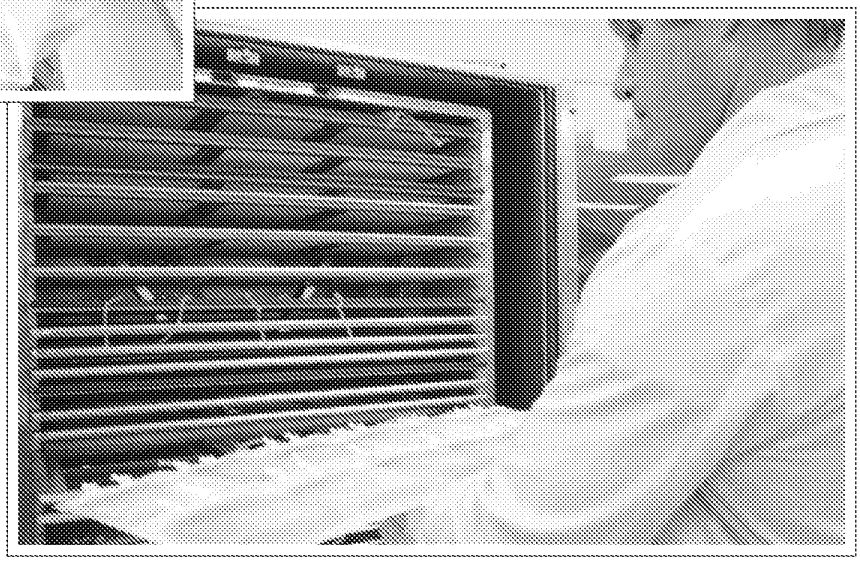
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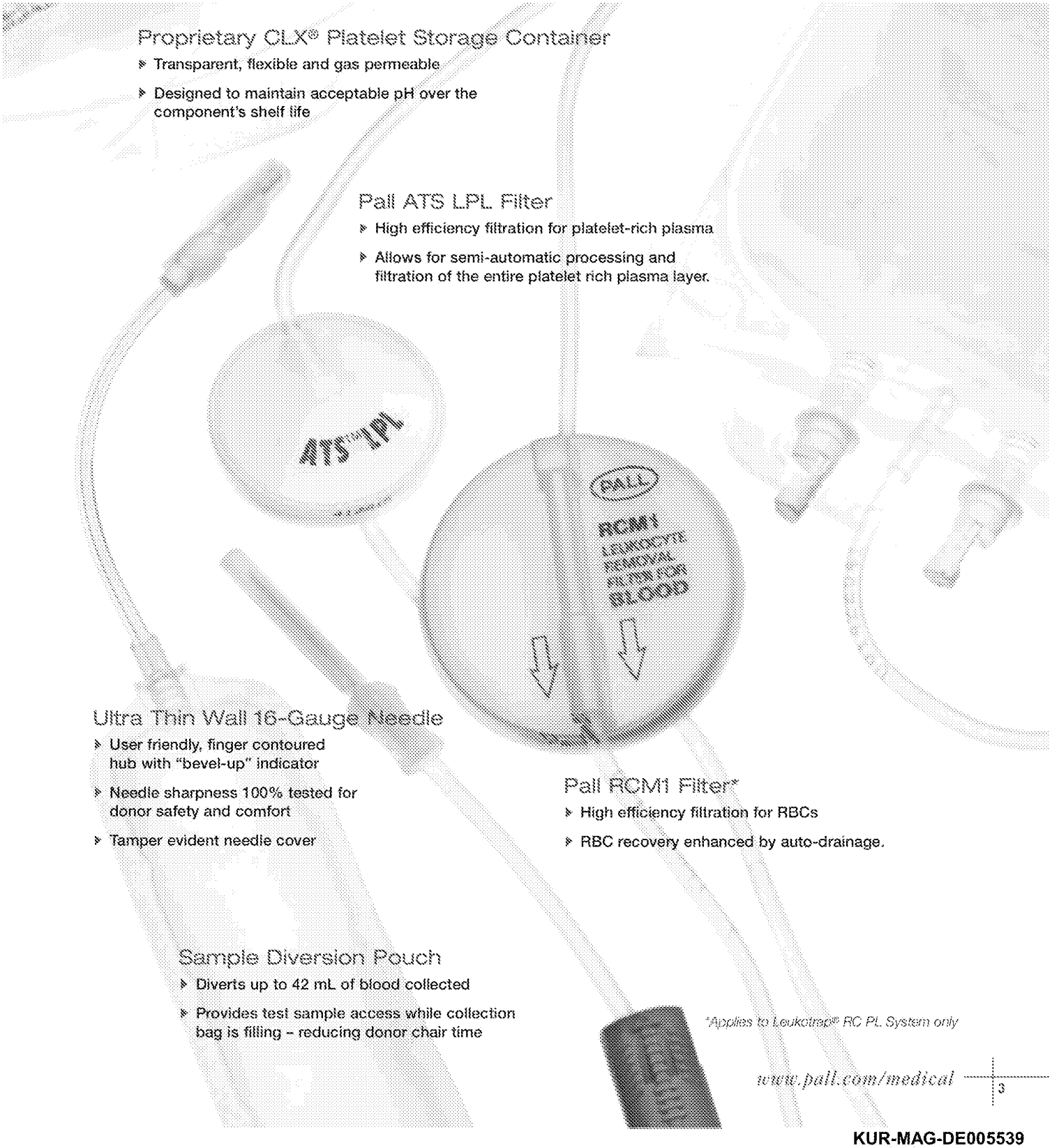
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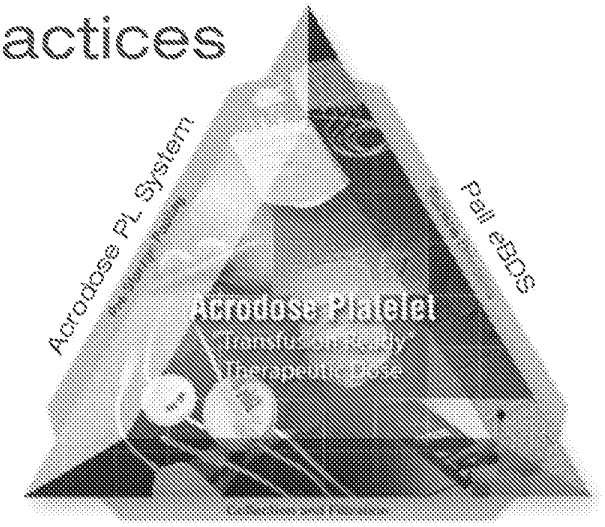
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Leukotrap RC PL and
Leukotrap PL Systems

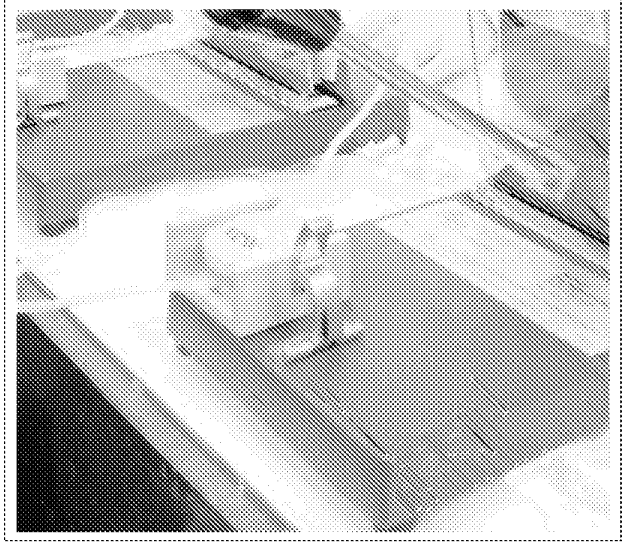
Collection and Filtration

Pall Sample Diversion Pouch



1 Automatically divert initial blood with the Pall Sample Diversion Pouch

Leukotrap RC PL or Leukotrap PL System



2 Prepare leukoreduced platelets with the Leukotrap RC PL or PL System

Provide Greater Platelet Transfusion Safety

Greater QC Assurance of Meeting Guidelines for Detecting Bacteria in *all* Platelet Products

- The American Association of Blood Banks (AABB)[5] and College of American Pathologists (CAP)[6] have issued guidelines for the detection of bacteria in all platelet products.
- All market cleared systems for detecting bacteria in platelet products require that these platelet products must be leukoreduced.
- The same standard of testing should be applied to all platelet products to make cGMP compliance easier.
- The Leukotrap RC PL System is the only closed system that can produce leukoreduced whole-blood derived platelet products.

Pre-storage Pooling and Bacteria Detection

Acrodose™ PL System



3 Pool leukoreduced platelets with the Pall Acrodose PL System.

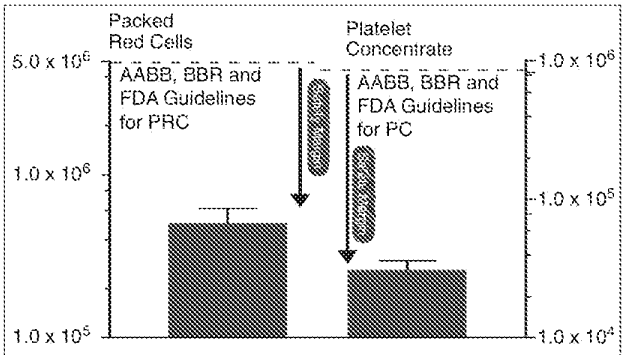
Pall *e*BDS and Pall Data



4 Detect bacteria with Pall *e*BDS, a market cleared quality control culture based system.

Consistent and Reliable Performance

Greater QC Assurance of Meeting White Blood Cell Residual Requirements



Safety margins for residual leukocytes in packed cells and platelet concentrates prepared with the Leukotrap RC PL System

Figure 1

Consistency of performance with RCM1 and ATS LPL Filters using the Leukotrap® RC PL System.

Data from actual field use.

Shown are mean residual WBC/unit and 95% confidence interval.

Greater QC Assurance of Platelet Recovery Requirements

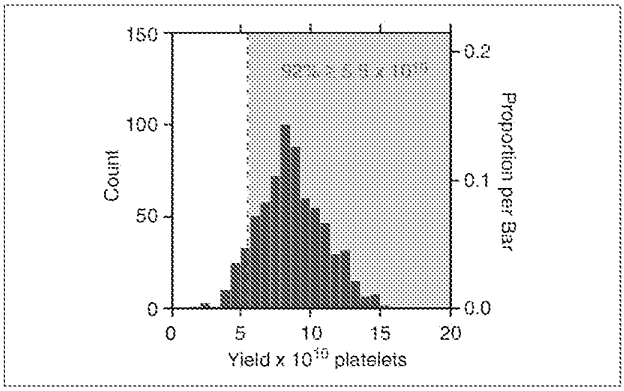


Figure 2

Platelet yield distribution of individual platelet concentrates (PC) prepared using the Leukotrap RC PL System.

Data from 500 mL WB (n=700) collections processed with the Leukotrap RC PL System.

Mean platelet yield = 8.87 x 10^{10} with a standard deviation of 2.42 x10^{10} platelets.

Ninety-two percent (92%) of PCs had a platelet count greater than the AABB Standards[7] for platelets prepared from whole blood (≥5.5 x 10^{10}).

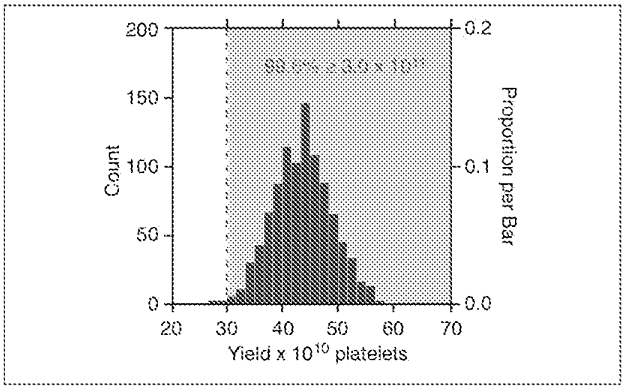


Figure 3

Platelet yield distribution of a pool of five (5) individual platelet concentrates (PC) prepared using the Leukotrap RC PL System.

The distribution was obtained by computer simulation using the individual PC yield data shown in Figure 2.

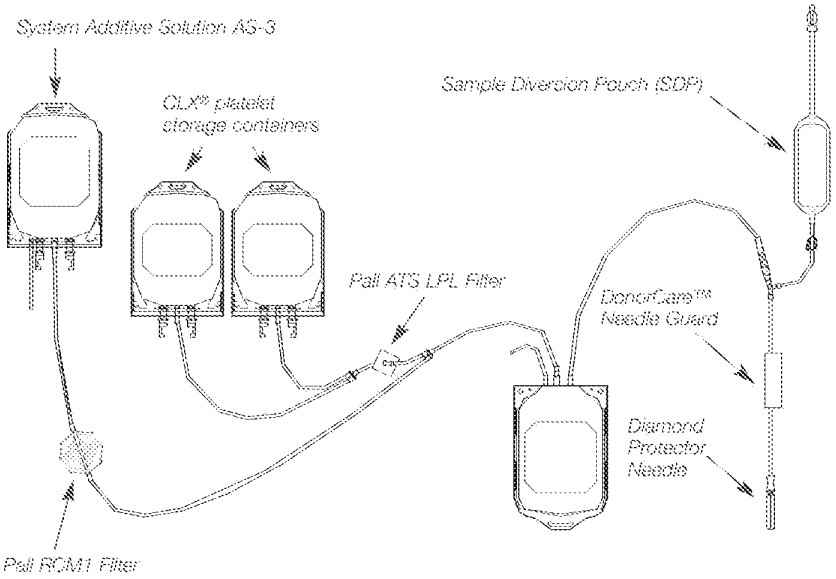
Mean platelet yield with a pool of 5 = 4.3 x 10^{11} with a standard deviation of 5.3 x 10^{10} platelets.

Over ninety-nine percent (99.6%) of the PC pools had a platelet yield greater than the AABB Standard for platelets prepared by cytapheresis[8] (≥3.0 x 10^{11}).

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Leukotrap® RC PL System

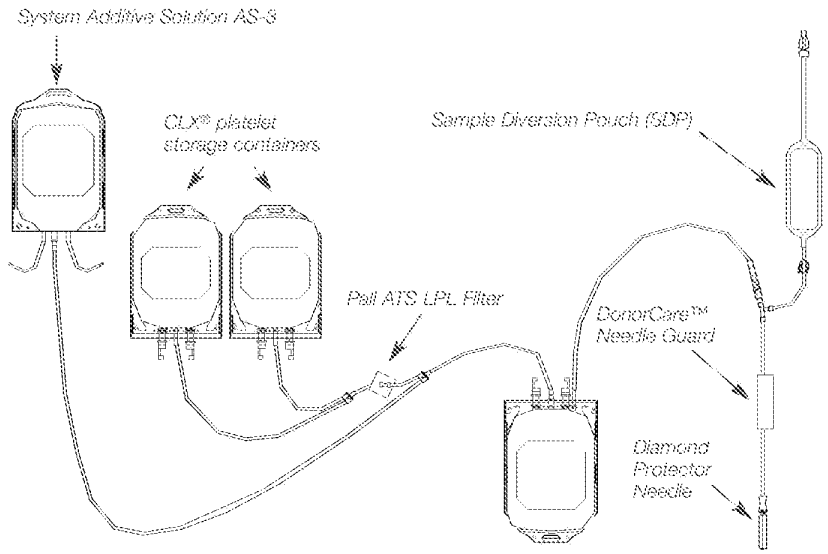


Ordering Information*

Leukotrap RC PL System

Reorder Code	Packaging
With SDP	
723-93	CP2D/AS-3, 450 mL capacity, Triple
123-93	CP2D/AS-3, 500 mL capacity, Triple
123-94	CP2D/AS-3, 500 mL capacity, Quad

Leukotrap PL System

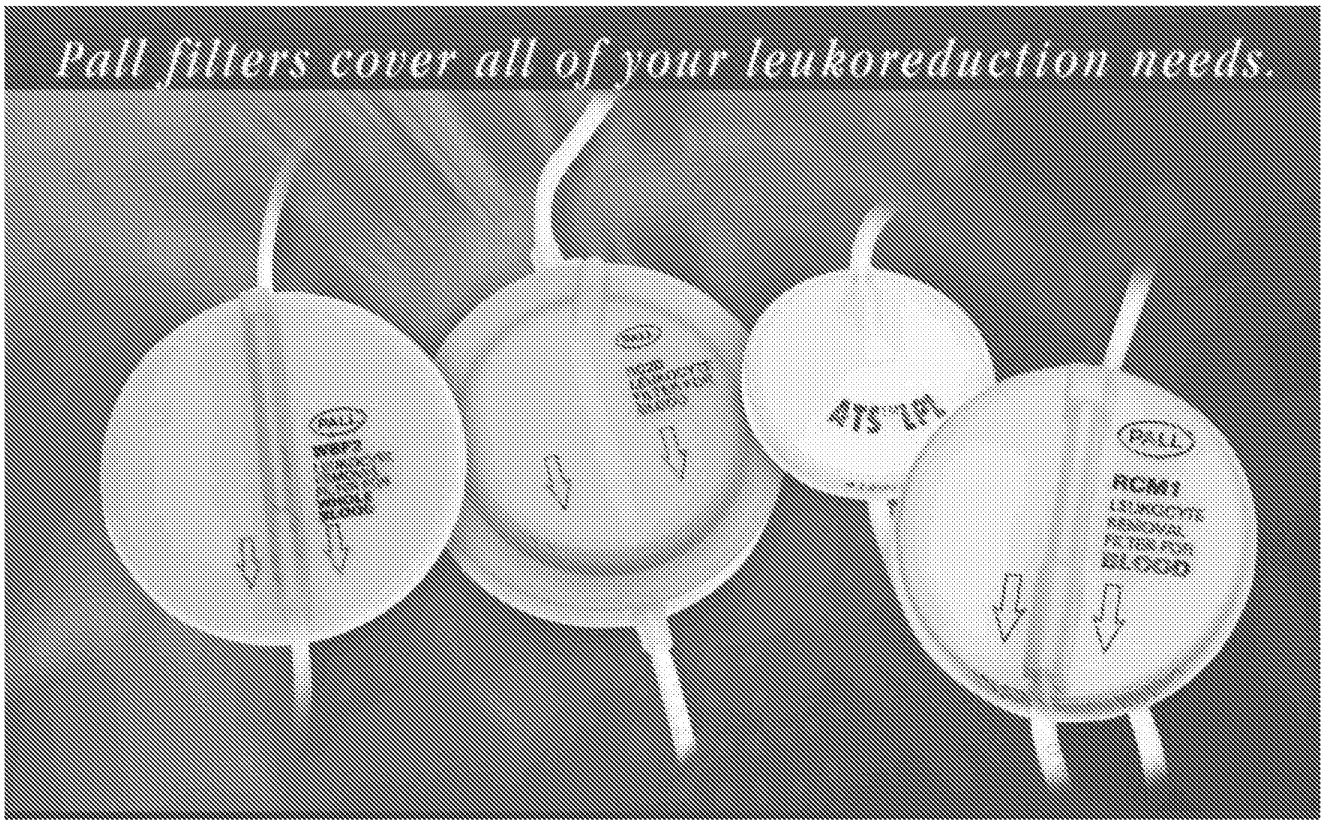


Ordering Information*

Leukotrap PL System

Reorder Code	Packaging
With SDP	
125-93	CP2D/AS-3, 500 mL capacity, Triple

**All sets come with DonorCare™ Needle Guard for reducing needlestick injury, enhanced paper labels for improved adhesion of overlabels and a QC leg on the collection bag for improved QC sampling. The System Additive Solution AS-3 (Nutricel® System) for RBC maintains viability for 42 days without manitol.*



References

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6 CAP Commission on Laboratory Accreditation, TRM. 44955 Phase I.

7 Standards 5.7.5.15 and 5.7.5.15.1 - Standards for Blood Banks and Transfusion Services, AABB 21st Edition, 2002.

8 Standard 5.7.5.18 - Standards for Blood Banks and Transfusion Services, AABB 21st Edition, 2002.

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Controlled Clinical Laboratory Comparison of Two Supplemented Aerobic and Anaerobic Media Used in Automated Blood Culture Systems To Detect Bloodstream Infections

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A 20-ml blood sample was collected from adult patients with suspected bloodstream infections and distributed equally into the four volume-controlled bottles of a blood culture set consisting of aerobic and anaerobic BACTEC Plus/F bottles and aerobic and anaerobic BacT/Alert FAN bottles. All bottles were incubated in their respective instruments for a standard 5-day protocol or until the instruments signalled positivity. Samples in all bottles with negative results by these instruments were terminally subcultured. A total of 8,390 blood culture sets were obtained during the study period, of which 4,402 (52.5%) met the study criteria. Of these, 946 (21.5%) were positive either by instrument signal or by additional terminal subculture of all negative bottles and yielded growth of microorganisms. Five hundred eighty-nine (13.4%) blood culture sets were considered to have recovered 663 clinically significant organisms. When both the BACTEC and the BacT/Alert systems were used, 465 positive sets were detected; BACTEC alone detected 52 positive sets and BacT/Alert alone detected 72 ($P = 0.09$). No differences were found between the two systems in microbial recovery rate from blood cultures obtained from patients on antibiotic therapy. Significantly more members of the family *Enterobacteriaceae* ($P < 0.01$) were detected from patients without antimicrobial therapy by BacT/Alert than by BACTEC. The false-negative rates were 0.20% for BACTEC and 0.32% for BacT/Alert. A significantly higher false-positive rate was found for BACTEC ($P < 0.0001$). Both systems were comparable for the time to detection of microorganisms. However, gram-positive bacteria were detected faster by BACTEC and *Enterobacteriaceae* were detected faster on average by BacT/Alert. We concluded that both systems are comparable in their abilities to recover aerobic and anaerobic organisms from blood cultures and a terminal subculture might not be necessary for either of the two systems. The increased positivity rate when using an anaerobic bottle in a two-bottle blood culture set is due to the additional blood volume rather than to the use of an anaerobic medium.

Due to the high morbidity and mortality associated with bacteremia (7), the rapid detection and subsequent identification of microorganisms from blood remain critical services of the clinical microbiology laboratory. Numerous blood culture methods are available, and selecting the optimal system for the diagnostic laboratory is an important and often difficult task (15). Many remarkable improvements have been made in an attempt to reduce the time to isolate pathogens from blood. Advancements in the use of liquid media linked with automation technology have enhanced the ability of laboratories to provide faster blood culture results. Two continuously monitored noninvasive blood culture systems, the BACTEC 9240 (Becton Dickinson, Heidelberg, Germany) and the BacT/Alert (Organon Teknika, Eppelheim, Germany), are in widespread use. The main advantages of the two systems over previous generations of blood culture instruments include full automation once the bottles are loaded, a shorter time to detection of blood pathogens, considerable labor savings, and improved laboratory workflow. The BacT/Alert and the BACTEC 9240 systems monitor the growth of organisms by checking for elaboration of CO_2 with a colorimetric and a fluorescent sensor, respectively.

New aerobic and anaerobic media were developed by the manufacturers to remove a variety of growth inhibitors from patients' blood, to enhance the recovery of fastidious organisms, and to improve the detection of bacteremia and fungemia in patients receiving antimicrobial therapy. BACTEC Plus/F medium consists of soybean-casein digest broth, primary supplements, and two types of resin, a nonionic absorbing resin and a cation-exchange resin. FAN medium (BacT/Alert) is a brain heart infusion broth base containing Ecosorb, a proprietary substance that contains adsorbent charcoal, Fuller's earth, and other components.

A number of studies comparing the two systems have been carried out, but to our knowledge, none of them compared the supplemented aerobic and anaerobic BACTEC Plus/F media with the supplemented aerobic and anaerobic BacT/Alert FAN media in one controlled clinical trial.

This study was conducted to compare the performances of the two blood culture systems, BACTEC 9240 and BacT/Alert, in terms of microbial recovery, time to detection, and false-positive and false-negative rates, thereby indicating the performance of the aerobic and anaerobic BACTEC Plus/F resin media and the aerobic and anaerobic BacT/Alert FAN media.

MATERIALS AND METHODS

Patient population. This monocenter study was conducted from August 1995 through February 1997 in a 2,500-bed acute-care community hospital which provides a full range of medical and surgical care. The hospital cares for an appreciable number of transplant, immunosuppressed patients, as well as patients presenting common community-acquired infections. Blood cultures were obtained from all adult patients with suspected bacteremia during the study

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period and processed in the hospital-related Institute of Microbiology and Hygiene.

Study design. Blood culture sets were prepared for the purposes of the study; each set contained four volume-controlled and randomized bottles, one each containing aerobic and anaerobic BACTEC Plus/F media and aerobic and anaerobic BacT/Alert FAN media. Written instructions for obtaining a blood culture, the required amount of blood, and the order of inoculation of the bottles for clinicians were included. In respect of the patient and with the agreement of the ethical commission of our hospital, a 20-ml amount of blood for one blood culture set was considered the maximum to obtain from a single venipuncture. This amount was distributed equally into each of the four bottles. The inoculum volume was determined in the microbiology laboratory by weight. Sets in which any one of the bottles did not contain a minimum of 3 ml of blood or in which the volume difference between two bottles was more than 3 ml were considered noncompliant and excluded from the study but processed for the bene@ of the patient.

On arrival in the laboratory, all bottles were placed in their respective instruments for a 5-day incubation time at 35°C and monitored in accordance with the manufacturers' recommendations. FAN aerobic bottles were vented before incubation.

Bottles indicated as positive by the instrument as well as bottles positive on arrival were Gram stained. Based on the Gram stain result, aliquots of the bottles were subcultured onto adequate media (chocolate agar incubated at 35°C in a 5% CO_2-enriched atmosphere or blood agar with aerobic and anaerobic incubation at 35°C). All microorganisms were identi@ed by standard microbiologic procedures. All false-positive bottles (i.e., bottles that were smear and subculture negative after instrument signal) were replaced into the instrument during the 5 days of protocol. A terminal blind subculture onto chocolate agar and blood agar (aerobic and anaerobic incubation as described above) was performed for all negative bottles. False-negative bottles had no positive signal by the instrument, but growth occurred on the terminal subculture.

Statistical methods. The following data of all blood cultures were entered in a computer database: collection time, loading time, blood volume of each bottle, detection of growth by each bottle, growth on subculture and identity of microorganisms recovered, antimicrobic therapy, and the detection time for each positive bottle. Detection time of a microorganism was de@ed as the time between loading a blood culture bottle into the instrument and the time when a positive signal occurred followed by growth on subculture. For comparison of detection times, only clinically signi@ant isolates recovered in both systems were taken into account. If both bottles of one system recovered the same organisms, the shorter time to detection was taken into account for comparison. The clinical importance of isolated microorganisms was determined after consultation with the patient's physician in accordance with published criteria (6, 10, 16, 18). Statistical analysis was done for blood cultures meeting the study criteria. Only isolates classi@d as being clinically signi@ant were taken into account. Sensitivities were calculated in two manners. For comparison of the two systems, the common denominator of positive cultures was determined by all four terminal blind subcultures. For evaluating the usefulness of terminal subcultures in clinical routines, the detection rate of each system was determined with reference only to the related terminal subculture. The common denominator for the determination of both the false-positive and the false-negative rates for each system was the total of 4,402 compliant sets of the study. The main scienti@ goal of the study was the comparison of the sensitivities and speci@cities of both systems. For these two analyses, the Bonferroni correction was used. All other analysis on subgroups of patients or isolates must be considered explorative without protection against the error of multiple testing. All comparisons were evaluated by McNemar's test ($\alpha = 0.05$, two-sided) by using the statistical package SPSSWIN.

RESULTS

A total of 8,390 blood culture sets were obtained during the study period. Of these, 4,402 (52.5%) met the study criteria; of these, 946 (21.5%) yielded growth of 1,083 bacteria or fungi. Five hundred eighty-nine (13.4%) compliant sets, positive by either instrument signal or terminal subculture only, detected 663 bacteria or fungi that were considered clinically signi@ant. Three hundred @fty-seven (8.1%) sets recovered only organisms classi@ed as contaminants.

Of the 589 positive blood culture sets with signi@ant isolates, 508 (86.3%) were positive by BACTEC 9240 and 523 (88.8%) sets were positive by BacT/Alert. BACTEC alone detected 52 (8.8%) positive sets, and BacT/Alert alone detected 72 (12.2%). With reference to the terminal blind subcultures of both systems, BACTEC and BacT/Alert showed sensitivity rates of 86.3 and 88.8% respectively. With reference to the system-related terminal subculture, the BACTEC instrument demonstrated a detection rate of 98.3% and the BacT/Alert instrument gave one of 97.4%.

TABLE 1. Comparative yields of clinically important bacteria and fungi in BACTEC Plus/F and FAN aerobic and anaerobic culture sets

Microorganism	No. of organisms detected by:			P
	BACTEC only	BacT/Alert only	Both systems	
Gram-positive bacteria	30	34	228	NS[a]
Staphylococcus aureus	11	14	124	
Staphylococcus epidermidis	2	2	9	
Viridans group streptococcus	2	5	18	
Enterococcus spp.	6	7	32	
Streptococcus pneumoniae	6	4	33	
Beta-hemolytic streptococci	3	1	9	
Listeria monocytogenes		1	3	
Enterobacteriaceae	21	45	187	<0.01
Escherichia coli	14	25	101	
Klebsiella spp.	3	12	27	
Enterobacter/Citrobacter spp.	2	5	31	
Salmonella spp.			6	
Proteus/Providencia/Morganella	1	1	11	
Serratia/Hafnia spp.	1	2	11	
Non-*Enterobacteriaceae*	18	13	36	NS
Haemophilus spp.		2	1	
Pseudomonas aeruginosa	7	7	8	
Stenotrophomonas maltophilia	3		6	
Neisseria meningitidis		1	1	
Acinetobacter spp.	8	3	18	
Other			2	
Anaerobic bacteria	6	3	4	NS
Clostridium perfringens	1	1	1	
Bacteroides spp.	3	2	2	
Candida spp.	5	6	14	NS
All microorganisms	80	101	482[b]	

[a] NS, not signi@ant.
[b] For some species with a single isolate, data were not depicted separately but were included in the total

Nine false-negative blood cultures occurred with the BACTEC instrument (three *Candida* species and single isolates of *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Listeria monocytogenes*, *Enterobacter agglomerans*, *Pseudomonas aeruginosa*, and *Pseudomonas stutzeri*) and 14 false negatives occurred with the BacT/Alert instrument (four *P. aeruginosa*, three *Acinetobacter* species, two *Stenotrophomonas maltophilia*, two *Candida* species, and single isolates of *Streptococcus sanguis*, *Escherichia coli*, and *Proteus mirabilis*).

The false-negative rates for the systems were 0.20% for BACTEC and 0.32% for BacT/Alert.

A signi@antly higher false-positive rate was found for BACTEC, 6.2%, than for BacT/Alert, 1.4% ($P < 0.0001$).

The comparative yields of bacteria and fungi from the two systems are indicated in Table 1. Of the 663 clinically signi@cant organisms from compliant sets, 482 (72.7%) were recovered from both systems, 80 (12%) were recovered by BACTEC only, and 101 (15.2%) were recovered by BacT/Alert only. The differences observed in the recovery of bacteria reached statistical signi@cance only for the *Enterobacteriaceae* group. The BacT/Alert system detected signi@antly more *Enterobacteriaceae* than the BACTEC system did ($P < 0.01$). A similar trend

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TABLE 2. Comparative speed of detection of clinically signi@cant organisms when both systems were positive and detection time was provided for both systems ($n = 421$)

Microorganism	Time to detection (h)		n	P
	BACTEC	BacT/Alert		
Staphylococcus aureus	8.4	11.2	124	<0.001
Viridans group streptococcus	4.0	6.6	18	<0.01
Enterococci	5.1	19.5	32	<0.05
Streptococcus pneumoniae	5.1	6.2	33	<0.05
Escherichia coli	7.6	6.9	101	<0.05
Klebsiella spp.	8.9	5.8	27	NS[a]
Enterobacter spp.	7.8	7.5	31	<0.05
Pseudomonas aeruginosa	15.4	20.7	8	NS
Acinetobacter spp.	6.9	10.2	18	<0.01
Mean values	9.0	10.4	482[b]	<0.05

[a] NS, not signi@cant.
[b] For some species with fewer than 10 isolates, data were not depicted separately but were included in the mean time to detection.

was seen in the recovery of yeasts from blood cultures obtained from patients without antibiotic therapy. For all other organisms, there were no signi@cant differences in the number of positive cultures between systems, neither by organism group nor by species.

Of all compliant blood culture sets, 41.9% (1,807 sets) were obtained from patients receiving antimicrobial therapy. Of the 589 positive compliant sets with signi@cant isolates, 35.5% (208) were obtained from patients receiving antibiotics. There were no signi@cant differences in isolation rates between the two systems for patients receiving antibiotics. The BacT/Alert system detected signi@cantly more *Enterobacteriaceae* than the BACTEC system did ($P < 0.01$) from patients without antibiotic therapy.

The times to detection of several bacterial groups were compared for the two systems (Table 2). Gram-positive bacteria were detected signi@cantly faster by the BACTEC system, whereas *Enterobacteriaceae* on average were recovered faster by the BacT/Alert system. There was no difference between the two systems in the cumulative percentage of positive cultures after 24, 48, and 72 h of incubation. Within the @rst 24 h, BACTEC detected 89.8% and BacT/Alert detected 89.6% of the positive cultures; after 48 h, 95.7 and 96.9% were detected by BACTEC and BacT/Alert, respectively; and after 72 h, 99.0 and 99.4% were detected by the two systems, respectively. The average times to detection were 9.0 h for the BACTEC system and 10.4 h for the BacT/Alert system ($P < 0.05$). The signi@cant difference in average time to detection between both systems was caused by the higher detection rate within the @rst 6 h of the BACTEC instrument (50.7% detected by BACTEC and 45.8% by BacT/Alert).

Delayed entry was de@ned as a time difference of >12 h between blood sample collection and placement of a blood culture bottle into the respective instrument. More than half of the compliant positive blood cultures had a transportation time of >12 h due to the fact that our new hospital building is separated from the laboratory. Delayed entry had no effect on the sensitivity of the BacT/Alert instrument, but for the BACTEC system, the detection rate was signi@cantly lower for blood cultures with delayed entry than for those with no delay ($P = 0.0097$). Differences also occurred in detection of the *Enterobacteriaceae* group: BacT/Alert recovered signi@cantly more *Enterobacteriaceae* from blood cultures with delayed entry than BACTEC did ($P = 0.0062$) when the subgroup of patients not receiving antibiotic therapy was considered.

The data of the two systems allow not only a system-versus-system comparison but also a comparison of the two media, i.e., resin aerobic versus FAN aerobic media and resin anaerobic versus FAN anaerobic media (Table 3). No signi@cant differences were seen between the aerobic media nor between the anaerobic media of the two systems in terms of detection rate. A comparison of the aerobic and anaerobic media of each system showed signi@cant differences. The false-positive rate was signi@cantly higher for both resin media than for the FAN media. The false-negative rates for both anaerobic media (4.7% for resin and 3.9% for FAN) were higher than those for the aerobic media (1.7% for resin and 2.2% for FAN).

Anaerobic bacteria causing septicemia were recovered from 13 compliant blood culture sets. Both systems detected four, the BACTEC system alone detected six, and the BacT/Alert system alone detected three anaerobic bacteria.

DISCUSSION

This monocenter-controlled evaluation compared the performances of the supplemented aerobic and anaerobic BACTEC resin media, under identical conditions of observation against the supplemented aerobic and anaerobic BacT/Alert FAN media in a clinical trial. Simultaneous inoculation of all four bottles from a single blood culture also enabled a system-versus-system comparison of the BACTEC 9240 and the BacT/Alert instruments. To our knowledge, no data have been published yet on this subject. In the past, several studies have evaluated the performance of the BACTEC (20) and BacT/Alert (2, 11) instruments, comparing either the two nonsupplemented media (19), the resin medium and the standard BacT/Alert medium (1, 9, 13), or the aerobic resin medium and the aerobic FAN medium (4, 8, 14). Outcomes have been quite different: the BACTEC system detected signi@cantly more gram-positive cocci and the BacT/Alert system recovered signi@cantly more *Enterobacteriaceae* in a @rst comparison (19) of the two nonsupplemented media.

Auckenthaler et al. (1) as well as Smith et al. (13) compared BACTEC resin medium to standard BacT/Alert medium, and both groups reported a better performance in terms of microbial recovery, false-positive rate, and detection time for the resin medium. A comparison of aerobic resin medium with aerobic FAN medium in a recent multicenter (4) study has demonstrated equal results. The previous single-center study by Pohlman et al. (8) showed a better recovery rate for *Entero-*

TABLE 3. Detection of positive cultures and false-positive signals by aerobic and anaerobic media

Medium	No. of positive cultures			No. of false-positive signals[b]
	Total	Detected by instrument[a]	Detected by terminal subculture	
Aerobic resin	466	456	10	185
Aerobic FAN	489	476	13	54
Anaerobic resin	448	420	28	116
Anaerobic FAN	429	406	23	11

[a] Values for aerobic resin versus aerobic FAN media and for anaerobic resin versus anaerobic FAN media are not signi@cantly different. Values for aerobic resin versus anaerobic resin media and aerobic FAN versus anaerobic FAN media are signi@cantly different ($P < 0.05$ and $P < 0.001$, respectively).
[b] Values for aerobic resin versus aerobic FAN media, anaerobic resin versus anaerobic FAN media, aerobic resin versus anaerobic resin media, and aerobic FAN versus anaerobic FAN media are signi@cantly different ($P < 0.001$).

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bacteriaceae and *Pseudomonas* by use of the BacT/Alert system with fewer false-positive results. In comparison with the results of other studies (4, 11, 12, 17), the positivity rate of blood cultures in our study was high (21.5% positive sets), with 13.4% sets recovering clinically signi@cant organisms. With the exception of members of the *Enterobacteriaceae* group, which were recovered signi@cantly ($P < 0.01$) more often by the BacT/Alert system alone, there were no signi@cant differences in terms of microbial recovery between the two systems. The *Enterobacteriaceae* that were detected signi@cantly more frequently by the BacT/Alert system resulted from blood cultures from patients without antimicrobial therapy. There was also a tendency towards a similar result for the fungi group: BacT/Alert detected slightly more *Candida* sp. isolates from patients without antibiotics than from patients with antimicrobial therapy. However, these are results of an explorative analysis in which, due to the small numbers of cases, a high beta error and the problems of multiple testing must be taken into account.

Reports of high false-negative rates, up to 6% (12, 13), suggest that terminal subculturing of negative BACTEC cultures after 5 days of incubation may be necessary, whereas others have suggested that this is not needed in the BacT/Alert system (3). In our trial, the false-negative rates were similarly low for both systems (0.20% for BACTEC and 0.32% for BacT/Alert) and the sensitivities for the BACTEC and BacT/Alert instruments with reference to the related terminal subcultures were 98.3 and 97.4%, respectively; therefore, we have concluded that a blind terminal subculture may not be necessary for either of the two systems.

The introduction of automated blood culture systems also serves the purpose of reducing the routine workload for laboratory personnel. A low false-positive rate is one important factor here. Our results showed a signi@cantly ($P < 0.0001$) higher false-positive rate for the aerobic and anaerobic resin media (6.2%) than for the FAN media (1.4%). During the study period, both instruments were used in accordance with the recommendations and speci@cations of each manufacturer. Laboratory facilities were equal for both systems. All false-positive blood cultures were replaced into the instrument, incubated for the rest of the 5-day incubation period, and terminally subcultured. A small percentage of the false-positive signals by the BACTEC instrument occurred after an electricity breakdown, which did not affect the BacT/Alert instrument.

Due to the need to reduce laboratory costs, many microbiology laboratories do not have 24-h coverage by technical personnel. Especially in smaller hospitals, there is no microbiology laboratory available, so that blood cultures must be sent to external laboratories. Therefore, a delay may occur from the time blood is drawn until the bottle is placed into a blood culture instrument. Our hospital consists of an original building complex with 1,500 beds and a new building with 1,000 beds which is situated 10 km away. All blood specimens from the new building must be transferred to the laboratory in the original building, so that a delay of >12 h may occur.

Those blood cultures that were obtained after the microbiology laboratory was closed for the day were collected in a central laboratory that is open 24 h per day and were incubated at 35°C, so that almost all blood cultures with delayed entry were preincubated at 35°C. Delayed entry did affect the sensitivity of the BACTEC instrument in that the detection rate was signi@cantly lower for blood cultures with delayed entry than for those with no delay ($P = 0.0097$).

The numbers of false-negative sets with delayed entry and of false negative sets with a transport time of <12 h were too small for valid comparison. For the BACTEC system, 6 of 9 false-negative sets were sets with delayed entry; for BacT/Alert, 8 of 14 false negatives were sets with delayed entry. In spite of the small number, there seems to be no need for blind terminal subculture either for sets with overnight preincubation at 35°C or for sets processed within the @rst 12 h after collection. Both systems detected organisms faster from culture sets with delayed entry since these sets were preincubated. With regards to the handling of preincubated blood culture bottles, the BacT/Alert system offers the advantage of a visible change on the bottom of a positive bottle so that the bottle can be processed onto subcultures before incubation into the instrument. The interpretation of Gram stain results for positive bottles was more dif@cult for FAN media than for resin media due to the charcoal particles in the media.

Staphylococcus epidermidis, which is considered a contaminant, was recovered more frequently from the FAN aerobic bottle ($n = 424$) than from the resin aerobic bottle ($n = 349$); this more frequent recovery may be due to the fact that the FAN aerobic bottle must be vented before incubation in the instrument. The use of needles to manually vent the aerobic FAN bottles may increase the probability of contaminating the bottle.

The question whether there is any advantage to using both aerobic and anaerobic blood culture media routinely (5) or whether anaerobic media should be used for the detection of bacteremia only in patients at risk of having an anaerobic infection is often raised. Only 13 positive blood cultures out of 589 sets with clinically signi@cant organisms recovered anaerobic bacteria, 11 being isolated from the anaerobic medium only and 2 being isolated from both the aerobic and anaerobic media. Four of the 11 blood culture sets with obligate anaerobic bacteria represented polymicrobial septicemia; in addition to the anaerobic bacteria, *Enterobacteriaceae*, *Staphylococcus aureus*, and *Candida* spp. were isolated from the corresponding aerobic bottle as well. De@nitively, seven (1.2%) blood cultures with monomicrobic obligate anaerobic pathogens would not have been detected by using only an aerobic bottle. By using the anaerobic resin bottle in addition to the aerobic one, the detection rate increased by 10.2%, with facultative anaerobic bacteria contributing 8.7% and obligate anaerobic bacteria contributing 1.6%. Analogously, the anaerobic FAN bottle increased the positivity by 9%, of which 8% was due to facultative anaerobic bacteria and 1% was due to strict anaerobic ones. Diagnoses of patients with septicemia due to obligate anaerobic bacteria included colitis ulcerosa, pancreatitis, diabetes mellitus with erysipelas, cholangitis, leukemia, and pneumonia, so that anaerobic infections could have been expected. According to Weinstein et al. (17), an increase in the volume of blood inoculated into BacT/Alert aerobic bottles (from 5 to 10 ml) increased the overall yield (7.2%) of clinically important organisms. From our results and those reported by Weinstein et al. (15, 17), we conclude that the higher recovery rate achieved when the anaerobic bottle is included is due to the inoculation of a larger blood volume rather than to the use of an additional anaerobic medium.

In summary, both systems are comparable for recovering clinically signi@cant microorganisms from adult patients with bacteremia and fungemia receiving antibiotic therapy at the time of blood culture collection. With blood from patients without antibiotic therapy, the BacT/Alert system detected signi@cantly more *Enterobacteriaceae*. The high false-positive rate of the BACTEC system caused additional work and material costs in our laboratory. With the BacT/Alert instrument, the software capabilities were more convenient for the user, and failure rarely occurred.

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THE STANDARD CLOTTING TIME

A METHOD BASED ON THE USE OF WHOLE VENOUS BLOOD IN CAPILLARY TUBES

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In 1955, Mayer[1] described a method for testing the coagulation time of whole blood that was later referred to as the *standard clotting time*.[2] The method was reported to be reliable and to reveal a rather narrow range of normal values, as compared with the more widely used Lee-White technic for clotting time, and with the now almost abandoned capillary method for clotting time. In the course of investigating possible clotting abnormalities in patients with prostatic cancer,[5] we re-evaluated the method, particularly because its claimed normal range of 11.9 ± 0.9 min. was based merely on values obtained from 40 healthy, fasting men, in the age group of 25 to 35 years.

MATERIALS AND METHODS

Because Mayer's procedure as outlined in 1957 was followed in detail,[2] it will not be described fully. It is necessary to note, however, that the No. 19 gage stainless steel needle was replaced by the Becton, Dickinson and Company No. 20 sterile disposable needle. With this method, venous blood is drawn and diverted by a special adapter to 3 capillary tubes, which are maintained at a temperature of 21 C. in a water bath. The end point is obtained by means of breaking off each capillary tube in succession and observing a fibrin clot. The average value determined from the 3 tubes represents the standard clotting time. It differs considerably from the ordinarily performed capillary clotting time because of the use of venous blood, with minimal admixture of tissue thromboplastin, and because the temperature is controlled. The test is readily performed by 1 technologist, and it is possible to examine 2 patients at the same time. Although it is of necessity performed at the bedside and requires minutes rather than seconds, the total time of performance is comparable to that of other coagulation tests if preparation of blood samples and reagents is considered. The following groups of persons, who were generally in a postprandial state, were examined:

1. Fifty-three women in the age group of 17 to 60 years.
2. Fifteen healthy men, 25 to 50 years of age.
3. Thirty healthy employees in the age group of 60 to 80 years, to serve as controls for patients with prostatic cancer.
4. Twenty-two men with cancer of the prostate gland, in the age group of 60 to 80 years.
5. Twelve persons on 2 different occasions, 1 to 12 months apart, in order to determine the standard deviation of the test.
6. Thirty-six outpatients maintained on anticoagulants (Coumadin) over a period of 1 year, for comparison of the standard clotting time with Quick's 1-stage prothrombin time.[4]
7. Twenty-five persons with miscellaneous cases who were investigated because of a history of a suspected bleeding tendency, for comparison with the clotting time (Lee-White) for whole blood, and a battery of other screening tests for blood coagulation.[4]

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RESULTS

1. Fifty-three healthy women (17 to 60 years) manifested a normal value of 11.2, with a standard deviation from the mean of ±1.1 min.

2. Fifteen healthy men (25 to 50 years) manifested normal values of 11.1 ± 1.1 min.

3. Thirty healthy male employees (60 to 80 years of age), with 42 determinations manifested normal values of 10.1 ± 1.3 min.

4. Twenty-two men (44 determinations) with cancer of the prostate gland manifested an average value of 10.5 ± 1.5 min. These men were also in the age group of 60 to 80 years.

5. Twelve controls taken on 2 different occasions (1 to 12 months apart) revealed a standard deviation from the mean of ±1.0 min.

6. One hundred thirty-nine determinations of the standard clotting time and also the prothrombin time on 36 patients being treated with anticoagulants revealed a poor correlation between these 2 tests. For the prothrombin activity in the so-called therapeutic range of from 20 to 30 per cent, the values in the standard clotting time ranged from 10.2 to 21.0 min. (Fig. 1). Prothrombin activity of less than 20 per cent revealed a range in the standard clotting time of 11.5 to 23.5 min.; values of prothrombin activity of more than 30 per cent manifested in the standard clotting time a range of 10.5 to 18.4 min. If, conversely, the therapeutic range of the standard clotting time is considered, which, according to Mayer and Connell[3] is between 15 and 20 min., the corresponding prothrombin activities revealed a range of 16 to 49 per cent (Fig. 1); taking values of the standard clotting time of less than 15 min., the range of the corresponding prothrombin activity varied from 15 to 70 per cent, and similarly, in values above 20 min., the variation of prothrombin activity was between 15 and 24 per cent.

7. Comparison of the standard clotting time with the clotting time for whole blood, and other screening tests, revealed that the standard clotting time was within the normal range whenever the clotting time for whole blood (Lee-White) was less than 20 min., with the following exceptions: 3 instances of patients treated with salicylates in whom the clotting time for whole blood was normal and the standard clotting time moderately prolonged (less than 20 min.); 3 other persons with a history of minor bleeding dif-

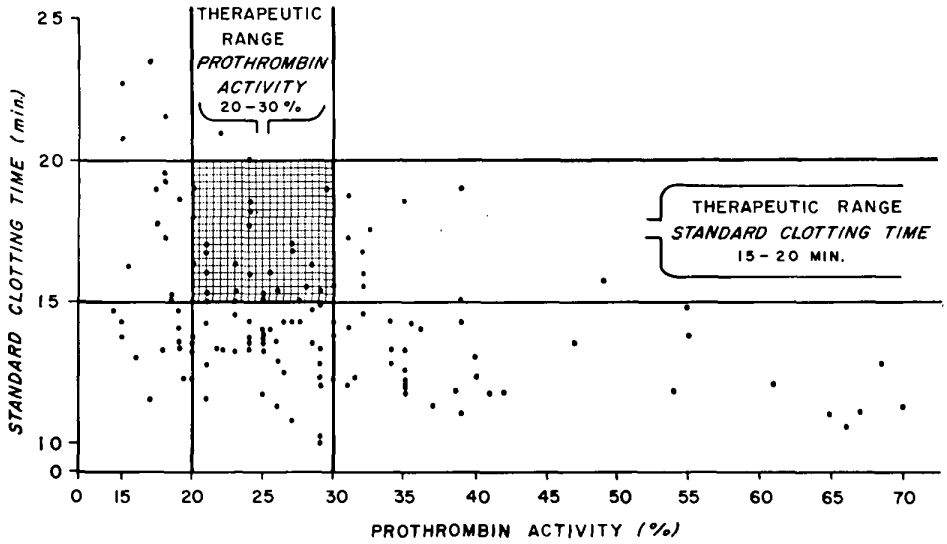


FIG. 1. A scattergram of the standard clotting time (min.) and prothrombin activity (per cent) of 139 determinations on 36 patients being treated with anticoagulants. Except for the *cross-hatched area*, there is no consistent correlation between the 2 tests.

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ficulty in whom the standard clotting time revealed a slight prolongation, in the range of from 15 to 20 min., whereas tests for other phases in blood coagulation, including the thromboplastin generation test, were normal. In addition, a patient with hemophilia A manifested a great prolongation of the standard clotting time, as well as the clotting time of the whole blood. There were 2 patients in whom, for unexplained reasons, the clotting time was less than normal, 9:00 and 7:33 min. One of these, a 34-year-old woman, had pulmonary coccidioidomycosis with multiple segmental pulmonary resections; her only other abnormality was a slightly positive tourniquet and petechiometer test. The other person, a 68-year-old man, is a patient with probable cirrhosis of the liver.

COMMENTS

We have found the standard clotting time a reliable and reproducible test for coagulation of whole blood. The normal range of values corresponds well with the figures reported by Mayer and Connell, except in the older age group, for whom the values are slightly less (approximately 1 min.).

The observation made by Mayer and Connell that there is poor correlation between the standard clotting time and the 1-stage prothrombin time is confirmed. The controversy[7] concerning which of the 2 tests more adequately represents a response to anticoagulation therapy is not resolved by our study; its resolution would require a very close clinical follow-up over a long period of time, which is not feasible for a study based on outpatients. According to Rapaport and Ames,[6] a Factor IX deficiency that is not measured by the prothrombin time does not seem to be the explanation. The standard clotting time may prove valuable whenever a discrepancy is encountered between 1 type of test, such as the 1-stage prothrombin time, and the clinical manifestations in anticoagulated patients. We also found that it may be a helpful procedure in evaluating a "borderline" prolonged clotting time, although it is by no means a substitute for detailed investigation of the patient with a history of definite bleeding. We have not determined whether or not values lower than normal (excluding faulty venipuncture) indicate a state of hypercoagulability. The greatest value of the test results from the fact that the normal range is rather narrow, as stated by Mayer and Connell.

SUMMARY

A re-evaluation of the standard clotting time, using several control groups, demonstrates that it is a reproducible test for coagulation of whole blood. It may be regarded as an additional useful test in the evaluation of an abnormal clotting time for whole blood, of patients with bleeding problems, and of patients being treated with anticoagulants.

SUMMARIO IN INTERLINGUA

Un re-evaluation del tempore standard de coagulation, utilisante plure gruppos de controlo, demonstra que illo es un reproducibile test pro le coagulation de sanguine total. Illo pote esser reguardate como un test additional de utilitate in le evalutation de anormal tempores de coagulation in sanguines total ab patientes con problemas hemorrhagic e ab patientes sub tractamento con anticoagulantes.

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Filing Date	2023-02-24
First Named Inventor	Bobby E. ROGERS
Art Unit	-
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Attorney Docket Number	069366-0574153_KUR2C04US

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	18113710
	Filing Date	2023-02-24
	First Named Inventor	Bobby E. ROGERS
	Art Unit	-
	Examiner Name	
	Attorney Docket Number	069366-0574153_KUR2C04US

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	Attorney Docket Number	069366-0574153_KUR2C04US

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See attached certification statement.

The fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

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Abstract of DE 29913417

Device for taking blood from a blood clot, (B), with a housing (1), with a hollow needle (10) that can be inserted through the blood vessel wall into the interior of the blood vessel (B), and with means for sucking the blood through the interior of the hollow needle, characterized, represents the hollow needle (10) between a retracted position, in which the hollow needle (10) remains at least substantially within the outer contours of the housing, and an extended position, in which the end to be inserted into the blood vessel (B) (19) the hollow needle (10) protrudes from the housing by a length, is displaceably arranged, and dar.. Means are provided with which the hollow needle (10) can be displaced from its retracted to its extended position.

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DESCRIPTION DE29913417U1

[0001]

13 PALGEN3 SCHUMACHER & KTUIN ·...."·· · ·· * ··*

[0002]

17 DUSSELDORF ESSEN PATENT ATTORNEYS

[0003]

21 OUR SIGNS: 99 328 K/at Düsseldorf, 5.

22 Aug 1999

[0004]

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28 Device for taking blood from a blood vessel

[0005]

32 The invention relates to a device for removing blood from a blood vessel of the type corresponding to the preamble of claim 1.

[0006]

37 Such devices always comprise a hollow needle that is beveled at one end for penetrating the

skin, the tissue lying between the skin and the vessel and the vessel wall, and which is usually equipped with a coupling at its other end, which is used to attach a container with a volume for receiving the blood taken .

[0007]

44 To generate the suction required for taking blood, it is known to design the containers as a piston/cylinder arrangement, after the hollow needle has been inserted into the blood vessel and the container has been coupled, the piston is actuated manually to increase the volume of the vessel.

[0008]

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[0009]

56 D-45133 ESSEN F^QM^JiSTl^SSE#*A .

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[0010]

61 POSTBANK COLOGNE (BLZ 370 100 50) 115 211 - 504

[0011]

65 The disadvantage of this device is that the patient can only prick the hollow needle into the blood vessel with considerable skill and practice if the person performing the puncture is almost painless for the patient.

68 Furthermore, when the plunger is actuated manually, the needle cannot usually be kept completely still, which means that the needle in the puncture area stretches or even injures the skin, the underlying tissue and the vessel wall, which regularly causes pain to the patient.

[0012]

74 For the latter reason, it is also known to pre-evacuate the vessels having the volume for receiving the blood taken and to seal them in their area to be connected to the coupling of the hollow needle with a closure or

77 Equip valve assembly, which is opened when coupled to the hollow needle, so that the blood to be removed is sucked into the volume of the container without requiring additional manual operation of the device.

[0013]

83 This measure prevents the risk of "wobbly pain" caused by the manual operation of the piston, but the disadvantage is that the insertion of the hollow needle, the subsequent coupling of the pre-evacuated vessel and the frequently necessary replacement of a full container with an empty one In turn, absorption of the blood removed leads to undesired movements of the needle which are painful for the patient.

[0014]

91 It is therefore the object of the invention to provide a device which allows blood to be taken from a blood vessel in a manner that is less painful for the patient.

[0015]

96 This object is solved by the invention presented in claim 1.

[0016]

100 Because in the device according to the invention the hollow needle can be moved between a retracted position, in which the hollow needle remains at least essentially within the outer contours of the housing of the device, and an extended position, in which the end of the hollow needle to be inserted into the blood vessel is pushed out of the housing by one certain length protrudes, is displaceably arranged, and that means are provided with which the hollow needle can be displaced from its retracted to its extended position, it is no longer necessary for the insertion of the needle that both the guide and the displacement during the insertion process of the needle must be accomplished by the person taking the blood sample.

108 Rather, the housing only needs to be positioned at the point on the body where the blood is to be taken and the means for extending the needle then activated.

110 The risk of "wobbling" during insertion of the hollow needle is therefore considerably reduced.

111 Since the means for moving the hollow needle can also be designed in such a way that it can be moved from its retracted to its extended position at high speed and the puncture process therefore only lasts a very short time, the pain associated with taking blood is reduced again.

114 Another advantage is that the high penetration speed of the needle reduces the pressure required in the blood vessel to prevent the vessel walls from collapsing when the needle is inserted, which is usually achieved by applying a pressure cuff, thereby reducing the risk of extravascular bruising.

[0017]

121 The means by which the hollow needle can be moved from its retracted position to its extended

position

[0018]

126 sen preferably have an arrangement which exerts an elastic force acting on the hollow needle in the direction of the retracted to the extended position.

128 In order to carry out the puncture, the hollow needle is then first moved into its retracted position, held in this position by suitable means, for example a locking device, and after the device has been brought to the suitable point on the body, by releasing the means, for example the locking moved to its extended position, with the tip of the hollow needle penetrating the blood vessel.

[0019]

136 In terms of its design, the arrangement for generating the elastic force can have a compression spring.

[0020]

141 However, it is also possible to generate the elastic force with the help of a compressed air reservoir or in a completely different way.

[0021]

146 The pain associated with taking blood from the patient can be further reduced if the housing of the device includes at least one internal volume for receiving the blood taken from the patient.

148 As a result of this measure, a coupling of a vessel for receiving blood taken after the puncture has been made is superfluous, so that "shaking pains" are prevented.

[0022]

153 If existing, commercially available containers are to continue to be used, an embodiment of the device according to the invention is recommended in which the housing includes an adapter arrangement for connecting at least one commercially available container for receiving the blood taken.

157 With this configuration, depending on the requirements, either several containers can be connected to the adapter at the same time,

[0023]

162 or - if this is not desired or possible - several containers can be connected one after the other.

[0024]

166 The means for sucking the blood through the interior of the hollow needle preferably include a negative pressure in the at least one interior volume compared to the outside environment.

168 This negative pressure can be generated, for example, by the inner volume being pre-evacuated and the interior of the hollow needle communicating with the inner volume in its extended position, in other words: only when the hollow needle is in the extended position is its interior connected to the pre-evacuated inner volume.

[0025]

175 However, it is also possible to provide means that only generate the negative pressure when the hollow needle is moved from its retracted to its extended position, to provide a manually or automatically actuated piston/cylinder device, or to bring about the negative pressure in any other way.

[0026]

182 Irrespective of the manner in which the negative pressure for sucking the blood is brought about, there are considerable advantages for the application if the device is designed in such a way that the negative pressure is applied to the hollow needle when it penetrates the blood vessel.

186 This measure effectively prevents painful extravascular bruising (hematoma) as a result of taking blood, which is regularly the case when blood can escape past the hollow needle from the blood vessel into the adjacent tissue during blood taking.

189 Because the suction in this preferred embodiment of the invention already exists when the hollow needle penetrates the blood vessel, blood that would otherwise have gotten into the tissue is also sucked out, even if the opening of the hollow needle is not completely drawn into the blood vessel

[0027]

196 Vessel has penetrated or partially exited the opposite vessel wall.

197 As a further consequence, in this embodiment the "penetration depth" of the tip of the hollow needle for carrying out the blood withdrawal method does not have to be specified as precisely as hitherto, which also makes it easier for the user to take the blood.

[0028]

203 For handling the device according to the invention, it is particularly advantageous to provide the side part of the housing from which the hollow needle protrudes in its extended position with at least one contact surface via which the device is supported on the body surface of a patient

during use.

207 To carry out the removal process, the device then only needs to be placed on a suitable part of the body and the displacement process of the hollow needle started.

[0029]

212 Tests have shown that the blood sampling process can be carried out particularly reliably and with little pain if the at least one contact surface is designed in such a way that when the device is supported on the body surface of the patient, the hollow needle forms an angle of between 5° and 30° with respect to the body surface in the support area - depending on the thickness of the tissue located between the vessel wall through which the hollow needle is intended to penetrate and the support surface.

[0030]

221 The device according to the invention can be used particularly variably when the at least one contact surface is designed in such a way that the angle that the hollow needle forms with the body surface during the removal process can be adjusted.

[0031]

227 In order to prevent the blood vessel intended for the removal process from being pushed away to the side when the device is put on, a particularly preferred

[0032]

232 Embodiment of the device according to the invention, a recess is provided in the at least one contact surface, into which the blood vessel can at least partially bulge and is thus positioned by the lateral boundary surfaces of the recess.

[0033]

238 If blood from a patient is used to carry out various diagnostic or

239 Therapy method required, so it is advantageous to provide a plurality of internal volumes separated from one another or an adapter arrangement for connecting a plurality of containers for receiving blood taken.

[0034]

245 The inner volumes or the containers can then optionally communicate with one another in series or also in parallel.

[0035]

250 In the drawing, exemplary embodiments of the invention are shown schematically.

251 Show it:

[0036]

255 1 shows a detail and diagrammatic view of a first exemplary embodiment of a device according to the invention in a longitudinal section, with the hollow needle being in its retracted position;

[0037]

260 FIG. 2 shows the same embodiment in the same view as in FIG. 1, but with the hollow needle being in its extended position; FIG.

[0038]

265 Fig .. 3 - in part - the same embodiment as in Fig. 1 in a partially cut

[0039]

269 NEN top view (view A in Fig. 1);

[0040]

273 FIG. 4 shows another embodiment of a device according to the invention in a view corresponding to FIG. 3; FIG.

[0041]

278 5--schematically and in detail--an exemplary embodiment corresponding to FIGS. 1 to 3 of a device according to the invention during a removal process, in a view in the direction of the blood vessel used for blood removal;

[0042]

284 6 - schematically - different positions of the beveled end of the hollow needle relative to the position of the blood vessel;

[0043]

289 7 shows an embodiment of a device according to the invention, which comprises a plurality of

volumes communicating with one another in series for receiving blood that has been taken (schematic);

[0044]

295 8 shows an embodiment of a device according to the invention in a view corresponding to FIG

[0045]

299 9 shows an embodiment of a device according to the invention in a view corresponding to FIGS. 7 and 8, which has an adapter plate for connecting two external containers for receiving blood that has been taken.

[0046]

305 The embodiment of a device according to the invention, denoted as 100 as a whole in FIGS. 1 to 3 and shown only partially and schematically in these figures, comprises a housing 1, which in its interior has two internal volumes 3, 4 fluidically connected to one another via a channel 2 for receiving blood.

309 The housing 1 has at its Fig. 1 downward-facing end face 5 on a housing extension 6 whose

[0047]

313 end 7 shown below in FIG. 1 is open.

[0048]

317 The interior 8 of the housing extension 6 serves to accommodate a hollow needle arrangement designated as a whole by 9, which essentially consists of the actual hollow needle 10 directed towards the open end 7 and a hollow needle carrier 11 serving to slidably mount the hollow needle arrangement 9 in the interior 8 of the housing extension 6 , which cooperates with the inner lateral surface 12 of the housing extension 6 at least approximately in a sealing manner.

[0049]

325 With its end face 13 facing away from the hollow needle 10 , the hollow needle carrier 11 is supported on a rigid contact surface 15 of the housing 1 via a pretensioned spiral spring 14 .

[0050]

330 A locking device 16 is used to lock the hollow needle arrangement 9 against the compressive force of the coil spring 14 in the retracted position.

[0051]

335 The hollow needle arrangement 9 has an inner channel 18 which extends from the tip 19 of the hollow needle 10 to a lateral opening 20 in the hollow needle carrier 11 .

[0052]

340 Furthermore, in the side wall of the housing extension 6 shown on the right in FIG.

[0053]

344 To move the hollow needle 10 from its retracted position shown in Fig. 1 to its extended position shown in Fig. 2, the locking device 16 is moved in such a way that the contact surface 17

[0054]

350 is released.

351 Due to the force exerted by the spiral spring 14 on the hollow needle arrangement 9, the latter snaps downwards according to FIG.

353 In this position, the inner channel 18 communicates with the channel 21 via the opening 22 so that the inner volumes 3 and 4 communicate with the inner channel 18 of the hollow needle and blood can flow through the channels 18, 21 and 2 into the inner volumes 3, 4.

[0055]

359 As can also be seen from FIG.

[0056]

363 As illustrated in FIG. 6, blood can only be taken if the hollow needle 10 penetrates just deep enough into the patient's tissue that its tip does not stop before penetrating the wall of the blood vessel B (see

366 6a)), nor does the area of the hollow needle 10 which is bevelled towards the tip 19 project completely through the blood vessel B (cf.

368 Fig. 6e)).

[0057]

372 In order to be able to adapt the "penetration depth" of the tip 19 of the hollow needle 10 required for blood sampling to the individual requirements, a cuff 24 is provided on the housing

extension 6, which is displaceably mounted in the direction of arrow P, with which the effective length of the housing extension 6 and thus the penetration depth the tip 19 of the hollow needle 10 can be changed.

377 The cuff 24 and the housing extension 6 can be equipped with latching means, not shown in the drawing, with which the cuff 24 can be locked in three different basic positions in which the penetration depth is at Kin-

[0058]

383 dern, normal-weight adults or overweight adults usual conditions is adapted.

[0059]

387 Extravascular bruising is also effectively prevented in end positions of the hollow needle 10 in which the tip 19 has not fully penetrated the blood vessel B (Fig. 6b)) or has partially penetrated the opposite wall of the blood vessel B (Fig. 6d)), since the negative pressure for sucking out the blood is already applied to the hollow needle as soon as it has entered the vessel.

[0060]

395 In principle, it is possible for the hollow needle 10 to pierce the blood vessel B essentially perpendicularly to its course.

397 However, such a procedure presupposes that the "penetration depth" must be predetermined almost exactly.

399 In order to avoid this, it is advisable to take the sample at an angle α between the hollow needle 10 and the blood vessel B, which is in the range between 5° and 30°.

401 For this purpose, the exemplary embodiment of the invention shown in FIGS. 1 and 2 has contact surfaces 25, through which the desired angle α is specified.

403 In the exemplary embodiments shown in the drawing, the angle α is fixed.

404 However, it is also within the scope of the invention to design the contact surfaces so variably that the angle α can be changed depending on the intended use of the device.

[0061]

409 As already described and shown again in detail in FIG. 1, a spiral spring 14 can be used to generate the force that drives the hollow needle arrangement from its retracted into its extended position.

412 However, as shown schematically in FIG. 4, it is also possible to provide a compressed air reservoir 26 between the end face 13 and the contact surface 15 or other means suitable for effecting an elastic force for propulsion.

[0062]

418 In order to prevent the vessel from which blood is to be taken from migrating laterally when the device 100 is placed on and the removal process thereby being frustrated, in a preferred embodiment of the invention a recess 27 is provided in the contact surfaces, into which the blood vessel B after the device 100 has been placed on the skin, it is at least partially pressed in and the blood vessel B is thus fixed laterally in the position required for taking blood (see Fig.

424 5).

[0063]

428 As illustrated in FIGS. 7 to 9, devices 100 according to the invention can be equipped in different ways with volumes for taking up blood that has been taken.

430 Thus, several volumes 28, 29, 30--three in FIG.

[0064]

434 It is also possible, as shown in FIG. 8, to provide inner volumes 31, 32, 33 which are arranged parallel to one another and are correspondingly filled approximately at the same time as one another.

[0065]

440 To generate the negative pressure required for filling, the volumes 28 to 33 can be pre-evacuated, or the negative pressure required in them can take place in any other way, for example by connecting the volumes to a piston/cylinder unit, an external pump, etc.

443 In order to avoid extravascular bruising, it is only essential that the negative pressure has already been generated when the tip 19 of the hollow needle 10 penetrates into the vessel.

[0066]

448 In the exemplary embodiment illustrated in FIG.

[0067]

452 Units 36/37 are formed in such a way that the pistons 36 can be displaced into the cylinder 37 by manually operable piston rods 38 .

454 An adapter arrangement 39 is used to attach the piston/cylinder unit 36/37 to this device, which is designated as a whole by 200, from which the housing extension 206 in turn extends downward according to FIG.

457 The hollow needle arrangement 209 and the channels 202 correspond in their technical design

and function to the hollow needle arrangement 9 and the channels 2 as they are described with reference to FIGS. 1 to 3 and therefore do not require any special discussion at this point.

[0068]

463 9 takes place in a manner already described with reference to FIGS. 1 to 3, by pulling out the piston rods 38 into the position shown in FIG of the cylinder 37 against the action of the negative pressure generated prior to the needle propelling and penetrating the blood vessel.

[0069]

469 14

[0070]

473 REFERENCE LIST

[0071]

477 1
478 Housing
479 34
480 volume

2

484 channel
485 35
486 volume

3

490 internal volume
491 36
492 Pistons

4

496 internal volume
497 37
498 cylinder

5

502 face

503 38

504 piston rods

6

508 Housing contζ

509 39

510 adapter assembly

7

514 End

515 40

516 locking protrusions

8

520 interior

521 100

522 contraption

9

526 hollow needle assembly

527 206

528 Housing contζ

10

532 hollow needle

533 209

534 hollow needle assembly

11

538 hollow needle carrier

539 202

540 channels

12

544 inner surface

13

548 face

549 H

550 skin

14

554 spiral spring

555 B

556 blood vessel

15

560 contact surface

561 A

562 Opinion

16

566 locking device

567 P

568 Arrow

17

572 plant area

18

576 inner canal

19

580 Top

20

584 opening

21
588 channel

22
592 End

23
596 attack

24
600 cuff

25
604 contact surface

26
608 compressed air reservoir

27
612 recess

28
616 volume

29
620 volume

30
624 volume

31

628 volume

32

632 volume

33

636 volume

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CLAIMS DE29913417U1

1.

13 Device for taking blood from a blood vessel (B), with a housing (1), with a hollow needle (10) that can be inserted through the blood vessel wall into the interior of the blood vessel (B), and with means for sucking the blood through the interior of the hollow needle, characterized in that the hollow needle (10) moves between a retracted position, in which the hollow needle (10) remains at least substantially within the outer contours of the housing, and an extended position, in which the end (19) to be inserted into the blood vessel (B) the hollow needle (10) protrudes from the housing by a length, and in that means are provided with which the hollow needle (10) can be displaced from its retracted to its extended position.

2.

24 Device according to Claim 1, characterized in that the means for displacing the hollow needle (10) from its retracted to its extended position comprise an arrangement which acts on the hollow needle (10) in a direction from the retracted to the extended position exert an acting elastic force.

3.

31 Device according to Claim 2, characterized in that the arrangement has a compression spring (14).

4.

36 Device according to Claim 2 or 3, characterized in that the arrangement has a compressed air reservoir (26).

5.

41 Device according to one of Claims 1 to 4, characterized in that the housing (1) comprises at least one internal volume (3, 4, 28-35) for receiving blood which has been removed.

6.

46 Device according to one of Claims 1 to 4, characterized in that the housing (1) comprises an adapter arrangement (39) for attaching at least one container, the internal volume (34, 35) of which is used to receive blood taken.

7.

52 Device according to Claim 5 or 6, characterized in that the means for sucking the blood through the interior of the hollow needles (10) comprise a negative pressure in the at least one interior volume (3, 4, 28-35) compared to the external environment.

8.

58 Device according to Claim 7, characterized in that the inner volume (3, 4, 28-35) is pre-evacuated and that the interior of the hollow needle (10) communicates with the inner volume (3, 4, 28-35) in its extended position.

9.

64 Device according to Claim 7, characterized in that means are provided which generate the negative pressure in the inner volume (3, 4, 28-35) when the hollow needle (10) is moved from its retracted to its extended position.

10.

70 Device according to Claim 9, characterized in that means for generating the negative pressure are a piston arrangement which is connected to the hollow needle (10) and which generates a negative pressure in a cylinder arrangement when the hollow needle (10) is moved into its extended position, and means which, in the extended Position of the hollow needle (10) connects the interior of the cylinder with the interior volume (3, 4, 28-35) for receiving the blood.

11.

78 Device according to one of Claims 1 to 10, characterized in that the side part of the housing (1) from which the hollow needle (10) protrudes in its extended position has at least one contact

surface (25) for supporting the device during use on the body surface of a patient.

12.

84 Device according to Claim 11, characterized in that the at least one contact surface (25) is designed in such a way that when the device is supported on the body surface of the patient, the hollow needle (10) forms an angle α to the body surface in the support area in the range between 5° and 30° includes.

13.

91 Device according to Claim 12, characterized in that the at least one contact surface (25) is designed such that the angle α between the hollow needle (10) and the body surface when the device is supported on the patient's body surface is adjustable.

14.

97 Device according to one of Claims 11 to 13, characterized in that the contact surface (25) has at least one recess (27) for fixing the blood vessel (B) used for taking blood.

15.

102 Device according to one of Claims 1 to 14, characterized in that the device comprises a plurality of separate inner volumes (3, 4, 28-33) for receiving the blood taken or an adapter arrangement (39) for connecting several containers for receiving blood taken includes.

16.

108 Device according to Claim 15, characterized in that the internal volumes (28, 29, 30) or the containers communicate with one another in series.

17.

113 Device according to Claim 15, characterized in that the inner volumes (31, 32, 33) or the containers communicate with one another in parallel.

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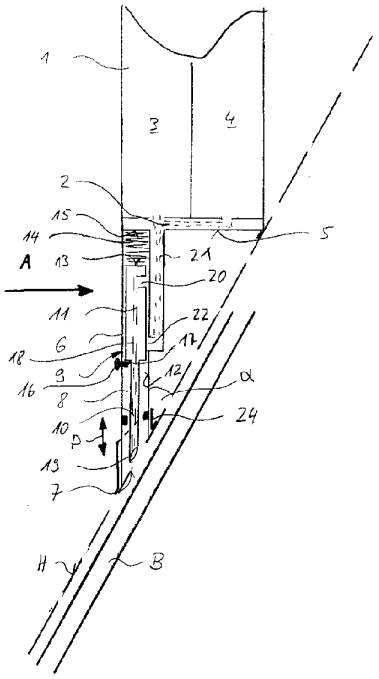
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(54) Vorrichtung zur Entnahme von Blut aus einem Blutgefäß

(57) Vorrichtung zur Entnahme von Blut aus einem Blutgefäß (B),
mit einem Gehäuse (1),
mit einer durch die Blutgefäßwandung ins Innere des Blutgefäßes (B) einführbaren Hohlnadel (10), und mit Mitteln zum Saugen des Bluts durch das Innere der Hohlnadel,
dadurch gekennzeichnet,
daß die Hohlnadel (10) zwischen einer zurückgezogenen Position, in der die Hohlnadel (10) zumindest im wesentlichen innerhalb der Außenkonturen des Gehäuses verbleibt, und einer ausgefahrenen Position, in der das in das Blutgefäß (B) einzuführende Ende (19) der Hohlnadel (10) aus dem Gehäuse um eine Länge hervorragt, verlagerbar angeordnet ist, und
daß Mittel vorgesehen sind, mit denen die Hohlnadel (10) aus ihrer zurückgezogenen in ihre ausgefahrene Position verlagerbar ist.



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Vorrichtung zur Entnahme von Blut aus einem Blutgefäß

Die Erfindung bezieht sich auf eine Vorrichtung zur Entnahme von Blut aus einem Blutgefäß der dem Oberbegriff des Anspruchs 1 entsprechenden Art.

Derartige Vorrichtungen umfassen stets eine zur Durchdringung der Haut, des zwischen Haut und Gefäß liegenden Gewebes sowie der Gefäßwandung einenends angeschrägte Hohlnadel, die an ihrem anderen Ende meist mit einer Kupplung ausgestattet ist, welche dem Ansetzen eines ein Volumen zur Aufnahme des entnommenen Blutes aufweisenden Behälters dient.

Zur Erzeugung des zur Blutentnahme erforderlichen Soges ist es bekannt, die Behältnisse als Kolben/Zylinderanordnung auszugestalten, wobei nach erfolgtem Einstich der Hohlnadel in das Blutgefäß und Ankuppeln des Behältnisses der Kolben manuell im Sinne einer Vergrößerung des Gefäßvolumens betätigt wird.

Nachteilig ist bei dieser Vorrichtung, daß ein für den Patienten nahezu schmerzloses Einstechen der Hohlnadel in das Blutgefäß nur bei erheblichem Geschick und erheblicher Übung der den Einstich vornehmenden Person möglich ist. Weiterhin kann bei manueller Betätigung des Kolbens die Nadel in der Regel nicht vollständig ruhig gehalten werden, was dazu führt, daß die Nadel im Einstechbereich die Haut, das darunter liegende Gewebe und die Gefäßwandung dehnt oder sogar verletzt, was regelmäßig zu Schmerzbeeinträchtigungen des Patienten führt.

Aus letzterem Grunde ist es ebenfalls bekannt, die das Volumen zur Aufnahme des entnommenen Blutes aufweisenden Gefäße vorzuevakuieren und in ihrem mit der Kupplung der Hohlnadel zu verbindenden Bereich mit einer Verschluß- bzw. Ventilanordnung auszustatten, die beim Ankuppeln an die Hohlnadel geöffnet wird, so daß das zu entnehmende Blut in das Volumen des Behältnisses eingesaugt wird, ohne daß es hierzu einer zusätzlichen manuellen Betätigung der Vorrichtung bedarf.

Durch diese Maßnahme wird die Gefahr, durch die manuelle Betätigung des Kolbens hervorgerufener "Wackelschmerzen" zwar verhindert, nachteilig ist jedoch, daß das Einstechen der Hohlnadel, das anschließende Ankuppeln des vorevakuierten Gefäßes und das in häufigen Fällen notwendige Auswechseln eines vollen gegen einen leeren Behälter zur Aufnahme des entnommenen Blutes wiederum zu unerwünschten, für den Patienten schmerzhaften Bewegungen der Nadel führt.

Es ist daher die Aufgabe der Erfindung, eine Vorrichtung zu schaffen, welche eine Blutentnahme aus einem Blutgefäß in für den Patienten weniger schmerzhafter Weise ermöglicht.

Diese Aufgabe wird durch die in Anspruch 1 wiedergegebene Erfindung gelöst.

Dadurch, daß bei der erfindungsgemäßen Vorrichtung die Hohlnadel zwischen einer zurückgezogenen Position, in der die Hohlnadel zumindest im wesentlichen innerhalb der Außenkonturen des Gehäuses der Vorrichtung verbleibt, und einer ausgefahrenen Position, in der das in das Blutgefäß einzuführende Ende der Hohlnadel aus dem Gehäuse um eine bestimmte Länge hervorragt, verlagerbar angeordnet ist, und daß Mittel vorgesehen sind, mit denen die Hohlnadel aus ihrer zurückgezogenen in ihre ausgefahrene Position verlagerbar ist, ist es zum Einstechen der Nadel nicht mehr erforderlich, daß während des Einstechvorganges sowohl die Führung, als auch die Verlagerung der Nadel von der die Blutabnahme durchführenden Person bewerkstelligt werden muß. Vielmehr braucht das Gehäuse lediglich an der Stelle des Körpers, an der die Blutabnahme erfolgen soll, positioniert und anschließend die Mittel zum Ausfahren der Nadel aktiviert zu werden. Die Gefahr des "Wackelns" während des Einstiches der Hohlnadel ist daher erheblich verringert. Da zudem die Mittel zur Verlagerung der Hohlnadel derart ausgebildet sein können, daß diese mit hoher Geschwindigkeit aus ihrer zurückgezogenen in ihre ausgefahrene Position erfolgt und damit der Einstichvorgang nur eine sehr kurze Zeit dauert, ist der mit der Blutentnahme verbundene Schmerz abermals reduziert. Weiterhin ist vorteilhaft, daß durch die hohe Eindringgeschwindigkeit der Nadel der in dem Blutgefäß zum Verhindern des Kollabierens der Gefäßwandungen beim Einstechen der Nadel erforderliche Druck der meist durch Anlegen einer Druckmanschette bewerkstelligt wird, verringert ist, wodurch das Risiko paravasaler Blutergüsse reduziert ist.

Die Mittel, mit denen die Hohlnadel aus ihrer zurückgezogenen in ihre ausgefahrene Position verlagerbar ist, wei-

sen vorzugsweise eine Anordnung auf, die auf die Hohlnadel eine in Richtung der zurückgezogenen auf die ausgefahrene Position wirkende, elastische Kraft ausüben. Zur Durchführung des Einstiches wird die Hohlnadel dann zunächst in ihre zurückgezogene Position verlagert, in dieser durch geeignete Mittel, beispielsweise einer Verriegelungseinrichtung, gehalten, und, nachdem die Vorrichtung an die geeignete Stelle des Körpers gebracht wurde, durch Lösen der Mittel, beispielsweise der Verriegelung, in ihre ausgefahrene Position gebracht, wobei die Spitze der Hohlnadel in das Blutgefäß eindringt.

In ihrer konstruktiven Ausgestaltung kann die Anordnung zur Erzeugung der elastischen Kraft eine Druckfeder aufweisen.

Es ist jedoch ebenfalls möglich, die elastische Kraft mit Hilfe eines Druckluftreservoirs oder auch in einer gänzlich anderen Weise zu erzeugen.

Der mit der Blutentnahme für den Patienten verbundene Schmerz kann nochmals verringert werden, wenn das Gehäuse der Vorrichtung mindestens ein Innenvolumen zur Aufnahme des dem Patienten entnommenen Blutes umfaßt. Durch diese Maßnahme wird ein Ankuppeln eines Gefäßes zur Aufnahme entnommenen Blutes nach erfolgtem Einstich überflüssig, so daß "Wackelschmerzen" verhindert werden.

Sollen bereits vorhandene, handelsübliche Behälter weiterhin Verwendung finden, so empfiehlt sich eine Ausführungsform der erfindungsgemäßen Vorrichtung, bei der das Gehäuse eine Adapteranordnung zum Anschluß mindestens eines handelsüblichen Behälters zur Aufnahme entnommenen Blutes umfaßt. Durch diese Ausgestaltung können an den Adapter je nach Anforderungen entweder mehrere Behälter gleichzeitig,

oder - falls dies nicht erwünscht oder möglich ist - auch mehrere Behälter nacheinander angeschlossen werden.

Die Mittel zum Saugen des Blutes durch das Innere der Hohlnadel umfassen vorzugsweise einen Unterdruck in dem mindestens einen Innenvolumen gegenüber der äußeren Umgebung. Dieser Unterdruck kann beispielsweise dadurch erzeugt werden, daß das Innenvolumen vorevakuiert ist und das Innere der Hohlnadel in ihrer ausgefahrenen Position mit dem Innenvolumen kommuniziert, mit anderen Worten: daß erst in der ausgefahrenen Position der Hohlnadel die Verbindung deren Inneren mit dem vorevakuierten Innenvolumen erfolgt.

Es ist jedoch ebenfalls möglich, Mittel vorzusehen, die den Unterdruck erst beim Verlagern der Hohlnadel aus ihrer zurückgezogenen in ihre ausgefahrene Position erzeugen, eine manuell oder automatisch betätigbare Kolben/Zylindereinrichtung vorzusehen oder den Unterdruck auf eine beliebige andere Weise zu bewerkstelligen.

Unabhängig davon, auf welche Weise der Unterdruck zum Saugen des Blutes bewirkt wird, ergeben sich für die Anwendung erhebliche Vorteile, wenn die Vorrichtung derart ausgebildet ist, daß der Unterdruck an der Hohlnadel anliegt, wenn diese in das Blutgefäß eindringt. Durch diese Maßnahme wird nämlich wirkungsvoll verhindert, daß infolge der Blutentnahme schmerzhafte paravasale Blutergüsse (Hämatome) entstehen, was regelmäßig dann der Fall ist, wenn während der Blutentnahme Blut an der Hohlnadel vorbei aus dem Blutgefäß in das angrenzende Gewebe austreten kann. Dadurch, daß der Sog bei dieser bevorzugten Ausführungsform der Erfindung bereits beim Eindringen der Hohlnadel in das Blutgefäß besteht, wird auch Blut, was ansonsten in das Gewebe gelangt wäre, abgesaugt, und zwar selbst dann, wenn die Öffnung der Hohlnadel nicht vollständig in das

Gefäß eingedrungen oder teilweise aus der gegenüberliegenden Gefäßwandung wieder ausgetreten ist. Als weitere Folge muß bei dieser Ausführungsform die "Eindringtiefe" der Spitze der Hohlnadel zur Durchführung des Blutentnahmeverfahrens nicht so exakt wie bislang vorgegeben werden, was die Blutentnahme auch dem Anwendungspersonal erleichtert.

Für die Handhabung der erfindungsgemäßen Vorrichtung ist es besonders vorteilhaft, das Seitenteil des Gehäuses, aus dem die Hohlnadel in ihrer ausgefahrenen Position herausragt, mit mindestens einer Anlagefläche zu versehen, über die sich die Vorrichtung während ihrer Verwendung auf der Körperoberfläche eines Patienten abstützt. Die Vorrichtung braucht zur Durchführung des Entnahmevorganges dann lediglich auf eine geeignete Körperstelle aufgesetzt und der Verlagervorgang der Hohlnadel in Gang gesetzt zu werden.

Versuche haben gezeigt, daß der Blutentnahmevorgang besonders zuverlässig und schmerzarm durchgeführt werden kann, wenn die mindestens eine Anlagefläche derart ausgestaltet ist, daß bei Abstützung der Vorrichtung auf der Körperoberfläche des Patienten die Hohlnadel zur Körperoberfläche im Abstützbereich einen Winkel im Bereich zwischen 5° und 30° - je nach Dicke des zwischen der Gefäßwandung, die die Hohlnadel durchdringen soll, und der Abstützfläche befindlichen Gewebes - einschließt.

Besonders variabel einsetzbar ist die erfindungsgemäße Vorrichtung dann, wenn die mindestens eine Anlagefläche derart ausgestaltet ist, daß der Winkel, den die Hohlnadel mit der Körperoberfläche während des Entnahmevorgangs einschließt, einstellbar ist.

Um zu verhindern, daß das jeweils für den Entnahmevorgang vorgesehene Blutgefäß beim Aufsetzen der Vorrichtung seitlich weggedrückt wird, ist bei einer besonders bevorzugten

Ausführungsform der erfindungsgemäßen Vorrichtung eine Aussparung in der mindestens einen Anlagefläche vorgesehen, in die das Blutgefäß sich zumindest teilweise hereinwölben kann und somit von den seitlichen Begrenzungsflächen der Aussparung positioniert wird.

Wird Blut eines Patienten zur Durchführung verschiedener Diagnose- bzw. Therapieverfahren benötigt, so ist es von Vorteil, eine Mehrzahl voneinander getrennter Innenvolumina oder eine Adapteranordnung zum Anschluß mehrerer Behälter zur Aufnahme entnommenen Blutes vorzusehen.

Die Innenvolumina oder die Behälter können dann wahlweise seriell oder auch parallel miteinander kommunizieren.

In der Zeichnung sind Ausführungsbeispiele der Erfindung schematisch dargestellt. Es zeigen:

Fig. 1 - ausschnittsweise und schematisch - ein erstes Ausführungsbeispiel einer erfindungsgemäßen Vorrichtung in einem Längsschnitt, wobei sich die Hohlnadel in ihrer zurückgezogenen Position befindet;

Fig. 2 dasselbe Ausführungsbeispiel in derselben Ansicht wie in Fig. 1, wobei sich jedoch die Hohlnadel in ihrer ausgefahrenen Position befindet;

Fig.. 3 - ausschnittsweise - dasselbe Ausführungsbeispiel wie in Fig. 1 in einer teilgeschnittenen Aufsicht (Ansicht A in Fig. 1);

Fig. 4 ein anderes Ausführungsbeispiel einer erfindungsgemäßen Vorrichtung in einer Fig. 3 entsprechenden Ansicht;

Fig. 5 - schematisch und ausschnittsweise - ein Fig. 1 bis 3 entsprechendes Ausführungsbeispiel einer erfindungsgemäßen Vorrichtung während eines Entnahmevorganges in einer Ansicht in Richtung des der Blutentnahme dienenden Blutgefäßes;

Fig. 6 - schematisch - verschiedene Positionen des abgeschrägten Endes der Hohlnadel relativ zur Lage des Blutgefäßes;

Fig. 7 eine Ausführungsform einer erfindungsgemäßen Vorrichtung, die mehrere seriell miteinander kommunizierende Volumina zur Aufnahme entnommenen Blutes umfaßt (schematisch);

Fig. 8 eine Ausführungsform einer erfindungsgemäßen Vorrichtung in einer Fig. 7 entsprechenden Ansicht, die mehrere parallel miteinander kommunizierende Innenvolumina zur Aufnahme entnommenen Blutes umfaßt sowie

Fig. 9 eine Ausführungsform einer erfindungsgemäßen Vorrichtung in einer Fig. 7 und 8 entsprechenden Ansicht, welche eine Adapterplatte zum Anschluß zweier externer Behältnisse zur Aufnahme entnommenen Bluts aufweist.

Die in den Fig. 1 bis 3 als Ganzes mit 100 bezeichnete, in diesen Figuren lediglich ausschnittsweise und schematisch dargestellte Ausführungsform einer erfindungsgemäßen Vorrichtung umfaßt ein Gehäuse 1, welches in seinem Inneren zwei fluidisch über einen Kanal 2 miteinander verbundene Innenvolumina 3, 4 zur Aufnahme entnommenen Blutes aufweist. Das Gehäuse 1 weist an seinen Fig. 1 nach unten weisenden Stirnseite 5 einen Gehäusefortsatz 6 auf, dessen

in Fig. 1 unten dargestelltes Ende 7 offen ausgebildet ist.

Das Innere 8 des Gehäusefortsatzes 6 dient der Aufnahme einer als Ganzes mit 9 bezeichneten Hohlnadelanordnung, die im wesentlichen aus der zum offenen Ende 7 hin gerichteten eigentlichen Hohlnadel 10 und einem der verschiebbaren Lagerung der Hohlnadelanordnung 9 in dem Inneren 8 des Gehäusefortsatzes 6 dienenden Hohlnadelträger 11 besteht, der mit der inneren Mantelfläche 12 des Gehäusefortsatzes 6 zumindest annähernd abdichtend zusammenwirkt.

Mit seiner der Hohlnadel 10 abgewandten Stirnseite 13 stützt sich der Hohlnadelträger 11 über eine vorgespannte Spiralfeder 14 an einer starren Anlagefläche 15 des Gehäuses 1 ab.

Der Arretierung der Hohlnadelanordnung 9 gegen die Druckkraft der Spiralfeder 14 in der zurückgezogenen Position dient eine Arretiereinrichtung 16, die in der zurückgezogenen Position der Hohlnadelanordnung 9 eine der Stirnseite 13 gegenüberliegende Anlagefläche 17 hintergreift.

Die Hohlnadelanordnung 9 weist einen Innenkanal 18 auf, der sich von der Spitze 19 der Hohlnadel 10 bis zu einer seitlichen Öffnung 20 des Hohlnadelträgers 11 erstreckt.

Ferner ist in der in Fig. 1 rechts dargestellten Seitenwandung des Gehäusefortsatzes 6 ein einenends in den Kanal 2 mündender Kanal 21 vorgesehen, dessen anderes Ende 22 in das Innere 8 des Gehäusefortsatzes 6 mündet.

Zur Verlagerung der Hohlnadel 10 aus ihrer in Fig. 1 dargestellten, zurückgezogenen Position in ihre in Fig. 2 dargestellte, ausgefahrene Position wird die Arretiereinrichtung 16 derart verlagert, daß die Anlagefläche 17

freigegeben wird. Durch die von der Spiralfeder 14 auf die Hohlnadelanordnung 9 ausgeübte Kraft schnellt letztere gemäß Fig. 2 nach unten, bis die Anlagefläche 17 an einem von der inneren Mantelfläche 12 nach innen ragenden Anschlag 23 anliegt und hierdurch der Verlagerungsweg begrenzt wird. In dieser Position kommuniziert der Innenkanal 18 über die Öffnung 22 mit dem Kanal 21, so daß die Innenvolumina 3 und 4 mit dem Innenkanal 18 der Hohlnadel kommunizieren und Blut durch die Kanäle 18, 21 und 2 in die Innenvolumina 3, 4 einströmen kann.

Wie ferner aus Fig. 2 ersichtlich ist, hat die Hohlnadel 10 mit ihrer Spitze 19 die Haut H im Bereich der Stelle, an der die Hohlnadel 10 in das Blutgefäß B eindringen soll, sowie eine Wandung des Blutgefäßes B durchsetzt.

Wie Fig. 6 veranschaulicht, ist eine Blutentnahme nur dann möglich, wenn die Hohlnadel 10 gerade so tief in das Gewebe des Patienten eindringt, daß ihre Spitze weder vor dem Durchdringen der Wandung des Blutgefäßes B zum Stillstand kommt (s. Fig. 6a)), noch der zur Spitze 19 hin angeschrägte Bereich der Hohlnadel 10 vollständig durch das Blutgefäß B hindurchragt (vgl. Fig. 6e)).

Um die zur Blutentnahme erforderliche "Eindringtiefe" der Spitze 19 der Hohlnadel 10 den individuellen Anforderungen anpassen zu können, ist an dem Gehäusefortsatz 6 eine in Richtung des Pfeiles P verschiebbar gelagerte Manschette 24 vorgesehen, mit der die wirksame Länge des Gehäusefortsatzes 6 und somit die Eindringtiefe der Spitze 19 der Hohlnadel 10 veränderbar ist. Die Manschette 24 und der Gehäusefortsatz 6 können mit in der Zeichnung nicht dargestellten Rastmitteln ausgestattet sein, mit denen sich die Manschette 24 in drei verschiedenen Grundstellungen arretieren läßt, bei denen die Eindringtiefe an die bei Kin-

dern, normalgewichtigen Erwachsenen bzw. übergewichtigen Erwachsenen üblichen Verhältnisse angepaßt ist.

Paravasale Blutergüsse werden auch bei Endpositionen der Hohlnadel 10, in denen die Spitze 19 nicht vollständig in das Blutgefäß B eingedrungen ist (Fig. 6b)) oder die gegenüberliegende Wandung des Blutgefäßes B teilweise durchdrungen hat (Fig. 6d)), wirksam verhindert, da der Unterdruck zum Absaugen des Blutes an der Hohlnadel bereits anliegt, sobald diese in das Gefäß eingedrungen ist. Prinzipiell ist es zwar möglich, den Einstich der Hohlnadel 10 in das Blutgefäß B im wesentlichen senkrecht zu dessen Verlauf vorzunehmen. Eine derartige Vorgehensweise setzt jedoch voraus, daß die "Eindringtiefe" nahezu exakt vorbestimmt werden muß. Um dies zu vermeiden, empfiehlt es sich, die Entnahme unter einem Winkel α zwischen der Hohlnadel 10 und dem Blutgefäß B vorzunehmen, der im Bereich zwischen 5° und 30° liegt. Hierzu weist das in den Fig. 1 und 2 dargestellte Ausführungsbeispiel der Erfindung Anlageflächen 25 auf, durch die der gewünschte Winkel α vorgegeben ist. Bei den in der Zeichnung dargestellten Ausführungsbeispielen ist der Winkel α fest eingestellt. Es liegt jedoch ebenfalls im Rahmen der Erfindung, die Anlageflächen derart variabel auszugestalten, daß der Winkel α je nach vorgesehener Anwendungsweise der Vorrichtung veränderbar ist.

Wie bereits beschrieben und in Fig. 1 nochmals im einzelnen dargestellt, kann der Erzeugung der die Hohlnadelanordnung aus ihrer zurückgezogenen in ihre ausgefahrene Position vortreibenden Kraft eine Spiralfeder 14 dienen. Es ist - wie in Fig. 4 schematisch dargestellt - jedoch ebenfalls möglich, zum Vortrieb ein Druckluftreservoir 26 zwischen der Stirnseite 13 und der Anlagefläche 15 oder andere zur Bewirkung einer elastischen Kraft geeignete Mittel vorzusehen.

Um zu verhindern, daß das Gefäß, aus dem Blut entnommen werden soll, beim Aufsetzen der Vorrichtung 100 seitlich auswandert und der Entnahmevorgang hierdurch vereitelt wird, ist bei einer bevorzugten Ausführungsform der Erfindung in den Anlageflächen eine Aussparung 27 vorgesehen, in die sich das Blutgefäß B nach dem Aufsetzen der Vorrichtung 100 auf die Haut zumindest teilweise eindrückt und somit das Blutgefäß B seitlich in der für die Blutentnahme erforderlichen Position fixiert wird (s. Fig. 5).

Wie in den Fig. 7 bis 9 verdeutlicht, können erfindungsgemäße Vorrichtungen 100 in unterschiedlicher Weise mit Volumina zur Aufnahme entnommenen Blutes ausgestattet sein. So können mehrere - in Fig. 7 drei - Volumina 28, 29, 30 in dem Gehäuse 1 vorgesehen sein, die seriell miteinander kommunizieren und somit während des Entnahmevorganges nacheinander mit Blut gefüllt werden.

Ferner ist es möglich, wie in Fig. 8 dargestellt, parallel zueinander angeordnete Innenvolumina 31, 32, 33 vorzusehen, die dementsprechend etwa zeitparallel zueinander aufgefüllt werden.

Zur Erzeugung des zum Auffüllen erforderlichen Unterdrucks können die Volumina 28 bis 33 vorevakuiert sein, oder der in selbigen erforderliche Unterdruck kann auf eine beliebige andere Weise, beispielsweise durch Verbindung der Volumina mit einer Kolben/Zylindereinheit, einer externen Pumpe usw. erfolgen. Zur Vermeidung paravasaler Blutergüsse ist es lediglich wesentlich, daß der Unterdruck bereits erzeugt ist, wenn die Spitze 19 der Hohlnadel 10 in das Gefäß eindringt.

Bei dem in Fig. 9 dargestellten Ausführungsbeispiel sind die zur Aufnahme des entnommenen Blutes vorgesehenen Volumina 34, 35 extern angeordnet und als Kolben/Zylinderein-

heiten 36/37 ausgebildet und zwar derart, daß die Kolben 36 durch manuell betätigbare Kolbenstangen 38 in den Zylinder 37 verlagerbar sind. Zur Anbringung der Kolben/-Zylindereinheit 36/37 an dieser als Ganzes mit 200 bezeichneten Vorrichtung dient eine Adapteranordnung 39, von der aus sich gemäß Fig. 9 wiederum nach unten der Gehäusefortsatz 206 erstreckt. Die Hohlnadelanordnung 209 und die Kanäle 202 entsprechen in ihrer technischen Ausgestaltung und Funktion der Hohlnadelanordnung 9 und den Kanälen 2, so wie sie anhand der Fig. 1 bis 3 beschrieben sind und bedürfen daher an dieser Stelle keiner besonderen Erörterung.

Die Blutentnahme bei der Vorrichtung gemäß Fig. 9 erfolgt in einer anhand von Fig. 1 bis 3 bereits beschriebenen Weise, wobei durch Herausziehen der Kolbenstangen 38 in die in Fig. 9 dargestellte Position, in der die Kolben 36 durch Arretiervorsprünge 40 an der Innenwandung des Zylinders 37 gegen die Wirkung des Unterdrucks gehalten werden, selbiger vor dem Vorschnellen der Nadel und Eindringen in das Blutgefäß erzeugt wird.

BEZUGSZEICHENLISTE

	1	Gehäuse	34	Volumen
5	2	Kanal	35	Volumen
	3	Innenvolumen	36	Kolben
	4	Innenvolumen	37	Zylinder
	5	Stirnseite	38	Kolbenstangen
	6	Gehäusefortsatz	39	Adapteranordnung
10	7	Ende	40	Arretiervorsprünge
	8	Inneres	100	Vorrichtung
	9	Hohlnadelanordnung	206	Gehäusefortsatz
	10	Hohlnadel	209	Hohlnadelanordnung
	11	Hohlnadelträger	202	Kanäle
15	12	innere Mantelfläche		
	13	Stirnseite	H	Haut
	14	Spiralfeder	B	Blutgefäß
	15	Anlagefläche	A	Ansicht
	16	Arretiereinrichtung	P	Pfeil
20	17	Anlagefläche		
	18	Innenkanal		
	19	Spitze		
	20	Öffnung		
	21	Kanal		
25	22	Ende		
	23	Anschlag		
	24	Manschette		
	25	Anlagefläche		
	26	Druckluftreservoir		
30	27	Aussparung		
	28	Volumen		
	29	Volumen		
	30	Volumen		
	31	Volumen		
35	32	Volumen		
	33	Volumen		

PALGEN, SCHUMACHER & KLUIN
PATENTANWÄLTE
DÜSSELDORF · ESSEN

07.08.99

UNSER ZEICHEN: 99 328 K/at

Düsseldorf, den 5. August 1999

Dr. Peter Zierden
Rudolf-Harbig-Weg 6

D - 40764 Langenfeld

Schutzansprüche

1. Vorrichtung zur Entnahme von Blut aus einem Blutgefäß (B),
mit einem Gehäuse (1),
mit einer durch die Blutgefäßwandung ins Innere des Blutgefäßes (B) einführbaren Hohlnadel (10),
und mit Mitteln zum Saugen des Bluts durch das Innere der Hohlnadel,
dadurch gekennzeichnet,
daß die Hohlnadel (10) zwischen einer zurückgezogenen Position, in der die Hohlnadel (10) zumindest im wesentlichen innerhalb der Außenkonturen des Gehäuses verbleibt, und einer ausgefahrenen Position, in der das in das Blutgefäß (B) einzuführende Ende (19) der Hohlnadel (10) aus dem Gehäuse um eine Länge hervorragt, verlagerbar angeordnet ist, und
daß Mittel vorgesehen sind, mit denen die Hohlnadel (10) aus ihrer zurückgezogenen in ihre ausgefahrene Position verlagerbar ist.

2. Vorrichtung nach Anspruch 1, **dadurch gekennzeichnet**, daß die Mittel, mit denen die Hohlnadel

D-40239 DÜSSELDORF · MULVANYSTRASSE 2 · TELEFON 49 / 211 / 96 145 - 0 · TELEFAX 49 / 211 / 96 145 - 20
D-45133 ESSEN · FRÜHLINGSTRASSE 43 A · TELEFON 49 / 201 / 84 230 - 0 · TELEFAX 49 / 201 / 84 230 - 20
POSTBANK KÖLN (BLZ 370 100 50) 115 211 - 504

(10) aus ihrer zurückgezogenen in ihre ausgefahrene Position verlagerbar ist, eine Anordnung umfassen, die auf die Hohlnadel (10) eine in Richtung von der zurückgezogenen auf die ausgefahrene Position wirkende, elastische Kraft ausüben.

3. Vorrichtung nach Anspruch 2, **dadurch gekennzeichnet**, daß die Anordnung eine Druckfeder (14) aufweist.

4. Vorrichtung nach Anspruch 2 oder 3, **dadurch gekennzeichnet**, daß die Anordnung ein Druckluftreservoir (26) aufweist.

5. Vorrichtung nach einem der Ansprüche 1 bis 4, **dadurch gekennzeichnet**, daß das Gehäuse (1) mindestens ein Innenvolumen (3, 4, 28 - 35) zur Aufnahme entnommenen Blutes umfaßt.

6. Vorrichtung nach einem der Ansprüche 1 bis 4, **dadurch gekennzeichnet**, daß das Gehäuse (1) eine Adapteranordnung (39) zum Anschluß mindestens eines Behälters umfaßt, dessen Innenvolumen (34, 35) zur Aufnahme von entnommenem Blut dient.

7. Vorrichtung nach Anspruch 5 oder 6, **dadurch gekennzeichnet**, daß die Mittel zum Saugen des Blutes durch das Innere der Hohlnadeln (10) einen Unterdruck in dem mindestens einen Innenvolumen (3, 4, 28 - 35) gegenüber der äußeren Umgebung umfassen.

8. Vorrichtung nach Anspruch 7, **dadurch gekennzeichnet**, daß das Innenvolumen (3, 4, 28 - 35) vorevakuiert ist und daß das Innere der Hohlnadel (10) in ihrer ausgefahrenen Position mit dem Innenvolumen (3, 4, 28 - 35) kommuniziert.

9. Vorrichtung nach Anspruch 7, **dadurch gekennzeichnet**, daß Mittel vorgesehen sind, die beim Verlagern der Hohlnadel (10) aus ihrer zurückgezogenen in ihre ausgefahrene Position den Unterdruck in dem Innenvolumen (3, 4, 28 - 35) erzeugen.

10. Vorrichtung nach Anspruch 9, **dadurch gekennzeichnet**, daß Mittel zur Erzeugung des Unterdrucks eine mit der Hohlnadel (10) verbundene Kolbenanordnung, die beim Verlagern der Hohlnadel (10) in ihre ausgefahrene Position in einer Zylinderanordnung einen Unterdruck erzeugt, und Mittel, die in der ausgefahrenen Position der Hohlnadel (10) das Innere des Zylinders mit dem Innenvolumen (3, 4, 28 - 35) zur Aufnahme des Bluts verbindet, umfaßt.

11. Vorrichtung nach einem der Ansprüche 1 bis 10, **dadurch gekennzeichnet**, daß das Seitenteil des Gehäuses (1), aus dem die Hohlnadel (10) in ihrer ausgefahrenen Position herausragt, mindestens eine Anlagefläche (25) zur Abstützung der Vorrichtung während ihrer Verwendung auf der Körperoberfläche eines Patienten aufweist.

12. Vorrichtung nach Anspruch 11, **dadurch gekennzeichnet**, daß die mindestens eine Anlagefläche (25) derart ausgestaltet ist, daß bei Abstützung der Vorrichtung auf der Körperoberfläche des Patienten die Hohlnadel (10) zur Körperoberfläche im Abstützbereich einen Winkel α im Bereich zwischen 5° und 30° einschließt.

13. Vorrichtung nach Anspruch 12, **dadurch gekennzeichnet**, daß die mindestens eine Anlagefläche (25) derart ausgestaltet ist, daß der Winkel α, den die Hohlnadel (10) mit der Körperoberfläche bei Abstüt-

zung der Vorrichtung auf der Körperoberfläche des Patienten aufweist, einstellbar ist.

14. Vorrichtung nach einem der Ansprüche 11 bis 13, **dadurch gekennzeichnet**, daß die Anlagefläche (25) mindestens eine Aussparung (27) zur Fixierung des der Blutentnahme dienenden Blutgefäßes (B) aufweist.

15. Vorrichtung nach einem der Ansprüche 1 bis 14, **dadurch gekennzeichnet**, daß die Vorrichtung eine Mehrzahl von einander getrennter Innenvolumina (3, 4, 28 - 33) zur Aufnahme des entnommenen Bluts umfaßt oder eine Adapteranordnung (39) zum Anschluß mehrerer Behälter zur Aufnahme entnommenen Blutes umfaßt.

16. Vorrichtung nach Anspruch 15, **dadurch gekennzeichnet**, daß die Innenvolumina (28, 29, 30) oder die Behälter seriell miteinander kommunizieren.

17. Vorrichtung nach Anspruch 15, **dadurch gekennzeichnet**, daß die Innenvolumina (31, 32, 33) oder die Behälter parallel miteinander kommunizieren.

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Fig. 1

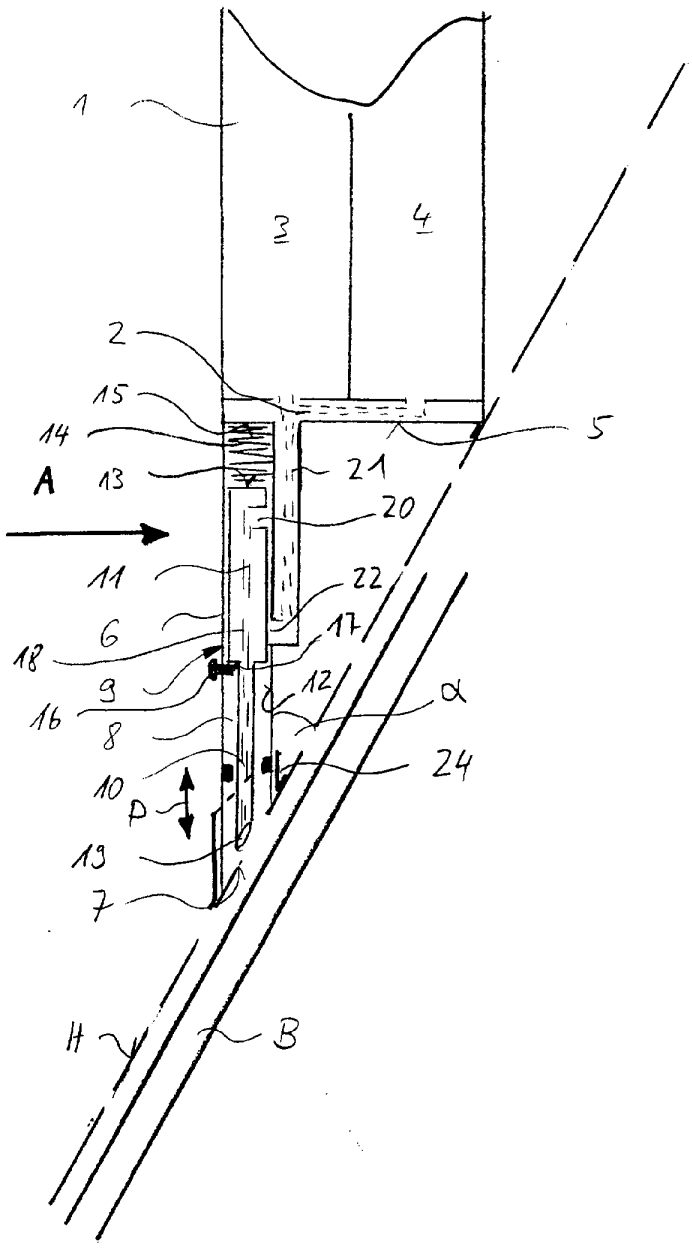
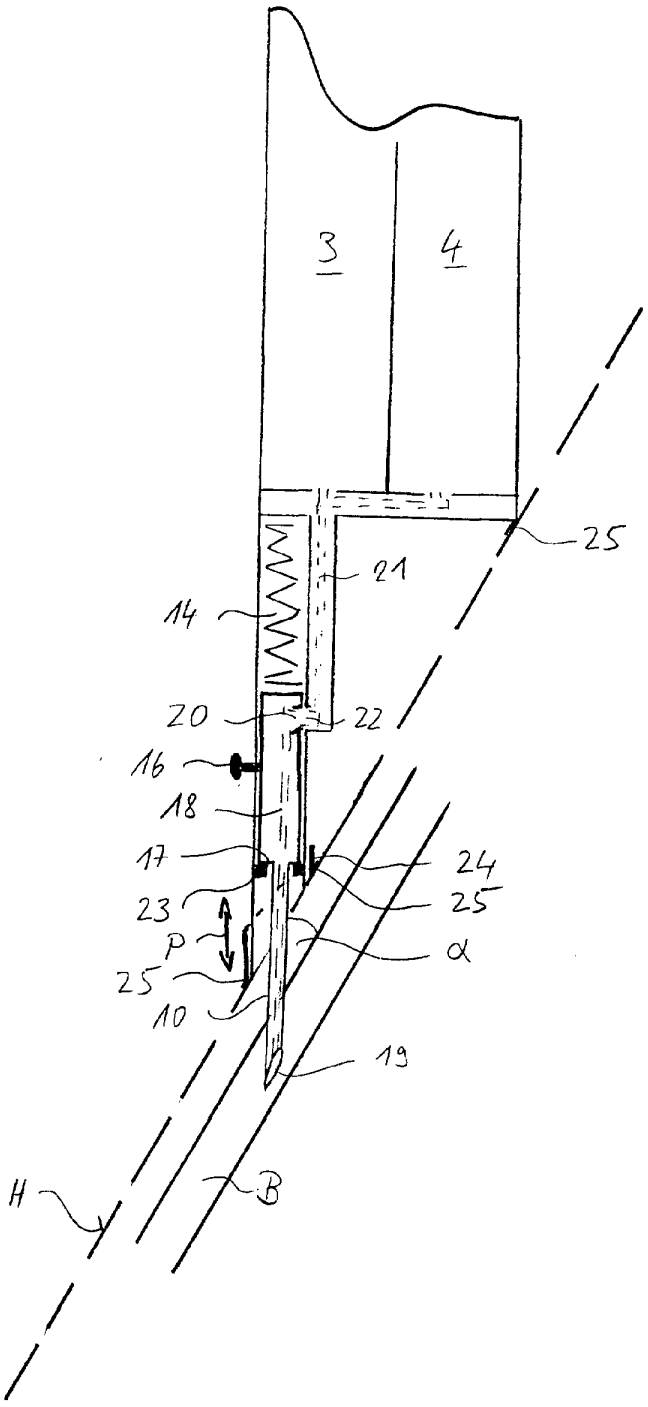


Fig. 2



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Fig.3

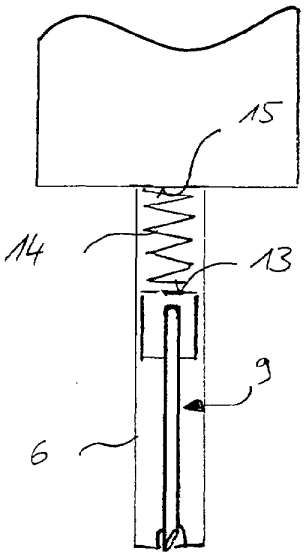
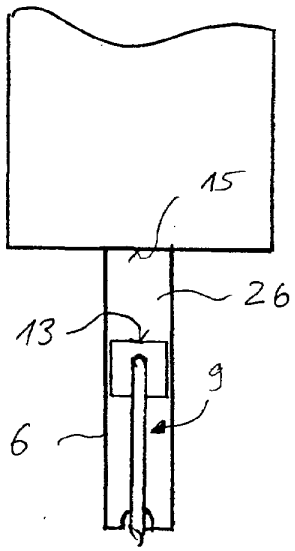


Fig.4



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Fig. 5

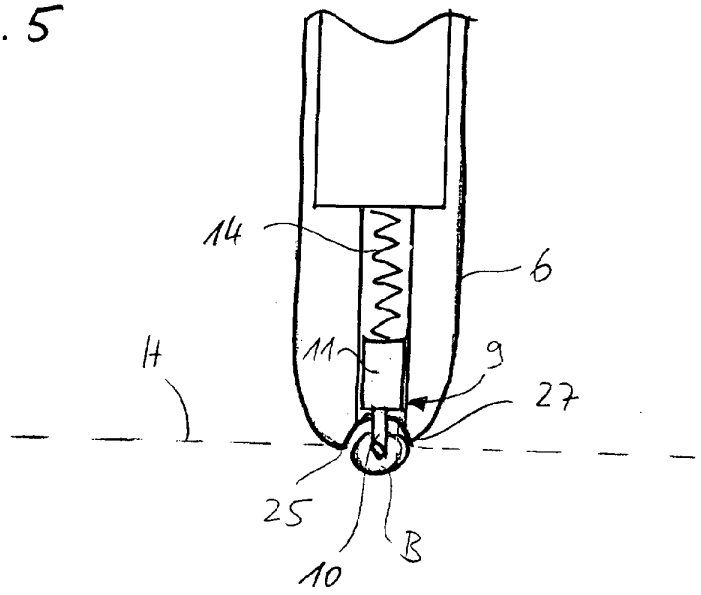


Fig. 6

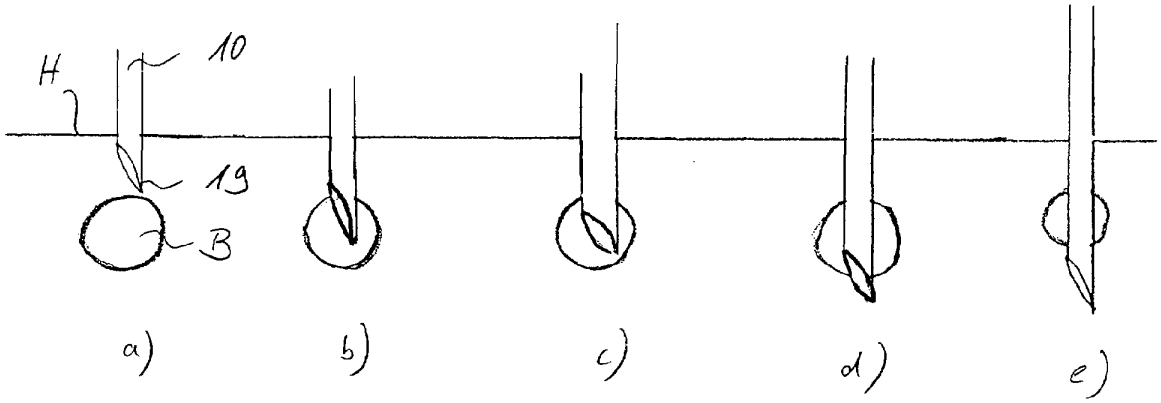


Fig. 7

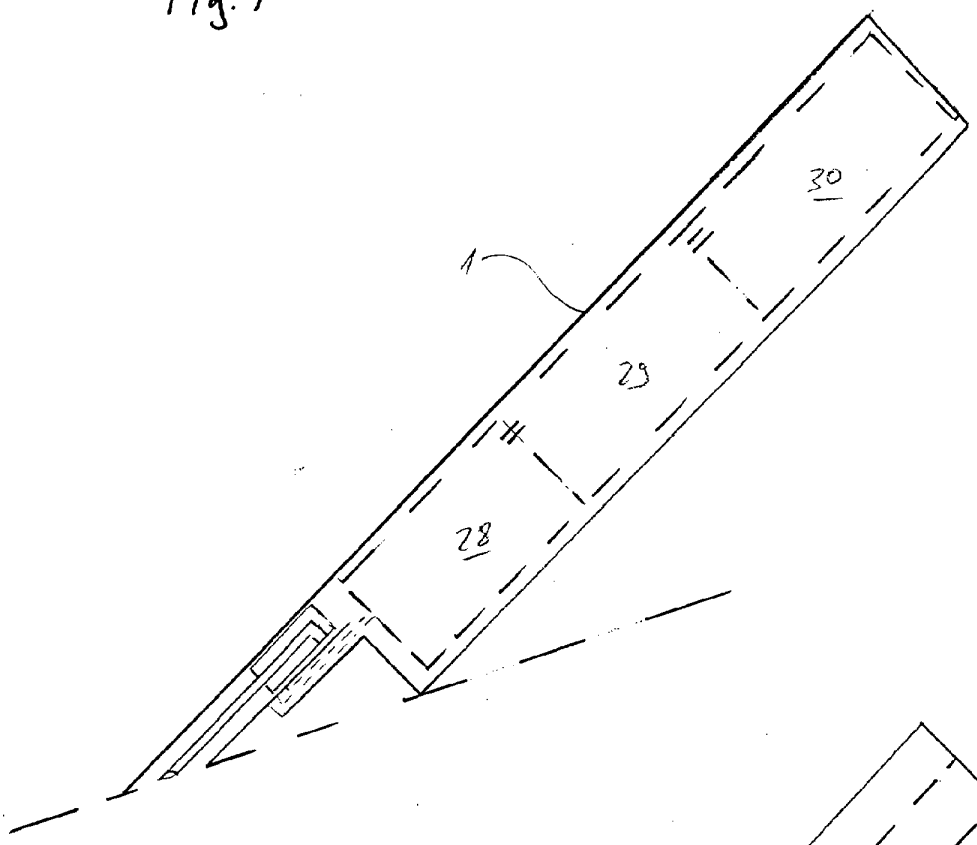
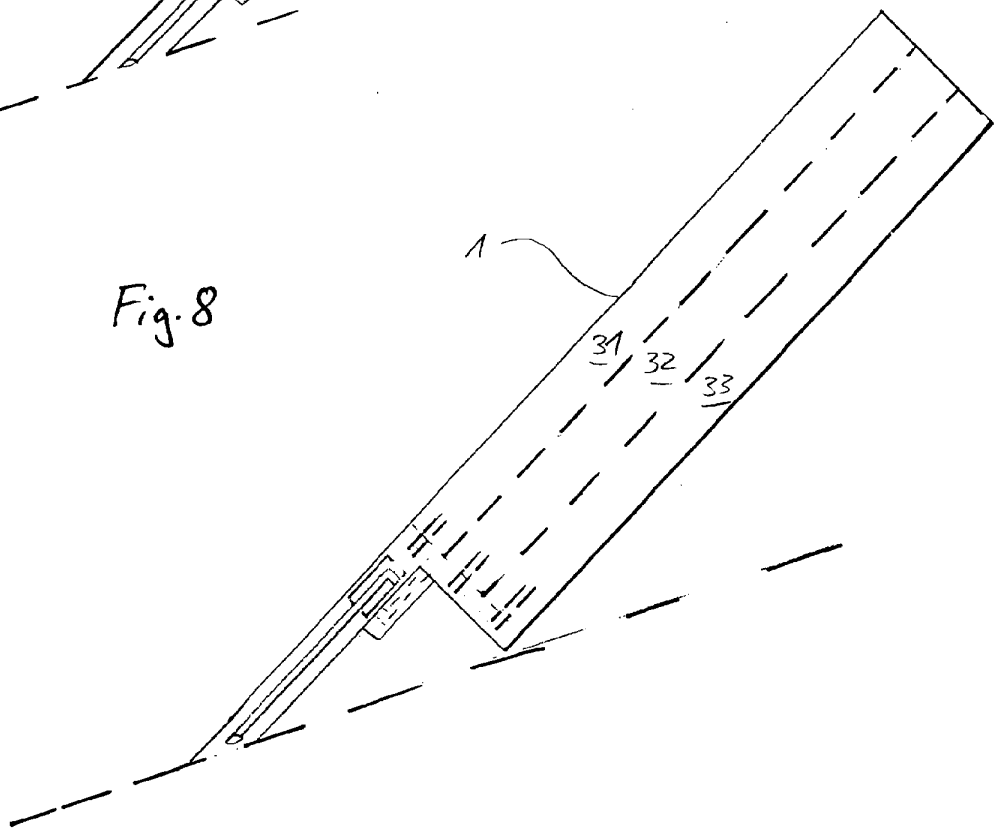
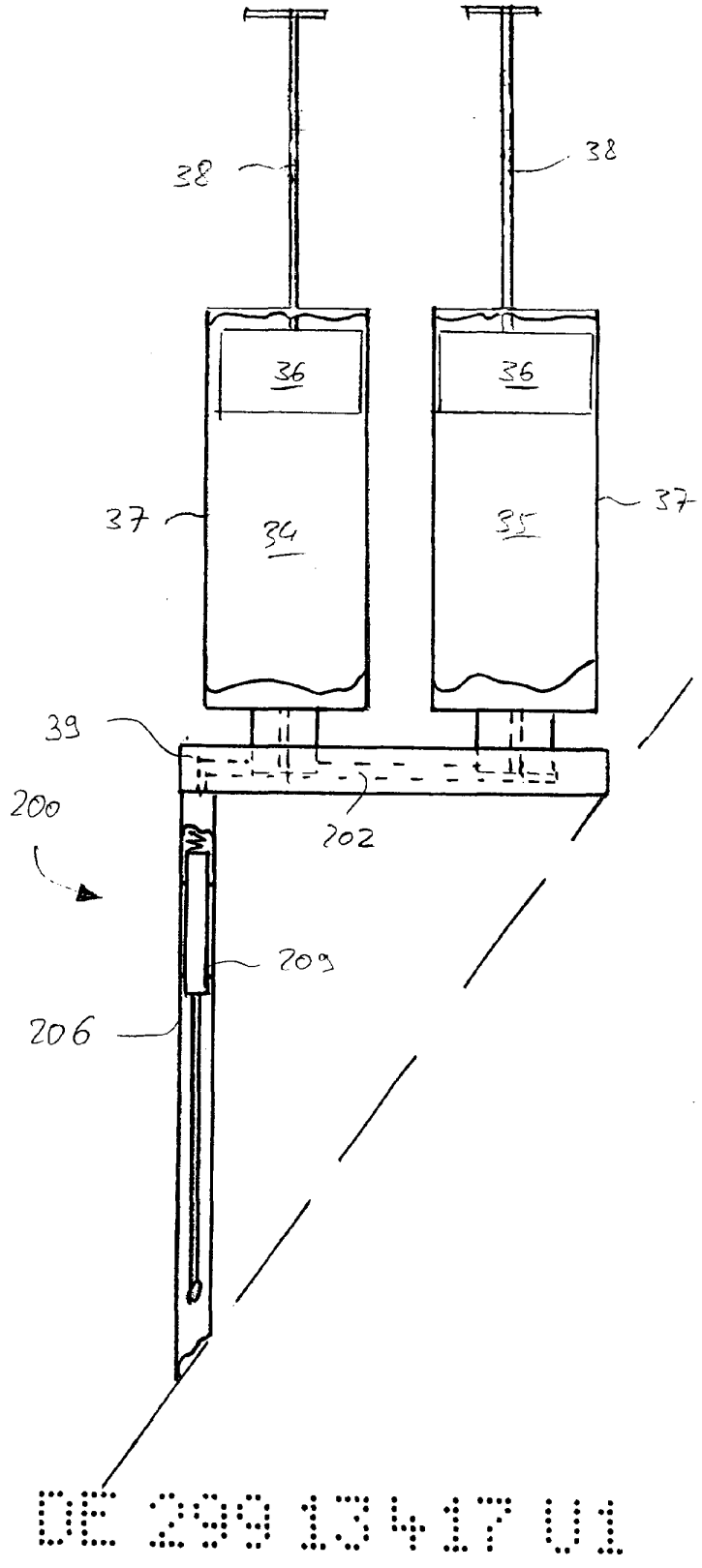


Fig. 8



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Fig. 9



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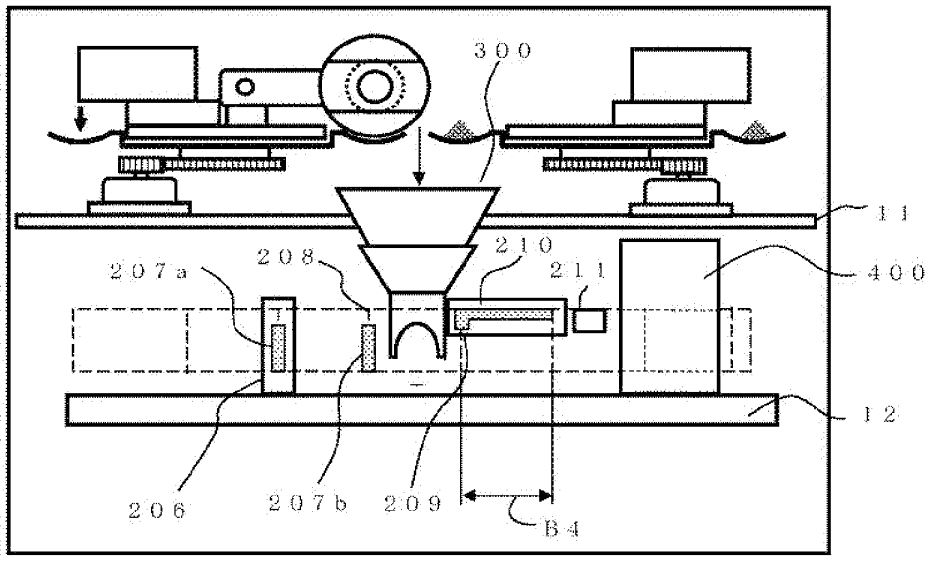
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4C047CC15
4C047JJ03
4C047JJ13
4C047JJ15
4C047JJ24
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4C047JJ40

wrap up close

(57) [Summary]
[Problem] To provide a drug packaging device and a method for manufacturing a packaged dr ug that does not break at the perforated portion of the packaging paper during transportation. A packaging paper storage unit in which V-shaped packaging paper is wound, a transport path for pulling out and transporting the packaging paper from the packaging paper storage unit, a nd a transport path provided in the middle of the transportation path. a heat sealing unit that forms a heat seal for dividing the packaging paper into individual packages; and a drive roller for sandwiching and driving the packaging paper containing the medicine supplied by the med icine supply unit, and a driving roller provided downstream in the transportation direction of t he packaging paper from the driving roller, and the heat seal a perforation forming part for for ming perforations in the portion heat-sealed by the part.
[Selection drawing] Fig. 4



The scope of the claims open —

Claims:

1.

A packaging paper storage unit around which V-shaped packaging paper is wound, a transport path for pulling out and transporting the packaging paper from the packaging paper storage unit,

A heat seal portion provided in the middle of the transport path for forming a heat seal for dividing the packaging paper into individual packages

; A drug supply unit that supplies each package,

a drive roller that sandwiches and drives the packaging paper containing the drug supplied by the drug supply unit, and a downstream downstream of the drive roller in the transportation direction of the packaging paper

. and a perforation forming section provided in the heat sealing section for forming perforations in the portion heat-sealed by the heat-sealing section

.

2.

The perforation creating section is

provided on one side of the transportation path for the packaging paper, and includes a blade storage section in which a perforation blade is retractably stored, and the transportation path for the packaging paper

. a blade receiving portion provided opposite to the blade housing portion on the other side of the blade housing portion and forming perforations in the packaging paper between the perf

orating blade protruding from the blade housing portion

; a first drive unit for moving the unit and the blade receiving portion toward the packing pa per to sandwich the packing paper

; and a second driving section for forming perforations in the packaging paper by driving the perforating blade of the blade accommodating section so as to protrude toward the blade rece iving section while holding

the A drug packaging device as described.

[Claim 3]

The perforating blade includes

a base portion and a

cutting edge portion including a plurality of blade pieces protruding from the base portion an d having a chevron-shaped cutting edge formed at the tip thereof, with a predetermined inter val between adjacent blade pieces. and

the second drive unit

forms perforations in the packaging paper by projecting partway of the blade piece of the pe rforation blade toward the blade receiving portion, and the base portion

of the perforation blade.

3. The medicine packaging device according to claim 2 , wherein the packaging paper is cut by protruding up to the blade receiving portion side .

4.

The perforating blade

is formed such that the width of the blades at both ends in the direction perpendicular to the conveying direction of the packing paper is larger than the width of the blades of the inner bla des,

4. The drug packaging device according to claim 3 , wherein the cutting start portions are fo rmed at both ends of the packaging paper in a direction orthogonal to the conveying direction of the packaging paper .

5.

The perforating blade

is formed so that each of the blade pieces has the longest length from the base of the centra l blade piece, and the length gradually decreases toward the end.

5. The medicine packaging device according to claim 3 or 4, characterized in that:

6.

The perforating blade has a horizontal blade having

a blade width larger than the thickness of said blade and inserted between said plurality of b lades.

By forming a plurality of cross-shaped blades, the cross-shaped blades form a perforation for med in the packaging paper to form a cutting start portion when separated along the perforati on

. The drug packaging device according to any one of claims 3 to 5.

7. A

pre-stored V-folded packaging sheet is pulled out to a conveying path, a

heat-sealed portion is formed on the pulled-out packaging sheet for dividing into individual p ackages, and the

heat-sealed portion is formed. The medicine is supplied and stored one by one between the packaging papers on which is formed, and the

packaging paper containing the medicine is nipped by the driving roller and driven to convey one by one, and the driving

roller

A method for manufacturing a packaged medicine , comprising: forming perforations in the heat-sealed portion of the packaging paper downstream of the packaging paper in the conveyi ng direction of the packaging paper.

detailed description open —

Description: BACKGROUND OF THE INVENTION 1.

Field of the Invention The present invention relates to a medicine packaging device for suppl ying and packaging medicines one by one and to a method for manufacturing divided medicin es. 2. Description of the Related Art A drug packaging device has been developed and put int o practical use for automating drug dispensing work. As an example of such a medicine packa ging device, there is one described in Patent Document 1. [0003] That is, the ends of the pa ckaging paper are pulled out from a roll around which the V-folded packaging paper is wound, and the end portion of the packaging paper is pulled through a plurality of support shafts onto a conveying path inclined downward in the conveying direction. and fed to a funnel-shaped dr ug hopper. A thermal pressure contact portion is provided downstream of the drug hopper, an d the thermal pressure contact portion is provided with a heat seal and a perforation forming portion. Then, a T-shaped heat seal for separating the individual packages is formed by heat s ealing, and perforations for separating the individual packages are formed. After heat-sealing, one packet of medicine is supplied from the medicine hopper to the space between the packa ging papers. [0004] When the drug is supplied, the packaging paper is nipped by driving roll ers provided downstream of the thermal pressure contact portion and pulled out by the length of one package to prepare for the next individual package. Heat sealing and perforation are p erformed. By repeating such an individual packaging operation, a single prescription of a pack aged drug is created. [Prior Art Document] [Patent Document] [Patent Document 1] Japanese Unexamined Patent Application Publication No. 2012-131551 [Summary of the Invention] [Pro

blems to be Solved by the Invention]

[0006]

In the device disclosed in Patent Document 1, the driving rollers for conveying the packaging paper are provided downstream of the perforation forming section. Therefore, when the packaging paper is pulled out by the drive roller, if an excessive load is applied to the packaging paper, there is a risk that the packaging paper will tear at the perforations. In addition, since the medicine is enclosed in the lower part between the packaging papers, the driving rollers must inevitably hold the upper side of the packaging papers to convey them. In order to prevent the packing paper from tearing during transportation, the upper edge of the packing paper cannot be perforated (cut). As a result, there is also the problem that it is difficult for an elderly person or a person with weakened muscles to cut along the perforations from the upper end side.

[0007]

Therefore, in some conventional packing machines, perforations (cuts) are made at the lower end of the paper so that the paper is cut from the lower side. then
In addition, the printing direction is reversed and the visibility is poor, and after cutting it off, it is necessary to turn it upside down again and cut it horizontally by hand to open it, which is inconvenient.

[0008]

An object of the present invention is to provide a drug packaging device and a method for manufacturing a packaged drug, in which paper for packaging is not cut at perforations (cuts) during transportation. aim. The second problem is that perforations (cuts) can be made on the upper end side of the packaging paper so that the patient can easily cut the single package along the perforations. An object of the present invention is to provide a highly convenient drug

packaging device and a method for manufacturing a packaged drug.

[0009]

Furthermore, as a secondary effect, by providing perforations (cuts) at the upper and lower ends of the packaging paper in this way, long packaging paper can be packed three times a d ay (morning, noon, evening), for example. I would also like to raise the point that the appear ance is neat when everything is folded because it is easy to make the creases firmly when fold ing it for storage.

Means for Solving the Problems

[0010]

A medicine packaging device of the present invention comprises a packaging paper storing s ection in which a V-folded packaging paper is wound, and a packaging paper from the packagi ng paper storing section. a transport path for pulling out and transporting paper, a heat seal p ortion provided in the middle of the transport path for forming a heat seal for separating the p acking paper into individual packages, and a heat seal portion provided in the middle of the tr ansport path , a medicine supply unit for supplying the medicine one package at a time betwe en the packaging papers; a drive roller for pinching and driving the packaging paper containin g the medicine supplied by the medicine supply unit; and the drive rollers. a perforation creati ng section provided downstream in the conveying direction of the packaging paper and formin g perforations in the portion heat-sealed by the heat-sealing section.

[0011]

Further, in the method for manufacturing a packaged medicine of the present invention, a pr e-stored V-folded packaging sheet is pulled out to a conveying path, and the pulled-out packa ging sheet is divided into individual packages by a heat-sealing section. is formed, and the me dicine is supplied and stored one by one between the packaging papers on which the heat-sea led portion is formed, and the packaging paper containing the medicine is sandwiched by the driving rollers to make one package. The perforations are formed in the heat-sealed portion of the packaging paper downstream of the drive roller in the transportation direction of the pack aging paper.

BRIEF DESCRIPTION OF THE DRAWINGS

[0012]

FIG. 1 is a plane cross-sectional view of a disc distribution unit of an automatic powder medici ne packaging machine according to an embodiment;

FIG. 2 is a front cross-sectional view showing the raised position of the drop hopper of the aut omatic powder medicine packaging machine of the embodiment;

FIG. 3 is a diagram showing the structure and operation outline of a drop hopper;

FIG. 4 is a front cross-sectional view showing the lowered position of the drop hopper of the a utomatic powder medicine packaging machine of the embodiment;

FIG. 5 is a cross-sectional plan view of the printing and packaging machine section of the auto matic powder medicine packaging machine of the embodiment;

FIG. 6 is a perspective view of the perforation forming device of the embodiment, showing a s tate in which the blade storage section and the blade receiving section are opened;
FIG. 7 is a perspective view of the perforation forming device of the embodiment, showing a s tate in which the packaging paper is being conveyed between the blade storage section and th e blade receiving section;
FIG. 8 is a perspective view of the perforation forming device of the embodiment, with the bla de housing portion and the blade receiving portion opened and the cover of the blade housing portion removed;
FIG. 9 is a perspective view of the perforation forming device of the embodiment, showing a s tate in which perforations are being formed with the blade storage section and the blade recei ving section closed;
FIG. 10 is a perspective view of the perforation forming device of the embodiment, with the c over of the blade housing section removed in a state where the blade housing section and the blade receiving section are closed to form perforations;
FIG. 11 is a perspective view of the perforation forming device of the embodiment, showing a state in which the blade storage section and the blade receiving section are closed to cut the packaging paper;
FIG. 12 is a perspective view of the perforation creating device of the embodiment, in which t he blade housing portion and the blade receiving portion are closed and the packaging is perf ormed;
FIG. 10 is a view of the blade storage section with the cover removed, in a state where the pa per is being cut;
13A and 13B are diagrams for explaining the shape and movement distance of the perforation blade of the perforation creating device according to the embodiment; FIG.
14A and 14B are diagrams for explaining the shape of a perforation blade of the perforation cr eating device according to the embodiment; FIG.
FIG. 15 is a diagram for explaining the relationship between the shape of the perforation blad e of the perforation creating device of the embodiment and the packaging paper;
FIG. 16 is a diagram showing an example of a packaged medicine manufactured by the autom atic powder medicine packaging machine of the embodiment;
17 is a plan view for explaining a printing packaging machine according to a second embodim ent; FIG.
FIG. 18 is a front view for explaining a printing packaging machine according to a second emb odiment; FIG.
BEST MODE FOR CARRYING OUT THE INVENTION
[0013]
An automatic powder medicine packaging machine according to an embodiment will be descr ibed below with reference to the drawings.
In the following description, an automatic powder medicine packing machine will be taken as

an example, but the present invention is not limited to the automatic powder medicine packing machine, and can also be applied to an automatic tablet packing machine. Further, it is needless to say that the present invention can also be applied to a medicine packaging device for packaging a plurality of medicines into one individual package as described in Japanese Patent No. 6255528 and Japanese Patent Application Laid-Open No. 2000-24087.

FIG .

1 is a plan view of an automatic powder medicine packing machine of this embodiment, and FIG. 2 is a front view of the automatic powder medicine packing machine. Above the intermediate table 11 of the housing 10 is arranged a disc distribution section 100 as a medicine supply section, and below the intermediate table 11 is arranged a printing packaging machine 200 as a medicine packaging section. A drop hopper 300 serves to introduce the powdered medicine discharged from the disc distribution unit 100 through the inner surface of the drop hopper 300 into the printing packaging machine 200 side.

[0015]

The disc distributor 100 is provided with two sets of distributors. In the disc distribution unit 100, 101 is a detachable powdered medicine cassette, which is loaded with powdered medicine in the amount necessary for the prescription at another place in advance, and manually operated by a staff member or by an automatic device such as a robot arm (not shown). It is placed on the vibration table 102 from another shelf. The vibration table 102 generates vibration by an electromagnet (not shown) or the like, and by transmitting the vibration force to the powdered medicine cassette 101, the powdered medicine in the powdered medicine cassette 101 is transported by vibration, and the powdered medicine is dropped little by little in the direction of the arrow 103. It is.

Reference

numeral 104 denotes a horizontally arranged distribution disk, a large wheel of which is rotated by a stepping motor 105 via a gear 106 in the direction of an arrow 104a. Further, an arc-shaped concave surface 107 is formed on the upper surface of the distribution disk 104 in the outer peripheral direction. Here, when the vibrating table 102 is driven while the stepping motor 105 is continuously rotated, the powdered medicine falls little by little onto the arcuate concave surface 107 of the distribution disc 104 to form a doughnut-shaped powdered medicine mountain P1. can be done. This operation is called a "circumferential scattering operation".

Reference numeral

108 denotes a scraping disk portion, and a lever 108a can rotate up and down around a shaft 109. As shown in FIG. A disc 110 whose circumference is made of silicone rubber is attached to the tip of the lever 108a, and can be rotated in the direction of an arrow 110a by a motor 111. As shown in FIG. This disc 110 has a waterwheel-like shape in which blades are provided between two discs. It should be noted that the disk diameter of the disk 110 is the same as the diameter of the concave surface of the arcuate concave surface 107 .

[0018]

In the case of the above-mentioned "circumferential scattering operation", the disk 110 is ro tated upward and retracted, and does not interfere with the formation of the donut-shaped po wdered drug pile P1. Next, during the "one-pack distribution operation", the disk 110 of the sc raping disk portion 108 rotates downward, and the disk 110 comes into close contact with the arc-shaped concave surface 107 without any gap. In this state, when the motor 111 is driven, the blades provided on the disk of the disk 110 scrape the powdered medicine on the arcuate concave surface 107 onto the drop hopper 300 . Then, when the stepping motor 105 is rotate d by a predetermined angle R, the amount of powdered medicine corresponding to that angle is dispensed to the drop hopper 300 side. Here, the predetermined angle R is not specified se parately.

This is the angle for the dose to be packaged in one package specified by the label. For exa mple, in the case of making a prescription for 36 packets of a powdered medicine of 1g per pa cket, 36g of powdered medicine is loaded in the powdered medicine cassette 101 in advance, and this is referred to as a "circumferential spreading operation"

.

", spread the entire amount evenly in a donut shape. Next, in the "distribution operation for o ne package", by rotating the stepping motor 105 by 10 degrees while rotating the disk 110, o ne package of 1 g of powdered medicine can be correctly dispensed to the drop hopper 300. b e. The disc distribution unit 100 and the drop hopper 300 constitute a medicine supply unit. Two sets of discs 112a and

112b are arranged in the disc distribution unit 100 in a symmetrical manner. is for enabling t he other disk portion 112b to perform a "single package dispensing operation" so that a plural ity of consecutive prescriptions can be continuously packaged without wasting time.

[0021]

FIG. 3 outlines the shape and operation of the drop hopper 300 . The drop hopper 300 has a double structure of an upper hopper 301 and a lower hopper 302, and a lower opening 303 of the upper hopper 301 is closed by a shutter 304 that can be opened and closed. The upper en d of the upper hopper 301 is formed with an upper opening 300a for receiving the powdered medicine from the disc distribution unit 100 . The lower end of the lower hopper 302 is forme d in a wedge shape as shown in FIGS.) 305c are formed. The drop hopper 300 can move up and down as a whole. Then, at the timing of dispensing the powdered medicine from the disc distribution unit 100 in the "one packet dispensing operation", it is positioned at the upper pos ition in FIGS. 3(a) and 3(b). At this time, the shutter 304 is closed as shown in the side view of FIG. At this time, the left and right claws 305a and 305b at the lower end of the drop hop per 300 are inserted into the open end B1 of the packaging paper B folded in two to be conve yed

. When the powdered medicine is discharged, as shown in FIG . 3(c), the entire drop hopper 300 moves downward. It acts as a guide when entering the When the shutter is opened as sh own in 304a in this state, the powdered medicine is stored inside the packaging paper B. FIG.

After that, the drop hopper 300 rises to the position shown in FIG. 3(b). [0024]

Next, the configuration and operation of the printing packaging machine 200 will be described with reference to FIGS. 4 and 5. FIG. FIG. 4 is a cross-sectional view of the front of the powder medicine packaging machine, showing a state in which the drop hopper 300 positioned above in FIG. 2 has moved downward. FIG. 5 is a top cross-sectional view of the printing and packaging machine 200. As shown in FIG. Reference numeral 201 denotes a packing paper roll as a packing paper storage unit, which is formed by winding a double-folded paper having thermal adhesiveness on a reel with the valley-fold side facing downward, and is placed on the lower stage 12. It is The packaging paper pulled out from the leading end of the paper on the outer peripheral side of the reel is conveyed along the conveying path along a route such as the one-dotted chain line B2 to B3. A printing unit 202 is composed of an ink ribbon 203, a thermal printing head 204, a platen roller 205, etc., and prints prescription information on the surface of the packaging paper B for each package.

Reference numeral

206 denotes a vertical sealing mechanism, which is a heat sealing portion provided on the lower table 12. By pressing the packing paper B from the front and back (top and bottom in FIG. 5) with a hot plate, the vertical sealing mechanism 207a is classified into individual packages by performing the sealing. 207b shows vertical sealing at a position moved by one package, but the upper open end 208 of the packaging paper B is not sealed. This is so that the packing sheets B can be transported in a state in which the claw portions 305a and 305b of the drop hopper 300 are inserted between the packing sheets B as shown in FIG. 3(a). The drop hook to be placed next

A drop hopper cleaning device 310 is attached to the back side of the hopper 300 . Since the drop hopper cleaning device 310 is not directly related to the present invention, detailed description thereof will be omitted.

Next , reference

numeral 209 denotes a horizontal sealing mechanism, which presses the packing paper B from the front and back with a hot plate to seal the unsealed portions in the horizontal direction and the vertical direction, as indicated by 210 . With the vertical seal 207 and the horizontal seal 210, the packaging paper B is sealed as a single package. Although not shown in the drawing, the vertical seal 7 does not seal the perforated portion but seals both sides of the perforated portion, which will be described in detail later.

A driving roller 211

is driven synchronously with the platen roller 205 of the printing unit 202, and rotates while nipping the upper end portion of the packaging paper B from both sides to cover the distance

of the one-packing pitch B4. , is driven as one step. Reference numeral 400 denotes a perfora tion forming device, which forms vertical perforations in the non-sealed portion provided in th e middle of the vertically sealed portion, thereby facilitating the separation of individual packe ts by the patient. 2 and 4 do not indicate perforations, but indicate boundaries between single packages. Also, in FIGS. 2 and 4, the description of the vertical seal downstream of the drop h opper 300 is omitted for the sake of clarity of explanation. As auxiliary equipment for the dr op hopper cleaning device 310, a dust collection blower 320 and a compressed air generating compressor 330 are arranged at the rear of the housing and used as air sources for the drop hopper cleaning device 310

.

.

[0029]

The configuration and operation of the perforation forming apparatus 400 will be described b elow with reference to FIGS. 6 to 15. FIG. FIG. 6 is a perspective view of the perforation formi ng device, showing a standby state in which the blade housing portion 402 and the blade rece iving portion 404 are open, and FIG. 4 is a diagram showing a state in which packing paper B is inserted. FIG. For the packaging paper B, the blade housing portion 402 and the blade recei ving portion 404 are arranged so as to be positioned between the blade housing portion 402 a nd the blade receiving portion 404 . FIG. 8 is a diagram showing a state in which the cover of the blade housing portion 402 is removed. A motor base 406 is fixed to the lower stage 12 s hown in FIGS. 4 and 5, and a stepping motor 408 is fixed to the motor base 406. As shown in FIG

.

A base 410 of a perforating blade unit 401 is fixed to the lower table 12 .

The base 410 of the perforating blade unit 401 is slidably provided with a supporting portion 4 28 to

which the blade housing portion 402 is fixed. A support portion 424 to which the blade recei ving portion 404 is fixed is slidably provided on the base 410, and slides integrally with a slide shaft 422 fixed to the support portion 424. As shown in FIG. The support portion 424 and the support portion 428 are slidable in the directions of contacting and separating from each othe r. A spring 426 is provided between the supporting portion 424 and the supporting portion 42 8 to bias them away from each other.

A shaft 434 is slidably provided inside the support portion 428 of the blade housing portion 40 2 , and

a sewing machine blade 432 is fixed to the left end of the shaft 434 . The perforating blade 4 32 is slidably provided between the two covers of the blade housing portion 402 in a direction in which the perforating blade 432 protrudes from the blade housing portion 402 .

[0033]

A timing belt is stretched between a shaft (not shown) of the stepping motor 408 and a pulle

y 414 fixed to the camshaft 412, so that the camshaft 412 is rotated by the rotation of the ste pping motor 408. .

Three cam plates 416 ,

418 and 420 are fixed to the camshaft 412 . The lowermost first cam plate 416 drives the bl ade receiving portion 404, and the first cam plate 416

By rotating , the slide shaft 422 is pulled rightward in the drawing by a cam follower (not sho wn). Since the supporting portion 424 to which the blade receiving portion 404 is fixed is conn ected to the slide shaft 422, the blade receiving portion 404 is also drawn rightward in the fig ure. A second cam plate 418 on the second stage from the bottom drives the blade housing portion 402. By rotating the cam plate 418, a cam follower attached to a support portion 428 to which the blade housing portion 402 is fixed is driven

.

430 is driven leftward in the figure. Therefore, by rotating the stepping motor 408, the blade accommodating portion 402 and the blade receiving portion 404 are moved in the direction of coming into contact with each other, and the packing paper B is sandwiched. The shape of the cam plates 416 and 418 keeps the packaging paper B sandwiched between the blade accomm odating portion 402 and the blade receiving portion 404 even if the cam plates 416 and 418 r otate further. Thus, the drive mechanism for the blade receiving portion 404 by the cam plate 416 and the drive mechanism for the blade housing portion 402 by the cam plate 418 constitu te a first drive portion. Further, the third cam plate 420 on the uppermost stage is for driving a perforating blade 432, and a cam follower 436 fixed to a shaft 434 is in contact with the thir d cam plate 420. As shown in FIG

.

As the stepping motor 408 rotates, the third cam plate 420 rotates and pushes the cam follow er 436 to drive the shaft 434 to the left in the figure. As a result, the perforating blade 432 fix ed to the shaft 434 protrudes from the blade accommodating portion 402 toward the blade re ceiving portion 404 to form perforations in the packing paper B. As shown in FIG. A mechanis m for driving the perforating blade by the cam plate 420 constitutes a second driving section.

[0037]

FIG. 8 shows the standby state of the perforating blade unit 401 . As shown in FIG. 8A, whe n the perforating blade unit 401 is in the standby state, the perforating blade 432 is sunk insi de the cover of the blade housing portion 402 . The state of cam plate 420 and cam follower 4 36 at this time is shown in FIG.

Next, FIGS

. 9 and 10 show a state in which the stepping motor 408 rotates to form perforations on the packaging paper B. FIG. As shown in FIGS. 9 and 10, by rotating the first cam plate 416 and t he second cam plate 418, the blade housing portion 402 and the blade receiving portion 404 c ome into contact with each other to sandwich the packing paper B. becomes. 9 and 10, illustr ation of the packaging paper B is omitted. When perforations are formed on the packaging pa

per B, the cam plate 420 pushes the cam follower 436 as shown in FIG. It will be in a protrudi ng state. After the perforations are formed on the packaging paper B, the stepping motor 40 8 rotates in reverse, so that the cam plate 420 reverses from the state shown in FIG. 9(b) to t he standby position shown in FIG. 8(b)

.

back to After the perforations are formed in the packaging paper B by such an operation, the packaging paper B is conveyed by the drive roller 211 to form the next individual package. Fo rmation of vertical seals, supply of medicine, and formation of horizontal seals are performed i n synchronism with the formation of perforations. When the perforations are formed, the pack aging paper B is stopped, and the vertical seal formation, drug supply, and horizontal seal for mation are performed while the packaging paper B is stopped. be. The above operation compl etes the cycle for one package.

[0040]

Here, the medicine is prescribed to the person taking the medicine, for example, 42 doses fo r two weeks in the morning, afternoon and evening. Perforations are made between 42 individ ual packages for one drug taker, and when individual packages for one drug taker are complet ed, the prescription drug is released by cutting the packaging paper B instead of the perforati ons. There is a need to. Therefore, in this embodiment, the perforation forming device 400 a lso cuts the packaging paper B. As shown in FIG

.

As shown in FIGS. 11 and 12, the cam plate 420 is shown in FIG. 9(b).

After the formation of the stitches, the stepping motor 408 is further rotated to rotate the ca m plate 420 to the position shown in FIG. 11(b). Cam follower 436 is then pushed to the farth est position from camshaft 412 . As a result, the perforating blade 432 further protrudes into t he blade receiving portion 404 to the base of the perforating blade 432 . As a result, the pack aging paper B is cut by the perforating blade 432 . When cutting the packaging paper B, the r otation of the camshaft 412 need only be rotated once without returning. Next, FIG. 13 sho ws the shape and amount of movement of the perforating blade 432. As shown in FIG . The perforating blade 432 is composed of a fixed portion 432a to the shaft 434, a blad e base portion 432b, and a cutting edge portion 432c protruding from the blade base portion 432b. A plurality of blades 432d each having a chevron-shaped blade edge formed at the tip o f the blade edge portion 432c are formed at predetermined intervals between adjacent blades 432d. Between the blades 432d and 432d, there are three horizontal blades having a blade wi dth wider than the thickness t of the blade edge, but they are omitted in FIGS. ing. As for the length to the tip of each blade 432d, the blade at the center is the longest, and the length gra dually decreases toward the ends. The angle θ between the straight line L1 connecting the tip s of the blades 432d and the straight line L2 parallel to the tips of the bases is set to about 4 degrees. As a result, when perforations are formed on the packaging paper B, the cutting port ion gradually shifts from the central blade 432d to the end blade 432d, so that the driving forc

e required to move the perforating blade 432 is small. done. [0043]

In addition, the lengthwise ends of the perforating blade 432, that is, the blade widths of the blade pieces 432e, 432e at the ends in the direction orthogonal to the transport direction of th e packaging paper B are formed larger than the blade width of the inner blade piece 432d. It i s 13(b), the width of the packaging paper B is configured so that the ends of the packaging p aper B are located at the positions of the edge pieces 432e, 432e of the perforating blade 43 2. It is Therefore, even if the transportation position of the packaging paper B is shifted, a cut ting start portion (cut) can be reliably formed at the end of the packaging paper B when the p atient cuts off the individual package, and the patient can easily separate. You can separate th e package.

FIG .

13(b) shows the projection distance of the perforation blade 432 when the perforation is for med by the perforation blade 432 and the packing paper B is cut. When forming perforations, the perforation blade 432 protrudes from the blade receiving portion 404 to the position M, w hich is the intermediate portion of the blade tip portion 432c of the perforation blade 432. As shown in FIG. When cutting the packaging paper B, the perforating blade 432 protrudes from the blade receiving portion 404 to the position C of the base portion 432b of the blade beyond the position of the blade tip portion 432c. With this configuration, the formation of perforation s between individual packages of the packaging paper B and the cutting of the packaging pap er B between one prescription can be achieved by changing the protruding amount of the perf oration blade 432. It is. Next, a cross-cut blade by inserting a horizontal blade piece betwee n the blade pieces 432d of the perforating blade 432 will be described with reference to FIGS. 14 and 15. FIG

.

14(a) is a perspective view, (b) is a left side view, (c) is a front view, and (d) is a top view. [0046]

That is, three horizontal blades are provided between the fifth and sixth blades, between the eighth and ninth blades, and between the eleventh and twelfth blades from the top in FIG. 43 2g is inserted. The horizontal blade 432g has a blade width larger than the thickness t of the blade 432d, and is press-fitted between the blades 432d. The base 432b of the blade 432 is p ress-fitted and held. By using the perforation blade 432 configured in this manner, perforation s are formed, and a cutting start portion (cut) is formed when opening each individual packag e when the packaging paper B is separated into individual packages. It is something to do. The insertion position and the number of horizontal blades 432g are

not limited to the above examples, and they can be inserted at any position between blades 432d. Especially when the amount of powdered medicine stored in each individual packet is s

mall, it is better to open it at the cross-cut position at the bottom of each individual packet to reduce the amount of leftovers.

Therefore, the insertion position and the number of sheets can be selected in consideration of this.

FIG .

15(a) illustrates the relationship between the perforating blade 432 and the packaging pape r. As shown in FIG. 15(a), the sealed portion (shaded portion) of the packing paper is formed by the vertical sealing mechanism 206 leaving a perforated portion (non-sealed portion) of, fo r example, 4 mm. It is formed in the sealing portion. Assuming that the width of the packagin g paper B, that is, the width in the direction perpendicular to the transport direction is, for exa mple, 70 mm, the length of the perforating blade 432 is set to 75 mm, which is larger than th e width of the packaging paper B. As a result, the ends of the packing paper B can be oppose d to the edge pieces 432e of the perforating blades 432, and as a result, the cutting start port ions (cuts) B1 are formed at both ends of the packing paper B. can be done. Further, as sho wn in FIG. 15(b), by setting the width of the horizontal blade to about 4 mm, which is larger t han the thickness t of the perforating blade 432 (=1 mm), the width of the unsealed portion o f the packing paper B is reduced

.

A cross cut portion B2 can be formed over 4 mm, which serves as a cutting start portion when opening the individual package. Therefore, it is possible to provide a packaged drug that can be easily opened by a patient/user.

FIG .

16 shows an example of a cross-sectional view of a manufactured packaged medicine, showi ng an example in which three cross-cut portions are formed at intervals of 9 mm from a positi on 20 mm from the upper end, for example. In the first embodiment, the packing paper B is conveyed in the horizontal direction, and along the conveying direction, the vertical sealing po rtion 206, the drop hopper 300 serving as the medicine supply portion, the horizontal sealing portion 209, and the conveying rollers

.

211 and the perforation creating unit 400 are arranged, but if the packaging paper B is config ured to be conveyed along the conveying path inclined downward in the conveying direction, t he vertical seal portion is located downstream of the medicine supply unit. It is also possible t o provide

Next ,

a printing packaging machine 500 of a second embodiment will be described with reference t o FIGS. 17 and 18. FIG. 17 is a plan view, and FIG. 18 is a front view of the same. The base p late 515 is provided with a packaging paper storage unit 533 in which the V-folded packaging paper B is wound into a roll. , is conveyed upward via a plurality of support rolls 534 and 535, the conveying direction is changed by the twist roller 531, and conveyed to a conveying path i

nclined downward by 45 degrees along the conveying direction. On the upper surface of the base plate 515, a conveying base 516 for the packaging paper B having an inclination of 45 d egrees with respect to the horizontal plane is provided

.

The sheet B is transported along the transport path. A drop hopper 518 having a lower exit en tered from the upper opening side of the valley-folded packaging paper B is provided substant ially vertically in the center of this transport path, and a drug supply hopper 519 is provided a bove it. The lower part of the medicine supply hopper 519 is open, and the shutter mechanis m 520 that blocks this opening temporarily holds the medicine to be put in one sachet, and op ens the medicine like 520a by an actuator (not shown), thereby lowering the medicine. Via th e drop hopper 518, the drug is dropped into the inner space of the folded packaging paper B a nd supplied.

[0054]

This space is blocked on the left and right by a paper holding plate 521 arranged on the upp er left upstream side of the transport and an inverted L-shaped heat seal portion 522 arrange d on the downstream lower right side. The paper pressing plate 521 is opened and closed by a rotating actuator 523, and is controlled to open when the packing paper B is being conveyed and to close when it is stopped. The heat seal portion 522 has a surface heating element 524 held by a carriage 525a. The carriage 525a is pivotally supported by a guide rod 526 and confi gured to be movable forward and backward by a feed screw 528 directly connected to a motor 527 . When the carriage 525a advances, the upper end of the packaging paper B is pressed a gainst the receiving plate 525b, and the packaging paper B is sealed by heating.

[0055]

With the packaging paper B stationary, the carriage 525a is advanced for a predetermined ti me, and the shutter mechanism 520 is opened as indicated by 520a at the timing when the p aper pressing plate 521 is closed. to fall. Next, when the packaging paper B is conveyed by a predetermined distance P and the carriage 525a is moved forward again, the portion containin g the medicine that has just dropped is sealed all at once. By repeating this operation, the pac kaging paper B is continuously sealed. At this time, if the types and amounts of the medicines to be put in sequentially are controlled according to the prescription and the dosing order, for example, two weeks' worth of medicine can be taken. , One dose is divided into each package and completed. The rubber roller pair 529 is means for sandwiching and conveying the packin g paper B, and by installing it at a plurality of locations of the continuous packing paper B, the paper can be conveyed without slack. The drive roller pair 529 is controlled by a pulse motor 530 to stop the conveyance of a predetermined distance. A perforation forming device 540 si milar to the perforation forming device 400 described as the first embodiment is provided dow nstream of the driving roller 529 on the downstream side

. [0057] In the operation of preparing a medicine package, the transported packaging paper B is longitudinally sealed by the heat seal portion 522 to separate one package. At this time, t

he previous individual package is laterally sealed at the same time. Next, one package of med icine is supplied between the packaging sheets B from the medicine supply 519 via the drop h opper 518 . The packaging paper B to which the medicine is supplied is conveyed by the drive roller 529 by the length of one package. [0058]

Next, the second medicine is supplied between the packaging papers B, and the packaging p apers B are further conveyed by the driving roller 529 . At this stage, the first vertical seal por tion comes to the perforation forming device 540, so the perforation forming device 540 forms a perforation in the central portion of the vertical seal portion. After this operation is repeated to complete one prescription of packaged medicine, the perforated line forming device 540 cut s the vertically sealed portion to manufacture the packaged medicine.

[0059]

Thus, the position of the heat seal portion is not limited to the upstream side of the drug sup ply section, but may be the downstream side of the drug supply section. While several embo diments and variations of the invention have been described, these embodiments and variatio ns are provided by way of example and are not intended to limit the scope of the invention .

These novel embodiments and modifications can be implemented in various other forms, and various omissions, replacements, and modifications can be made without departing from the s cope of the invention. These embodiments and modifications thereof are included in the scope and gist of the invention, and are included in the scope of the invention described in the claim s and equivalents thereof.

[Description of Reference Numerals]

100

... Disk distribution section (medicine supply section)

200... Printing and packaging machine

201... Packaging paper roll (packaging paper storage section)

206... Vertical sealing mechanism

209 ... Horizontal sealing mechanism

211 ... Driving roller

300 ... Dropping hopper (medicine supply section)

400 ... Perforation creating device

402 ... Blade storage section

404... Blade receiving portions

416, 418... Cam plate

420... Cam plate

432 Perforating blade

432b Perforating blade base

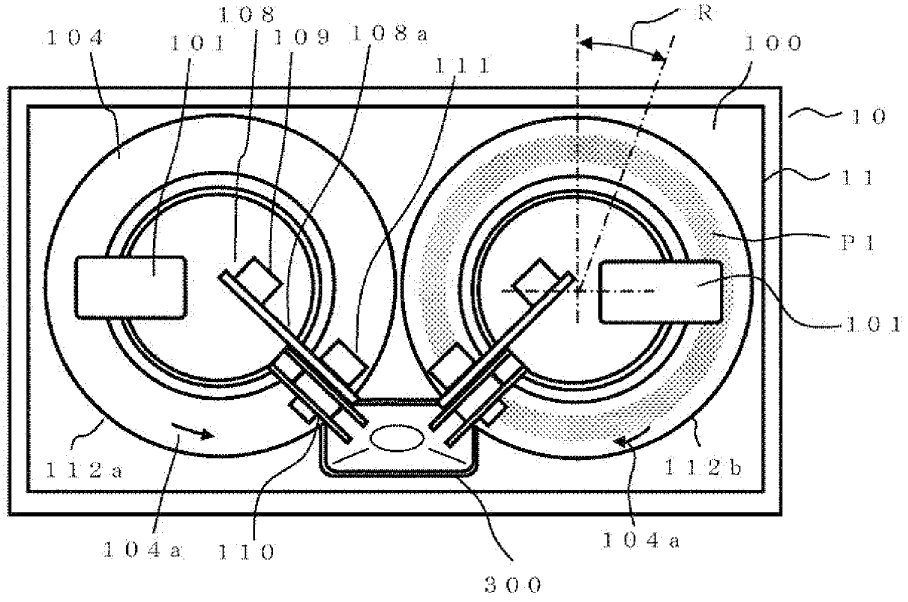
432c Perforating blade tip

B Packaging paper

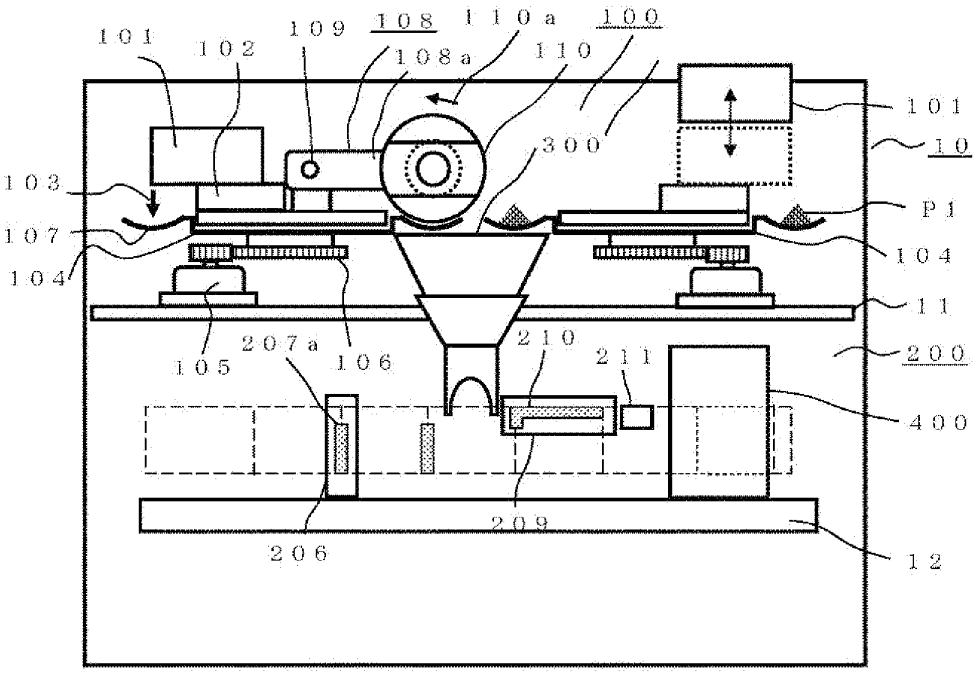
B2, B3 Conveyance path (conveyance path)

drawing open —

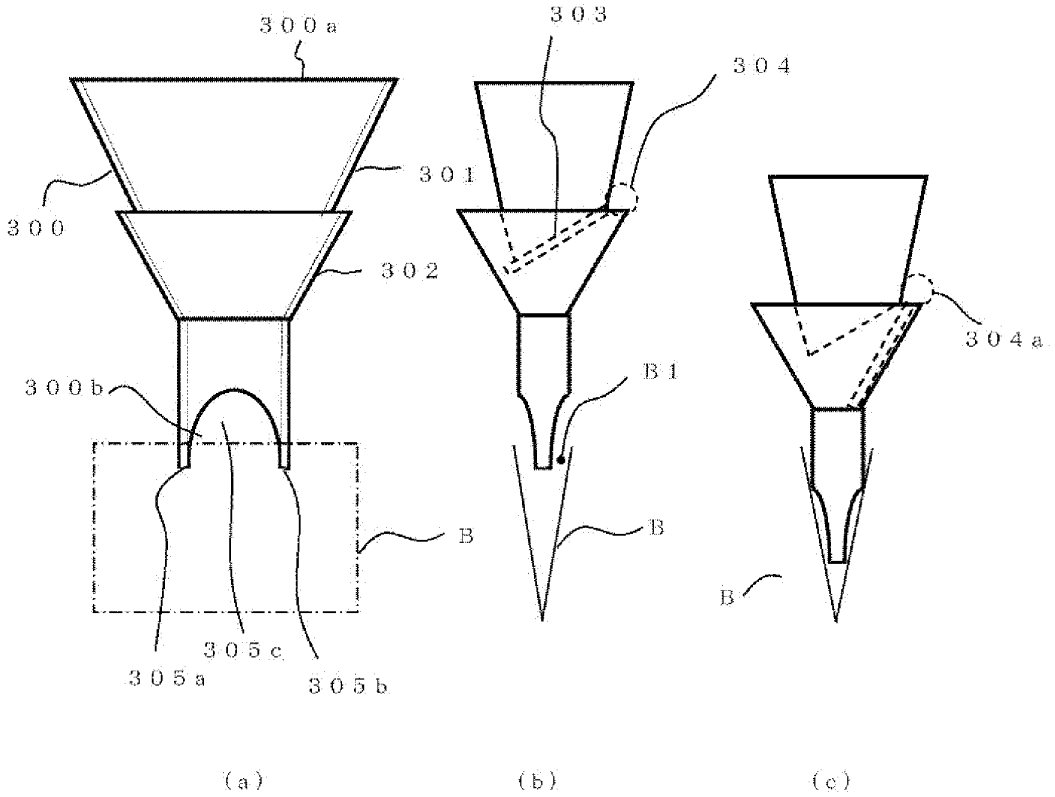
[Fig. 1]



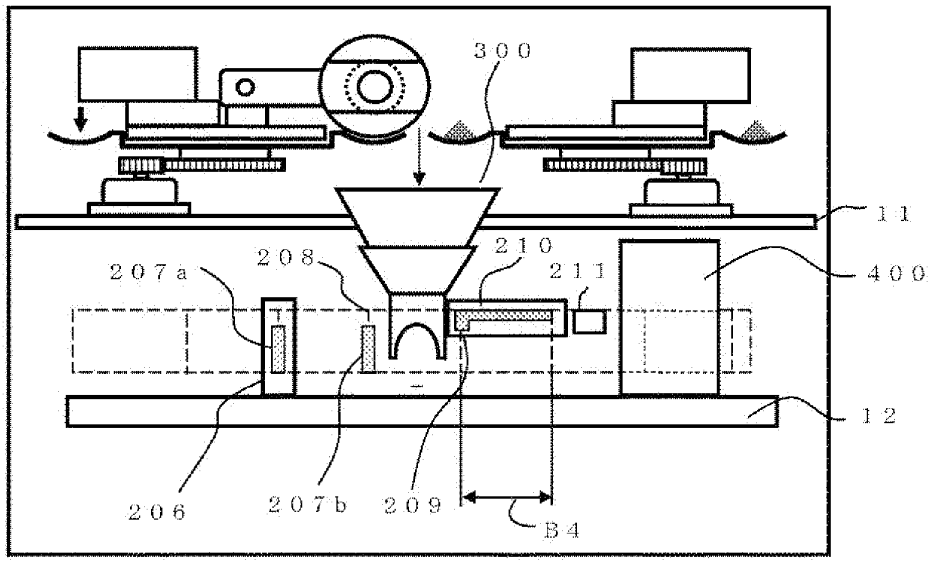
[Figure 2]



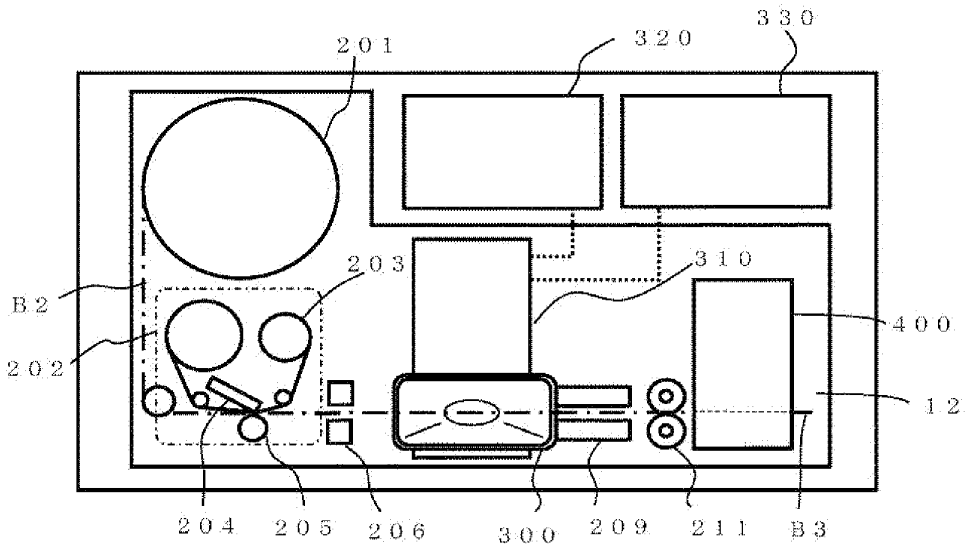
[Figure 3]



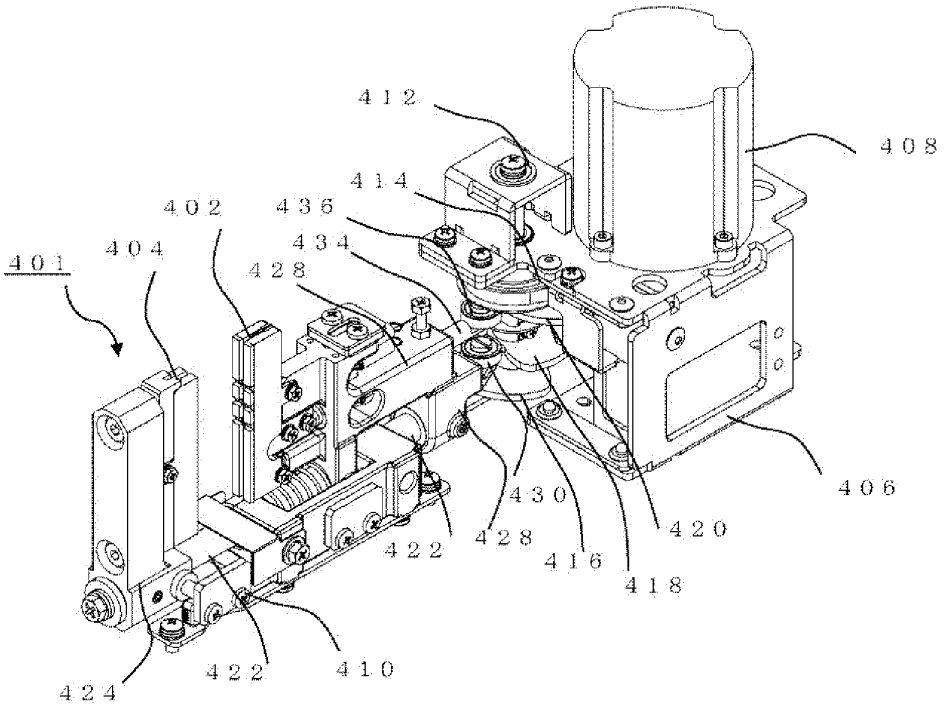
[Figure 4]



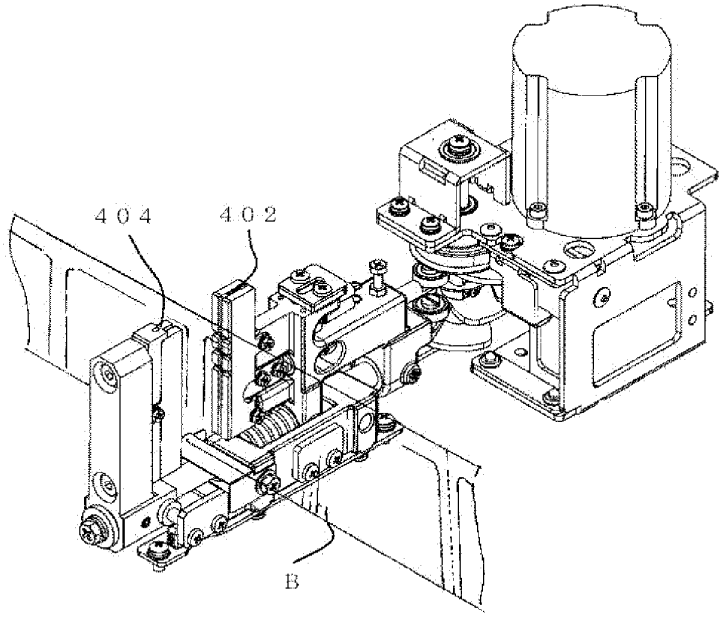
[Figure 5]



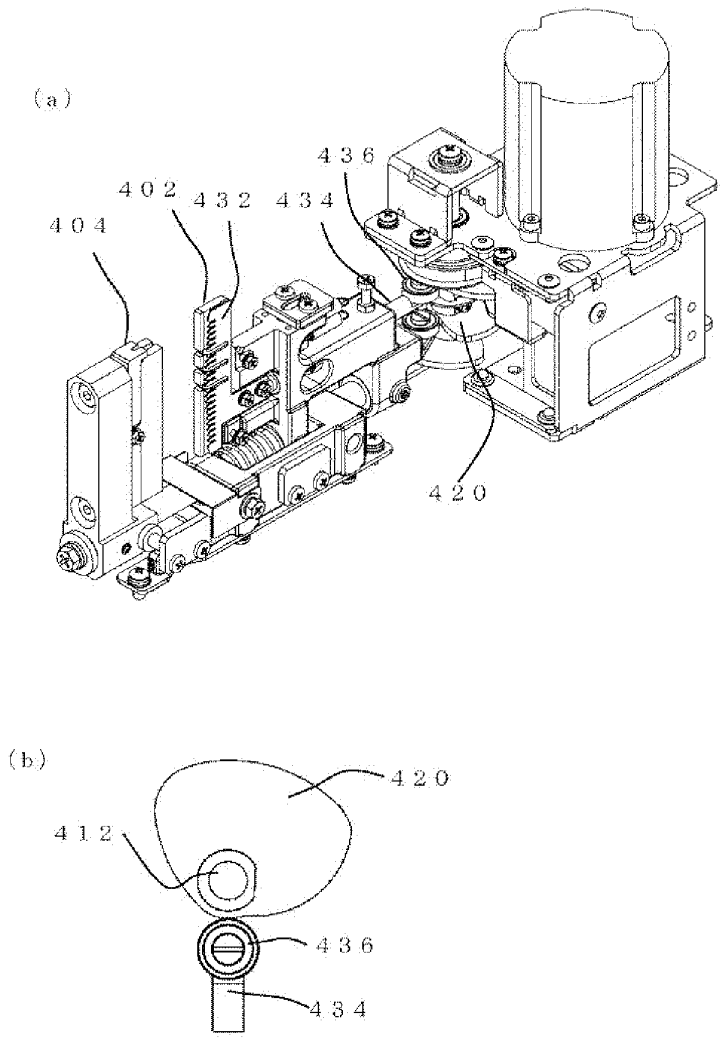
[Fig. 6]


412
408
414
402
436
434
401
404
428
406
430
420
422
428
416
418
422
410
424

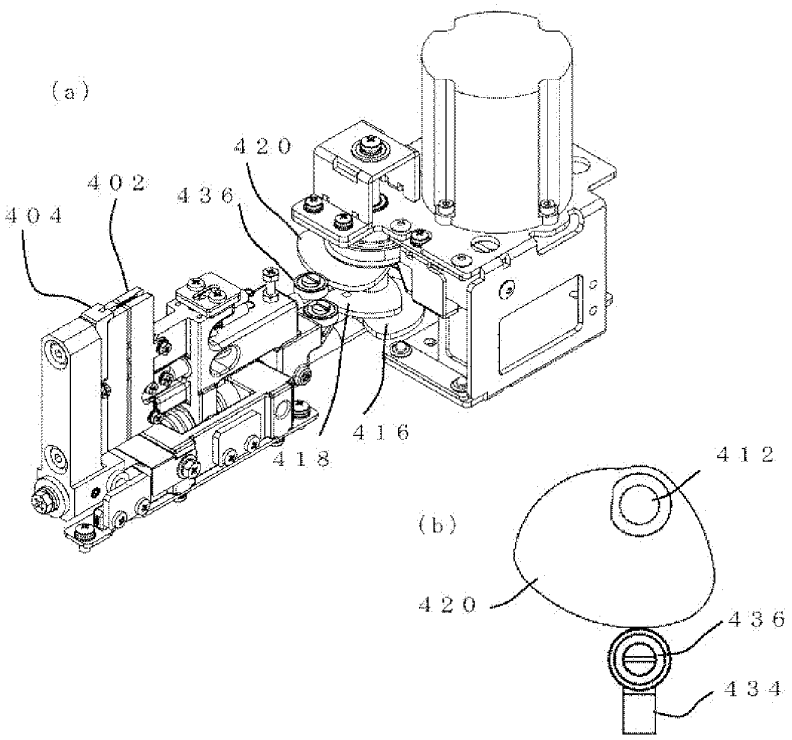
[Fig. 7]


404
402
B

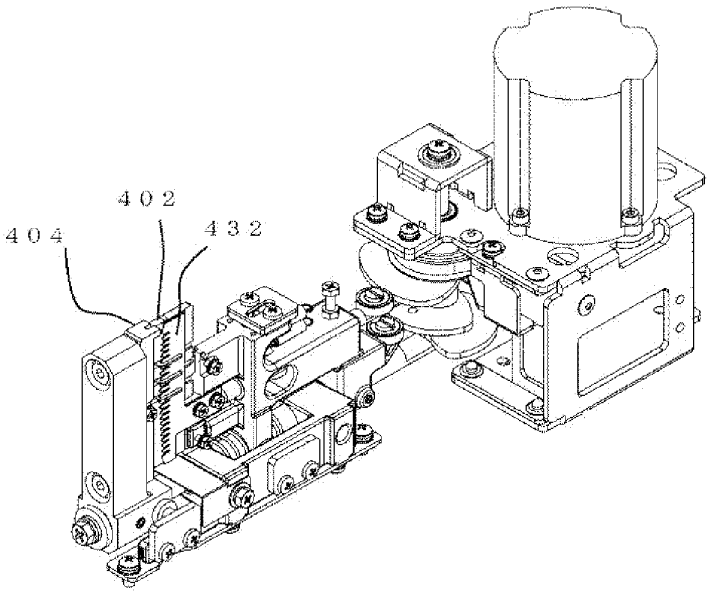
[Fig. 8]



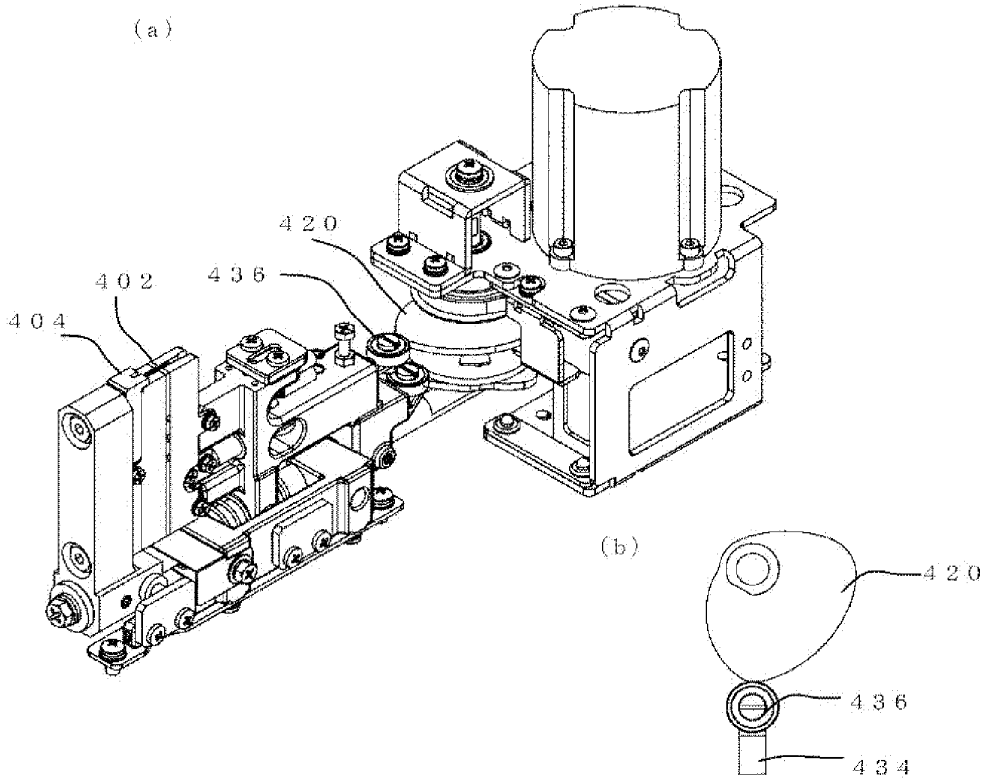
[Fig. 9]



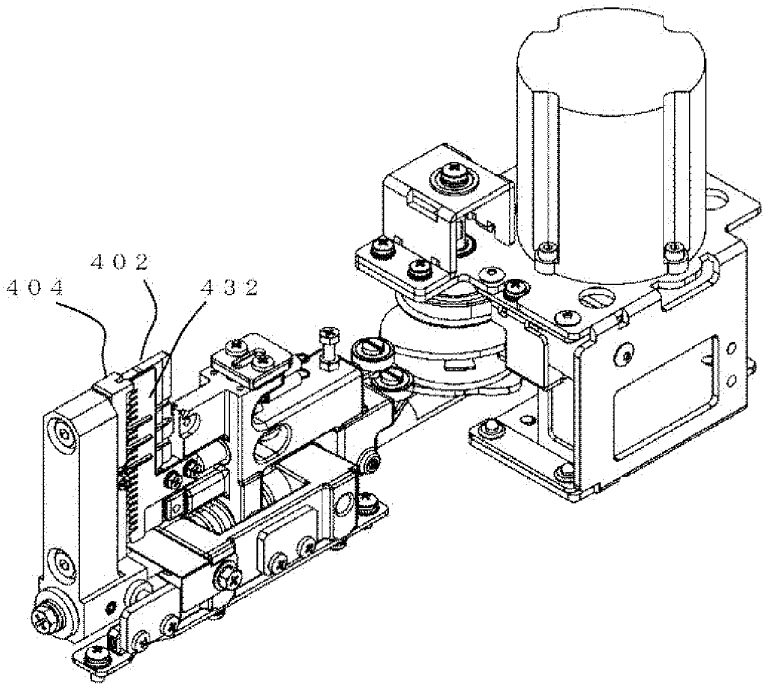
[Fig. 10]



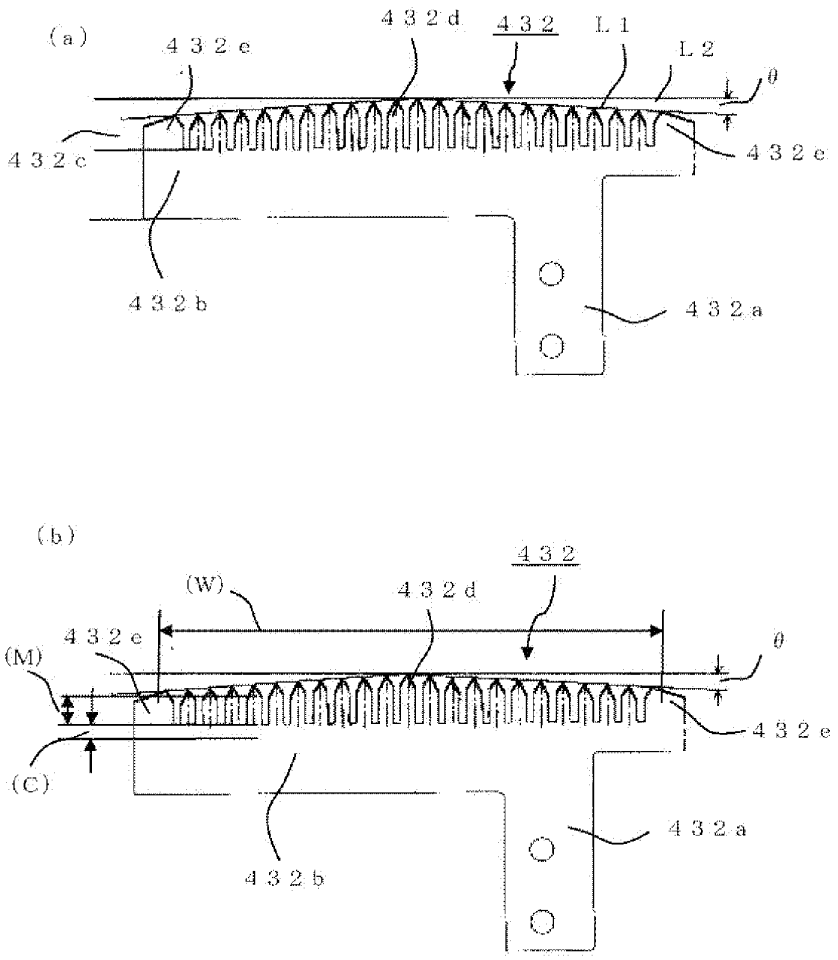
[Fig. 11]



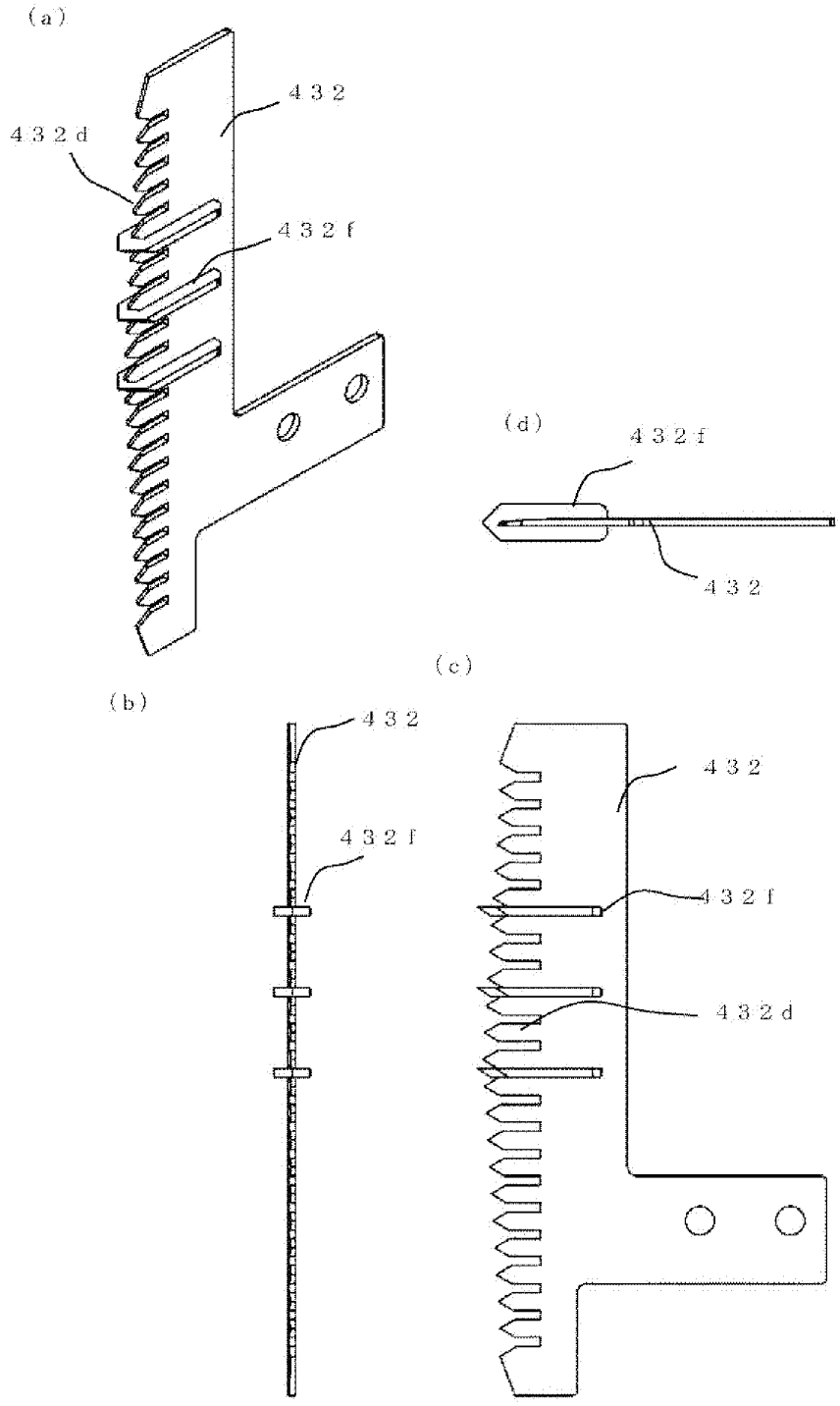
[Fig. 12]



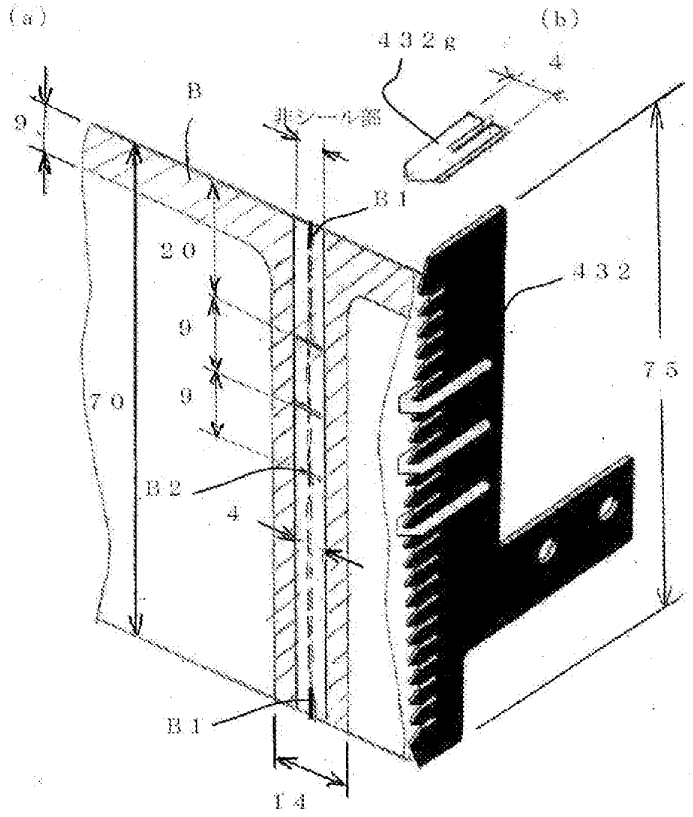
[Fig. 13]


(a)
432e
432d
432
L1
L2
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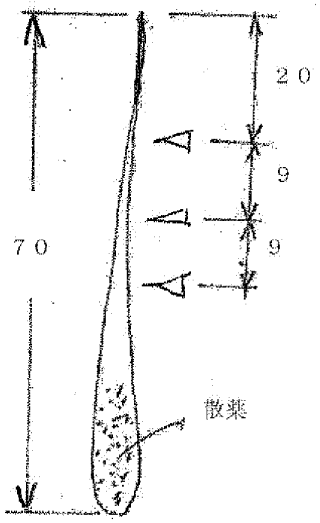
[Fig. 14]



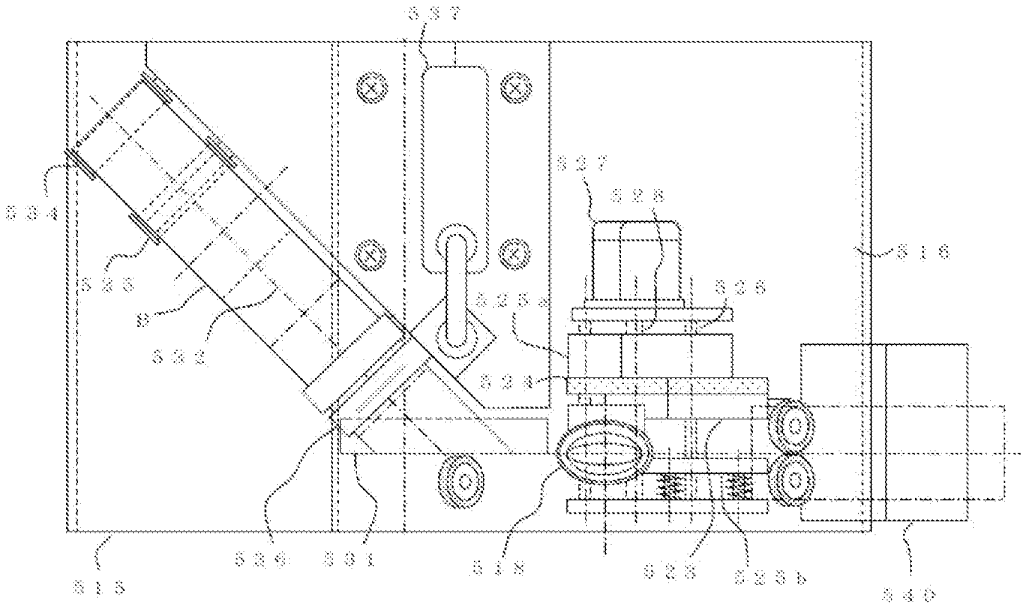
[Fig. 15]



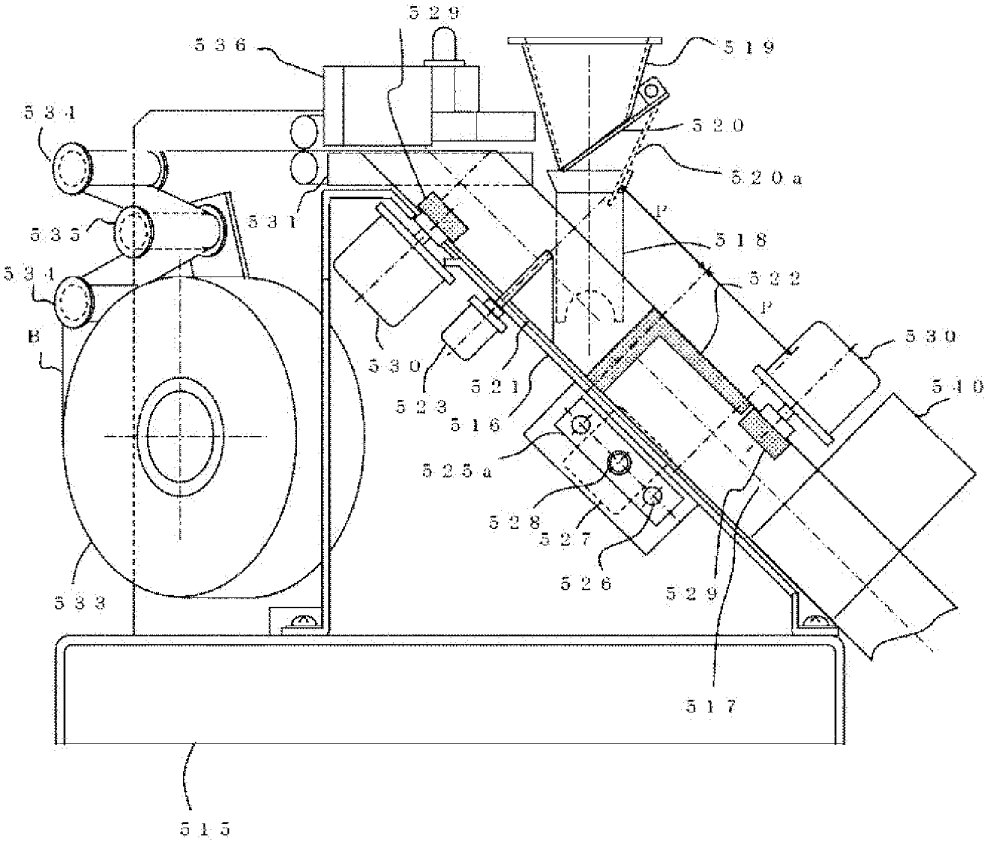
[Fig. 16]



[Fig. 17]



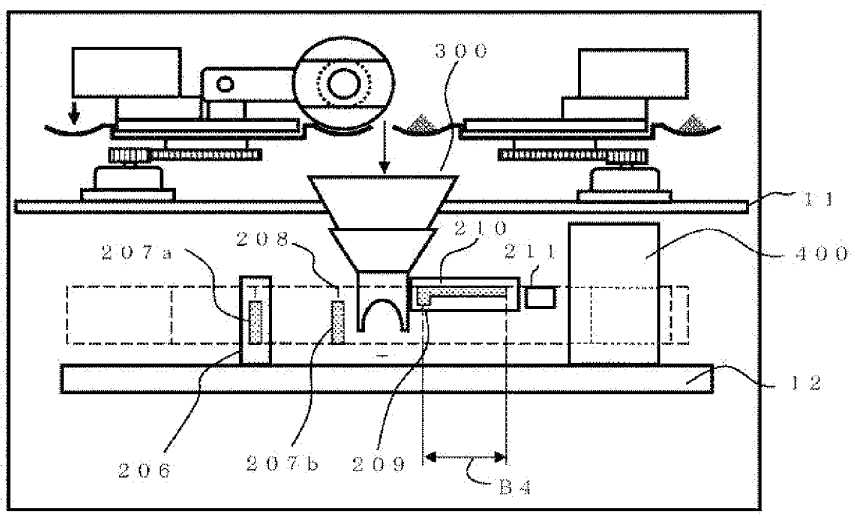
[Fig. 18]



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Bibliographic data: JP2020000340 (A) — 2020-01-09

MEDICINE DISPENSING/PACKAGING DEVICE AND PRODUCTION METHOD OF DISPENSING/PACKAGING MEDICINE

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Applicant(s): TOSHO INC ± (株式会社トーショー)

Classification: **- international:** ***A61J3/00; B65B61/00***
- cooperative:

Application number: JP20180120789 20180626 Global Dossier

Priority number(s): JP20180120789 20180626

Abstract of JP2020000340 (A)

To provide a medicine dispensing/packaging device that is never cut in a perforation portion of the dispensing/packaging paper during conveyance, and provide a production method of the dispensing/packaging medicine.SOLUTION: A medicine dispensing/packaging device has: a dispensing/packaging paper storage part where the V-folded dispensing/packaging paper is wound; a conveyance path for drawing the dispensing/packaging paper out of the dispensing/packaging paper storage part, and conveying it; a heat seal part provided in the middle of the conveyance path, and forming a heat seal to divide a dispensing/packaging paper into one package at a time; a medicine supplying part provided in the middle of the conveyance path, and supplying medicine by one package at a time between the dispensing/packaging papers; a drive roller for holding the dispensing/packaging paper where the medicine supplied by the medicine supplying part is stored, and performing conveyance drive; and a perforation making part provided at a conveyance direction down-stream of the dispensing/packaging paper from the drive roller, and forming the perforation in a portion heat-sealed by the heat seal part.SELECTED DRAWING: Figure 4

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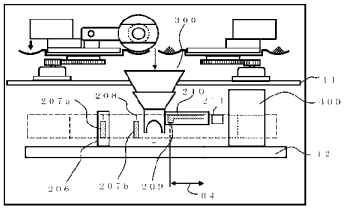
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最終頁に続く

(54)【発明の名称】薬剤分包装置及び分包薬剤の製造方法

【要約】
【課題】搬送中に分包用紙のミシン目部分で切れることの無い薬剤分包装置及び分包薬剤の製造方法を提供する。
【解決手段】Ｖ字折りされた分包用紙が巻回された分包用紙収納部と、前記分包用紙収納部から分包用紙を引出して搬送する搬送路と、前記搬送路の途中に設けられ、前記分包用紙を１個包分ずつに区分するヒートシールを形成するヒートシール部と、前記搬送路の途中に設けられ、前記分包用紙間に薬剤を１包分ずつ供給する薬剤供給部と、前記薬剤供給部によって供給された薬剤が収納された分包用紙を挟持して搬送駆動する駆動ローラと、前記駆動ローラよりも前記分包用紙の搬送方向下流に設けられ、前記ヒートシール部によってヒートシールされた部分にミシン目を形成するミシン目作成部と、を有する。
【選択図】図４



【特許請求の範囲】
【請求項１】
Ｖ字折りされた分包用紙が巻回された分包用紙収納部と、
前記分包用紙収納部から分包用紙を引出して搬送する搬送路と、
前記搬送路の途中に設けられ、前記分包用紙を１個包分ずつに区分するヒートシールを形成するヒートシール部と、
前記搬送路の途中に設けられ、前記分包用紙間に薬剤を１包分ずつ供給する薬剤供給部と、
前記薬剤供給部によって供給された薬剤が収納された分包用紙を挟持して搬送駆動する駆動ローラと、
前記駆動ローラよりも前記分包用紙の搬送方向下流に設けられ、前記ヒートシール部によってヒートシールされた部分にミシン目を形成するミシン目作成部と、
を有する薬剤分包装置。
【請求項２】
前記ミシン目作成部は、
前記分包用紙の搬送路の一方の面側に設けられ、ミシン刃が突没自在に収納された刃収納部と、
前記分包用紙の搬送路の他方の面側に、前記刃収納部と対向して設けられ、前記刃収納部から突出した前記ミシン刃との間で前記分包用紙にミシン目を形成する刃受け部と、
前記刃収納部と前記刃受け部とをそれぞれ前記分包用紙側に移動させて分包用紙を挟持するように駆動する第１の駆動部と、
前記刃収納部と前記刃受け部とによって前記分包用紙を挟持した状態で、前記刃収納部のミシン刃を前記刃受け部側に突出するように駆動することにより前記分包用紙にミシン目を形成する第２の駆動部と、
を有する請求項１記載の薬剤分包装置。
【請求項３】
前記ミシン刃は、
基部と、
前記基部から突出して設けられ、先端に山形の刃先が形成された複数の刃片が、隣接する刃片との間に所定の間隔を設けて形成された刃先部と、を有し、
前記第２の駆動部は、
前記ミシン刃の刃片の途中まで前記刃受け部側に突出させることにより、前記分包用紙にミシン目を形成し、
前記ミシン刃の基部まで前記刃受け部側に突出させることにより、前記分包用紙を切断する、
ことを特徴とする請求項２記載の薬剤分包装置。
【請求項４】
前記ミシン刃は、
前記分包用紙の搬送方向と直交する方向の両端部の刃片の刃の幅が内側の刃片の刃の幅よりも大きく形成され、これら両端部の刃片により分包用紙の搬送方向と直交する方向の両端部に切断開始部を形成する、
ことを特徴とする請求項３記載の薬剤分包装置。
【請求項５】
前記ミシン刃は、
前記それぞれの刃片が、中央部の刃片の基部からの長さが最も長く、端部に行くにつれて長さが徐々に短くなるように形成された、
ことを特徴とする請求項３又は請求項４記載の薬剤分包装置。
【請求項６】
前記ミシン刃は、
前記複数の刃片と刃片との間に、前記刃片の厚さよりも刃幅の広い横刃片を挿入するこ

とにより、十字状の刃を複数形成し、この十字状の刃により分包用紙に形成されるミシン目に、ミシン目に沿って分離されたときの切断開始部を形成する、
ことを特徴とする請求項３乃至請求項５のいずれか１項記載の薬剤分包装置。
【請求項７】
予め収納されたＶ字折りされた分包用紙を搬送路に引出し、
前記引出された分包用紙に１個包分ずつに区分するヒートシール部を形成し、
前記ヒートシール部が形成された分包用紙間に薬剤を１個包分ずつ供給して収納し、
前記薬剤が収納された分包用紙を駆動ローラにより挟持して１個包分ずつ搬送駆動し、
前記駆動ローラよりも前記分包用紙の搬送方向の下流側で、前記分包用紙のヒートシールされた部分にミシン目を形成する、
分包薬剤の製造方法。
【発明の詳細な説明】
【技術分野】
【０００１】
本発明は、薬剤を１個包分ずつ供給して分包する薬剤分包装置及び分包薬剤の製造方法に関する。
【背景技術】
【０００２】
薬剤調剤業務の自動化のために薬剤分包装置が開発され実用に供している。このような薬剤分包装置の例として特許文献１記載のものがある。
【０００３】
すなわち、Ｖ字折りされた分包用紙が巻回されたロールから、分包用紙の端部が引出され、複数の支持軸を介して搬送方向に向かって下方に傾斜した搬送路に沿って搬送され、漏斗状の薬剤ホッパ部に供給される。薬剤ホッパよりも下流側には、熱圧接部が設けられており、この熱圧接部にはヒートシール及びミシン目形成部が設けられている。そして、ヒートシールによって１個包を分離するＴ字形状のヒートシールが成されるとともに、各個包に分離するためのミシン目が形成される。ヒートシールが成された後に１個包分の薬剤が薬剤ホッパから分包用紙間に供給される。
【０００４】
薬剤が供給されると、熱圧接部よりも下流側に設けられた駆動ローラによって分包用紙が挟持されて１個包分の長さだけ引き出されて、次の個包のためのヒートシールとミシン目の作成が行われる。このような個包化動作を繰返すことによって１処方分の分包薬剤が作成される。
【先行技術文献】
【特許文献】
【０００５】
【特許文献１】特開２０１２－１３１５５１号公報
【発明の概要】
【発明が解決しようとする課題】
【０００６】
特許文献１記載の装置では、分包用紙を搬送する駆動ローラがミシン目作成部よりも下流側に設けられている。このため、駆動ローラによって分包用紙を引出した際に、分包用紙に過大な負荷が掛かるとミシン目部分で分包用紙が切れてしまうという虞があった。また、分包用紙間の下部には薬剤が封入されているので駆動ローラは必然的に分包用紙の上方を挟持して搬送する必要がある。搬送中に分包用紙が切れないようにするためには、分包用紙の上端にはミシン目（カット）を入れることができない。その結果、老人や筋力の衰えた人は上端側からミシン目に沿って切り取ることが困難であるという問題もあった。
【０００７】
そこで従来の分包機では、用紙の下端にミシン目（カット）を入れて、下側から切り取るようにする場合もあったが、これでは都度分包用紙を逆さにする必要があり、そのとき

に印字の向きが逆になって視認性が悪く、さらに切り取った後、もう一度逆さに元の状態にして、手で横方向に切って開封する必要があり、その不便さが指摘されていた。
【０００８】
本発明が解決しようとする課題は、搬送中に分包用紙のミシン目（カット）部分で切れることの無いようにした薬剤分包装置及び分包薬剤の製造方法を提供することを目的とする。また、第２の課題は、服用者が１個包をミシン目に沿って切断するのが容易なように分包用紙の上端部側にミシン目（カット）が入れられることのできる服用者にとって利便性の高い薬剤分包装置及び分包薬剤の製造方法を提供することを目的とする。
【０００９】
さらに、副次的な効果としては、このように分包用紙の上下端にミシン目（カット）を設けることで、長い分包用紙を例えば１日３包（朝・昼・晩）ごとに折りたたんで保管するような場合に、その折り目がしっかり付けやすいので、全て折りたたんだときの外観がきちんとしているという点も上げておきたい。
【課題を解決するための手段】
【００１０】
本発明の薬剤分包装置は、Ｖ字折りされた分包用紙が巻回された分包用紙収納部と、前記分包用紙収納部から分包用紙を引出して搬送する搬送路と、前記搬送路の途中に設けられ、前記分包用紙を１個包分ずつに区分するヒートシールを形成するヒートシール部と、前記搬送路の途中に設けられ、前記分包用紙間に薬剤を１包分ずつ供給する薬剤供給部と、前記薬剤供給部によって供給された薬剤が収納された分包用紙を挟持して搬送駆動する駆動ローラと、前記駆動ローラよりも前記分包用紙の搬送方向下流に設けられ、前記ヒートシール部によってヒートシールされた部分にミシン目を形成するミシン目作成部と、を有する。
【００１１】
また、本発明の分包薬剤の製造方法は、予め収納されたＶ字折りされた分包用紙を搬送路に引出し、前記引出された分包用紙に１個包分ずつに区分するヒートシール部を形成し、前記ヒートシール部が形成された分包用紙間に薬剤を１個包分ずつ供給して収納し、前記薬剤が収納された分包用紙を駆動ローラにより挟持して１個包分ずつ搬送駆動し、前記駆動ローラよりも前記分包用紙の搬送方向の下流側で、前記分包用紙のヒートシールされた部分にミシン目を形成する。
【図面の簡単な説明】
【００１２】
【図１】実施形態の散薬自動分包機の円盤配分部の平面の断面図。
【図２】実施形態の散薬自動分包機の落下ホッパの上昇位置を示す正面の断面図。
【図３】落下ホッパの構造と動作概要を示す図。
【図４】実施形態の散薬自動分包機の落下ホッパの下降位置を示す正面の断面図。
【図５】実施形態の散薬自動分包機の印刷包装機部の平面の断面図。
【図６】実施形態のミシン目作成装置の斜視図で、刃収納部と刃受け部とが開いた状態を示す図。
【図７】実施形態のミシン目作成装置の斜視図で、刃収納部と刃受け部との間に分包用紙が搬送されている状態を示す図。
【図８】実施形態のミシン目作成装置の斜視図で、刃収納部と刃受け部とが開いた状態で刃収納部のカバーを外した図。
【図９】実施形態のミシン目作成装置の斜視図で、刃収納部と刃受け部とが閉じてミシン目を作成している状態を示す図。
【図１０】実施形態のミシン目作成装置の斜視図で、刃収納部と刃受け部とが閉じてミシン目を作成している状態の刃収納部のカバーを外した図。
【図１１】実施形態のミシン目作成装置の斜視図で、刃収納部と刃受け部とが閉じて分包用紙を切断している状態を示す図。
【図１２】実施形態のミシン目作成装置の斜視図で、刃収納部と刃受け部とが閉じて分包

用紙を切断している状態の刃収納部のカバーを外した図。
【図１３】実施形態のミシン目作成装置のミシン刃の形状と移動距離を説明するための図。
【図１４】実施形態のミシン目作成装置のミシン刃の形状を説明するための図。
【図１５】実施形態のミシン目作成装置のミシン刃の形状と分包用紙との関係を説明するための図。
【図１６】実施形態の散薬自動分包機で製造された分包薬剤の例を示す図。
【図１７】第２の実施形態の印刷包装機を説明するための平面図。
【図１８】第２の実施形態の印刷包装機を説明するための正面図。
【発明を実施するための形態】
【００１３】
以下、実施形態に係る散薬自動分包機を、図面を用いて説明する。
以下の説明では散薬自動分包機を例にとって説明するが、本発明は散薬自動分包機に限定されるものではなく、錠剤自動分包機にも適用可能である。また、特許第６２５５５２８号公報や特開２０００－２４０８７号公報に記載されたような複数の薬剤を１つの個包に分包する薬剤分包装置にも適用可能なことは勿論である。
【００１４】
図１は本実施形態の散薬自動分包機の平面図、図２は散薬自動分包機の正面図である。筐体１０の中間台１１の上部には薬剤供給部である円盤配分部１００、中間台１１の下部には、薬剤包装部である印刷包装機２００が配置されている。また３００は落下ホッパであって、円盤配分部１００から放出される散薬をこの落下ホッパ３００の内面側を通して、印刷包装機２００側に導入する働きをなすものである。
【００１５】
円盤配分部１００には２組の配分部が設けられている。円盤配分部１００において、１０１は着脱自在な散薬カセットで、事前に別の場所で、当該処方に必要な分量の散薬が装填され、係員の手動操作か、図示しないロボットアーム等の自動装置によって、別の棚から振動台１０２に載置される。振動台１０２は、図示しない電磁石などによって振動を発生させ、この振動力を散薬カセット１０１に伝達させることで、散薬カセット１０１内の散薬を振動輸送し、矢印１０３の方向に散薬を少量ずつ落下させるものである。
【００１６】
１０４は水平に配置された配分円盤で、大きな円輪がステッピング・モータ１０５によって、歯車１０６を介して矢印１０４ａ方向に回転させられるようになっている。さらに配分円盤１０４の外周方向の上面には円弧状凹面１０７を形成していている。ここで、ステッピング・モータ１０５を連続的に回転しながら、振動台１０２を駆動すると、散薬が配分円盤１０４の円弧状凹面１０７に少量ずつ落下して、ドーナツ状の散薬の山Ｐ１を形成することができる。この動作を「円周撒き動作」と呼ぶこととする。
【００１７】
また、１０８は掻き出しディスク部で、レバー１０８ａが軸１０９を中心にして上下に回動できる。このレバー１０８ａの先端には、その円周外周がシリコンゴム製のディスク１１０が取り付けられ、モータ１１１で矢印１１０ａ方向に回転可能である。このディスク１１０は２枚の円板の間に羽根が設けられた水車状の形状である。なお、このディスク１１０の円板の直径は、円弧状凹面１０７の凹面の直径と同一である。
【００１８】
先の「円周撒き動作」の場合は、このディスク１１０は上方に回動して待避していて、ドーナツ状の散薬の山Ｐ１の形成を妨げない。次に「１包分配分動作」時は、掻き出しディスク部１０８のディスク１１０が下方に回動して、ディスク１１０が、円弧状凹面１０７に隙間なく密着する。この状態で、モータ１１１を駆動するとディスク１１０の円板に設けられた羽根によって円弧状凹面１０７の上の散薬が落下ホッパ３００に掻き落とされる。そして、ステッピング・モータ１０５を所定角度Ｒだけ回転させると、その角度分の散薬の量が、落下ホッパ３００側に払出される。ここで、先の所定角度Ｒとは、別に処方

箋から指定される１個包に包装すべき用量分の角度である。
【００１９】
例えば、処方箋で、ある散薬を１個包あたり１ｇで３６個包作成する場合にあっては、事前に散薬カセット１０１に３６ｇの散薬を装填しておき、これを「円周撒き動作」で、全量をドーナツ状に均一に撒く。次に「１包分配分動作」で、ディスク１１０を回転させながら、ステッピング・モータ１０５を１０度回転させると、正しく１個包分の１ｇの散薬が落下ホッパ３００に払出させることができるものである。このような円盤配分部１００と落下ホッパ３００で薬剤供給部を構成する。
【００２０】
円盤配分部１００には、左右に対称形に、２組の円盤部１１２ａと１１２ｂが配置しているが、これは、一方の円盤部１１２ａで「円周撒き動作」しているときは、他方の円盤部１１２ｂが「１包分配分動作」を出来るようにして、複数の連続する処方において無駄時間がなく、連続的に分包できるようにするためのものである。
【００２１】
図３は落下ホッパ３００の形状と動作の概要を示すものである。落下ホッパ３００は上ホッパ３０１と下ホッパ３０２の二重構造となっており、上ホッパ３０１の下開放部３０３を開閉自在なシャッタ３０４で閉鎖している。上ホッパ３０１の上端は、円盤配分部１００からの散薬を受け入れる上開口部３００ａが形成されている。下ホッパ３０２の下端部は図３（ａ）（ｂ）に示すように楔状に形成され、両端に突部である爪部３０５ａ、３０５ｂが形成され、その間に散薬を払出す凹部（下開口部）３０５ｃが形成されている。この落下ホッパ３００は全体として上下移動できるようになっている。そして、「１包分配分動作」で、円盤配分部１００から散薬を払出すタイミングでは、図３（ａ）（ｂ）の上位置に位置する。この時、シャッタ３０４は図３（ｂ）の側面図に示すように閉鎖しているので、落下した散薬は一旦このシャッタ３０４上に保持される。
【００２２】
このとき落下ホッパ３００の下端の左右の爪部３０５ａと３０５ｂは、搬送される谷折り状に二つ折された分包用紙Ｂの開放端Ｂ１にその先端を入れ込んでいる。
【００２３】
散薬の放出時は図３（ｃ）のように、落下ホッパ３００全体を下方に移動するが、左右の爪部３０５ａ、３０５ｂｃ楔状の形状が、落下ホッパ３００が分包用紙Ｂ間に進入するときのガイドの働きをしている。この状態でシャッタを３０４ａのように開くと、散薬は分包用紙Ｂの内部に収納されるものである。その後、落下ホッパ３００は図３（ｂ）の位置まで上昇する。
【００２４】
次に、図４と図５を用いて印刷包装機２００の構成と動作を説明する。図４は散薬分包機の正面の断面図であって、図２で上方に位置していた落下ホッパ３００は、下方に移動した状態を示している。図５は印刷包装機２００の上面の断面図である。２０１は分包用紙収納部としての分包用紙ロールであって、熱接着性を持つ二つ折りした用紙が谷折側を下にして、リールに巻き上げたものであり、下段台１２の上に設置されている。リールの外周側の用紙先端から引き出された分包用紙は、一点鎖線Ｂ２からＢ３のような経路で搬送路を搬送されるようになっている。２０２は印刷部で、インクリボン２０３、感熱印刷ヘッド２０４、プラテンローラ２０５等によって構成され、分包用紙Ｂの表面に、１包分ずつの処方情報を印字するものである。
【００２５】
２０６は下段台１２上に設けられたヒートシール部である縦シール機構で、分包用紙Ｂを前後（図５では上下）から熱板によって圧接することで、２０７ａのように縦方向のシールが行われることで１個包分ずつに区分する。１包分移動した位置での縦シールを２０７ｂに示すが、分包用紙Ｂの上開放端２０８はシールしないようになっている。これは、図３（ａ）のように、落下ホッパ３００の爪部３０５ａ、３０５ｂが、分包用紙Ｂ間に挿入した状態で、分包用紙Ｂを搬送できるようにするためである。次に配置される落下ホッ

パ３００の奥側には落下ホッパ洗浄装置３１０が取り付けられている。この落下ホッパ洗浄装置３１０については、本発明と直接関係しないので詳細な説明は省略する。
【００２６】
次の２０９は横シール機構で、分包用紙Ｂを前後から熱板によって圧接することで、２１０のように横方向と縦方向の未シール部分とのシールが行われる。先の縦シール２０７と横シール２１０とによって、分包用紙Ｂは１個包としてシールされるものである。なお、図では省略しているが、縦シール７はミシン目が形成される部分をシールせずに、ミシン目形成部を挟んだ両側をシールするようになっており、詳細は後述する。
【００２７】
２１１は駆動ローラであって、印刷部２０２のプラテンローラ２０５と同期駆動され、分包用紙Ｂの上端部分を両面から挟持して回転することにより、１個包分ピッチＢ４の距離を、１工程として駆動される。４００はミシン目作成装置で、縦シールされた部分の中間に設けられた非シール部に、縦方向のミシン目を形成することにより、服薬者が１個包ずつに分離しやすくなっている。なお、図２及び図４に示す縦方向の破線はミシン目ではなく、１個包の境目を示したものである。また、図２及び図４においては、説明を判りやすくするために落下ホッパ３００より下流側の縦シールの記載は省略している。
【００２８】
なお、落下ホッパ洗浄装置３１０の補機として、集塵ブロア３２０と、圧縮空気発生コンプレッサ３３０が、筐体後方に配置されて、それぞれ、落下ホッパ洗浄装置３１０の空気源として利用される。
【００２９】
以下、図６～図１５を用いてミシン目作成装置４００の構成と動作について説明する。図６はミシン目作成装置の斜視図であり、刃収納部４０２と刃受け部４０４とが開いている待機状態を示す図で、図７は刃収納部４０２と刃受け部４０４との間に分包用紙Ｂを挿入した状態を示す図である。分包用紙Ｂは刃収納部４０２と刃受け部４０４との中間に位置するように刃収納部４０２と刃受け部４０４とが配置されている。図８は刃収納部４０２のカバーを外した状態を示す図である。
【００３０】
図４及び図５に記載された下段台１２にはモータ用ベース４０６が固定され、このモータ用ベース４０６にはステッピング・モータ４０８が固定されている。また、下段台１２にはミシン刃ユニット４０１のベース４１０が固定されている。
【００３１】
ミシン刃ユニット４０１のベース４１０には刃収納部４０２が固定された支持部４２８が摺動自在に設けられている。また、ベース４１０には刃受け部４０４が固定された支持部４２４が摺動自在に設けられ、支持部４２４に固定されたスライド軸４２２と一体になって摺動するものである。そして、支持部４２４と支持部４２８とは互いに接離する方向に摺動自在である。これら支持部４２４と支持部４２８との間にはスプリング４２６が設けられ、互いに離間する方向に付勢されている。
【００３２】
刃収納部４０２の支持部４２８の内部にはシャフト４３４がスライド自在に設けられ、このシャフト４３４の左端にはミシン刃４３２が固定されている。そして、ミシン刃４３２は刃収納部４０２の２枚のカバーの間に、ミシン刃４３２が刃収納部４０２から突没する方向にスライド自在に設けられている。
【００３３】
ステッピング・モータ４０８の図示しない軸とカムシャフト４１２に固定されたプーリ４１４との間にはタイミングベルトが掛け渡され、ステッピング・モータ４０８が回転することによりカムシャフト４１２が回転するようになっている。
【００３４】
また、カムシャフト４１２には３つのカム板４１６，４１８，４２０が固定されている。最下段の第１のカム板４１６は刃受け部４０４を駆動するもので、第１のカム板４１６

を回転することで図示しないカムフォロワによってスライド軸４２２を図中右方向に引き寄せる。スライド軸４２２には刃受け部４０４が固定された支持部４２４が接続されているので、刃受け部４０４も図中右方向に引き寄せられる。

【００３５】

下から２段目の第２のカム板４１８は刃収納部４０２を駆動するもので、カム板４１８を回転することにより刃収納部４０２が固定された支持部４２８に取付けられたカムフォロワ４３０を図中、左方向に駆動するものである。したがって、ステッピング・モータ４０８を回転することによって刃収納部４０２と刃受け部４０４とが互いに接触する方向に移動して分包用紙Ｂを挟持する。カム板４１６と４１８の形状はそれ以上回転しても刃収納部４０２と刃受け部４０４とは分包用紙Ｂを挟持したままである。このようにカム板４１６による刃受け部４０４の駆動機構、及びカム板４１８による刃収納部４０２の駆動機構で第１の駆動部を構成している。

【００３６】

さらに最上段の第３のカム板４２０はミシン刃４３２駆動用のもので、シャフト４３４に固定されたカムフォロワ４３６が第３のカム板４２０に接触している。そして、ステッピング・モータ４０８が回転することによって第３のカム板４２０が回転し、カムフォロワ４３６を押すことによりシャフト４３４を図中左側に駆動する。その結果、シャフト４３４に固定されたミシン刃４３２が刃収納部４０２から刃受け部４０４側に突出して、分包用紙Ｂにミシン目を形成するものである。カム板４２０によるミシン刃の駆動機構が第２の駆動部を構成する。

【００３７】

ミシン刃ユニット４０１の待機状態を図８に示す。図８（ａ）に示すようにミシン刃ユニット４０１の待機状態ではミシン刃４３２は刃収納部４０２のカバー内に没した状態である。このときのカム板４２０とカムフォロワ４３６の状態を図８（ｂ）に示すが、カムフォロワ４３６がカムシャフト４１２に最も近い位置にある。

【００３８】

次に、ステッピング・モータ４０８が回転して分包用紙Ｂにミシン目を形成している状態を図９及び図１０に示す。図９及び図１０に示すように第１のカム板４１６及び第２のカム板４１８が回転することにより、刃収納部４０２と刃受け部４０４とは接触して分包用紙Ｂを挟持した状態となる。なお、図９及び図１０では分包用紙Ｂの記載は省略している。分包用紙Ｂにミシン目を形成する状態ではカム板４２０は図９（ｂ）に示すようにカムノォロワ４３６を押し込んでおり、図１０に示すようにミシン刃４３２の先端が刃受け部４０４内に突出した状態となる。

【００３９】

分包用紙Ｂにミシン目を形成した後は、ステッピング・モータ４０８が逆転することにより、カム板４２０が図９（ｂ）の状態から逆転して図８（ｂ）に示す待機位置に戻る。このような動作によって分包用紙Ｂにミシン目を形成すると、次の個包を形成するために駆動ローラ２１１によって分包用紙Ｂの搬送が行われる。なお、ミシン目の形成と同期して縦シールの形成、薬剤の供給、横シールの形成が行われる。これは、ミシン目の形成時には分包用紙Ｂが停止した状態にあり、分包用紙Ｂの停止した状態での作業である縦シールの形成、薬剤の供給、横シールの形成が行われるものである。以上の動作で１個包分のサイクルが終了する。

【００４０】

ここで、薬剤の処方は服薬者に対して、例えば朝昼晩で２週間分４２回分を処方する。１人の服薬者に対する４２回分の個包の間はミシン目を入れ、１人の服薬者に対する個包が完了した段階ではミシン目ではなく、分包用紙Ｂを切断することにより処方薬を放出する必要がある。

【００４１】

このため、本実施の形態では、ミシン目作成装置４００によって分包用紙Ｂの切断も行うようになっている。図１１及び図１２に示すように、カム板４２０が図９（ｂ）のミシ

ン目を形成する状態を越えて、ステッピング・モータ４０８をさらに回転させ、カム板４２０を図１１（ｂ）に示す位置まで回転させる。すると、カムフォロワ４３６はカムシャフト４１２から最も離れた位置まで押される。これによりミシン刃４３２がさらに突出してミシン刃４３２の基部まで刃受け部４０４内に突出する。これにより、分包用紙Ｂはミシン刃４３２により切断されることになる。なお、分包用紙Ｂの切断時はカムシャフト４１２の回転を戻すことなく、１回転させるのみでよい。

【００４２】

次に、ミシン刃４３２の形状と移動量とを図１３に示す。

ミシン刃４３２はシャフト４３４への固定部４３２ａ、刃の基部４３２ｂ、及び刃の基部４３２ｂから突出して設けられた刃先部４３２ｃとからなる。刃先部４３２ｃの先端に山形の刃先が形成された複数の刃片４３２ｄが、隣接する刃片４３２ｄとの間に所定の間隔を設けて形成されている。刃片４３２ｄと刃片４３２ｄとの間には３箇所に、刃先部の厚さｔよりも刃幅の広い横刃片が設けられているが、図１３（ａ）、（ｂ）では省略している。そして各刃片４３２ｄの先端までの長さは中央部の刃片が最も長く、端部に行くにつれて徐々に長さが短くなっている。各刃片４３２ｄの先端を結ぶ直線Ｌ１と基部の先端に平行な直線Ｌ２とのなす角度θは約４度の角度が設けられている。これにより、分包用紙Ｂにミシン目を形成する際は、カット部が中央の刃片４３２ｄから徐々に端部の刃片４３２ｄへと移るので、ミシン刃４３２の移動に要する駆動力も小さいもので済む。

【００４３】

また、ミシン刃４３２の長さ方向の端部、すなわち分包用紙Ｂの搬送方向に直交する方向の端部の刃片４３２ｅ、４３２ｅの刃幅は内側の刃片４３２ｄの刃幅よりも大きく形成されている。そして分包用紙Ｂの幅は図１３（ｂ）に記号Ｗと記載したように、分包用紙Ｂの端部が、ミシン刃４３２の端部の刃片４３２ｅ、４３２ｅの位置になるように構成されている。従って、分包用紙Ｂの搬送位置がずれても、分包用紙Ｂの端部に、服薬者が個包を切り離すときの切断開始部（カット）を確実に形成でき、服薬者が容易に分包を切り離すことができる。

【００４４】

図１３（ｂ）にミシン刃４３２によるミシン目形成と分包用紙Ｂの切断のときのミシン刃４３２の突出距離を示す。ミシン目形成時にはミシン刃４３２の刃先部４３２ｃの中間部であるＭの位置まで刃受け部４０４にミシン刃４３２が突出する。また、分包用紙Ｂの切断時は刃先部４３２ｃの位置を越えた刃の基部４３２ｂの位置Ｃまで刃受け部４０４にミシン刃４３２が突出する。このように構成することによって分包用紙Ｂの個包間へのミシン目の形成と、１処方間の分包用紙Ｂの切断とがミシン刃４３２の突出量を変えることによって達成することができるものである。

【００４５】

次に、ミシン刃４３２の刃片４３２ｄ間に横刃片を挿入することによる、十字カット刃について図１４及び図１５を参照して説明する。図１４（ａ）は斜視図、（ｂ）は左側面図、（ｃ）は正面図、（ｄ）は上面図をそれぞれ示している。

【００４６】

すなわち、ミシン刃４３２の、図１４で上から５枚目と６枚目の間、８枚目と９枚目の間、及び１１枚目と１２枚目の間の３箇所には、横刃４３２ｇが挿入されている。この横刃片４３２ｇは刃片４３２ｄの厚さｔよりも刃の幅が広く形成されており、各刃片４３２ｄの間に圧入されるとともに、横刃４３２ｆの基部側に設けられた溝部にミシン刃４３２の基部４３２ｂが圧入されることにより保持されている。このように構成されたミシン刃４３２とすることにより、ミシン目が形成されるとともに、分包用紙Ｂが各個包に分離されたときに各個包を開封するときの切断開始部（カット）を形成するものである。

【００４７】

横刃４３２ｇの挿入位置と枚数は上述の例に限定されるものではなく、刃片４３２ｄの間であればどの位置にも挿入できるものである。特に各個包に収納される散薬の量が少ないときは、各個方の下のほうの十字カット位置で開封したほうが飲み残しの量が少なくな

るので、それを考慮して挿入する位置、枚数を選択することができる。
【００４８】
図１５（ａ）にミシン刃４３２と分包用紙との関係を例示する。図１５（ａ）に示すように、分包用紙のシール部（斜線部）は、縦シール機構２０６によって、ミシン目形成部（非シール部）を例えば４ｍｍ残して形成され、ミシン目はこの非シール部に形成される。そして、例えば、分包用紙Ｂの幅、すなわち、搬送方向と直交する方向の幅が例えば７０ｍｍであると仮定すると、ミシン刃４３２の長さを分包用紙Ｂの幅よりも大きい７５ｍｍとする。これにより、分包用紙Ｂの端部はミシン刃４３２の端部の刃片４３２ｅに対向するようにでき、その結果、分包用紙Ｂの両端部に切断開始部（カット）Ｂ１を形成することができる。
【００４９】
また、図１５（ｂ）に示すように、横刃の刃幅をミシン刃４３２の厚さｔ＝１ｍｍよりも大きい４ｍｍ程度とすることにより、分包用紙Ｂの非シール部の幅４ｍｍに亘って十字カット部Ｂ２を形成することができ、個包の開封のときの切断開始部となる。よって、患者・利用者による開封が容易な分包薬剤を提供できるものである。
【００５０】
なお、図１６は製造された分包薬剤の断面図の例を示すもので、例えば、上端から２０ｍｍの位置から、９ｍｍ間隔で３個の十字カット部形成した例を示している。
【００５１】
なお、第１の実施形態では、分包用紙Ｂを水平方向に搬送し、搬送方向に沿って、縦シール部２０６、薬剤供給部である落下ホッパ３００、横シール部２０９、搬送ローラ２１１及びミシン目作成部４００を配置したが、分包用紙Ｂを搬送方向に向かって下方に傾斜した搬送路に沿って搬送するように構成すれば、縦シール部は薬剤供給部の下流側に設けることも可能である。
【００５２】
次に図１７及び図１８を用いて第２の実施形態の印刷包装機５００について説明する。図１７は平面図、図１８は、同じく正面図である。ベース板５１５にはＶ字折りされた分包用紙Ｂをロール状に巻回した分包用紙収納部５３３が設けられ、この分包用紙収納部５３３から１端を引出された分包用紙Ｂは、複数の支持ロール５３４，５３５を介して上方へ搬送され、ひねりローラ５３１によって搬送方向が変換され、搬送方向に沿って下方に４５度傾斜した搬送経路に搬送される。
【００５３】
ベース板５１５の上面には水平面に対して４５度の傾きを有する分包用紙Ｂの搬送ベース５１６が設けられ、この４５度平面に平行な中心線５１７に沿って立位の分包用紙Ｂの搬送経路にそって搬送される。この搬送経路の中央部には谷折りした分包用紙Ｂの上部開口側から下出口を侵入させた落下ホッパ５１８がほぼ垂直に設けられ、さらにその上部に薬剤供給ホッパ５１９が設けられる。薬剤供給ホッパ５１９の下部は開口していて、この開口を遮るシャッタ機構５２０は、一つの分包に入れるべき薬剤を一旦保持し、図示しないアクチュエータによって５２０ａのように開放することで、薬剤を下の落下ホッパ５１８を介して、谷折りした分包用紙Ｂの内部空間に薬剤を落下させて供給する。
【００５４】
この空間は左上の搬送上流に配置された紙押さえ板５２１と、下流側右下に配置された逆Ｌ字型ヒートシール部５２２によって左右を遮られている。紙押さえ板５２１は回動アクチュエータ５２３によって開閉動作し、分包用紙Ｂが搬送されているときは開き、停止している時は閉じるように制御される。ヒートシール部５２２は、面発熱体５２４をキャリッジ５２５ａに保持されている。キャリッジ５２５ａはガイドロッド５２６に軸支され、モータ５２７に直結された送りネジ５２８によって前進後退可能なごとくに構成される。キャリッジ５２５ａが前進すると、分包用紙Ｂの上端横方向と縦方向とが、受け板５２５ｂに圧接され、加熱によって、分包用紙Ｂはシールされるように構成される。
【００５５】

分包用紙Ｂが静止した状態で、キャリッジ５２５ａを所定時間前進させた状態で、かつ紙押さえ板５２１を閉じたタイミングで、シャッタ機構５２０を５２０ａのように開くと、薬剤が分包用紙Ｂ内に落下する。次に分包用紙Ｂを所定間隔Ｐ搬送して、再度キャリッジ５２５ａを前進させると、先ほど落下した薬剤の収納部分が一括してシールされる。この動作を繰り返すことで、分包用紙Ｂが連続的にシールされるが、この時、順次投入する薬剤の種類と量を処方箋に従って、服用順序に従って制御すれば、例えば２週間分の服用薬剤が、一回の服用分は一包毎に分割されて完成する。なお、ゴムローラ対５２９は分包用紙Ｂを挟持して搬送する手段であり、連続する分包用紙Ｂの複数箇所に設置することによって、用紙をたるみなく搬送できるようになっている。駆動ローラ対５２９はパルスモータ５３０によって、所定距離の搬送停止制御ができるようになっている。

【００５６】

下流側の駆動ローラ５２９の下流には第１の実施形態として説明したミシン目作成装置４００と同様のミシン目作成装置５４０が設けられている。

【００５７】

薬剤の分包を作成する動作は、搬送される分包用紙Ｂをヒートシール部５２２によって１包分を区分する縦シールを行う。なお、このとき前の個包に対して横シールも同時に成される。次に薬剤供給５１９から落下ホッパ５１８を介して１包分の薬剤を分包用紙Ｂ間に供給する。薬剤が供給された分包用紙Ｂは駆動ローラ５２９によって１個包分の長さ分搬送される。

【００５８】

次に２包目の薬剤が分包用紙Ｂ間に供給されて、さらに駆動ローラ５２９によって分包用紙Ｂが搬送される。この段階で最初の縦シール部がミシン目作成装置５４０の部分に来るので、ミシン目作成装置５４０によって縦シール部の中央部にミシン目が形成される。以下、この動作を繰返して１処方分の分包薬剤が完成したら、ミシン目作成装置５４０によって縦シール部をミシン目作成装置５４０によって切断することにより分包薬剤を製造するものである。

【００５９】

このように、ヒートシール部の位置は薬剤供給部の上流に限定されず、薬剤供給部の下流側であっても良いものである。

【００６０】

本発明のいくつかの実施形態、変形例を説明したが、これらの実施形態、変形例は、例として提示したものであり、発明の範囲を限定することは意図していない。これら新規な実施形態、変形例は、その他の様々な形態で実施されることが可能であり、発明の要旨を逸脱しない範囲で、種々の省略、置き換え、変更を行うことができる。これら実施形態やその変形は、発明の範囲や要旨に含まれるとともに、特許請求の範囲に記載された発明とその均等の範囲に含まれる。

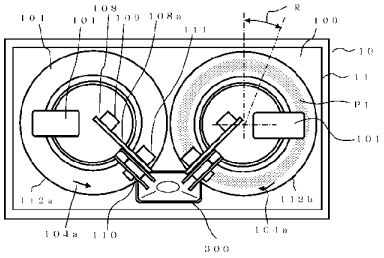
【符号の説明】

【００６１】

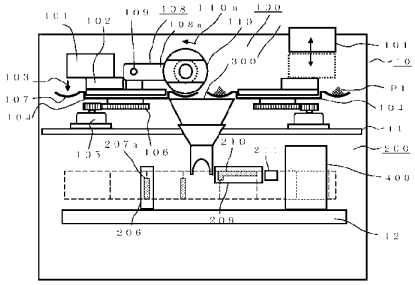
１００・・・円盤配分部（薬剤供給部）
２００・・・印刷包装機
２０１・・・分包用紙ロール（分包用紙収納部）
２０６・・・縦シール機構
２０９・・・横シール機構
２１１・・・駆動ローラ
３００・・・落下ホッパ（薬剤供給部）
４００・・・ミシン目作成装置
４０２・・・刃収納部
４０４・・・刃受け部
４１６，４１８・・・カム板
４２０・・・カム板

４３２・・・ミシン刃
４３２ｂ・・・ミシン刃の基部
４３２ｃ・・・ミシン刃の刃先
Ｂ・・・分包用紙
Ｂ２，Ｂ３・・・搬送経路（搬送路）

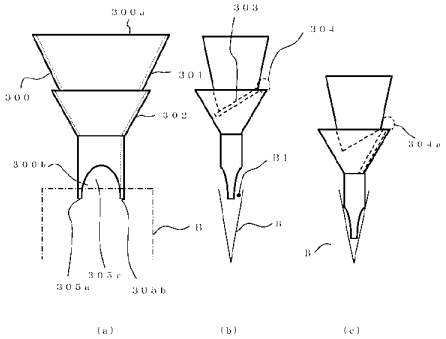
【図１】



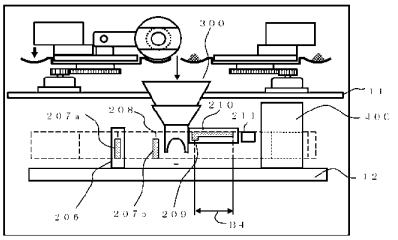
【図２】



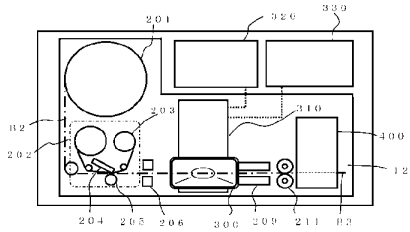
【図３】



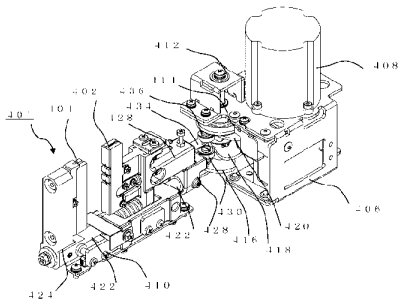
【図４】



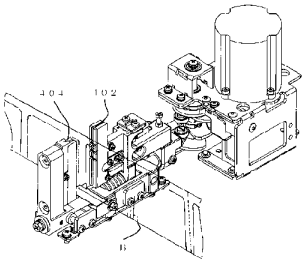
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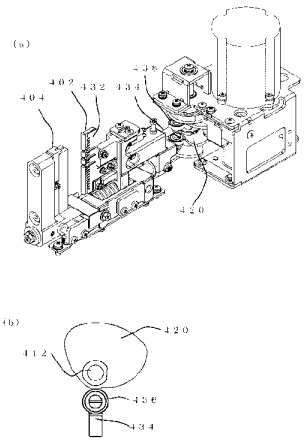
【図６】



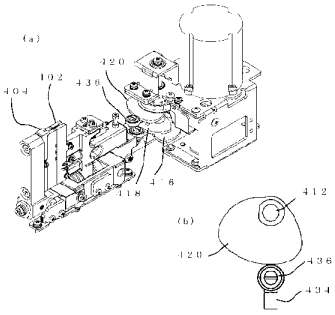
【図７】



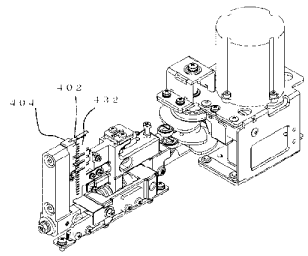
【図８】



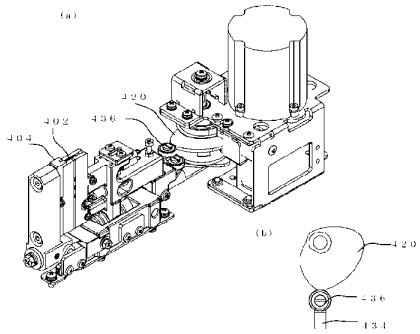
【図９】



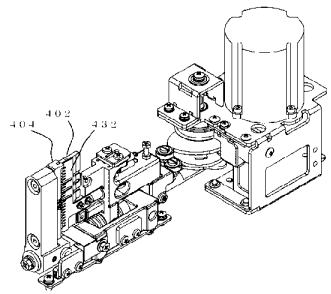
【図１０】



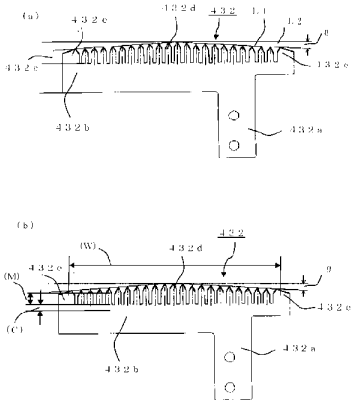
【図１１】



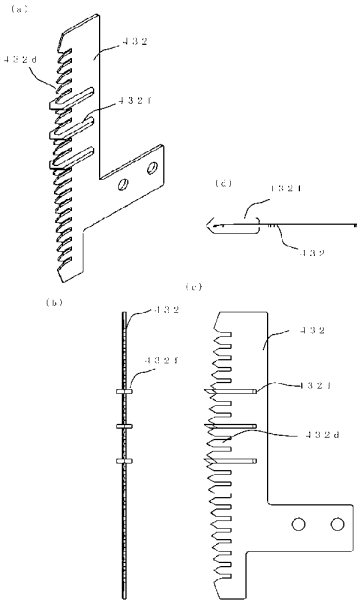
【図１２】



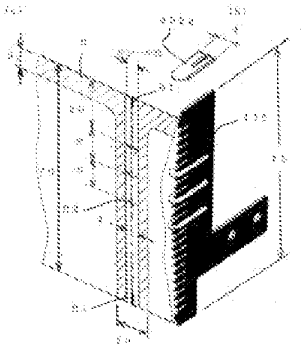
【図１３】



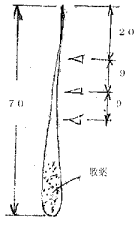
【図１４】



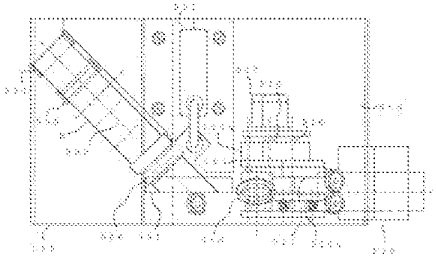
【図１５】



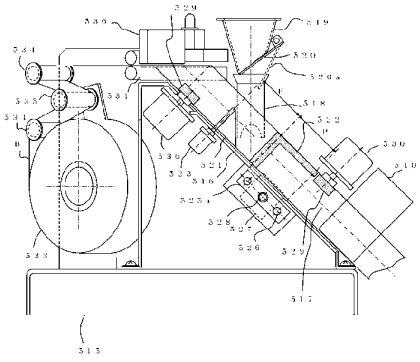
【図１６】



【図１７】



【図１８】



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(54) Title: FLUID DIVERSION MECHANISM FOR BODILY-FLUID SAMPLING

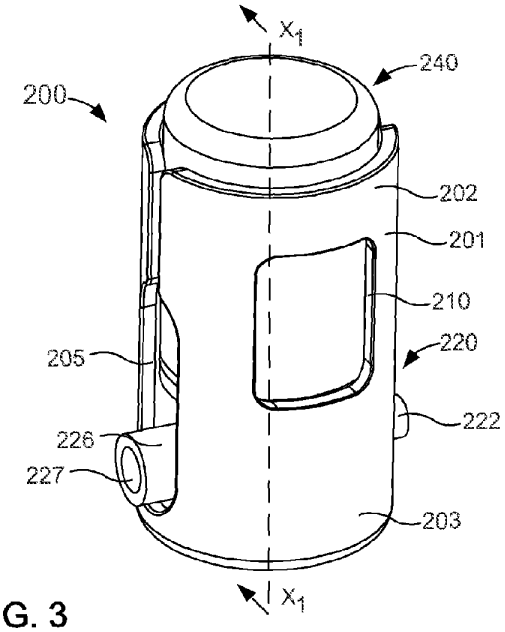


FIG. 3

(57) Abstract: An apparatus includes a housing, a fluid reservoir, a flow control mechanism, and an actuator. The housing defines an inner volume and has an inlet port that can be fluidically coupled to a patient and an outlet port. The fluid reservoir is disposed in the inner volume to receive and isolate a first volume of a bodily-fluid. The flow control mechanism is rotatable in the housing from a first configuration, in which a first lumen places the inlet port is in fluid communication with the fluid reservoir, and a second configuration, in which a second lumen places the inlet port in fluid communication with the outlet port. The actuator is configured to create a negative pressure in the fluid reservoir and is configured to rotate the flow control mechanism from the first configuration to the second configuration after the first volume of bodily-fluid is received in the fluid reservoir.

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FLUID DIVERSION MECHANISM FOR BODILY-FLUID SAMPLING

Cross-Reference to Related Applications

[1001] This application is a continuation-in-part of and claims priority to U.S. Patent Application No. 13/904,691, filed May 29, 2013, entitled "Fluid Diversion Mechanism For Bodily-Fluid Sampling," which claims priority to and the benefit of U.S. Provisional Application No. 61/652,887, filed May 30, 2012, entitled "Fluid Diversion Mechanism for Bodily-Fluid Sampling," both of which are hereby incorporated by reference in their entirety.

[1002] This application also claims priority to and the benefit of U.S. Provisional Application Serial No. 61/652,887, filed May 30, 2012, entitled, "Fluid Diversion Mechanism for Bodily-Fluid Sampling," the disclosure of which is hereby incorporated by reference in its entirety.

Background

[1003] The invention relates generally to the parenteral procurement of bodily-fluid samples, and more particularly to devices and methods for parenterally-procuring bodily-fluid samples with reduced contamination from microbes or other contaminants exterior to the bodily-fluid source, such as dermally-residing microbes.

[1004] Health care practitioners routinely perform various types of microbial tests on patients using parenterally-obtained bodily-fluids. Patient samples (e.g., bodily-fluids) are sometimes tested for the presence of one or more potentially undesirable microbes, such as bacteria, fungi, or yeast (e.g., Candida). Microbial testing may include incubating patient samples in one or more sterile vessels containing culture media that is conducive to microbial growth. Generally, when microbes tested for are present in the patient sample, the microbes flourish over time in the culture medium. After a pre-determined amount of time (e.g., a few hours to several days), the culture medium can be tested for the presence of the microbes. The presence of microbes in the culture medium suggests the presence of the same microbes in the patient sample which, in turn, suggests the presence of the same microbes in the bodily-fluid of the patient from which the sample was obtained. Accordingly, when microbes are determined to be present in the culture medium, the patient may be prescribed one or

more antibiotics or other treatments specifically designed to treat or otherwise remove the undesired microbes from the patient.

[1005] Patient samples, however, can sometimes become contaminated during procurement. One way in which contamination of a patient sample may occur is by the transfer of microbes from a bodily surface (e.g., dermally-residing microbes) dislodged during needle insertion into a patient and subsequently transferred to a culture medium with the patient sample. The bodily surface microbes may be dislodged either directly or via dislodged tissue fragments, hair follicles, sweat glands and other adnexal structures. The transferred microbes may thrive in the culture medium and eventually yield a positive microbial test result, thereby falsely indicating the presence of such microbes in vivo. Such inaccurate results are a concern when attempting to diagnose or treat a suspected illness or condition. For example, false positive results from microbial tests may result in the patient being unnecessarily subjected to one or more anti-microbial therapies, which may cause serious side effects to the patient including, for example, death, as well as produce an unnecessary burden and expense to the health care system.

[1006] As such, a need exists for improved bodily-fluid transfer devices and methods that reduce microbial contamination in bodily-fluid test samples.

Summary

[1007] Devices for parenterally-procuring bodily-fluid samples with reduced contamination from microbes exterior to the bodily-fluid source, such as dermally-residing microbes, are described herein. In some embodiments, a device for procuring bodily-fluid samples from a patient includes a housing, a fluid reservoir, a flow control mechanism, and an actuator. The housing includes a proximal end portion and a distal end portion and defines an inner volume therebetween. The housing has an inlet port that is configured to be fluidically coupled to a patient and an outlet port that is configured to be fluidically coupled to a sample reservoir. The fluid reservoir is disposed within the inner volume of the housing and is configured to receive and isolate a first volume of a bodily-fluid withdrawn from the patient. The flow control mechanism defines a first lumen and a second lumen and is disposed in the housing for rotational movement from a first configuration, in which the inlet port is placed in fluid communication with the fluid reservoir such that the bodily-fluid can

flow from the inlet port, through the first lumen, and to the fluid reservoir, to a second configuration, in which the inlet port is placed in fluid communication with the outlet port such that the bodily-fluid can flow from the inlet, through the second lumen and to the outlet port. The actuator is configured to create a negative pressure in the fluid reservoir when actuated by a user. The actuator is operably coupled to the flow control mechanism and is configured to rotate the flow control mechanism from the first configuration to the second configuration after the first volume of bodily-fluid is received in the fluid reservoir from the patient.

Brief Description of the Drawings

[1008] FIG. 1 is a schematic illustration of a bodily-fluid transfer device according to an embodiment.

[1009] FIG. 2 is a front view of a bodily-fluid transfer device according to an embodiment.

[1010] FIG. 3 is a perspective view of the bodily-fluid transfer device of FIG. 2.

[1011] FIG. 4 is an exploded view of the bodily-fluid transfer device of FIG. 2.

[1012] FIG. 5 is a perspective view of a housing included in the bodily-fluid transfer device illustrated in FIG. 2.

[1013] FIG. 6 is a cross-sectional view of the housing illustrated in FIG. 5 taken along the line X_2-X_2.

[1014] FIG. 7 is a perspective view of a diverter included in the bodily-fluid transfer device of FIG. 2.

[1015] FIG. 8 is a cross-sectional view of the diverter illustrated in FIG. 8 taken along the line X_3-X_3.

[1016] FIG. 9 is a perspective view of a flow control mechanism included in the bodily-fluid transfer device of FIG. 2.

[1017] FIG. 10 is an exploded view of an actuator mechanism included in the bodily-fluid transfer device of FIG. 2.

[1018] FIG. 11 is a cross-sectional view of the bodily-fluid transfer device of FIG. 2 taken along the line X_1-X_1, in a first configuration.

[1019] FIG. 12 is a cross-sectional view of the bodily-fluid transfer device of FIG. 2 taken along the line X_1-X_1, in a second configuration.

[1020] FIG. 13 is a front view of a bodily-fluid transfer device according to an embodiment.

[1021] FIG. 14 is a perspective view of the bodily-fluid transfer device of FIG. 13.

[1022] FIG. 15 is an exploded view of the bodily-fluid transfer device of FIG. 13.

[1023] FIG. 16 is a cross-sectional view of a housing included in the bodily-fluid transfer device of FIG. 13 taken along the line X_5-X_5 in FIG. 14.

[1024] FIG. 17 is a cross-sectional view of the bodily-fluid transfer device taken along the line X_4-X_4 in FIG. 14, in a first configuration.

[1025] FIG. 18 is a perspective view of the bodily-fluid transfer device of FIG. 13, in a second configuration.

[1026] FIG. 19 is a cross-sectional view of the bodily-fluid transfer device of FIG. 18 taken along the line X_6-X_6.

[1027] FIG. 20 is a front view of a bodily-fluid transfer device according to an embodiment.

[1028] FIG. 21 is a perspective view of the bodily-fluid transfer device of FIG. 20.

[1029] FIG. 22 is an exploded view of the bodily-fluid transfer device of FIG. 20.

[1030] FIG. 23 is a cross-sectional view of a housing included in the bodily-fluid transfer device of FIG. 20 taken along the line X_8-X_8 in FIG. 21.

[1031] FIG. 24 is a perspective view of a first control member and a second control member included in a flow control mechanism of the bodily-fluid transfer device of FIG. 20.

[1032] FIG. 25 is a cross-sectional view of the bodily-fluid transfer device of FIG. 20 taken along the line X_7-X_7 in FIG. 21, in a first configuration.

[1033] FIG. 26 is a perspective view of the bodily-fluid transfer device of FIG. 20, in a second configuration.

[1034] FIG. 27 is a cross-sectional view of the bodily-fluid transfer device of FIG. 25 taken along the line X_9-X_9.

[1035] FIGS. 28 and 29 schematic illustrations of a bodily-fluid transfer device according to an embodiment, in a first and second configuration, respectively.

[1036] FIG. 30 is a perspective view of a bodily-fluid transfer device according to an embodiment.

[1037] FIG. 31 is an exploded perspective view of the bodily-fluid transfer device of FIG. 30.

[1038] FIG. 32 is a perspective view of a housing included in the bodily-fluid transfer device of FIG. 30.

[1039] FIG. 33 is a cross-sectional view of the housing illustrated in FIG. 32 taken along the line X_{11}-X_{11}.

[1040] FIG. 34 is a perspective view of a diverter included in the bodily-fluid transfer device of FIG. 30.

[1041] FIG. 35 is a cross-sectional view of the diverter illustrated in FIG. 34 taken along the line X_{12}-X_{12}.

[1042] FIG. 36 is a perspective view of a portion of a flow control mechanism included in the bodily-fluid transfer device of FIG. 30.

[1043] FIG. 37 is a cross-sectional view of the portion of the flow control mechanism illustrated in FIG. 36 taken along the line X_{13}-X_{13}.

[1044] FIGS. 38-41 are cross-sectional views of the bodily-fluid transfer device of FIG. 32 taken along the line X_{10}-X_{10}, in a first, second, third, and fourth configuration, respectively.

[1045] FIG. 42 is a perspective view of a bodily-fluid transfer device according to an embodiment.

[1046] FIG. 43 is an exploded perspective view of the bodily-fluid transfer device of FIG. 42.

[1047] FIG. 44 is a perspective exploded view of a flow control mechanism included in the bodily-fluid transfer device of FIG. 42.

[1048] FIGS. 45 and 46 are cross-sectional views of the bodily-fluid transfer device of FIG. 42 taken along the line X_{14}-X_{14}, in a first configuration and a second configuration, respectively.

[1049] FIG. 47 is a flowchart illustrating a method for parenterally procuring a bodily-fluid sample that is substantially free from microbes.

Detailed Description

[1050] Devices for parenterally procuring bodily-fluid samples with reduced contamination from microbes exterior to the bodily-fluid source, such as dermally-residing microbes, are described herein. In some embodiments, a device for procuring bodily-fluid samples from a patient includes a housing, a fluid reservoir, a flow control mechanism, and an actuator. The housing includes a proximal end portion and a distal end portion and defines an inner volume therebetween. The housing has an inlet port that is configured to be fluidically coupled to a patient and an outlet port that is configured to be fluidically coupled to a sample reservoir. The fluid reservoir is disposed within the inner volume of the housing and is configured to receive and isolate a first volume of a bodily-fluid withdrawn from the patient. The flow control mechanism defines a first lumen and a second lumen and is disposed in the housing for rotational movement from a first configuration, in which the inlet port is placed in fluid communication with the fluid reservoir such that the bodily-fluid can flow from the inlet port, through the first lumen, and to the fluid reservoir, to a second configuration, in which the inlet port is placed in fluid communication with the outlet port

such that the bodily-fluid can flow from the inlet, through the second lumen and to the outlet port. The actuator is configured to create a negative pressure in the fluid reservoir when actuated by a user. The actuator is operably coupled to the flow control mechanism and is configured to rotate the flow control mechanism from the first configuration to the second configuration after the first volume of bodily-fluid is received in the fluid reservoir from the patient.

[1051] In some embodiments, a device for procuring bodily-fluid samples from a patient includes a housing, an actuator, a diverter, and a flow control mechanism. The housing has a proximal end portion and a distal end portion and defines an inner volume therebetween. The actuator is movably disposed in the housing. The actuator includes a sealing member and a fluid reservoir defined, at least in part, by the sealing member. The actuator is configured to create a negative pressure in the fluid reservoir when actuated by a user. The diverter is disposed in the housing and has an inlet port that is configured to be fluidically coupled to the patient, a first outlet port that is configured to be fluidically coupled to the fluid reservoir, and a second outlet port that is configured to be fluidically coupled to a sample reservoir. The flow control mechanism defines a first lumen and a second lumen. The flow control mechanism is disposed in the diverter and is rotatable from a first configuration, in which the inlet port is placed in fluid communication with the first outlet port such that bodily-fluid can flow from the inlet port, through the first lumen and to the first outlet port, to a second configuration, in which the inlet port is placed in fluid communication with the second outlet port such that the bodily-fluid can flow from the inlet, through the second lumen and to the second outlet port.

[1052] In some embodiments, a device for procuring bodily-fluid samples from a patient includes a housing, a flow control mechanism, and an actuator. The housing has a proximal end portion and a distal end portion and defines an inner volume therebetween. The housing has an inlet port configured to be fluidically coupled to the patient and an outlet port configured to be fluidically coupled to a sample reservoir. The flow control mechanism defines a first lumen and a second lumen. The flow control mechanism is disposed in the housing and is rotatable between a first configuration, in which the inlet port is placed in fluid communication with a fluid reservoir defined, at least in part, by the housing such that bodily-fluid can flow from the inlet port, through the first lumen and to the fluid reservoir, to a second configuration, in which the inlet port is placed in fluid communication with the

outlet port such that the bodily-fluid can flow from the inlet, through the second lumen and to the outlet port. The actuator is movably disposed in the housing and is operably coupled to the flow control mechanism. The actuator is configured to create a negative pressure in the fluid reservoir when actuated by the user. The actuator is further configured to rotate the flow control mechanism from the first configuration to the second configuration after a first volume of bodily-fluid is received in the fluid reservoir from the patient.

[1053] In some embodiments, a device for procuring bodily-fluid samples from a patient includes a housing, a seal member, a fluid reservoir, a flow control mechanism, and an actuator. The housing has a proximal end portion and a distal end portion and defines an inner volume therebetween. The housing has an inlet port configured to be fluidically coupled to the patient. The seal member is movably disposed in the inner volume and is configured to define, at least partially, the fluid reservoir disposed in the inner volume. The fluid reservoir is configured to receive and isolate a first volume of bodily-fluid withdrawn from the patient. The flow control mechanism is movably disposed in the housing and is configured to move between a first configuration, in which the bodily-fluid can flow from the inlet port, through the flow control mechanism and to the fluid reservoir, to a second configuration, in which the fluid reservoir is fluidically isolated from the inlet port. The actuator is operably coupled to the seal member and the flow control mechanism. The actuator includes a spring configured to move the seal member from a first position to a second position to create a negative pressure in the fluid reservoir. The actuator is configured to move the flow control mechanism from the first configuration to the second configuration after a first volume of bodily-fluid is received in the fluid reservoir from the patient.

[1054] In some embodiments, a device for procuring bodily-fluid samples from a patient includes a housing, a flow control mechanism, and an actuator. The housing has a proximal end portion and a distal end portion and defines an inner volume therebetween. The housing has an inlet port configured to be fluidically coupled to the patient and an outlet port configured to be fluidically coupled to a sample reservoir. The flow control mechanism is disposed in the housing and includes a first control member and a second control member. The second control member defines a first lumen and a second lumen and is rotatably movable between a first configuration, in which the inlet port is placed in fluid communication with a fluid reservoir defined, at least in part, by the housing such that bodily-fluid can flow from the inlet port, through the first lumen and to the fluid reservoir, to

a second configuration, in which the inlet port is placed in fluid communication with the outlet port such that the bodily-fluid can flow from the inlet, through the second lumen and to the outlet port. The actuator is movably disposed in the housing and is operably coupled to the flow control mechanism. The actuator is configured to create a negative pressure in the fluid reservoir when actuated by the user. The actuator is further configured to rotate the second control member from the first configuration to the second configuration after a first volume of bodily-fluid is received in the fluid reservoir from the patient.

[1055] In some embodiments, a device for procuring bodily-fluid samples from a patient includes a diverter, a flow control mechanism, and an actuator mechanism. The diverter defines an inlet port, a first outlet port, and a second outlet port. The first outlet port is fluidically coupled to a first fluid reservoir and the second outlet port is fluidically coupled to a second reservoir, fluidically isolated from the first fluid reservoir. The flow control mechanism is configured to be disposed, at least partially within the diverter. The actuator mechanism is configured to engage the flow control mechanism to move the flow control mechanism between a first configuration, in which a flow of bodily-fluid can enter the first fluid reservoir, and a second configuration, in which a flow of bodily-fluid can enter the second fluid reservoir.

[1056] In some embodiments, a bodily-fluid transfer device can be configured to selectively divert a first, predetermined amount of a flow of a bodily-fluid to a first reservoir before permitting the flow of a second amount of the bodily-fluid into a second reservoir. In this manner, the second amount of bodily-fluid can be used for diagnostic or other testing, while the first amount of bodily-fluid, which may contain microbes from a bodily surface, is isolated from the bodily-fluid to be tested. The first amount of bodily-fluid can be subsequently used for different types of testing (e.g., CBC, other blood chemistry tests) or can be simply sequestered.

[1057] In some embodiments, a bodily-fluid transfer device is configured to automatically move from a first configuration to a second configuration, for example, without requiring an input or other action by a health care practitioner. In some embodiments, the bodily-fluid transfer device prevents bodily-fluid from flowing or otherwise being introduced into a second reservoir before at least a first amount of bodily-fluid (e.g., a predetermined amount) is first introduced into a first reservoir.

[1058] In some embodiments, a method for procuring a bodily-fluid sample using a parenteral sampling device that has a needle with a lumen and a fluid reservoir fluidically coupled to the needle includes inserting the needle of the device into a patient. The method includes establishing fluid communication between the needle and the fluid reservoir. An actuator is moved a first distance to create a negative pressure in the fluid reservoir to withdraw a predetermined volume of the bodily-fluid. The actuator is moved a second distance to engage a flow control mechanism and rotate the flow control mechanism from a first configuration to a second configuration. The first configuration is operable in allowing bodily-fluid to flow through a first flow path from the needle to the fluid reservoir and the second configuration is operable in allowing bodily-fluid to flow through a second flow path from the needle to a sample reservoir.

[1059] As used in this specification, "bodily-fluid" can include any fluid obtained from a body of a patient, including, but not limited to, blood, cerebrospinal fluid, urine, bile, lymph, saliva, synovial fluid, serous fluid, pleural fluid, amniotic fluid, and the like, or any combination thereof.

[1060] As used herein, the term "set" can refer to multiple features or a singular feature with multiple parts. For example, when referring to set of walls, the set of walls can be considered as one wall with distinct portions, or the set of walls can be considered as multiple walls. Similarly stated, a monolithically constructed item can include a set of walls. Such a set of walls can include, for example, multiple portions that are in discontinuous from each other. A set of walls can also be fabricated from multiple items that are produced separately and are later joined together (e.g., via a weld, an adhesive or any suitable method).

[1061] As used herein, the words "proximal" and "distal" refer to the direction closer to and away from, respectively, a user who would place the device into contact with a patient. Thus, for example, the end of a device first touching the body of the patient would be the distal end, while the opposite end of the device (e.g., the end of the device being manipulated by the user) would be the proximal end of the device.

[1062] As used herein, the singular forms "a," "an" and "the" include plural referents unless the context clearly dictates otherwise. Thus, for example, the term "an engagement surface" is intended to mean a single surface or multiple surfaces unless explicitly expressed otherwise.

[1063] FIG. 1 is a schematic illustration of a portion of a bodily-fluid transfer device 100, according to an embodiment. Generally, the bodily-fluid transfer device 100 (also referred to herein as "fluid transfer device" or "transfer device") is configured to permit the withdrawal of bodily-fluid from a patient such that a first portion or amount of the withdrawn fluid is diverted away from a second portion or amount of the withdrawn fluid that is to be used as a biological sample, such as for testing for the purpose of medical diagnosis and/or treatment. In other words, the transfer device 100 is configured to transfer a first, predetermined amount of a bodily-fluid to a first collection reservoir and a second amount of bodily-fluid to one or more bodily-fluid collection reservoirs fluidically isolated from the first collection reservoir, as described in more detail herein.

[1064] The transfer device 100 includes a diverter 120, a first reservoir 170, and a second reservoir 180, different from the first reservoir 170. The diverter 120 includes an inlet port 122 and two or more outlet ports, such as a first outlet port 124 and a second outlet port 126 shown in FIG. 1. The inlet port 122 is configured to be fluidically coupled to a medical device defining a pathway **P** for withdrawing and/or conveying the bodily-fluid from the patient to the transfer device 100. For example, the inlet port 122 can be fluidically coupled to a needle or other lumen-containing device (e.g., flexible sterile tubing). In this manner, the diverter 120 can receive the bodily-fluid from the patient via the needle or other lumen-containing device.

[1065] The first outlet port 124 of the diverter 120 is configured to be fluidically coupled to the first reservoir 170. In some embodiments, the first reservoir 170 is monolithically formed with the first outlet port 124 and/or a portion of the diverter 120. In other embodiments, the first reservoir 170 can be mechanically and fluidically coupled to the diverter 120 via an adhesive, a resistance fit, a mechanical fastener, any number of mating recesses, a threaded coupling, and/or any other suitable coupling or combination thereof. Similarly stated, the first reservoir 170 can be physically (e.g., mechanically) coupled to the diverter 120 such that an interior volume defined by the first reservoir 170 is in fluid communication with the first outlet port 120 of the diverter 120. In still other embodiments, the first reservoir 170 can be operably coupled to the first outlet port 124 of the diverter 120 via an intervening structure (not shown in FIG. 1), such as a flexible sterile tubing. More particularly, the intervening structure can define a lumen configured to place the first reservoir 170 in fluid communication with the first outlet port 124.

[1066] The first reservoir 170 is configured to receive and contain the first, predetermined amount of the bodily-fluid. In some embodiments, the first reservoir 170 is configured to contain the first amount of the bodily-fluid such that the first amount is fluidically isolated from a second amount of the bodily-fluid (different from the first amount of bodily-fluid) that is subsequently withdrawn from the patient. The first reservoir 170 can be any suitable reservoir for containing a bodily-fluid, such as a pre-sample reservoir described in detail in U.S. Patent No. 8,197,420 ("the '420 Patent"), the disclosure of which is incorporated herein by reference in its entirety. As used in this specification, the terms "first, predetermined amount" and "first amount" describe an amount of bodily-fluid configured to be received or contained by the first reservoir 170. Furthermore, while the term "first amount" does not explicitly describe a predetermined amount, it should be understood that the first amount is the first, predetermined amount unless explicitly described differently.

[1067] The second outlet port 126 of the diverter 120 is configured to be fluidically coupled to the second reservoir 180. In some embodiments, the second reservoir 180 is monolithically formed with the second outlet port 126 and/or a portion of the diverter 120. In other embodiments, the second reservoir 180 can be mechanically coupled to the second outlet port 126 of the diverter 120 or operably coupled to the second outlet port 126 via an intervening structure (not shown in FIG. 1), such as described above with reference to the first reservoir 170. The second reservoir 180 is configured to receive and contain the second amount of the bodily-fluid. For example, the second amount of bodily-fluid can be an amount withdrawn from the patient subsequent to withdrawal of the first amount. In some embodiments, the second reservoir 180 is configured to contain the second amount of the bodily-fluid such that the second amount is fluidically isolated from the first amount of the bodily-fluid.

[1068] The second reservoir 170 can be any suitable reservoir for containing a bodily-fluid, including, for example, a sample reservoir as described in the '420 Patent incorporated by reference above. As used in this specification, the term "second amount" describes an amount of bodily-fluid configured to be received or contained by the second reservoir 180. In some embodiments, the second amount can be any suitable amount of bodily-fluid and need not be predetermined. In other embodiments, the second amount received and contained by the second reservoir 180 is a second predetermined amount.

[1069] In some embodiments, the first reservoir 170 and the second reservoir 180 can be coupled to (or formed with) the diverter 120 in a similar manner. In other embodiments, the first reservoir 170 and the second reservoir need not be similarly coupled to the diverter 120. For example, in some embodiments, the first reservoir 170 can be monolithically formed with the diverter 120 (e.g., the first outlet port 124) and the second reservoir 180 can be operably coupled to the diverter 120 (e.g., the second outlet port 126) via an intervening structure, such as a flexible sterile tubing.

[1070] As shown in FIG. 1, the transfer device 100 further includes an actuator 140 and a flow control mechanism 130 defining a first channel 138 and a second channel 139. In some embodiments, the actuator 140 can be included in or otherwise operably coupled to the diverter 120. In this manner, the actuator 140 can be configured to control a movement of the flow control mechanism 130 (e.g., between a first configuration and a second configuration). For example, the actuator 140 can be movable between a first position corresponding to the first configuration of the flow control mechanism 130, and a second position, different from the first position, corresponding to the second configuration of the flow control mechanism 130. In some embodiments, the actuator 140 is configured for uni-directional movement. For example, the actuator 140 can be moved from its first position to its second position, but cannot be moved from its second position to its first position. In this manner, the flow control mechanism 130 is prevented from being moved to its second configuration before its first configuration, thus requiring that the first amount of the bodily-fluid be directed to the first reservoir 170 and not the second reservoir 180.

[1071] The flow control mechanism 130 is configured such that when in the first configuration, the first channel 138 fluidically couples the inlet port 122 to the first outlet port 124 and when in the second configuration, the second channel 139 fluidically couples the inlet portion 122 to the second outlet port 126. In some embodiments, the actuator 140 is coupled to the flow control mechanism 130 and is configured to move the flow control mechanism 130 in a translational motion between the first configuration and the second configuration. For example, in some embodiments, the flow control mechanism 130 can be in the first configuration when the flow control mechanism 130 is in a distal position relative to the transfer device 100. In such embodiments, the actuator 140 can be actuated to move the flow control device 130 in the proximal direction to a proximal position relative to the transfer device 100, thereby placing the flow control mechanism 130 in the second

configuration. In other embodiments, the actuator 140 can be actuated to move the flow control mechanism 130 in a rotational motion between the first configuration and the second configuration.

[1072] Accordingly, when the flow control mechanism 130 is in the first configuration, the second outlet port 126 is fluidically isolated from the inlet port 122. Similarly, when the flow control mechanism 130 is in the second configuration, the first outlet port 124 is fluidically isolated from the inlet port 122. In this manner, the flow control mechanism 130 can direct, or divert the first amount of the bodily-fluid to the first reservoir 170 via the first outlet port 124 when the flow control mechanism 130 is in the first configuration and can direct, or divert the second amount of the bodily-fluid to the second reservoir 180 via the second outlet port 126 when the flow control mechanism 130 is in the second configuration.

[1073] In some embodiments, at least a portion of the actuator 140 can be operably coupled to the first reservoir 170. In this manner, the actuator 140 (or at least the portion of the actuator 140) can be configured to cause a vacuum within the first reservoir 170, thereby initiating flow of the bodily-fluid through the transfer device 100 and into the first reservoir 170 when the diverter 120 is in its first configuration. The actuator 140 can include any suitable mechanism for actuating the transfer device 100 (e.g., at least the flow control mechanism 130), such as, for example, a rotating disc, a plunger, a slide, a dial, a button, and/or any other suitable mechanism or combination thereof. Examples of suitable actuators are described in more detail herein with reference to specific embodiments.

[1074] In some embodiments, the diverter 120 is configured such that the first amount of bodily-fluid need be conveyed to the first reservoir 170 before the diverter 120 will permit the flow of the second amount of bodily-fluid to be conveyed through the diverter 120 to the second reservoir 180. In this manner, the diverter 120 can be characterized as requiring compliance by a health care practitioner regarding the collection of the first, predetermined amount (e.g., a pre-sample) prior to a collection of the second amount (e.g., a sample) of bodily-fluid. Similarly stated, the diverter 120 can be configured to prevent a health care practitioner from collecting the second amount, or the sample, of bodily-fluid into the second reservoir 180 without first diverting the first amount, or pre-sample, of bodily-fluid to the first reservoir 170. In this manner, the health care practitioner is prevented from including (whether intentionally or unintentionally) the first amount of bodily-fluid, which is more likely to contain bodily surface microbes and/or other undesirable external contaminants that

are not representative of the in vivo conditions of a patient's bodily-fluid system, in the bodily-fluid sample to be used for analysis. The forced-compliance aspect of the diverter 120 is described in more detail herein with reference to specific embodiments.

[1075] In some embodiments, the diverter 120 is configured to automatically (i.e., without requiring an input or other action by a health care practitioner or other operator of the transfer device 100) fluidically isolate the inlet port 122 from the first outlet port 124. For example, the diverter 120 can be configured such that the flow control mechanism 130 will automatically fluidically isolate the first outlet port 124 from the inlet port 122 when the first reservoir 170 has received the first, predetermined amount of bodily-fluid. As such, additional flow of bodily-fluid in excess of the first amount into the first reservoir 170 is prevented. In some embodiments, the diverter 120 is configured such that the flow control mechanism 130 automatically moves from its first configuration to its second configuration after the first amount of bodily-fluid is conveyed to the first reservoir 170.

[1076] In some embodiments, the actuator 140 can have a third position, different from the first and second positions, which corresponds to a third configuration of the flow control mechanism 130. When in the third configuration, the flow control mechanism 130 can fluidically isolate the inlet port 122 from both the first outlet port 124 and the second outlet port 126 simultaneously. Therefore, when the flow control mechanism 130 is in its third configuration, flow of bodily-fluid from the inlet port 122 to either the first reservoir 170 or the second reservoir 180 is prevented. In use, for example, the actuator 140 can be actuated to place the flow control mechanism 130 in the first configuration such that a bodily-fluid can flow from the inlet port 122 to the first reservoir 170, then moved to the second configuration such that the bodily-fluid can flow from the inlet port 122 to the second reservoir 180, then moved to the third configuration to stop the flow of bodily-fluid into and/or through the diverter 120. In some embodiments, the flow control mechanism 130 can be moved to the third configuration between the first configuration and the second configuration. In some embodiments, the flow control mechanism 130 can be in the third configuration before being moved to either of the first configuration or the second configuration.

[1077] In some embodiments, one or more portions of the transfer device 100 are disposed within a housing (not shown in FIG. 1). For example, in some embodiments, at least a portion of one or more of the diverter 120, the first reservoir 170, and the actuator 140 can be disposed within the housing. In such an embodiment, at least a portion of the actuator

140 is accessible through the housing. Examples of suitable housings are described in more detail herein with reference to specific embodiments.

[1078] Referring now to FIGS. 2-12, a transfer device 200 includes a housing 201, a diverter 220, a flow control mechanism 230, and an actuator 240. The transfer device 200 can be any suitable shape, size, or configuration. For example, while shown in FIGS. 2 and 3 as being substantially cylindrical, the transfer device 200 can be square, rectangular, polygonal, and/or any other non-cylindrical shape.

[1079] The housing 201 includes a proximal end portion 202 and a distal end portion 203. The distal end portion 203 includes a base 206 from which a set of walls 204 extend. More specifically, the walls 204 of the housing 201 define a substantially annular shape and define an inner volume 211 therebetween. The proximal end portion 202 of the housing 201 is configured to be open such that the inner volume 211 can receive at least a portion of the diverter 220, a portion of the flow control mechanism 230, and a portion of the actuator 240 (FIG. 4). Similarly stated, the housing 201 is configured to house at least the portion of the diverter 220, the portion of the flow control mechanism 230, and the portion of the actuator 240

[1080] The walls 204 of the housing 201 define a set of status windows 210 and a set of channels 205. The status windows 210 can be any suitable shape or size and are configured to allow a user to visually inspect at least a portion of the transfer device 200. While shown in FIG. 5 as including two status windows 210, in other embodiments, the housing 201 can define any number of status windows 210, such as, for example, one, three, four, or more. The channels 205 defined by the housing 201 are configured to extend from the distal end portion 203 and through the proximal end portion 202. Similarly stated, the channels 205 extend through a proximal surface of the housing 201. Said yet another way, the channels 205 are open ended at the proximal end portion 202 of the housing 201.

[1081] The housing 201 further includes a set of guide posts 207 and a set of flow control protrusions 208. While shown in FIGS. 5 and 6 as cylindrical protrusions, the guide posts 207 can be any suitable shape or size and are configured to extend from the base 206 in the proximal direction. In this manner, the guide posts 207 are configured to engage a portion of the diverter 220 and a portion of the actuator 240, as further described herein. The flow control protrusions 208 extend from the base 206 in the proximal direction and define notches

209. In this manner, the flow control protrusions 208 are configured to selectively engage the flow control mechanism 230 to move the flow control mechanism 230 between a first configuration and a second configuration, as described in further detail herein. While only one flow control protrusion 208 is shown in FIGS. 5 and 6, the housing 201 is configured to include two flow control protrusions 208. In other embodiments, the housing 201 can include any number flow control protrusions 208 such as for example, one, three, four, or more.

[1082] As shown in FIGS. 7 and 8, the diverter 220 includes a proximal end portion 228 and a distal end portion 229 and defines an inner volume 221. The inner volume 221 is configured to receive at least a portion of the flow control mechanism 230, as further described herein. The proximal end portion 228 of the diverter 220 includes a first outlet port 224 and can engage a portion of the actuator 240. The distal end portion 229 includes an inlet port 222 and a second outlet port 226. As shown in FIGS. 1 and 2, the diverter 220 is disposed within the inner volume 211 of the housing 201 such that a portion of the inlet port 222 extends through a first channel 205 defined by the walls 204 of the housing 201 and a portion of the second outlet port 226 extends through a second channel 205 opposite the first channel. While not explicitly shown in FIGS. 2-12, the distal end portion 229 of the diverter 220 is configured to engage the guide posts 207 such that lateral movement of the diverter 220 is limited. Similarly stated, the distal end portion 229 of the diverter 220 can engage the guide posts 207 of the housing 201 such that the diverter 220 is substantially limited to movement in the proximal or distal direction, relative to the housing 201, as further described herein.

[1083] The inlet port 222 included in the distal end portion 229 of the diverter 220 defines an inlet lumen 223. As shown in FIG. 8, the inlet lumen 223 is configured to be in fluid communication with the inner volume 221. Similarly stated, the inlet lumen 223 of the inlet port 222 extends through a wall defining the inner volume 221 of the diverter 220. The inlet port 222 is further configured to be fluidically coupled to a medical device (not shown) defining a fluid flow pathway for withdrawing and/or conveying the bodily-fluid from a patient to the transfer device 200. For example, the inlet port 222 can be fluidically coupled to a needle or other lumen-containing device (e.g., flexible sterile tubing). Similarly stated, the inlet lumen 223 defined by the inlet port 222 is placed in fluid communication with a lumen defined by a lumen-containing device, when the lumen-containing device is coupled to the inlet port 222. Expanding further, when the lumen-containing device is disposed within a

portion of a body of the patient (e.g., within a vein of the patient), the inner volume 221 of the diverter 220 is placed in fluid communication with the portion of the body of the patient.

[1084] The first outlet port 224 included in the proximal end portion 228 of the diverter 220 defines a first outlet lumen 225. As shown in FIG. 8, the first outlet lumen 225 is configured to be in fluid communication with the inner volume 221 of the diverter 220 (e.g., the first outlet lumen 225 extends through the wall defining the inner volume 221). Similarly, the second outlet port 226 included in the distal end portion 229 of the diverter 220 defines a second outlet lumen 227 in fluid communication with the inner volume 221.

[1085] As shown in FIG. 9, the flow control mechanism 230 includes a first control member 231 and a second control member 235. At least a portion of the flow control mechanism 230 is configured to be disposed within the inner volume 221 defined by the diverter 220. In this manner, the flow control mechanism 230 defines a circular cross-sectional shape such that when the flow control mechanism 230 is disposed within the inner volume 221, a portion of the flow control mechanism 230 forms a friction fit with the walls of the diverter 220 defining the inner volume 221, as described in further detail herein.

[1086] The first control member 231 includes a set of activation protrusions 232 and a set of cross members 234 (only one of each is shown in FIG. 9). The activation protrusions 232 are configured to engage the flow control protrusion 208 of the housing 201. More specifically, the activation protrusions 232 can be disposed within the notch 209 defined by the flow control protrusion 208. Therefore, in use, the flow control protrusions 208 can engage the activation protrusions 232 to move the flow control mechanism 230 between a first configuration and a second configuration.

[1087] The second control member 235 defines a first lumen 238, a second lumen 239, and a set of channels 237 and is configured to be disposed, at least partially, within the first control member 231. More particularly, the first control member 231 has a first diameter D_1 and the second control member 235 has a second diameter D_2 larger than the first diameter D_1. Therefore, when the second control member 235 is disposed within the first control member 231 a portion of the second control member 235 extends beyond a surface of the first control member 231 that defines the first diameter D_1.

[1088] The channels 237 defined by the second control member 235 receive the cross members 234 of the first control member 231. The arrangement of the cross members 234

disposed within the channels 237 is such that the second control member 235 is maintained in a desired position relative to the first control member 231. In this manner, the second control member 235 is configured to move concurrently with the first control member 231 when the flow control protrusions 208 engage the activation protrusions 232 of the first control member 231. Similarly stated, the flow control mechanism 230 is moved between the first configuration and the second configuration when the first control member 231 and the second control member 235 are moved between the first configuration and the second configuration, respectively. Furthermore, when the flow control mechanism 230 is in the first configuration, the first lumen 238 is placed in fluid communication with the inlet lumen 223 defined by the inlet port 222 and the first outlet lumen 225 defined by the first outlet port 224. When the flow control mechanism 230 is in the second configuration, the second lumen 239 is placed in fluid communication with the inlet lumen 223 defined by the inlet port 222 and the second outlet lumen 227 defined by the second outlet port 226, as described in further detail herein.

[1089] As shown in FIG. 10, the actuator mechanism 240 includes an actuator housing 262, a plunger 248, a cap 255, and a spring 261. The actuator mechanism 240 is configured to move between a first configuration and a second configuration, thereby moving the transfer device 200 between a first configuration and a second configuration, as described in further detail herein. The actuator housing 262 includes a proximal end portion 263 and a distal end portion 264 and defines an inner volume 265. The actuator housing 262 can be any suitable shape, size or configuration. For example, the actuator housing 262 can be substantially cylindrical and be configured to be disposed, at least partially, within the housing 201. The inner volume 265 is configured to receive the plunger 248, the spring 261, and at least a portion of the cap 255. The plunger 248 includes a proximal end portion 249 and a distal end portion 249 and a side wall 251. The distal end portion 250 is configured to receive the guide posts 207 of the housing 201, as described in further detail herein. The proximal end portion 249 includes a set of retention tabs 253 and can receive a portion of the spring 261. More particularly, the retention tabs 253 included in the proximal end portion 249 of the plunger 248 are configured to engage the spring 261 to removably couple the spring 261 to the plunger 248.

[1090] The side wall 251 of the plunger 248 define a set of notches 252 configured to receive a set of seal members 254. The seal members 254 can be any suitable seal members 254 such as for example, o-rings formed from any suitable elastomeric material. In this

manner, the plunger 248 is disposed within the inner volume 265 of the actuator housing 262 such that the seal members 254 define a friction fit with the inner walls (not shown in FIG. 10) that define the inner volume 265 of the actuator housing 262. Similarly stated, the seal members 254 define a fluidic seal with the inner walls of the actuator housing 262. Furthermore, the plunger 248 is disposed within the inner volume 265 such that the plunger 248 divides the inner volume 265 into a first portion 267 that is fluidically isolated from a second portion 270 (see e.g., FIGS. 11 and 12). The first portion 267 of the inner volume 265 is defined between a surface of the proximal end portion 263 of the actuator housing 262 and the proximal end portion 249 of the plunger 248. As such, the first portion 267 of the inner volume 265 is configured contain the spring 261 such that the spring 261 is in contact with the surface of the proximal end portion 263 of the actuator housing 262 and the proximal end portion 249 of the plunger 248.

[1091] The cap 255 can be any suitable shape or size and is configured to be disposed, at least partially, within the inner volume 265 of the actuator housing 262. Furthermore, the cap 255 can be formed from any suitable material. For example, in some embodiments, the cap 255 is formed from an elastomeric material such as silicone. In other embodiments, the cap 255 can be formed from any polymeric material such as, for example, rubber, vinyl, neoprene, or the like.

[1092] The cap 255 includes a proximal end portion 256 and a distal end portion 257. The proximal end portion 256 is disposed within the inner volume 265 of the actuator housing 262 such that the distal end portion 250 of the plunger 248 and the proximal end portion 256 of the cap defines the second portion 270 of the inner volume (referred to henceforth as "first reservoir") of the inner volume 265. Expanding further, the proximal end portion 256 of the cap 255 is configured to define a friction fit with the inner walls (not shown in FIG. 10) that define the inner volume 265. Similarly stated, the proximal end portion 254 defines a fluidic seal with the inner walls of the actuator housing 262. Therefore, the fluidic seal defined by the actuator housing 262 and the plunger 248 and the fluidic seal defined by the actuator housing 262 and the proximal end portion 256 of the cap 255 fluidically isolate the fluid reservoir 270 from a portion outside of the fluid reservoir 270 (i.e., the second portion of the inner volume 265).

[1093] The distal end portion 257 of the cap 255 includes a set of notches 260 configured to receive a set of protrusions 266 of the actuator housing 262 when the proximal end portion

256 is disposed within the inner volume 265. The arrangement of the notches 260 defined by the cap 255 and the protrusions 266 of the actuator housing 262 is such that the protrusions 266 form a friction fit with the walls defining the notches 260. In this manner, the protrusions 266 engage the walls defining the notches 260 to maintain the cap 255 in a desired position relative to the actuator housing 262 when the proximal end portion 256 is disposed within the inner volume 265. Moreover, the actuator mechanism 240 and the diverter 220 are disposed within the housing 201 such that the distal end portion 257 of the cap 255 is in contact with the proximal end portion 228 of the diverter 220, as described in further detail herein.

[1094] The cap 255 further defines an inlet port 258 and a set of guide post ports 259. The inlet port 258 is configured to receive a portion of the first outlet port 224 included in the diverter 220. More specifically, the inlet port 258 receives the first outlet port 224 such that the inlet port 258 form a fluidic seal with an outer surface of the first outlet port 224. Similarly, the guide post ports 259 receive a portion of the guide posts 207 of the housing 201 such that the guide post ports 259 form a fluidic seal with an outer surface of the guide posts 207. In this manner, a portion of the guide posts 207 and a portion of the first outlet port 224 are disposed within the fluid reservoir 270 defined by the actuator housing 262. Furthermore, with the portion of the first outlet port 224 disposed within the fluid reservoir 270, the fluid reservoir 270 (i.e., the second portion of the inner volume 265) is in fluid communication with the first outlet lumen 225, as described in further detail herein.

[1095] In some embodiments, the transfer device 200 can be stored in a storage configuration in which the second control member 235 of the flow control mechanism 230 fluidically isolates the inlet port 222, the first outlet port 224, and the second outlet port 226 from the inner volume 221 defined by the diverter 220. In such embodiments, first lumen 238 and the second lumen 239 are fluidically isolated from the inlet lumen 223, the first outlet lumen 225, and the second outlet lumen 227. Furthermore, the friction fit defined by the second control member 235 and the walls of the diverter 220 defining the inner volume 221 maintain the flow control mechanism 230 in the storage configuration until the flow control mechanism 230 is moved from the storage configuration.

[1096] In use, a user can engage the transfer device 200 to couple the inlet port 222 to a proximal end portion of a lumen-defining device (not shown) such as, for example, a butterfly needle or, as an additional example, surgical tubing coupleable with a Luer-Lok-

type connection that allows for mating to an indwelling catheter or hub or other general vascular access device(s)/product(s). With the inlet port 222 coupled to the lumen-defining device the inlet lumen 223 is placed in fluid communication with the lumen defined by the lumen-defining device. Furthermore, the distal end portion of the lumen-defining device can be disposed within a portion of the body of a patient (e.g., a vein), thus, the inlet lumen 223 is in fluid communication with the portion of the body of the patient. In a similar manner, the second outlet port 226 can be coupled to an external fluid reservoir (not shown). The external fluid reservoir can be any suitable reservoir. For example, in some embodiments, the external fluid reservoir can be a BacT/ALERT® SN or a BacT/ALERT® FA, manufactured by BIOMERIEUX, INC.

[1097] With the inlet port 222 coupled to the lumen-defining device and the second outlet port 226 coupled to the external fluid reservoir, a user can place the transfer device 200 in the first configuration by applying an activation force to the actuator mechanism 240, thereby moving at least a portion of the actuator mechanism 240, the diverter 220, and the flow control mechanism 230 in the distal direction towards the first configuration, as shown by the arrow **AA** in FIG. 11. More specifically and as described above, the distal end portion 250 of the plunger 248 engages the guide posts 207 of the housing 201. The arrangement of the plunger 248 and the guide posts 207 is such that as the user applies the activation force to the actuator mechanism 240, the position of the plunger 248, relative to the housing 201, is maintained. Therefore, the activation force applied by the user moves the actuator housing 262, the cap 255, the diverter 220, and the flow control mechanism 230 in the direction of the arrow **AA**, but not the plunger 248. Thus, the distal movement of the actuator housing 262 is such that a portion of the activation force is configured to compress the spring 261, and as such, the height of the second portion 267 of the inner volume is reduced. The compression of the spring 261 is such that the spring 261 exerts a reaction force (e.g., a force of expansion) in response to the portion of the activation force compressing the spring 261. Similarly stated, the spring 261 is configured return to an expanded configuration when the activation force is removed.

[1098] The distal movement of the actuator housing 262 relative to the plunger 248 is such that the height of the fluid reservoir 270 is increased. With the fluid reservoir 270 being fluidically isolated (as described above) the increase in the height (i.e., the increase in volume) produces a negative pressure within the fluid reservoir 270. Furthermore, as the

actuator mechanism 240 is moved from the storage configuration toward the first configuration, the flow control protrusions 208 engage the activation protrusions 232 (not shown in FIG. 11) included in the first control member 231 to move the flow control mechanism 230 toward the first configuration, as indicated by the arrow **BB**. Thus, when the flow control mechanism 230 is moved to the first configuration, the first lumen 238 defined by the second control member 235 is placed in fluid communication with the inlet lumen 223 defined by the inlet port 222 and the first outlet lumen 225 defined by the first outlet port 224.

[1099] As shown by the arrow **CC**, the inlet lumen 223 of the inlet port 222, the first lumen 238 of the second control member 235, and the first outlet lumen 225 of the first outlet port 224 define a fluid flow path such that the fluid reservoir 270 defined by the actuator housing 262 is in fluid communication with the inlet port 222. Furthermore, with the inlet port 222 coupled to the lumen-defining device the fluid reservoir 270 of the actuator housing 262 is placed in fluid communication with the portion of the patient (e.g., the vein). The negative pressure within the fluid reservoir 270 is such that the negative pressure differential introduces a suction force within the portion of the patient. In this manner, a bodily-fluid is drawn into the fluid reservoir 270 of the actuator housing 262. In some embodiments, the bodily-fluid can contain undesirable microbes such as, for example, dermally-residing microbes.

[1100] In some embodiments, the magnitude of the suction force can be modulated by increasing or decreasing the amount of activation force applied to the actuator mechanism 240. Excess suction force can, in some cases, collapse a patient's vein thereby cutting off sample flow. Once a vein is collapsed, one or more additional venipunctures may be required to access a non-collapsed vein. Excess suction force may also cause hemolysis at the needle tip within the vein due to excessive negative pressure. Thus, in some embodiments, it can be desirable to limit the amount of suction force (i.e., modulate the negative pressure during a blood draw) introduced to a vein to reduce, minimize, or even eliminate vein collapse and/or one potential source of hemolysis. In such embodiments, the user can reduce the amount of force applied to the actuator mechanism 240. In this manner, the reaction force exerted by the expansion of the spring 261 (e.g., as described above) is sufficient to overcome a portion of the activation force applied by the user. Thus, the spring 261 can expand to move the plunger 248 and the housing 201 in the distal direction, relative to the actuator housing 262,

the cap 255, the diverter 220, and the flow control mechanism 230. The distal movement of the plunger 248 and housing 201 is such that the flow control protrusions 208 engage the activation protrusions 232 of the flow control mechanism 230 to move the flow control mechanism 230 towards the storage configuration. The rotation of the flow control mechanism 230 (e.g., in a direction opposite the arrow **BB**) reduces the size of the fluid pathway (e.g., an inner diameter) between the inlet lumen 223 and the first lumen 238 and the first outlet port 225 and the first lumen 238, thereby reducing the suction force introduced into the vein of the patient.

[1101] With the desired amount of bodily-fluid transferred to the fluid reservoir 270 defined by the actuator housing 262, a user can engage the transfer device 200 to move the transfer device 200 from the first configuration to the second configuration, wherein a flow of bodily-fluid is transferred to the external reservoir (e.g., such as those described above). In some embodiments, the desired amount of bodily-fluid transferred to the actuator housing 262 is a predetermined amount of fluid. For example, in some embodiments, the transfer device 200 can be configured to transfer bodily-fluid until the pressure within the fluid reservoir 270 defined by the actuator housing 262 is in equilibrium with the pressure of the portion of the body in which the lumen-defining device is disposed (e.g., the vein). In such embodiments, the equalizing of the pressure between the second portion 176 of the inner volume 265 and the portion of the body stops the flow of the bodily-fluid into the actuator housing 262. In some embodiments, the predetermined amount of bodily-fluid (e.g., volume) is at least equal to the combined volume of the inlet lumen 223, the first lumen 238, the first outlet lumen 225, and the lumen-defining device.

[1102] As shown in FIG. 12, the transfer device 200 can be moved from the first configuration to the second configuration by further moving the actuator mechanism 240 in the distal direction, as indicated by the arrow **DD**. Expanding further, the user can apply an activation force to the actuator mechanism 240 such that the actuator housing 262, the cap 255, the diverter 220, and the flow control mechanism 230 move in the distal direction. With the desired amount of the bodily-fluid disposed within the fluid reservoir 270 the volume of the fluid reservoir 270 is configured to remain constant as the actuator housing 262 and the cap 255 move relative to the plunger 248. Similarly stated, the pressure of the fluid reservoir 270 is configured to remain substantially unchanged as the transfer device 200 is moved from the first configuration to the second configuration.

[1103] As the actuator mechanism 240 is moved from the first configuration toward the second configuration, the flow control protrusions 208 engage the activation protrusions 232 (not shown in FIG. 12) included in the first control member 231 to move the flow control mechanism 230 toward the second configuration, as indicated by the arrow **EE**. Thus, when the flow control mechanism 230 is moved to the second configuration, the second lumen 239 defined by the second control member 235 is placed in fluid communication with the inlet lumen 223 defined by the inlet port 222 and the second outlet lumen 227 defined by the second outlet port 226.

[1104] As shown by the arrow **FF**, the inlet lumen 223 of the inlet port 222, the second lumen 239 of the second control member 235, and the second outlet lumen 227 of the second outlet port 226 define a fluid flow path such that the external reservoir (not shown in FIG. 12) is in fluid communication with the inlet port 222 and, therefore, the portion of the patient (e.g., the vein). Furthermore, the external reservoir is configured to define a negative pressure (e.g., the known external reservoirs referred to herein are vessels defining a negative pressure). The negative pressure within the external reservoir is such that the negative pressure differential between the external reservoir and the portion of the body of the patient introduces a suction force within the portion of the patient. Therefore, a desired amount of bodily-fluid is drawn into the external reservoir and is fluidically isolated from the first, predetermined amount of bodily-fluid contained within the fluid reservoir 270 defined by the actuator housing 262. In this manner, the bodily-fluid contained in the external reservoir is substantially free from microbes generally found outside of the portion of the patient (e.g., dermally residing microbes, microbes within a lumen defined by the transfer device 200, microbes within the lumen defined by the lumen defining device, and/or any other undesirable microbe(s)). With the desired amount of bodily-fluid contained in the external fluid reservoir, the user can remove the activation force from the actuator mechanism 240 (e.g., remove the portion of the hand engaging the actuator mechanism 240). With the removal of the activation force, the spring 261 exerts the force of expansion (described above) to move the transfer device 200 from the second configuration to the storage configuration. With the transfer device 200 in the storage configuration, the first outlet port 224 is fluidically isolated from the first lumen 238 and/or the second lumen 239 of the flow control mechanism 230. Thus, the bodily-fluid contained within the actuator housing 262 is fluidically isolated from a volume outside the actuator housing 262 and the external reservoir can be decoupled from the transfer device 200. In addition, the bodily-fluid contained within

the actuator housing 262 is isolated from the patient and the healthcare worker, and can be safely disposed of (e.g., in a biohazard materials container) in a "closed" device.

[1105] While the transfer device 200 is shown and described in FIGS. 2-12 as disposing the diverter 220 within the housing 201, in some embodiments, a transfer device can include a diverter and housing that are monolithically formed. For example, FIGS. 13-19 illustrate a transfer device 300 according to an embodiment. FIGS. 13 and 14 illustrate the transfer device 300 in a first configuration. The transfer device 300 includes a housing 301, having a diverter 320 and defining a fluid reservoir 370, a flow control mechanism 330, and an actuator 340.

[1106] The housing 301 includes a proximal end portion 302 and a distal end portion 303. The distal end portion 303 of the housing 301 includes a set of walls 304 that define a channel 305 configured to receive a distal portion 342 of the actuator 340. The walls 304 can be configured to define the channel 305 with any suitable shape, size, or configuration. For example as shown in FIG. 16, the walls 304 can be configured to further define a slot 319 in the channel 305 configured to receive an activation extension 346 included in the actuator 340 (FIG. 15). Similarly stated, the slot 319 can be configured to receive the activation extension 346 included in the distal portion 342 of the actuator 340, disposed within the channel 305, such that the activation extension 346 can pass through the walls 304 and be disposed substantially outside the channel 305, as described in further detail herein.

[1107] The walls 304 of the distal end portion 303 of the housing 301 also include a recessed surface 315 and a stop 313 (FIGS. 15 and 16). The stop 313 defines a proximal boundary of the channel 305 that can limit the movement of the actuator 340 within the channel 305. Furthermore, the stop 313 defines a passageway 314 configured to receive a portion of the actuator 340 such that the portion of the actuator 340 can extend in the proximal direction beyond the stop 313, as further described herein. The recessed surface 315 is configured to be a flat surface from which the diverter 320 can extend. Similarly stated, the diverter 320 is a set of walls configured to extend perpendicularly from the recessed surface 315. In this manner, the diverter 320 receives at least a portion of the flow control mechanism 340, as described in further detail herein. While shown and described as extending perpendicularly from the recessed surface 315, in other embodiments, the diverter 320 can extend from the recessed surface 315 at any suitable angular orientation.

[1108] As shown in FIG. 15, the proximal end portion 302 of the housing 301 includes a set of walls 318 that extend from the stop 313 in the proximal direction. In this manner, the walls 318 define a tubular shape substantially enclosed at the distal end by the stop 313 and open at the proximal end. The walls 318 define a slot 312 and an inner volume 311 configured to receive a proximal end portion 341 of the actuator 340. As further described herein, the proximal end portion 302 of the housing 301, the stop 313, and the proximal end portion 341 of the actuator 340 define a fluid reservoir 370 configured to receive and/or contain a bodily fluid.

[1109] As shown in FIG. 16, the diverter 320 includes an inlet port 322, a first outlet port 324, and a second outlet port 326, and defines an inner volume 321. The inner volume 321 is configured to receive at least a portion of the flow control mechanism 330, as further described herein. The inlet port 322 of the diverter 320 defines an inlet lumen 323. The inlet lumen 323 is configured to be in fluid communication with the inner volume 321. Similarly stated, the inlet lumen 323 of the inlet port 322 extends through a wall defining the inner volume 321 of the diverter 320.

[1110] The inlet port 322 is further configured to be fluidically coupled to a medical device (not shown) defining a fluid flow pathway for withdrawing and/or conveying the bodily-fluid from a patient to the transfer device 300. For example, the inlet port 322 can be fluidically coupled to a needle or other lumen-containing device (e.g., flexible sterile tubing). Similarly stated, the inlet lumen 323 defined by the inlet port 322 is placed in fluid communication with a lumen defined by a lumen-containing device, when the lumen-containing device is coupled to the inlet port 322. Expanding further, when the lumen-containing device is disposed within a portion of a body of the patient (e.g., within a vein of the patient), the inner volume 321 of the diverter 320 is placed in fluid communication with the portion of the body of the patient.

[1111] The first outlet port 324 of the diverter 320 defines a first outlet lumen 325. The first outlet lumen 325 is configured to be in fluid communication with the inner volume 321 of the diverter 320 and the fluid reservoir 370 (described above). Similarly stated, the first outlet lumen 325 is configured to extend through the wall defining the inner volume 321 and through a portion of the stop 313 defining the fluid reservoir 370, thereby placing the fluid reservoir 370 in fluid communication with the inner volume 321. The second outlet port 326 of the diverter 320 defines a second outlet lumen 327 and can be coupled to an external fluid

reservoir. In this manner, the second outlet lumen 327 can extend through the wall defining the inner volume 321 to be in fluid communication with the inner volume 321 and can be fluidically coupled to the external reservoir to place the external fluid reservoir in fluid communication with the inner volume 321.

[1112] As shown in FIG. 15, the flow control mechanism 330 includes a first control member 331 and a second control member 335. At least a portion of the flow control mechanism 330 is configured to be disposed within the inner volume 321 defined by the diverter 320. In this manner, the flow control mechanism 330 defines a circular cross-sectional shape such that when the flow control mechanism 330 is disposed within the inner volume 321, a portion of the flow control mechanism 330 forms a friction fit with the walls of the diverter 320 defining the inner volume 321, as described in further detail herein.

[1113] The first control member 331 includes a set of activation protrusions 332 configured to engage a set of protrusion 347 included in the activation extension 346 of the actuator 340. Therefore, in use, the actuator 340 can engage the activation protrusions 332 to move the flow control mechanism 330 between a first configuration and a second configuration. The second control member 335 defines a first lumen 338 and a second lumen 339 and can be formed from any suitable material. For example, in some embodiments, the second control member 335 is formed from silicone. In other embodiments, the second control member 335 can be any suitable elastomer configured to deform when disposed within the inner volume 321 of the diverter. Expanding further, the second control member 335 has a diameter larger than the diameter of the inner volume 321. In the manner, the diameter of the second control member 335 is reduced when the second control member 335 is disposed within the inner volume 321. Thus, the outer surface of the second control member 335 forms a friction fit with the inner surface of the walls defining the inner volume 321.

[1114] The second control member 335 is configured to be coupled to the first control member 331. For example, in some embodiments, the first control member 331 can be coupled to the second control member 335 via a mechanical fastener and/or adhesive. In other embodiments, the first control member 331 and the second control member 335 can be coupled in any suitable manner. In this manner, the second control member 335 is configured to move concurrently with the first control member 331 when the activation extension 347 of the actuator 340 engages the activation protrusions 332 of the first control

member 331. Similarly stated, the flow control mechanism 330 is moved between the first configuration and the second configuration when the first control member 331 and the second control member 335 are moved between the first configuration and the second configuration, respectively. Furthermore, when the flow control mechanism 330 is in the first configuration, the first lumen 338 is placed in fluid communication with the inlet lumen 323 defined by the inlet port 322 and the first outlet lumen 325 defined by the first outlet port 324. When the flow control mechanism 330 is in the second configuration, the second lumen 339 is placed in fluid communication with the inlet lumen 323 defined by the inlet port 322 and the second outlet lumen 327 defined by the second outlet port 326, as described in further detail herein.

[1115] As described above, the actuator mechanism 340 includes the proximal end portion 341, the distal end portion 342, and an actuator arm 343 therebetween. The actuator mechanism 340 is configured to move between a first configuration and a second configuration, thereby moving the transfer device 300 between a first configuration and a second configuration, as described in further detail herein. The proximal end portion 341 includes a plunger 348 configured to be disposed within the inner volume 311 of the housing 301. More particularly, the plunger 348 includes a seal member 354 configured to define a friction fit with the inner surface of the walls 318 defining the inner volume 311. Similarly stated, the seal member 354 defines a fluidic seal with the inner surface of the walls 318 defining the inner volume 311 such that a portion of the inner volume 311 proximal of the seal member 354 is fluidically isolated from a portion of the inner volume 311 distal of the seal member 354.

[1116] The actuator arm 343 is configured to extend from the proximal end portion 341 of the actuator 340 through the passageway 314 defined by the stop 313. Therefore, as described above, the distal end portion 342 of the actuator 340 is disposed on a distal side of the stop 313. More specifically, the distal end portion 342 includes an engagement portion 344 and the activation portion 346. The engagement portion 344 and at least a portion (e.g., a distal portion) of the actuator arm 343 are configured to be disposed within the channel 305 such that the activation portion 346 can extend through the slot 319, as described above. In this manner, a user can engage the engagement portion 344 to move the actuator 340 in a distal direction between a first configuration and a second configuration, as further described herein.

[1117] In some embodiments, the transfer device 300 can be stored in the first configuration in which the first lumen 338 of the second control member 335 is in fluid communication with the inlet port 322 and the first outlet port 324. In such embodiments, the friction fit defined by the second control member 335 and the walls of the diverter 320 defining the inner volume 321 maintain the flow control mechanism 330 in the first configuration until the actuator 340 moves the flow control mechanism 330 to the second configuration.

[1118] In use, a user can engage the transfer device 300 to couple the inlet port 322 to a proximal end portion of a lumen-defining device (not shown) such as, for example, a butterfly needle. With the inlet port 322 coupled to the lumen-defining device the inlet lumen 323 is placed in fluid communication with the lumen defined by the lumen-defining device. Furthermore, the distal end portion of the lumen-defining device can be disposed within a portion of the body of a patient (e.g., a vein), thus, the inlet lumen 323 is in fluid communication with the portion of the body of the patient. In a similar manner, the second outlet port 326 can be coupled to an external fluid reservoir (not shown). The external fluid reservoir can be any suitable reservoir. For example, in some embodiments, the external fluid reservoir can be a BacT/ALERT® SN or a BacT/ALERT® FA blood culture collection bottle with media specifically designed to facilitate the growth of certain types of microbes (e.g., aerobic media/broth and/or aerobic media/broth), manufactured by BIOMERIEUX, INC.

[1119] With the inlet port 322 coupled to the lumen-defining device and the second outlet port 326 coupled to the external fluid reservoir, a user can begin the transfer of a bodily-fluid by applying an activation force to the engagement portion 344 of the actuator 340, thereby moving the actuator 340 the distal direction, as shown by the arrow **GG** in FIG. 17. More specifically and as described above, the plunger 348 engages the inner surface of the walls 318 defining the inner volume 311 such that the volume of the fluid reservoir 370 is increased (e.g., as defined by the plunger 348, the walls 318 of the housing 301 and the stop 313). With the fluid reservoir 370 being fluidically isolated (as described above) from a volume on the proximal side of the seal member 354, the increase in the volume of the fluid reservoir 370 produces a negative pressure within the fluid reservoir 370. Moreover, with the flow control mechanism 330 in the first configuration, negative pressure differential introduces a suction force within the first lumen 338, the inlet lumen 323, and the first outlet lumen 325.

[1120] As shown by the arrow **HH**, the inlet lumen 323 of the inlet port 322, the first lumen 338 of the second control member 335, and the first outlet lumen 325 of the first outlet port 324 define a fluid flow path such that the second portion 376 of the inner volume 373 defined by the fluid reservoir 370 is in fluid communication with the inlet port 322. Furthermore, with the inlet port 322 coupled to the lumen-defining device the fluid reservoir 370 is in fluid communication with the portion of the patient (e.g., the vein) and at least a portion of the suction force is introduced to the portion of the patient. In this manner, a bodily-fluid is drawn into the fluid reservoir 370. In some embodiments, the bodily-fluid can contain undesirable microbes such as, for example, dermally-residing microbes dislodged during the insertion of the lumen-defining device.

[1121] In some embodiments, the magnitude of the suction force can be modulated by moving the actuator 340 in the proximal or distal direction. For example, in some embodiments, it can be desirable to limit the amount of suction force introduced to a vein. In such embodiments, the user can move the actuator 340 in the proximal direction (e.g., the direction of the arrow **II** in FIG. 18) such the activation extension 346 can engage the protrusions 332 of the first control member 331. In this manner, the protrusions 347 included in the activation extension 346 can mesh with the protrusions 332 of the first control member 331 to rotate the first control member 331 in the direction of the arrow **JJ**. The rotation of the flow control mechanism 330 (e.g., in a direction opposite the arrow **JJ**) reduces the size of the fluid pathway (e.g., an inner diameter) between the inlet lumen 323 and the first lumen 338 and the first outlet port 325 and the first lumen 338, thereby reducing the suction force introduced into the vein of the patient.

[1122] With the desired amount of bodily-fluid transferred to the fluid reservoir 370, a user can engage the transfer device 300 to move the transfer device 300 from the first configuration to the second configuration, wherein a flow of bodily-fluid is transferred to the external reservoir (e.g., such as those described above). In some embodiments, the desired amount of bodily-fluid transferred to the fluid reservoir 370 is a predetermined amount of fluid. For example, in some embodiments, the transfer device 300 can be configured to transfer bodily-fluid until the pressure within the fluid reservoir 370 is equilibrium with the pressure of the portion of the body in which the lumen-defining device is disposed (e.g., the vein). In such embodiments, the equalizing of the pressure between the fluid reservoir 370 and the portion of the body stops the flow of the bodily-fluid into the fluid reservoir 370. In

some embodiments, the predetermined amount of bodily-fluid (e.g., volume) is at least equal to the combined volume of the inlet lumen 323, the first lumen 338, the first outlet lumen 325, and the lumen-defining device.

[1123] As shown in FIG. 18, the transfer device 300 can be moved from the first configuration to the second configuration by further moving the actuator mechanism 340 in the distal direction, as indicated by the arrow **II**. As the actuator mechanism 340 is moved from the first configuration toward the second configuration, the protrusions 347 of the activation extension 346 further engage the activation protrusions 332 included in the first control member 331 to move the flow control mechanism 330 to the second configuration, as indicated by the arrow **KK** in FIG. 19. In this manner, the flow control mechanism 330 is moved to the second configuration, and the first lumen 238 is fluidically isolated from the inlet lumen 223 and the first outlet lumen 225. In addition, the second lumen 339 defined by the second control member 335 is placed in fluid communication with the inlet lumen 323 defined by the inlet port 322 and the second outlet lumen 327 defined by the second outlet port 326.

[1124] As shown by the arrow **LL**, the inlet lumen 323 of the inlet port 322, the second lumen 339 of the second control member 335, and the second outlet lumen 327 of the second outlet port 326 define a fluid flow path such that the external reservoir (not shown in FIG. 19) is in fluid communication with the inlet port 322 and, therefore, the portion of the patient (e.g., the vein). Furthermore, the external reservoir is configured to define a negative pressure (e.g., the known external reservoirs referred to herein are vessels defining a negative pressure). The negative pressure within the external reservoir is such that the negative pressure differential between the external reservoir and the portion of the body of the patient introduces a suction force within the portion of the patient. Therefore, a desired amount of bodily-fluid is drawn into the external reservoir and is fluidically isolated from the first, predetermined amount of bodily-fluid contained within the fluid reservoir 370.

[1125] The bodily-fluid contained in the external reservoir is substantially free from microbes generally found outside of the portion of the patient (e.g., dermally residing microbes, microbes within a lumen defined by the transfer device 300, microbes within the lumen defined by the lumen defining device, and/or any other undesirable microbe). In some embodiments, with the desired amount of bodily-fluid contained in the external fluid reservoir, the user can further move the actuator 340 in the proximal direction to place the

transfer device 300 in a third configuration. In such embodiments, the actuator 340 can be moved in the proximal direction such that the engagement portion 344 and/or the activation extension 346 contact the stop 313, thereby limiting further proximal movement of the actuator 340. In this configuration, the actuator 340 can place the flow control mechanism 330 in a third configuration configured to fluidically isolate the first lumen 338 and the second lumen 339 from the inlet lumen 323, the first outlet lumen 325, and the second outlet lumen 327. Thus, the bodily-fluid contained within the fluid reservoir 370 is fluidically isolated from a volume outside the fluid reservoir 370 and the external reservoir can be decoupled from the transfer device 300.

[1126] While the transfer device 300 is shown and described in FIGS. 13-19 as being configured to actuated by continual user influence (e.g., the user manually moves the actuator 340 in the proximal direction), in some embodiments, a transfer device need not require continual user influence. For example, FIGS. 20-26 illustrate a transfer device 400 according to an embodiment. FIGS. 20 and 21 illustrate the transfer device 400 in a first configuration. The transfer device 400 includes a housing 401, having a diverter 420 and defining a fluid reservoir 470, a flow control mechanism 430, and an actuator mechanism 440.

[1127] The housing 401 includes a proximal end portion 402 and a distal end portion 403. The distal end portion 403 of the housing 401 includes a set of walls 404 having a recessed portion 415 and a stop 413 (FIGS. 22 and 23). The stop 413 defines a distal boundary of the recessed portion 415 and defines a passageway 414. The passageway 414 is configured to receive an activation extension 346 included in the actuator mechanism 440 such that the activation extension 346 extends through the stop 413, as further described herein. The recessed portion 415 includes a substantially flat surface from which the diverter 420 can extend (FIG. 22). Similarly stated, the diverter 420 is a set of walls configured to extend perpendicularly from the surface of the recessed portion 415. In this manner, the diverter 420 receives at least a portion of the flow control mechanism 430, as described in further detail herein. While shown and described as extending perpendicularly from the surface of the recessed portion 415, in other embodiments, the diverter 420 can extend from the surface at any suitable angular orientation.

[1128] The proximal end portion 402 of the housing 401 includes a set of walls 418 that extend from the stop 413 in the proximal direction. In this manner, the walls 418 define a tubular shape substantially enclosed at the distal end by the stop 413 and open at the proximal

end. The proximal end portion 402 of the housing 401 can be formed from any suitable material. For example, in some embodiments, the proximal end portion 402 can be formed from a relatively flexible material. In such embodiments, the proximal end portion 402 can be configured to deform (e.g., bend, compress, or otherwise reconfigure) under a given force, as described in further detail herein. As shown in FIG. 23, the walls 418 include shoulder 416 and retention tabs 417 and define an inner volume 411 configured to receive a portion of the actuator mechanism 440. As further described herein, the proximal end portion 402 of the housing 401, the stop 413, and a portion of the actuator mechanism 440 define a fluid reservoir 470 configured to receive and/or contain a bodily fluid.

[1129] As shown in FIG. 23, the diverter 420 includes an inlet port 422, a first outlet port 424, and a second outlet port 426, and defines an inner volume 421. The inner volume 421 is configured to receive at least a portion of the flow control mechanism 430, as further described herein. The inlet port 422 of the diverter 420 defines an inlet lumen 423. The inlet lumen 423 is configured to be in fluid communication with the inner volume 421. Similarly stated, the inlet lumen 423 of the inlet port 422 extends through a wall defining the inner volume 421 of the diverter 420.

[1130] The inlet port 422 is further configured to be fluidically coupled to a medical device (not shown) defining a fluid flow pathway for withdrawing and/or conveying the bodily-fluid from a patient to the transfer device 400. For example, the inlet port 422 can be fluidically coupled to a needle or other lumen-containing device (e.g., flexible sterile tubing). Similarly stated, the inlet lumen 423 defined by the inlet port 422 is placed in fluid communication with a lumen defined by a lumen-containing device, when the lumen-containing device is coupled to the inlet port 422. Expanding further, when the lumen-containing device is disposed within a portion of a body of the patient (e.g., within a vein of the patient), the inner volume 421 of the diverter 420 is placed in fluid communication with the portion of the body of the patient.

[1131] The first outlet port 424 of the diverter 420 defines a first outlet lumen 425. The first outlet lumen 425 is configured to be in fluid communication with the inner volume 421 of the diverter 420 and the fluid reservoir 470 (described above). Similarly stated, the first outlet lumen 425 is configured to extend through the wall defining the inner volume 421 and through a portion of the stop 413 defining the fluid reservoir 470, thereby placing the fluid reservoir 470 in fluid communication with the inner volume 421. The second outlet port 426

of the diverter 420 defines a second outlet lumen 427 and is configured to be coupled to an external fluid reservoir. In this manner, the second outlet lumen 427 can extend through the wall defining the inner volume 421 to be in fluid communication with the inner volume 421 and can be fluidically coupled to the external reservoir to place the external fluid reservoir in fluid communication with the inner volume 421.

[1132] As shown in FIG. 24, the flow control mechanism 430 includes a first control member 431 and a second control member 435. At least a portion of the flow control mechanism 430 is configured to be disposed within the inner volume 421 defined by the diverter 420. In this manner, the flow control mechanism 430 defines a circular cross-sectional shape such that when the flow control mechanism 430 is disposed within the inner volume 421, a portion of the flow control mechanism 430 forms a friction fit with the walls of the diverter 420 defining the inner volume 421, as described in further detail herein.

[1133] The first control member 431 includes an activation protrusion 432 and engagement protrusions 433. The activation protrusion 432 is configured to engage a protrusion 447 included in the activation extension 446 of the actuator mechanism 440. Therefore, in use, the actuator mechanism 440 can engage the activation protrusion 432 to move the flow control mechanism 430 between a first configuration and a second configuration. The second control member 435 defines a first lumen 438, a second lumen 439, and a set of grooves 437. The second control member 435 can be formed from any suitable material such as, for example, silicone. In other embodiments, the second control member 435 can be any suitable elastomer configured to deform when disposed within the inner volume 421 of the diverter. Expanding further, the second control member 435 has a diameter larger than the diameter of the inner volume 421. In the manner, the diameter of the second control member 435 is reduced when the second control member 435 is disposed within the inner volume 421. Thus, the outer surface of the second control member 435 forms a friction fit with the inner surface of the walls defining the inner volume 421.

[1134] The grooves 437 defined by the second control member 435 are configured to receive the engagement protrusions 433. In this manner, the first control member 431 can selectively engage the second control member 435 such that the second control member 435 is moved concurrently with the first control member 431 when the activation extension 447 of the actuator mechanism 440 engages the activation protrusion 432 of the first control member 431. Similarly stated, the flow control mechanism 430 is moved between the first

configuration and the second configuration when the first control member 431 and the second control member 435 are moved between the first configuration and the second configuration, respectively. Furthermore, when the flow control mechanism 430 is in the first configuration, the first lumen 438 is placed in fluid communication with the inlet lumen 423 defined by the inlet port 422 and the first outlet lumen 425 defined by the first outlet port 424. When the flow control mechanism 430 is in the second configuration, the second lumen 439 is placed in fluid communication with the inlet lumen 423 defined by the inlet port 422 and the second outlet lumen 427 defined by the second outlet port 426, as described in further detail herein.

[1135] As shown in FIGS. 22 and 25, the actuator mechanism 440 includes an engagement member 444, the activation extension 446, a plunger 448, and a spring 461. The engagement member 444 is configured to be coupled to the distal end portion 403 of the housing 401. In this manner, the housing 401 and the engagement member 444 house the flow control mechanism 430 and at least a portion of the diverter 420. The engagement member 444 includes a throttling button 445. The throttling button 445 is configured such that when engaged by a user, the throttling button 445 interacts with the flow control mechanism 430 to modulate the movement of the flow control mechanism 440, as described in further detail herein.

[1136] The plunger 448 includes a proximal end portion 449 and a distal end portion 450 and is configured to be disposed within the inner volume 411 defined by the housing 401. The proximal end portion 449 of the plunger 448 is configured to selectively engage the retention protrusions 417 included in the housing 401. The plunger 448 further includes a sealing member 454 disposed at the distal end portion 450. The seal member 454 is configured to define a friction fit with the inner surface of the walls 418 defining the inner volume 411. Similarly stated, the seal member 454 defines a fluidic seal with the inner surface of the walls 418 defining the inner volume 411 such that a portion of the inner volume 411 proximal of the seal member 454 is fluidically isolated from a portion of the inner volume 411 distal of the seal member 454.

[1137] The spring 461 includes a proximal end portion 462 and a distal end portion 463 and is configured to circumscribe the plunger 448. Similarly stated, the plunger 448 is disposed within the spring 461 when the spring 461 and the plunger 448 are disposed within the housing 401. Furthermore, when disposed within the inner volume 411, the distal end portion 463 of the spring 461 is configured to engage the shoulder 416 of the housing 401

and the proximal end portion 462 is configured to engage the proximal end portion 449 of the plunger 448. In this manner, the spring 461, when urged to move from a first (compressed) configuration to a second (expanded) configuration, is configured to move the plunger 448 in the proximal direction, as described in further detail herein.

[1138] The activation extension 446 can be any suitable size, shape, or configuration. For example, as shown in FIG. 22, the activation extension 446 can be a flexible tether formed from, for example, nylon. In this manner, the activation extension 446 can be substantially flexible in a lateral direction and substantially rigid in an axial direction. Similarly stated, in some embodiments, the activation extension 446 is configured to bend, twist, conform, and/or otherwise reconfigure without stretching. Said yet another way, the length of the activation extension 446 is configured to remain substantially unchanged as the activation extension 446 is bent or otherwise reconfigured.

[1139] The activation extension 446 is configured to be coupled to the distal end portion 450 of the plunger 448. More specifically, a proximal end portion of the activation extension 446 is disposed within the inner volume 411 of the housing 401 and is coupled to the plunger 448 and a distal end portion of the activation extension 446 passes through the stop 413 and is disposed within the recessed portion 415 of the housing 401. In this manner, the activation extension 446 is configured engage the activation protrusion 432 of the first control member 431 to move the flow control mechanism 430 between the first configuration and the second configuration, as described in further detail herein.

[1140] In some embodiments, the transfer device 400 can be stored in a storage configuration in which the second control member 435 of the flow control mechanism 430 fluidically isolates the inlet port 422, the first outlet port 424, and the second outlet port 426 from the inner volume 421 defined by the diverter 420. In such embodiments, first lumen 438 and the second lumen 439 are fluidically isolated from the inlet lumen 423, the first outlet lumen 425, and the second outlet lumen 427. Furthermore, the friction fit defined by the second control member 435 and the walls of the diverter 420 defining the inner volume 421 maintain the flow control mechanism 430 in the storage configuration until the flow control mechanism 430 is moved from the storage configuration.

[1141] In use, a user can engage the transfer device 400 to couple the inlet port 422 to a proximal end portion of a lumen-defining device (not shown) such as, for example, a

butterfly needle. With the inlet port 422 coupled to the lumen-defining device the inlet lumen 423 is placed in fluid communication with the lumen defined by the lumen-defining device. Furthermore, the distal end portion of the lumen-defining device can be disposed within a portion of the body of a patient (e.g., a vein), thus, the inlet lumen 423 is in fluid communication with the portion of the body of the patient. In a similar manner, the second outlet port 426 can be coupled to an external fluid reservoir (not shown). The external fluid reservoir can be any suitable reservoir. For example, in some embodiments, the external fluid reservoir can be a BacT/ALERT® SN or a BacT/ALERT® FA, manufactured by BIOMERIEUX, INC.

[1142] With the inlet port 422 coupled to the lumen-defining device and the second outlet port 426 coupled to the external fluid reservoir, a user can begin a transfer of a bodily-fluid by applying an activation force to the transfer device 400. More specifically, the user can introduce an activation force to the proximal end portion 402 of the housing 401 by squeezing, for example, the sides of the proximal end portion 402 such that the proximal end portion 402 deforms in response to the activation force, as described above. Thus, the proximal end portion 402 is urged (in response to the activation force) to reconfigure such that the retention tabs 417 are removed from contact with the proximal end portion 449 of the plunger 448. Expanding further, the retention tabs 417 are configured to apply a reaction force to the proximal end portion 449 of the plunger 448 in response to an expansion force exerted by the spring 461, thereby maintaining the spring 461 in the compressed configuration. With the retention tabs 417 removed from contact with the plunger 448 and with the distal end portion 463 of the spring 461 in contact with the shoulder 416 of the housing 401, the proximal end portion 462 of the spring 462 expands to move the plunger 448 in the direction of the arrow **MM** in FIG. 25.

[1143] As described above, the plunger 448 engages the inner surface of the walls 418 defining the inner volume 411 such that the volume of the fluid reservoir 470 is increased (e.g., as defined by the plunger 448, the walls 418 of the housing 401 and the stop 413). With the fluid reservoir 470 being fluidically isolated (as described above) from a volume on the proximal side of the seal member 454, the increase in the volume of the fluid reservoir 470 produces a negative pressure within the fluid reservoir 470. Moreover, movement of the plunger 448 in the proximal direction is such that the activation extension 446 is moved in the proximal direction. In this manner, the protrusion 447 of the activation extension 446

engages the protrusion 432 of the first control member 431 to move the flow control mechanism 430 from the storage configuration to the first configuration, as indicated by the arrow **NN**. With the flow control mechanism 430 in the first configuration, the negative pressure of the fluid reservoir 470 introduces a suction force within the first lumen 438, the inlet lumen 423, and the first outlet lumen 425.

[1144] As shown by the arrow **OO**, the inlet lumen 423 of the inlet port 422, the first lumen 438 of the second control member 435, and the first outlet lumen 425 of the first outlet port 424 define a fluid flow path such that the second portion 476 of the inner volume 473 defined by the fluid reservoir 470 is in fluid communication with the inlet port 422. Furthermore, with the inlet port 422 coupled to the lumen-defining device the fluid reservoir 470 is in fluid communication with the portion of the patient (e.g., the vein) and at least a portion of the suction force is introduced to the portion of the patient. In this manner, a bodily-fluid is drawn into the fluid reservoir 470. In some embodiments, the bodily-fluid can contain undesirable microbes such as, for example, dermally-residing microbes dislodged during the insertion of the lumen-defining device.

[1145] In some embodiments, the rate of expansion of the spring 461 can be modulated by engaging the throttling button 445 included in the engagement portion 444 of the actuator mechanism 440. For example, in some embodiments, it can be desirable to limit the amount of suction force introduced to a vein. In such embodiments, the user can exert a force on the throttling button 445 such that the throttling button 445 is moved to engage the flow control mechanism 430. In this manner, the throttling button 445 can increase the friction between, for example, the second control member 435 and the walls defining the inner volume 421 of the diverter. Thus, the increase in friction between the second control member 435 and the walls defining the inner volume 411 resist the force exerted by the activation extension 446, thereby slowing the rate of expansion of the spring. In this manner, the reduction of pressure (e.g., the increase in negative pressure) of the fluid reservoir 470 can be controlled to maintain a desired pressure differential between the vein and the fluid reservoir 470 and limit the suction force introduced to the vein.

[1146] In some embodiments, the user can depress the throttling button 445 to maintain the transfer device 400 in the first configuration. With the desired amount of bodily-fluid transferred to the fluid reservoir 470, a user can disengage the throttling button 445 to disengage the throttling button 445 from the flow control mechanism 430. In this manner,

the friction between the second control member 435 and the walls defining the inner volume 411 is reduced and the force of expansion exerted by the spring is sufficient to again overcome the friction between the second control member 435 and the walls defining the inner volume 411. Therefore, the transfer device 400 is moved 400 from the first configuration to the second configuration, wherein a flow of bodily-fluid is transferred to the external reservoir (e.g., such as those described above).

[1147] In some embodiments, the desired amount of bodily-fluid transferred to the fluid reservoir 470 is a predetermined amount of fluid. For example, in some embodiments, the transfer device 400 can be configured to transfer bodily-fluid until the pressure within the fluid reservoir 470 is equilibrium with the pressure of the portion of the body in which the lumen-defining device is disposed (e.g., the vein). In such embodiments, the equalizing of the pressure between the fluid reservoir 470 and the portion of the body stops the flow of the bodily-fluid into the fluid reservoir 470. In some embodiments, the predetermined amount of bodily-fluid (e.g., volume) is at least equal to the combined volume of the inlet lumen 423, the first lumen 438, the first outlet lumen 425, and the lumen-defining device.

[1148] As described above, the transfer device 400 is moved from the first configuration to the second configuration by further moving the plunger 448 in the distal direction. As the plunger 448 is moved from the first configuration toward the second configuration, the protrusions 447 of the activation extension 446 further engage the activation protrusions 432 included in the first control member 431 to move the flow control mechanism 430 to the second configuration, as indicated by the arrow **PP** in FIG. 26. In this manner, the flow control mechanism 430 is moved to the second configuration, and the first lumen 438 is fluidically isolated from the inlet lumen 423 and the first outlet lumen 425. In addition, the second lumen 439 defined by the second control member 435 is placed in fluid communication with the inlet lumen 423 defined by the inlet port 422 and the second outlet lumen 427 defined by the second outlet port 426.

[1149] As shown by the arrow **QQ** in FIG. 27, the inlet lumen 423 of the inlet port 422, the second lumen 439 of the second control member 435, and the second outlet lumen 427 of the second outlet port 426 define a fluid flow path such that the external reservoir (not shown in FIG. 19) is in fluid communication with the inlet port 422 and, therefore, the portion of the patient (e.g., the vein). Furthermore, the external reservoir is configured to define a negative pressure (e.g., the known external reservoirs referred to herein are vessels defining a negative

pressure). The negative pressure within the external reservoir is such that the negative pressure differential between the external reservoir and the portion of the body of the patient introduces a suction force within the portion of the patient. In some embodiments, the user can engage throttling button 445 to again increase the friction between the second control member 435 and the walls defining the inner volume 411. In this manner, further expansion of the spring 461 is limited and a desired amount of bodily-fluid can be drawn into the external reservoir such that the desired amount of bodily fluid is fluidically isolated from the first, predetermined amount of bodily-fluid contained within the fluid reservoir 470.

[1150] The bodily-fluid contained in the external reservoir is substantially free from microbes generally found outside of the portion of the patient (e.g., dermally-residing microbes, microbes within a lumen defined by the transfer device 400, microbes within the lumen defined by the lumen defining device, and/or any other undesirable microbe). In some embodiments, with the desired amount of bodily-fluid contained in the external fluid reservoir, the user can disengage the throttling button 445 such that the transfer device returns to the storage configuration. As described above, in this configuration the actuator mechanism 440 can place the flow control mechanism 430 in a third configuration configured to fluidically isolate the first lumen 438 and the second lumen 439 from the inlet lumen 423, the first outlet lumen 425, and the second outlet lumen 427. Thus, the bodily-fluid contained within the fluid reservoir 470 is fluidically isolated from a volume outside the fluid reservoir 470 and the external reservoir can be decoupled from the transfer device 400.

[1151] While the transfer device 400 is described above with reference to FIGS. 20-27 as being stored in a storage configuration, in some embodiments, a transfer device can be stored in a first configuration (e.g., defining a flow path between an inlet port and a fluid reservoir). For example, FIGS. 28 and 29 illustrate a transfer device 500 according to an embodiment. In some embodiments, aspects of the transfer device 500 can be substantially similar to corresponding aspects of the transfer device 200. In this manner, details of certain aspects are not described in further detail herein and it should be understood that such aspects are substantially similar in form or function to the corresponding aspects.

[1152] The transfer device 500 includes a housing 501, a diverter 520, a flow control mechanism 530, and an actuator 540. The housing 501 includes a proximal end portion 502 and a distal end portion 503. The proximal end portion 502 defines an inner volume configured to receive at least a portion of the actuator mechanism 540, as described in further

detail herein. The distal end portion 503 of the housing 501 includes the diverter 520. Similarly stated, the diverter 520 is monolithically formed with the distal end portion 503 of the housing 501. The diverter 520 receives at least a portion of the flow control mechanism 530, as described in further detail herein.

[1153] As shown in FIG. 28, the diverter 520 includes an inlet port 522, a first outlet port 524, and a second outlet port 526, and defines an inner volume 521. The inner volume 521 is configured to receive at least a portion of the flow control mechanism 530, as further described herein. The inlet port 522 of the diverter 520 defines an inlet lumen 523. The inlet lumen 523 is configured to be in fluid communication with the inner volume 521. Similarly stated, the inlet lumen 523 of the inlet port 522 extends through a wall defining the inner volume 521 of the diverter 520.

[1154] The flow control mechanism 530 includes a first control member 531 and a second control member 535. At least a portion of the flow control mechanism 530 is configured to be disposed within the inner volume 521 defined by the diverter 520. In this manner, the flow control mechanism 530 defines a circular cross-sectional shape such that when the flow control mechanism 530 is disposed within the inner volume 521, a portion of the flow control mechanism 530 forms a friction fit with the walls of the diverter 520 defining the inner volume 521, as described further detail herein.

[1155] The first control member 53 is configured to engage an activation extension 546 of the actuator mechanism 540 and move between a first configuration and a second configuration. The second control member 535 defines a first lumen 538 and a second lumen 539and is configured to be coupled to the first control member 531. Therefore, the second control member 535 is configured to move concurrently with the first control member 531 when the activation extension 546 engages the first control member 531. Similarly stated, the flow control mechanism 530 is moved between the first configuration and the second configuration when the first control member 531 and the second control member 535 are moved between the first configuration and the second configuration, respectively. Furthermore, when the flow control mechanism 530 is in the first configuration, the first lumen 538 is placed in fluid communication with the inlet lumen 523 defined by the inlet port 522 and the first outlet lumen 525 defined by the first outlet port 524. When the flow control mechanism 530 is in the second configuration, the second lumen 539 is placed in fluid

communication with the inlet lumen 523 defined by the inlet port 522 and the second outlet lumen 527 defined by the second outlet port 526, as described in further detail herein.

[1156] The actuator mechanism 540 is configured to move between a first configuration and a second configuration, thereby moving the transfer device 500 between a first configuration and a second configuration, as described in further detail herein. The actuator mechanism 540 includes a plunger 548 and the activation extension 546. The plunger 548 includes a proximal end portion 549, a distal end portion 550, and an engagement portion 544 and is configured to be disposed, at least partially within the inner volume 511 of the housing 501. The engagement portion 544 is configured to extend in the distal direction from the proximal end portion 549 of the plunger 548. In this manner, the engagement portion 544 can be engaged by a user to move the actuator mechanism 540 between the first configuration and the second configuration, as described in further detail herein.

[1157] The distal end portion 550 of the plunger 548 includes a seal member 554 configured to define a friction fit with the inner surface of the walls defining the inner volume 511. Similarly stated, the seal member 554 defines a fluidic seal with the inner surface of the walls defining the inner volume 511 such that a portion of the inner volume 511 proximal of the seal member 554 is fluidically isolated from a portion of the inner volume 511 distal of the seal member 554. Furthermore, the portion of the inner volume 511 distal of the seal member 554 defines a fluid reservoir 570. Similarly stated, the fluid reservoir 570 defined by the walls defining the inner volume 511 and the seal member 554 of the plunger 548.

[1158] The activation extension 546 includes a protrusion 547 configured to selectively engage the proximal end portion 549 of the plunger 548. In this manner, the proximal end portion 549 of the plunger 548 can move the activation extension 546 when the plunger 548 moves from a first configuration to a second configuration, as further described herein.

[1159] As described above, the transfer device 500 is stored in the first configuration in which the first lumen 538 of the second control member 535 is in fluid communication with the inlet port 522 and the first outlet port 524. In such embodiments, the friction fit defined by the second control member 535 and the walls of the diverter 520 defining the inner volume 521 maintain the flow control mechanism 530 in the first configuration until the actuator 540 moves the flow control mechanism 530 to the second configuration.

[1160] In use, a user can engage the transfer device 500 to couple the inlet port 522 to a proximal end portion of a lumen-defining device (not shown) such as, for example, a butterfly needle. With the inlet port 522 coupled to the lumen-defining device the inlet lumen 523 is placed in fluid communication with the lumen defined by the lumen-defining device. Furthermore, the distal end portion of the lumen-defining device can be disposed within a portion of the body of a patient (e.g., a vein), thus, the inlet lumen 523 is in fluid communication with the portion of the body of the patient. In a similar manner, the second outlet port 526 can be coupled to an external fluid reservoir (not shown).

[1161] With the inlet port 522 coupled to the lumen-defining device and the second outlet port 526 coupled to the external fluid reservoir, a user can begin the transfer of a bodily-fluid by applying an activation force to the engagement portion 544 of the actuator 540, thereby moving the plunger 548 in the distal direction, as shown by the arrow **RR** in FIG. 28. More specifically and as described above, the plunger 548 engages the inner surface of the walls defining the inner volume 511 such that the volume of the fluid reservoir 570 is increased (e.g., as defined by the plunger 548 and the housing 501). With the fluid reservoir 570 being fluidically isolated (as described above) from a volume on the proximal side of the seal member 554, the increase in the volume of the fluid reservoir 570 produces a negative pressure within the fluid reservoir 570. Moreover, with the flow control mechanism 530 in the first configuration, negative pressure differential introduces a suction force within the first lumen 538, the inlet lumen 523, and the first outlet lumen 525.

[1162] As shown by the arrow **SS**, the inlet lumen 523 of the inlet port 522, the first lumen 538 of the second control member 535, and the first outlet lumen 525 of the first outlet port 524 define a fluid flow path such that the second portion 576 of the inner volume 573 defined by the fluid reservoir 570 is in fluid communication with the inlet port 522. Furthermore, with the inlet port 522 coupled to the lumen-defining device the fluid reservoir 570 is in fluid communication with the portion of the patient (e.g., the vein) and at least a portion of the suction force is introduced to the portion of the patient. In this manner, a bodily-fluid is drawn into the fluid reservoir 570. In some embodiments, the bodily-fluid can contain undesirable microbes such as, for example, dermally-residing microbes dislodged during the insertion of the lumen-defining device.

[1163] As shown in FIG. 28, the actuator mechanism 540 is configured such that the proximal end portion 549 of the plunger 548 is spaced apart from the protrusion 547 of the

activation extension 546. In this manner, the plunger 548 can move in the proximal direction without engaging the protrusion 547 of the activation extension 546. Thus, the plunger 548 can move to introduce the change of the volume in the fluid reservoir 570 without the activation extension 546 moving the first control member 531 from the first configuration toward the second configuration. Therefore, the transfer device 500 can be stored in the first configuration, as described above.

[1164] With a desired amount of bodily-fluid transferred to the fluid reservoir 570, a user can move the transfer device 500 from the first configuration to the second configuration, wherein a flow of bodily-fluid is transferred to the external reservoir (e.g., such as those described above). In some embodiments, the desired amount of bodily-fluid transferred to the fluid reservoir 570 is a predetermined amount of fluid. For example, in some embodiments, the transfer device 500 can be configured to transfer bodily-fluid until the pressure within the fluid reservoir 570 is equilibrium with the pressure of the portion of the body in which the lumen-defining device is disposed (e.g., the vein). In such embodiments, the equalizing of the pressure between the fluid reservoir 570 and the portion of the body stops the flow of the bodily-fluid into the fluid reservoir 570. In some embodiments, the predetermined amount of bodily-fluid (e.g., volume) is at least equal to the combined volume of the inlet lumen 523, the first lumen 538, the first outlet lumen 525, and the lumen-defining device.

[1165] As shown in FIG. 29, the transfer device 500 can be moved from the first configuration to the second configuration by further moving the actuator mechanism 540 in the distal direction, as indicated by the arrow **TT**. As the actuator mechanism 540 is moved from the first configuration toward the second configuration, the protrusions 547 of the activation extension 546 is engaged by the proximal end portion 549 of the plunger 548 such that the activation extension 546 is moved in the direction **TT**. Furthermore, the proximal motion of the activation extension 546 moves the first control member 331 and places the flow control mechanism 530 in the second configuration, as indicated by the arrow **UU**. In this manner, the first lumen 538 is fluidically isolated from the inlet lumen 523 and the first outlet lumen 525. In addition, the second lumen 539 defined by the second control member 535 is placed in fluid communication with the inlet lumen 523 defined by the inlet port 522 and the second outlet lumen 527 defined by the second outlet port 526.

[1166] As shown by the arrow **VV**, the inlet lumen 523 of the inlet port 522, the second lumen 539 of the second control member 535, and the second outlet lumen 527 of the second

outlet port 526 define a fluid flow path such that the external reservoir (not shown in FIGS. 28 and 29) is in fluid communication with the inlet port 522 and, therefore, the portion of the patient (e.g., the vein). Furthermore, the external reservoir is configured to define a negative pressure (e.g., the known external reservoirs referred to herein are vessels defining a negative pressure). The negative pressure within the external reservoir is such that the negative pressure differential between the external reservoir and the portion of the body of the patient introduces a suction force within the portion of the patient. Therefore, a desired amount of bodily-fluid is drawn into the external reservoir and is fluidically isolated from the first, predetermined amount of bodily-fluid contained within the fluid reservoir 570.

[1167] The bodily-fluid contained in the external reservoir is substantially free from microbes generally found outside of the portion of the patient (e.g., dermally residing microbes, microbes within a lumen defined by the transfer device 500, microbes within the lumen defined by the lumen defining device, and/or any other undesirable microbe). As described above, the bodily-fluid contained within the fluid reservoir 570 is fluidically isolated from a volume outside the fluid reservoir 570 and the external reservoir can be decoupled from the transfer device 500.

[1168] While some embodiments described above include a flow control mechanism that can be rotated to control the flow of a bodily-fluid (e.g., the flow rate) and/or to control the amount of negative pressure within a fluid reservoir, in other embodiments, bodily-fluid transfer device can include any suitable device, mechanism, and/or assembly that can control, at least partially, a flow of bodily-fluid (e.g., the flow rate of the bodily-fluid). For example, FIGS. 30-41 illustrate a transfer device 600 according to an embodiment. The transfer device 600 includes a housing 601, a diverter 620, a flow control mechanism 630, and adjustment mechanism 685, and an actuator 640. The transfer device 600 can be any suitable shape, size, or configuration. For example, the transfer device 600 can have a shape and size that is substantially similar to the transfer device 200 described above with reference to FIGS. 2-12. As such, portions of the transfer device 600 can be substantially similar in form and/or function to corresponding portions of the transfer device 200 of FIGS. 2-12. Thus, aspects of the transfer device 600 are not described in further detail herein.

[1169] The housing 601 of the transfer device 600 includes a proximal end portion 602 and a distal end portion 603. The distal end portion 603 includes a base 606 from which a set of walls 604 extend. The walls 604 of the housing 601 define a substantially annular shape

and define an inner volume 611 between the proximal end portion 602 and the distal end portion 603. The proximal end portion 602 of the housing 601 is open to receive at least a portion of the diverter 620, a portion of the flow control mechanism 630, and a portion of the actuator 640 within the inner volume 611 (see e.g., FIG. 31). The walls 604 of the housing 601 define a set of status windows 610 and a set of channels 605. The status windows 610 and the channels 605 can be any suitable shape or size. For example, the status windows 610 and the channels 605 can be substantially similar in form and function to the status windows 210 and the channels 205 of the transfer device 200.

[1170] As shown in FIGS. 32 and 33, the housing 601 includes a set of guide posts 607 and a set of flow control protrusions 608 and defines a passageway 614. The guide posts 607 engage a portion of the diverter 620 and a portion of the actuator 640, as further described herein. The flow control protrusions 608 extend from the base 606 in the proximal direction and can be arranged to selectively engage a portion of the flow control mechanism 630 to move the flow control mechanism 630 between a first configuration and a second configuration, as described in further detail herein. While only one flow control protrusion 608 is shown in FIGS. 32 and 33, the housing 601 can include, for example, two flow control protrusions 608 that are disposed adjacent to a guide post 607. As shown in FIG. 33, the passageway 614 extends through the base 606 and can be arranged to receive a portion of the flow control mechanism 630, as described in further detail herein.

[1171] As shown in FIG. 31, the actuator mechanism 640 includes the actuator housing 662, a plunger 648, and a cap 655. The actuator mechanism 640 is configured to move between a first configuration and a second configuration, thereby moving the transfer device 600 between a first configuration and a second configuration, as described in further detail herein. The actuator housing 662 includes a proximal end portion 663 and a distal end portion 664 and defines an inner volume 665. The inner volume 665 of the actuator housing 662 receives the plunger 648 and at least a portion of the cap 655. The plunger 648 includes a set of seal member 654 that can form a friction fit with an inner surface (not shown in FIG. 31) of the actuator housing 662 that defines the inner volume 665 of the actuator housing 662. Thus, the plunger 648 can be configured to divide the inner volume 665 into a first portion 667 that is fluidically isolated from a second portion 670 (also referred to herein as "fluid reservoir"). The cap 655 defines an inlet port 658 and a set of guide post ports 659. The inlet port 658 receives a portion of a first outlet port 624 of the diverter 620. The guide

post ports 659 movably receive the guide posts 607 of the housing 601 to allow the guide posts 607 to be in contact with the plunger 648. In this manner, the actuator housing 662, the plunger 648, and the cap 655 of the actuator mechanism 640 can be substantially similar to or the same as the actuator housing 262, the plunger 248, and the cap 255, respectively, of the actuator mechanism 640 included in the transfer device 200 described above with reference to FIGS. 2-12. Thus, aspects of the actuator housing 662, the plunger 648, and the cap 655 are not described in further detail herein. As shown in FIG. 31, the actuator mechanism 640 can differ from the actuator mechanism 240 in that the actuator mechanism 640 does not include a spring such as the spring 261 of the actuator mechanism 240. In other embodiments, however, the actuator mechanism 640 can include a spring that is substantially similar to the spring 261.

[1172] As shown in FIGS. 34 and 35, the diverter 620 of the transfer device 600 includes a proximal end portion 628 and a distal end portion 629 and defines an inner volume 621. The inner volume 621 can receive at least a portion of the flow control mechanism 630, as described above with reference to the transfer device 200. The proximal end portion 628 of the diverter 620 includes a first outlet port 624. The distal end portion 629 includes an inlet port 622 and a second outlet port 626. The diverter 620 is movably disposed within the inner volume 611 of the housing 601 such that a portion of the inlet port 622 extends through a first channel 605 defined by the walls 604 of the housing 601 and a portion of the second outlet port 626 extends through a second channel 605 opposite the first channel (see e.g., FIG. 30). While not explicitly shown in FIGS. 30-41, the distal end portion 629 of the diverter 620 can engage the guide posts 607 to limit, for example, lateral movement of the diverter 620 as the diverter 620 is moved in the inner volume 611. Similarly stated, the guide posts 607 of the housing 601 can engage the diverter 620 to substantially limit its movement to a proximal direction or distal direction relative to the housing 601, as further described herein.

[1173] As shown in FIG. 35, the inlet port 622, the first outlet port 624, and the second outlet port 626 define an inlet lumen 623, a first outlet lumen 625, and a second outlet lumen 627, respectively, that are each in fluid communication with the inner volume 621. The inlet port 622 can be fluidically coupled to a needle or other lumen-containing device (not shown in FIGS. 30-41) that can be disposed within a portion of a body of the patient (e.g., within a vein of the patient), the first outlet port 624 can be fluidically coupled to a portion of the actuator 640, and the second outlet port 626 can be fluidically coupled to an external

reservoir (e.g., a sample reservoir not shown in FIGS. 30-41). In this manner, the diverter 620 can be arranged to selectively place the portion of the actuator 640 or the external reservoir in fluid communication with the portion of the body via the inlet port 622 and the first outlet port 624 or via the inlet port 622 and the second outlet port 626, respectively. As shown in FIG. 35, the diverter 620 also defines an opening 689 that can receive a portion of the flow control mechanism 630, as described in further detail herein.

[1174] As shown in FIGS. 36 and 37, the flow control mechanism 630 includes a first activation mechanism 631A, a second activation mechanism 631B, a control member 635, and an adjustment mechanism 685. At least a portion of the flow control mechanism 630 is configured to be disposed within the inner volume 621 defined by the diverter 620. More specifically, the flow control mechanism 630 has a circular cross-sectional shape such that when the flow control mechanism 630 is disposed in the inner volume 621, a portion of the control member 635 forms a friction fit with the walls of the diverter 620 defining the inner volume 621, as described in further detail herein. Although not shown in FIGS. 30-41, the flow control mechanism 630 can be arranged within the inner volume 611 of the housing 601 and the inner volume 621 of the diverter 620 such that the first activation mechanism 631A and the second activation mechanism 631B are disposed adjacent to and in contact with the control member 635. More specifically, the first activation mechanism 631A and the second activation mechanism 631B can be in frictional contact with the control mechanism 635. In other embodiments, the first activation mechanism 631A and the second activation mechanism 631B can be coupled to the control member 635 via a mechanical fastener and/or an adhesive. In this manner, the first activation mechanism 631A and the second activation mechanism 631B can be moved concurrently to move the control member 635, as described in further detail herein.

[1175] The first activation mechanism 631A and the second activation mechanism 631B include a set of engagement members 634A and 634B, respectively (although only one engagement member 634B is shown in FIG. 36, the second activation mechanism 631B is arranged in similar manner as the first activation mechanism 631A). The engagement members 634A and 634B are configured to engage the flow control protrusion 608 of the housing 601. For example, the diverter 620 and the flow control mechanism 630 can be moved within the inner volume 611 of the housing 601 to place the engagement members 634A and 634B in contact with the flow control protrusions 608. Moreover, once the

engagement members 634A and 634B are placed in contact with the flow control protrusions 608, further movement of the diverter 620 and the flow control mechanism 630 can rotate the flow control mechanism 630 relative to the diverter 620 between a first configuration and a second configuration, as described in further detail herein.

[1176] As shown in FIG. 37, the control member 635 defines a first lumen 638, a second lumen 639, and a set of channels 637. The channels 637 can be configured to receive a portion of the adjustment mechanism 685, as described in further detail herein. The flow control mechanism 630 can be arranged such that when in its first configuration, the first lumen 638 is placed in fluid communication with the inlet lumen 623 defined by the inlet port 622 and the first outlet lumen 625 defined by the first outlet port 624. Similarly, when the flow control mechanism 630 is in the second configuration, the second lumen 639 is placed in fluid communication with the inlet lumen 623 defined by the inlet port 622 and the second outlet lumen 627 defined by the second outlet port 626. Therefore, the flow control mechanism 630 can be rotated relative to the diverter 620 to selectively place the first outlet port 624 or the second outlet port 626 in fluid communication with the inlet port 622.

[1177] The adjustment mechanism 685 includes a dial 686 and an adjustment member 688 (see e.g., FIG. 31). In some embodiments, the adjustment member 688 can be, for example, a screw or the like. As shown in FIG. 30, the adjustment mechanism 685 can be disposed adjacent to the base 606 of the housing 601. More specifically, the dial 686 includes a receiving portion 686A that can be inserted into the passageway 614 defined by the base 606. In this manner, a coupler 687 (e.g., a retaining ring or the like) can be positioned about the receiving portion 686 to limit movement of the dial 686 relative to the base 606. For example, the coupler 687 can be configured to limit translational movement of the dial 686 relative to the base 606 while allowing rotational movement of the dial 686 relative to the base 606. The adjustment mechanism 685 can be arranged such that at least a portion of the adjustment member 688 is movably disposed in the opening 689 defined by the diverter 620. For example, the adjustment member 688 and a set of walls defining the opening 689 of the diverter 620 can define a threaded coupling. Thus, the adjustment member 688 can be rotated relative to the diverter 620 and, as such, the adjustment member 688 can be moved in a translation motion (e.g., proximal or distal direction) relative to the diverter 620. For example, a portion of the adjustment member 688 (e.g., a head of a bolt or screw) can be disposed within the receiving portion 686A of the dial 686 such that as the dial

686 is rotated relative to the housing 601, the adjustment member 688 is rotated relative to the diverter 620. Moreover, a portion of the adjustment member 688 can be disposed within one of the channels 637 of the control member 635. As such, the adjustment mechanism 685 can be manipulated to advance the adjustment member 688 relative to the diverter 620 to place the adjustment member 688 in contact with an engagement surface 636 of the control member 635 (see e.g., FIG. 37). In this manner, the movement of the adjustment member 688 can exert a force on the engagement surface 636 that can be sufficient to deform, bend, or otherwise reconfigure a wall of the control member 635 defining either the first lumen 638 or the second lumen 639, as described in further detail herein.

[1178] In some embodiments, the transfer device 600 can be stored in a storage configuration (e.g., a first configuration) in which the control member 635 of the flow control mechanism 630 fluidically isolates the inlet port 622, the first outlet port 624, and the second outlet port 626 from the inner volume 621 defined by the diverter 620. In such embodiments, first lumen 638 and the second lumen 639 are fluidically isolated from the inlet lumen 623, the first outlet lumen 625, and the second outlet lumen 627, as shown in FIG. 38. Furthermore, the friction fit defined by the control member 635 and the walls of the diverter 620 defining the inner volume 621 maintain the flow control mechanism 630 in the storage configuration until the flow control mechanism 630 is moved from the storage configuration.

[1179] In use, a user can manipulate the transfer device 600 to couple the inlet port 622 to a proximal end portion of a lumen-defining device (not shown) such as, for example, a butterfly needle. The distal end portion of the lumen-defining device can be disposed within a portion of the body of a patient (e.g., a vein), thereby placing the inlet lumen 623 in fluid communication with the portion of the body of the patient. In a similar manner, the second outlet port 626 can be coupled to an external fluid reservoir (not shown). The external fluid reservoir can be any suitable reservoir. For example, in some embodiments, the external fluid reservoir can be a BacT/ALERT® SN or a BacT/ALERT® FA, manufactured by BIOMERIEUX, INC.

[1180] With the inlet port 622 coupled to the lumen-defining device and the second outlet port 626 coupled to the external fluid reservoir, a user can move the transfer device 600 from the first configuration to a second configuration by applying an activation force to the actuator mechanism 640. In this manner, at least a portion of the actuator mechanism 640, the diverter 620, and the flow control mechanism 630 are moved in the distal direction

toward the second configuration, as indicated by the arrow **WW** in FIG. 39. More specifically and as described above, the arrangement of the plunger 648 and the guide posts 607 is such that as the user applies the activation force to the actuator mechanism 640, the position of the plunger 648, relative to the housing 601, is maintained. Therefore, the activation force applied by the user moves the actuator housing 662, the cap 655, the diverter 620, and the flow control mechanism 630 in the direction of the arrow **WW**, but not the plunger 648. The distal movement of the actuator housing 662 is such that the height of the first portion 667 of the inner volume 665 is reduced and the height of the fluid reservoir 670 is increased. With the fluid reservoir 670 being fluidically isolated (as described above) the increase in the height (i.e., the increase in volume) produces a negative pressure within the fluid reservoir 670. Said another way, the movement of the plunger 648 increases the volume of the fluid reservoir 670, which, in turn, produces a negative pressure therein.

[1181] As the actuator mechanism 640 is moved from the storage configuration toward the first configuration, the flow control protrusions 608 engage the engagement members 634A and 634B of the first activation mechanism 631A and the second activation member 631B, respectively, (not shown in FIG. 39) to move the flow control mechanism 630 toward the first configuration, as indicated by the arrow **XX** in FIG. 39. Thus, when the flow control mechanism 630 is moved to its first configuration, the first lumen 638 defined by the control member 635 is placed in fluid communication with the inlet lumen 623 defined by the inlet port 622 and the first outlet lumen 625 defined by the first outlet port 624. As indicated by the arrow **YY** in FIG. 39, the inlet lumen 623 of the inlet port 622, the first lumen 638 of the control member 635, and the first outlet lumen 625 of the first outlet port 624 define a fluid flow path such that the fluid reservoir 670 defined by the actuator housing 662 is placed in fluid communication with the inlet port 622. Thus, the negative pressure within the fluid reservoir 670 is such that the negative pressure differential introduces a suction force within the portion of the patient. In this manner, a bodily-fluid is drawn into the fluid reservoir 670 of the actuator housing 662, as indicated by the arrow **YY**. In some embodiments, the bodily-fluid can contain undesirable microbes such as, for example, dermally-residing microbes. In some instances, the magnitude of the suction force can be modulated by increasing or decreasing the amount of activation force applied to the actuator mechanism 640. In this manner, the change in the volume of the fluid reservoir 670 can be modulated such that a desired amount of a suction force is exerted within the vein of the patient.

[1182] With the desired amount of bodily-fluid transferred to the fluid reservoir 670 defined by the actuator housing 662, a user can manipulate the transfer device 600 to move the transfer device 600 from the second configuration to the third configuration, wherein a flow of bodily-fluid is transferred to the external reservoir (e.g., such as those described above). In some embodiments, the desired amount of bodily-fluid transferred to the actuator housing 662 is a predetermined amount of fluid, as described in detail above.

[1183] The transfer device 600 can be moved from the second configuration to the third configuration by further moving the actuator mechanism 640 in the distal direction, as indicated by the arrow **ZZ** in FIG. 40. Expanding further, the user can apply an activation force to the actuator mechanism 640 such that the actuator housing 662, the cap 655, the diverter 620, and the flow control mechanism 630 move in the distal direction. With the desired amount of the bodily-fluid disposed within the fluid reservoir 670 the volume of the fluid reservoir 670 is configured to remain constant as the actuator housing 662 and the cap 655 move relative to the plunger 648. Similarly stated, the pressure of the fluid reservoir 670 is configured to remain substantially unchanged as the transfer device 600 is moved from the first configuration to the second configuration. As the actuator mechanism 640 is moved from its first configuration toward its second configuration, the flow control protrusions 608 engage the engagement members 634A and 634B to rotate the flow control mechanism 630 toward the second configuration, as indicated by the arrow **AAA**. Thus, when the flow control mechanism 630 is moved to its second configuration, the second lumen 639 defined by the control member 635 is placed in fluid communication with the inlet lumen 623 defined by the inlet port 622 and the second outlet lumen 627 defined by the second outlet port 626.

[1184] As shown by the arrow **BBB**, the inlet lumen 623 of the inlet port 622, the second lumen 639 of the control member 635, and the second outlet lumen 627 of the second outlet port 626 define a fluid flow path such that the external reservoir (not shown in FIG. 40) is in fluid communication with the inlet port 622 and, therefore, the portion of the patient (e.g., the vein). Furthermore, the external reservoir is configured to define a negative pressure (e.g., the known external reservoirs referred to herein are vessels defining a negative pressure). The negative pressure within the external reservoir is such that the negative pressure differential between the external reservoir and the portion of the body of the patient introduces a suction force within the portion of the patient. Therefore, a desired amount of bodily-fluid can be drawn into the external reservoir that is fluidically isolated from the first,

predetermined amount of bodily-fluid contained within the fluid reservoir 670 defined by the actuator housing 662. In this manner, the bodily-fluid contained in the external reservoir is substantially free from microbes generally found outside of the portion of the patient (e.g., dermally residing microbes, microbes within a lumen defined by the transfer device 600, microbes within the lumen defined by the lumen defining device, and/or any other undesirable microbe).

[1185] In some instances, it may be desirable to limit and/or modulate the amount of a suction force exerted on the vein of the patient and/or a flow rate of the bodily-fluid. In such instances, the user can manipulate the adjustment mechanism 685 to move the adjustment member 688 relative to the control member 635. For example, the distal movement of the diverter 620 relative to the housing 601 is such that a portion of the adjustment member 688 is disposed in the receiving portion 686A of the dial 686. In this manner, the dial 686 can be rotated to advance the adjustment member 688 relative to the control member 635, as indicated by the arrow **CCC** in FIG. 41. Thus, the adjustment member 688 can be moved into contact with the engagement surface 636 to deform a portion of the control member 635 defining the second lumen 639. As such, the wall of the control member 635 constricts the second lumen 639 (e.g., reduces a diameter of at least a portion of the second lumen 639), thereby reducing the suction force exerted within the vein and/or slowing the rate at which the bodily-fluid flows within the second lumen 639. In some embodiments, the dial 686 can be rotated in alternating directions to alternately move the adjustment member 688 in the proximal direction and the distal direction. In this manner, the flow of the bodily-fluid can be, for example, pulsed or the like. In this manner, bodily-fluid that is substantially free from microbes (e.g., dermally residing microbes or the like) can flow with a desired set of characteristics into the external reservoir.

[1186] While the transfer device 200 is described above with reference to FIGS. 2-12 as including a linear spring 261 (e.g., a compression spring), in other embodiments, a transfer device can include any suitable spring that can be configured to modulate, change, and/or control a negative pressure within a fluid reservoir and/or a flow rate of a bodily-fluid. For example, FIGS. 42-47 illustrate a transfer device 700 according to another embodiment. The transfer device 700 includes a housing 701, a diverter 720, a flow control mechanism 730, and adjustment mechanism 785, and an actuator 740. The transfer device 700 can be any suitable shape, size, or configuration. For example, portions of the transfer device 700 can be

substantially similar to or the same as corresponding portions of the transfer device 200 (described above with reference to FIGS. 2-12) and/or the transfer device 600 (described above with reference to FIGS. 30-41). As such, aspects of the transfer device 700 of the transfer device 700 are not described in further detail herein.

[1187] The housing 701 of the transfer device 700 includes a proximal end portion 702 and a distal end portion 703. The distal end portion 703 includes a base 706 from which a set of walls 704 extend. The walls 704 of the housing 701 define a substantially annular shape and define an inner volume 711 between the proximal end portion 702 and the distal end portion 703. The proximal end portion 702 of the housing 701 is open to receive at least a portion of the diverter 720, a portion of the flow control mechanism 730, and a portion of the actuator 740 within the inner volume 711 (see e.g., FIG. 31). The walls 704 of the housing 701 define a set of status windows 710 and a set of channels 705. The status windows 710 and the channels 705 can be any suitable shape or size. For example, the status windows 710 and the channels 705 can be substantially similar in form and function to the status windows 210 and the channels 205 of the transfer device 200. The housing 701 includes a set of guide posts 707 and a set of flow control protrusions (not shown in FIGS. 43-46). In this manner, the housing 701 can function similarly to the housing 601 included in the transfer device 600 described above.

[1188] As shown in FIG. 31, the actuator mechanism 740 includes the actuator housing 762, a plunger 748, and a cap 755. The actuator mechanism 740 is configured to move between a first configuration and a second configuration, thereby moving the transfer device 700 between a first configuration and a second configuration, as described in further detail herein. The actuator housing 762 includes a proximal end portion 763 and a distal end portion 764 and defines an inner volume 765. The inner volume 765 of the actuator housing 762 receives the plunger 748 and at least a portion of the cap 755. As such, the actuator mechanism 740 can be substantially similar in form and function as the actuator mechanism 640 included in the transfer device 600 described above with reference to FIGS. 30-41. Thus, the plunger 748 can be disposed in the actuator housing 762 to divide the inner volume 765 into a first portion 767 and a second portion 770 (also referred to herein as "fluid reservoir").

[1189] As shown in FIGS. 43, the diverter 720 of the transfer device 700 includes an inlet port 722, a first outlet port 724, and a second outlet port 726 and defines an inner volume 721. The inner volume 721 can receive at least a portion of the flow control mechanism 730,

as described above with reference to the transfer device 200. The diverter 720 is movably disposed within the inner volume 711 of the housing 701 such that a portion of the inlet port 722 extends through a first channel 705 defined by the walls 704 of the housing 701 and a portion of the second outlet port 726 extends through a second channel 705 opposite the first channel (see e.g., FIG. 42). While not explicitly shown in FIGS. 42-46, the distal end portion 729 of the diverter 720 can engage the guide posts 707 to limit, for example, lateral movement of the diverter 720 as the diverter 720 is moved in the inner volume 711. Similarly stated, the guide posts 707 of the housing 701 can engage the diverter 720 to substantially limit its movement to a proximal direction or distal direction relative to the housing 701, as further described herein.

[1190] The inlet port 722, the first outlet port 724, and the second outlet port 726 define an inlet lumen 723, a first outlet lumen 725, and a second outlet lumen 727, respectively, that are each in fluid communication with the inner volume 721 (see e.g., FIGS. 45 and 46). The inlet port 722 can be fluidically coupled to a needle or other lumen-containing device (not shown in FIGS. 30-41) that can be disposed within a portion of a body of the patient (e.g., within a vein of the patient), the first outlet port 724 can be fluidically coupled to a portion of the actuator 740, and the second outlet port 726 can be fluidically coupled to an external reservoir (e.g., a sample reservoir not shown in FIGS. 30-41). In this manner, the diverter 720 can be arranged to selectively place the portion of the actuator 740 or the external reservoir in fluid communication with the portion of the body via the inlet port 722 and the first outlet port 724 or via the inlet port 722 and the second outlet port 726, respectively.

[1191] As shown in FIG. 44, the flow control mechanism 730 includes a first activation mechanism 731A, a second activation mechanism 731B, a control member 735, a first torsion spring 761A, and a second torsion spring 761B. At least a portion of the flow control mechanism 730 is configured to be disposed within the inner volume 721 defined by the diverter 720, as described above. Although not shown in FIGS. 42-46, the flow control mechanism 730 can be arranged within the inner volume 711 of the housing 701 and the inner volume 721 of the diverter 720 such that the first activation mechanism 731A and the second activation mechanism 731B are disposed adjacent to and in contact with the control member 735. More specifically, the first activation mechanism 731A and the second activation mechanism 731B can be in frictional contact with the control mechanism 735. In other embodiments, the first activation mechanism 731A and the second activation

mechanism 731B can be coupled to the control member 735 via a mechanical fastener and/or an adhesive. In this manner, the first activation mechanism 731A and the second activation mechanism 731B can be moved concurrently to move the control member 735, as described in further detail herein.

[1192] The first activation mechanism 731A and the second activation mechanism 731B include a set of engagement members 734A and 734B, respectively (although only one engagement member 734B is shown in FIG. 36, the second activation mechanism 731B is arranged in similar manner as the first activation mechanism 731A). The engagement members 734A and 734B are configured to engage the flow control protrusion 708 of the housing 701, as described with reference to the transfer device 600 of FIGS. 30-41. In use, once the engagement members 734A and 734B are placed in contact with the flow control protrusions 708, further movement of the diverter 720 and the flow control mechanism 730 can rotate the flow control mechanism 730 relative to the diverter 720 between a first configuration and a second configuration. As such, the torsion springs 761A and 761B can be moved from a first configuration having a substantially smaller potential energy to a second configuration having a substantially larger potential energy. In other words, the rotational movement of the flow control mechanism 730 relative to the diverter 720 can transfer the torsion springs 761A and 761B to a configuration having a larger potential energy than the potential energy prior to the rotation of the flow control mechanism 730 relative to the diverter 720, as described in further detail herein.

[1193] As shown in FIG. 44, the control member 735 defines a first lumen 738, a second lumen 739. The flow control mechanism 730 can be arranged such that when in its first configuration, the first lumen 738 is placed in fluid communication with the inlet lumen 723 defined by the inlet port 722 and the first outlet lumen 725 defined by the first outlet port 724. Similarly, when the flow control mechanism 730 is in the second configuration, the second lumen 739 is placed in fluid communication with the inlet lumen 723 defined by the inlet port 722 and the second outlet lumen 727 defined by the second outlet port 726. Therefore, the flow control mechanism 730 can be rotated relative to the diverter 720 to selectively place the first outlet port 724 or the second outlet port 726 in fluid communication with the inlet port 722.

[1194] In some embodiments, the transfer device 700 can be stored in a storage configuration in which the control member 735 of the flow control mechanism 730 fluidically

isolates the inlet port 722, the first outlet port 724, and the second outlet port 726 from the inner volume 721 defined by the diverter 720. In such embodiments, first lumen 738 and the second lumen 739 are fluidically isolated from the inlet lumen 723, the first outlet lumen 725, and the second outlet lumen 727. Furthermore, the friction fit defined by the control member 735 and the walls of the diverter 720 defining the inner volume 721 maintain the flow control mechanism 730 in the storage configuration until the flow control mechanism 730 is moved from the storage configuration.

[1195] In use, a user can manipulate the transfer device 700 to couple the inlet port 722 to a proximal end portion of a lumen-defining device (not shown) such as, for example, a butterfly needle. The distal end portion of the lumen-defining device can be disposed within a portion of the body of a patient (e.g., a vein), thereby placing the inlet lumen 723 in fluid communication with the portion of the body of the patient. In a similar manner, the second outlet port 726 can be coupled to an external fluid reservoir (not shown). The external fluid reservoir can be any suitable reservoir. For example, in some embodiments, the external fluid reservoir can be a BacT/ALERT® SN or a BacT/ALERT® FA, manufactured by BIOMERIEUX, INC.

[1196] With the inlet port 722 coupled to the lumen-defining device and the second outlet port 726 coupled to the external fluid reservoir, a user can move the transfer device 700 from the first configuration to a second configuration by applying an activation force to the actuator mechanism 740. In this manner, at least a portion of the actuator mechanism 740, the diverter 720, and the flow control mechanism 730 are moved in the distal direction toward the second configuration, as indicated by the arrow **DDD** in FIG. 45. More specifically and as described above, the distal movement of the actuator housing 762 is such that a height of the first portion 767 of the inner volume 765 is reduced and a height of the fluid reservoir 770 is increased. With the fluid reservoir 770 being fluidically isolated (as described above) the increase in the height (i.e., the increase in volume) produces a negative pressure within the fluid reservoir 770. Said another way, the movement of the plunger 748 increases the volume of the fluid reservoir 770, which, in turn, produces a negative pressure therein.

[1197] As shown in FIG. 45, when the flow control mechanism 730 is moved to its first configuration (e.g., from a storage configuration), the first lumen 738 defined by the control member 735 is placed in fluid communication with the inlet lumen 723 defined by the inlet

port 722 and the first outlet lumen 725 defined by the first outlet port 724. As indicated by the arrow **EEE** in FIG. 45, the inlet lumen 723 of the inlet port 722, the first lumen 738 of the control member 735, and the first outlet lumen 725 of the first outlet port 724 define a fluid flow path such that the fluid reservoir 770 defined by the actuator housing 762 is placed in fluid communication with the inlet port 722. Thus, the negative pressure within the fluid reservoir 770 is such that the negative pressure differential introduces a suction force within the portion of the patient. In this manner, a bodily-fluid is drawn into the fluid reservoir 770 of the actuator housing 762, as indicated by the arrow **EEE**. In some embodiments, the bodily-fluid can contain undesirable microbes such as, for example, dermally-residing microbes.

[1198] In some instances, the magnitude of the suction force can be modulated by increasing or decreasing the amount of activation force applied to the actuator mechanism 740. More specifically and as described above, the rotational movement of the flow control mechanism 730 can increase the potential energy of the torsion springs 761A and 761B (not shown in FIG. 45). For example, in some embodiments, an end portion of the torsion springs 761A and 761B can be placed in contact with the flow control protrusions 708 to substantially limit the movement of the end portion of the torsion springs 761A and 761B. Thus, the rotational movement of the first activation mechanism 731A and the second activation mechanism 731B rotates a second end portion of the torsion springs 761A and 761B, respectively, relative to the end portion in contact with the flow control protrusions 708, thereby changing the potential energy of the torsion springs 761A and 761B. In this manner, the torsion springs 761A and 761B can exert a reaction force that can resist the activation force applied to the user on the actuator mechanism 740. Therefore, by reducing the activation force, the flow control mechanism 730 can rotate relative to the diverter 720 to change the alignment of the first lumen 738 of the control member 735 relative to the inlet lumen 723 and the first outlet lumen 725 of the diverter 720. As such, the negative pressure within the fluid reservoir 770 can be reduced and/or otherwise changed.

[1199] With the desired amount of bodily-fluid transferred to the fluid reservoir 770 defined by the actuator housing 762, a user can manipulate the transfer device 700 to move the transfer device 700 from the second configuration to the third configuration, wherein a flow of bodily-fluid is transferred to the external reservoir (e.g., such as those described above). In some embodiments, the desired amount of bodily-fluid transferred to the actuator

housing 762 is a predetermined amount of fluid, as described in detail above. The transfer device 700 can be moved from the first configuration to the second configuration by further moving the actuator mechanism 740 in the distal direction, as indicated by the arrow **FFF** in FIG. 46. Expanding further, the user can apply an activation force to the actuator mechanism 740 such that the actuator housing 762, the cap 755, the diverter 720, and the flow control mechanism 730 move in the distal direction. As the actuator mechanism 740 is moved from its first configuration toward its second configuration, the flow control protrusions 708 engage the engagement members 734A and 734B to rotate the flow control mechanism 730 toward the second configuration, as indicated by the arrow **GGG**. Thus, when the flow control mechanism 730 is moved to its second configuration, the second lumen 739 defined by the control member 735 is placed in fluid communication with the inlet lumen 723 defined by the inlet port 722 and the second outlet lumen 727 defined by the second outlet port 726.

[1200] As shown by the arrow **HHH** in FIG. 46, the inlet lumen 723 of the inlet port 722, the second lumen 739 of the control member 735, and the second outlet lumen 727 of the second outlet port 726 define a fluid flow path such that the external reservoir (not shown in FIG. 46) is in fluid communication with the inlet port 722 and, therefore, the portion of the patient (e.g., the vein). Furthermore, the external reservoir is configured to define a negative pressure (e.g., the known external reservoirs referred to herein are vessels defining a negative pressure). The negative pressure within the external reservoir is such that the negative pressure differential between the external reservoir and the portion of the body of the patient introduces a suction force within the portion of the patient. Therefore, a desired amount of bodily-fluid can be drawn into the external reservoir that is fluidically isolated from the first, predetermined amount of bodily-fluid contained within the fluid reservoir 770 defined by the actuator housing 762. In this manner, the bodily-fluid contained in the external reservoir is substantially free from microbes generally found outside of the portion of the patient (e.g., dermally residing microbes, microbes within a lumen defined by the transfer device 700, microbes within the lumen defined by the lumen defining device, and/or any other undesirable microbe).

[1201] In some instances, it may be desirable to limit and/or modulate the amount of a suction force exerted on the vein of the patient and/or a flow rate of the bodily-fluid. In such instances, the user can decrease the activation force applied to the actuator mechanism 740. In this manner, the torsion springs 761A and 761B can exert a force that is operable in

rotating the control member 735 relative to the diverter 720. Thus, the flow control mechanism 730 can rotate relative to the diverter 720 to change the alignment of the first lumen 738 of the control member 735 relative to the inlet lumen 723 and the first outlet lumen 725 of the diverter 720. As such, the negative pressure within the fluid reservoir 770 can be reduced, modulated, pulsed and/or otherwise changed.

[1202] Referring now to FIG. 47, a flowchart illustrates a method 1000 for parenterally procuring a bodily-fluid sample that is substantially free from microbes. In some embodiments, the method 1000 includes inserting a needle of a parenteral sampling device into a patient, at 1001. In some embodiments, the parenteral sampling device can be, for example, a fluid transfer device such as those described herein. As such, the parenteral sampling device (also referred to herein as "device") can include at least the needle, an actuator, a flow control mechanism, and a fluid reservoir. As described above with reference to the transfer devices 100, 200, 300, 400, 500, 600, and/or 700, the device can be configured to selectively place the needle in fluid communication with the fluid reservoir.

[1203] The method 1000 includes establishing fluid communication between the needle and the fluid reservoir, at 1002. For example, in some embodiments, the device can be in a storage configuration prior to use in which the needle is fluidically isolated from the fluid reservoir. Therefore, in use, the device can be manipulated to define a fluid flow path between the needle and the fluid reservoir. In some embodiments, for example, the device can be manipulated to arrange the flow control mechanism included in the device in a first configuration such that the flow control mechanism defines at least a portion of the fluid flow path. For example, the flow control mechanism can be substantially similar to the flow control mechanism 230 included in the transfer device 200 described above with reference to FIGS. 2-12.

[1204] With the flow path defined between the needle and the fluid reservoir, an actuator is moved a first distance to create a negative pressure in the fluid reservoir and to withdraw a predetermined volume of bodily-fluid, at 1003. For example, in some embodiments, a user can exert an activation force on the actuator to move the actuator relative to a portion of the device. In such embodiments, the actuator can include a plunger or the like that can be disposed within a portion of the actuator and arranged such that the plunger defines, at least partially, the fluid reservoir. Thus, when the activation force is applied to the actuator, the actuator can move relative to the plunger such that a negative pressure is produced within the

fluid reservoir. In this manner, a bodily-fluid can flow through a first flow path from the needle to the fluid reservoir (e.g., via a lumen defined by the flow control mechanism). In some instances, the negative pressure in the fluid reservoir can be reduced, for example, by reducing the activation force applied to the actuator and/or releasing the actuator, at 1004. For example, in some embodiments, the actuator can include a spring and/or any other suitable device, mechanism, or member that can be operable in constricting at least a portion of the fluid flow path. The negative pressure in a subsequent sample reservoir can also be reduced, for example, by apply an activation force to the actuator, at 1004, as described herein.

[1205] The method 1000 includes moving the actuator a second distance to engage the flow control mechanism to move the flow control mechanism between the first configuration and a second configuration that is operable in allowing bodily-fluid to flow through a second flow path from the needle to a sample reservoir, at 1005. For example, in some embodiments, by moving the actuator the second distance, the flow control mechanism is rotated such that a lumen defined therein defines at least a portion of the second fluid flow path. In this manner, bodily-fluid can flow through the second flow path to be disposed within the sample reservoir. In some embodiments, the collection and/or the isolation of a first volume of the bodily-fluid can reduce and/or eliminate, for example, an amount of microbes (e.g., dermally-residing microbes, other undesirable external contaminants, or the like) in the sample volume.

[1206] While various embodiments have been described above, it should be understood that they have been presented by way of example only, and not limitation. Where methods and steps described above indicate certain events occurring in certain order, those of ordinary skill in the art having the benefit of this disclosure would recognize that the ordering of certain steps may be modified and that such modifications are in accordance with the variations of the invention. Additionally, certain of the steps may be performed concurrently in a parallel process when possible, as well as performed sequentially as described above. Additionally, certain steps may be partially completed and/or omitted before proceeding to subsequent steps.

[1207] While various embodiments have been particularly shown and described, various changes in form and details may be made. Although various embodiments have been described as having particular features and/or combinations of components, other

embodiments are possible having any combination or sub-combination of any features and/or components from any of the embodiments described herein. For example, while the not shown in FIGS. 28 and 29, in some embodiments, the transfer device 500 can include a throttling button, similar in form and function to the throttling button 445 included in the transfer device 400. By way of another example, although not shown in FIGS. 30-41, in some embodiments, the transfer device 600 can include one or more springs such as, for example, the spring 261 of the transfer device and/or the torsion springs 761A and 761B of the transfer device 700.

[1208] The specific configurations of the various components can also be varied. For example, the size and specific shape of the various components can be different than the embodiments shown, while still providing the functions as described herein. More specifically, the size and shape of the various components can be specifically selected for a desired rate of bodily-fluid flow into a fluid reservoir.

Claims

1. A device for procuring bodily-fluid samples from a patient, the device comprising:

a housing including a proximal end portion and a distal end portion and defining an inner volume therebetween, the housing having an inlet port configured to be fluidically coupled to the patient, and an outlet port configured to be fluidically coupled to a sample reservoir;

a fluid reservoir disposed in the inner volume and configured to receive and isolate a first volume of bodily-fluid withdrawn from the patient;

a flow control mechanism disposed in the housing and defining a first lumen and a second lumen, the flow control mechanism configured for rotational movement from a first configuration, in which the inlet port is placed in fluid communication with the fluid reservoir such that bodily-fluid can flow from the inlet port, through the first lumen and to the fluid reservoir, to a second configuration, in which the inlet port is placed in fluid communication with the outlet port such that the bodily-fluid can flow from the inlet, through the second lumen and to the outlet port; and

an actuator operably coupled to the flow control mechanism and configured to create a negative pressure in the fluid reservoir when actuated by a user, the actuator further configured to rotate the flow control mechanism from the first configuration to the second configuration after the first volume of bodily-fluid is received in the fluid reservoir from the patient.

2. The device of claim 1, wherein the actuator is further configured to move a first distance to create the negative pressure in the fluid reservoir when actuated by a user.

3. The device of claim 2, wherein the actuator is further configured to move a second distance to rotate the flow control mechanism from the first configuration to the second configuration.

4. The device of claim 1, wherein the actuator is configured to move in a first direction to create the negative pressure in the fluid reservoir, and to move in a second direction to reduce the negative pressure created in the fluid reservoir from movement in the first direction.

5. The device of claim 1, wherein the actuator is configured to allow the user to modulate the negative pressure created in the fluid reservoir.

6. A device for procuring bodily-fluid samples from a patient, the device comprising:

a housing including a proximal end portion and a distal end portion and defining an inner volume therebetween;

an actuator movably disposed in the housing, the actuator including a sealing member and a fluid reservoir defined at least in part by the sealing member, the actuator configured to create a negative pressure in the fluid reservoir when actuated by a user;

a diverter disposed in the housing, the diverter having an inlet port configured to be fluidically coupled to the patient, a first outlet port configured to be fluidically coupleable to the fluid reservoir, and a second outlet port configured to be fluidically coupled to a sample reservoir; and

a flow control mechanism disposed in the diverter and defining a first lumen and a second lumen, the flow control mechanism configured for rotational movement between a first configuration, in which the inlet port is placed in fluid communication with the first outlet port such that bodily-fluid can flow from the inlet port, through the first lumen and to the first outlet port, to a second configuration, in which the inlet port is placed in fluid communication with the second outlet port such that the bodily-fluid can flow from the inlet, through the second lumen and to the second outlet port.

7. The device of claim 6, wherein the actuator is further configured to rotate the flow control mechanism from the first configuration to the second configuration after a first volume of bodily-fluid is received in the fluid reservoir from the patient.

8. The device of claim 7, wherein the actuator is configured to move a first distance to create the negative pressure in the fluid reservoir, and to move a second distance to rotate the flow control mechanism from the first configuration to the second configuration, when actuated by a user.

9. The device of claim 6, wherein the actuator is configured to move in a first direction to create the negative pressure in the fluid reservoir, and to move in a second direction to

reduce the negative pressure created in the fluid reservoir from movement in the first direction.

10. The device of claim 6, wherein the actuator further includes a plunger operably coupled to the sealing member.

11. The device of claim 10, wherein the actuator further includes a spring operably coupled to the plunger, the spring configured to compress in response to an activation force when the actuator is actuated by a user.

12. The device of claim 11, wherein the spring is configured to expand and exert a reaction force when the activation force is removed.

13. The device of claim 12, wherein the spring is configured to allow the user to modulate the negative pressure created in the fluid reservoir.

14. A device for procuring bodily-fluid samples from a patient, the device comprising:

a housing including a proximal end portion and a distal end portion and defining an inner volume therebetween, the housing having an inlet port configured to be fluidically coupled to the patient, and an outlet port configured to be fluidically coupled to a sample reservoir;

a flow control mechanism disposed in the housing and defining a first lumen and a second lumen, the flow control mechanism configured for rotational movement between a first configuration, in which the inlet port is placed in fluid communication with a fluid reservoir defined at least in part by the housing such that bodily-fluid can flow from the inlet port, through the first lumen and to the fluid reservoir, to a second configuration, in which the inlet port is placed in fluid communication with the outlet port such that the bodily-fluid can flow from the inlet, through the second lumen and to the outlet port; and

an actuator movably disposed in the housing and operably coupled to the flow control mechanism, the actuator configured to create a negative pressure in the fluid reservoir when actuated by a user, the actuator further configured to rotate the flow control mechanism from the first configuration to the second configuration after a first volume of bodily-fluid is received in the fluid reservoir from the patient.

15. The device of claim 14, wherein the actuator includes an activation mechanism configured to rotate the flow control mechanism from the first configuration to the second configuration.

16. The device of claim 15, wherein the activation mechanism includes a first set of protrusions and the flow control mechanism includes a second set of protrusions, the first set of protrusions configured to operably engage the second set of protrusions to rotate the flow control mechanism from the first configuration to the second configuration.

17. The device of claim 14, wherein the actuator is further configured to create the negative pressure in the fluid reservoir when the actuator is moved from a first position to a second position by the user.

18. The device of claims 17, wherein the actuator is further configured to rotate the flow control mechanism from the first configuration to the second configuration when the actuator is moved from the second position to a third position by the user.

19. The device of claim 18, wherein the actuator includes an activation mechanism and the flow control mechanism includes a set of protrusions, the activation mechanism configured to operably engage the set of protrusions to rotate the flow control mechanism from the first configuration to the second configuration when the actuator is moved from the second position to a third position by the user.

20. A device for procuring bodily-fluid samples from a patient, the device comprising:

a housing including a proximal end portion and a distal end portion and defining an inner volume therebetween, the housing having an inlet port configured to be fluidically coupled to the patient;

a seal member movably disposed in the inner volume;

a fluid reservoir disposed in the inner volume and at least partially defined by the seal member, the fluid reservoir configured to receive and isolate a first volume of bodily-fluid withdrawn from the patient;

a flow control mechanism movably disposed in the housing, the flow control mechanism configured to move between a first configuration, in which the bodily-fluid can flow from the inlet port, through the flow control mechanism and to the fluid reservoir, and a

second configuration, in which the fluid reservoir is fluidically isolated from the inlet port; and

an actuator operably coupled to the seal member and to the flow control mechanism, the actuator including a spring configured to move the seal member from a first position to a second position to create a negative pressure in the fluid reservoir, the actuator further configured to move the flow control mechanism from the first configuration to the second configuration after a first volume of bodily-fluid is received in the fluid reservoir from the patient.

21. The device of claim 20, further comprising:

a throttling button operably coupled to the actuator and configured to modulate the rate at which the spring moves the seal member from the first position to the second position based on user manipulation of the throttling button.

22. The device of claim 20, wherein the flow control mechanism includes a first control member and a second control member, the second control member defining a first lumen and a second lumen, the flow control mechanism configured for rotational movement between the first configuration in which the inlet port is placed in fluid communication with the fluid reservoir such that bodily-fluid can flow from the inlet port, through the first lumen and to the fluid reservoir, to a second configuration, in which the inlet port is placed in fluid communication with a sample reservoir such that the bodily-fluid can flow from the inlet, through the second lumen and to the sample reservoir.

23. The device of claim 22, wherein the first control member includes a protrusion movably disposed in a grove defined by the second control member, the protrusion configured to move in the grove as the spring moves the seal member from the first position to the second position.

24. The device of claim 23, wherein the protrusion is configured to rotate the second control member when the spring moves the seal member from the second position to a third position.

25. A device for procuring bodily-fluid samples from a patient, the device comprising:

a housing including a proximal end portion and a distal end portion and defining an inner volume therebetween, the housing having an inlet port configured to be fluidically coupled to the patient, and an outlet port configured to be fluidically coupled to a sample reservoir;

a flow control mechanism disposed in the housing, the flow control mechanism including a first control member and a second control member, the second control member defining a first lumen and a second lumen and configured for rotational movement between a first configuration in which the inlet port is placed in fluid communication with a fluid reservoir defined at least in part by the housing such that bodily-fluid can flow from the inlet port, through the first lumen and to the fluid reservoir, to a second configuration, in which the inlet port is placed in fluid communication with the outlet port such that the bodily-fluid can flow from the inlet, through the second lumen and to the outlet port; and

an actuator movably disposed in the housing and operably coupled to the first control member, the actuator configured to create a negative pressure in the fluid reservoir when actuated by a user, the actuator further configured to rotate the second control member from the first configuration to the second configuration after a first volume of bodily-fluid is received in the fluid reservoir from the patient.

26. The device of claim 25, wherein the actuator includes an activation mechanism operably coupled to the first control member and configured to rotate the second control member from the first configuration to the second configuration.

27. The device of claim 25, wherein the actuator is further configured to create the negative pressure in the fluid reservoir when the actuator is moved from a first position to a second position by the user.

28. The device of claims 27, wherein the actuator is further configured to rotate the second control member from the first configuration to the second configuration when the actuator is moved from the second position to a third position by the user.

29. The device of claim 28, further comprising:

an activation mechanism coupled to the first control member, the activation mechanism including a protrusion configured to operably engage the actuator when the actuator is moved from the second position to a third position by the user.

30. A method for procuring bodily-fluid samples using a parenteral sampling device, the device including a needle having a lumen configured for insertion into the patient, and a fluid reservoir fluidically coupleable to the needle, the method comprising:

inserting the needle of the device into the patient;

establishing fluid communication between the needle and the fluid reservoir;

moving an actuator a first distance to create a negative pressure in the fluid reservoir and to withdraw a predetermined volume of bodily-fluid;

moving the actuator a second distance to engage a flow control mechanism and rotate the flow control mechanism from a first configuration to a second configuration, the first configuration operable to allow bodily-fluid to flow through a first flow path from the needle to the fluid reservoir, the second configuration operable to allow bodily-fluid to flow through a second flow path from the needle to a sample reservoir.

31. The method of claim 30, wherein moving the actuator the first distance includes applying an activation force to the actuator in a first direction.

32. The method of claim 31, wherein releasing the activation force allows the actuator to move in a second direction opposite the first direction, to reduce the negative pressure created in the fluid reservoir.

33. The method of claim 30, further comprising:

moving the actuator a third distance to reduce the flow rate of bodily-fluid through the second flow path to the sample reservoir in the second configuration.

34. The method of claim 33, further comprising:

moving the actuator a third distance to engage a control member and deform the second flow path reduce the flow rate of bodily-fluid through the
second flow path to the sample reservoir in the second configuration.

35. A method for procuring bodily-fluid samples using a parenteral sampling device, the device including a needle having a lumen configured for insertion into the patient, and a fluid reservoir fluidically coupleable to the needle, the method comprising:

inserting the needle of the device into the patient;

establishing fluid communication between the needle and the fluid reservoir;

applying a first activation force to an actuator to create a negative pressure in the fluid reservoir and to withdraw a predetermined volume of bodily-fluid;

reducing the first activation force applied to the actuator to reduce the negative pressure created in the fluid reservoir; and

applying a second activation force to the actuator to engage a flow control mechanism and move the flow control mechanism from a first configuration to a second configuration, the first configuration operable to allow bodily-fluid to flow through a first flow path from the needle to the fluid reservoir, the second configuration operable to allow bodily-fluid to flow through a second flow path from the needle to a sample reservoir.

36. The method of claim 35, wherein the first activation force moves the actuator a first distance in a first direction to create the negative pressure in the fluid reservoir.

37. The method of claim 36, wherein reducing the first activation force allows the actuator to move in a second direction opposite the first direction, to reduce the negative pressure created in the fluid reservoir.

38. The method of claim 35, wherein the second activation force moves the actuator a second distance in the first direction to move the flow control mechanism from the first configuration to the second configuration.

39. The method of claim 35, further comprising:

applying a third activation force to reduce the flow rate of bodily-fluid through the second flow path to the sample reservoir in the second configuration.

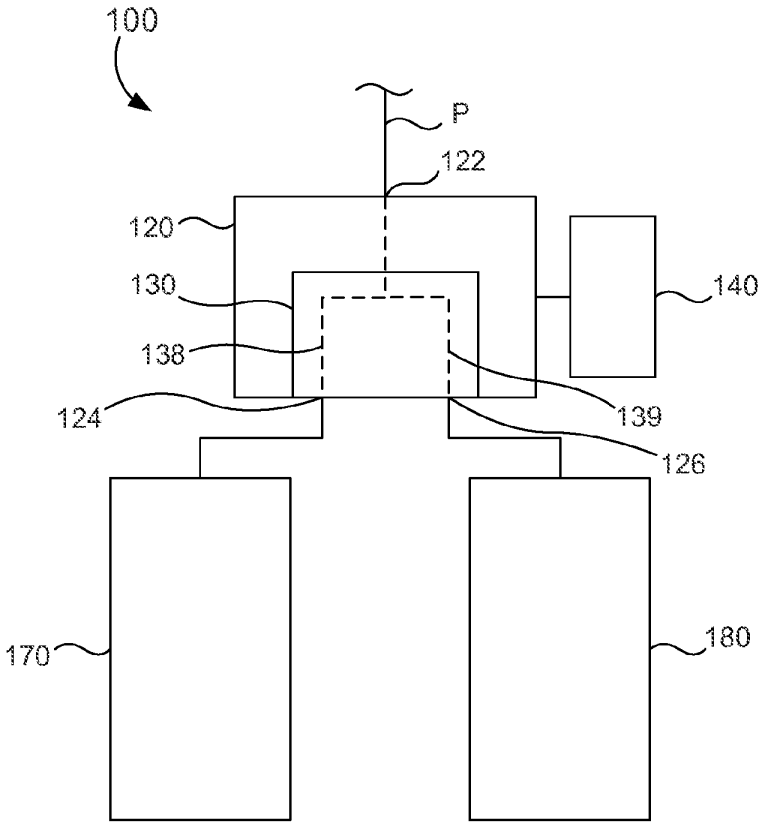


FIG. 1

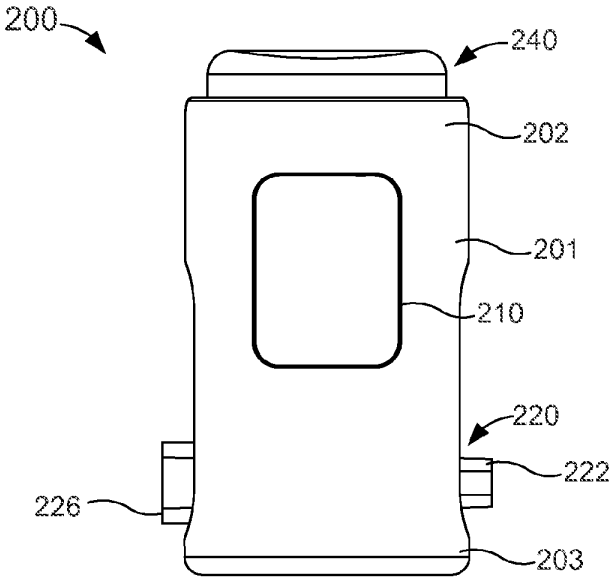

200
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FIG. 2

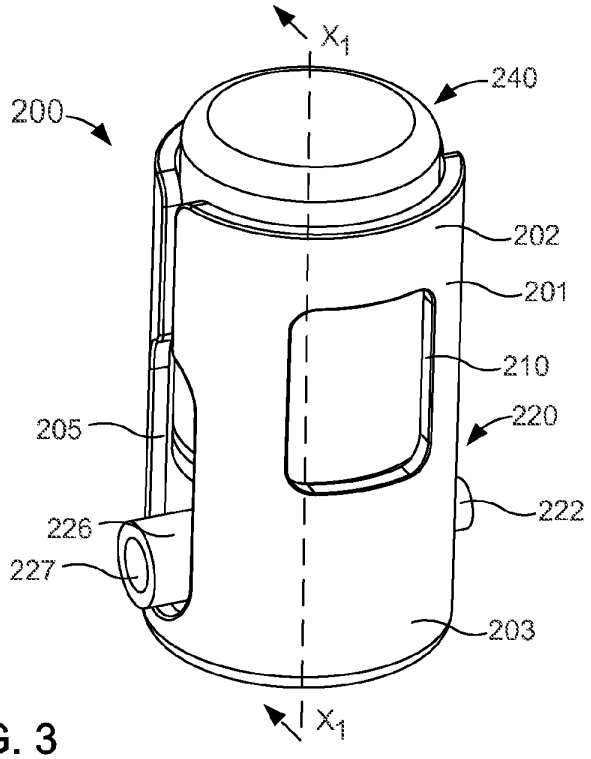

X1
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227
203
X1

FIG. 3

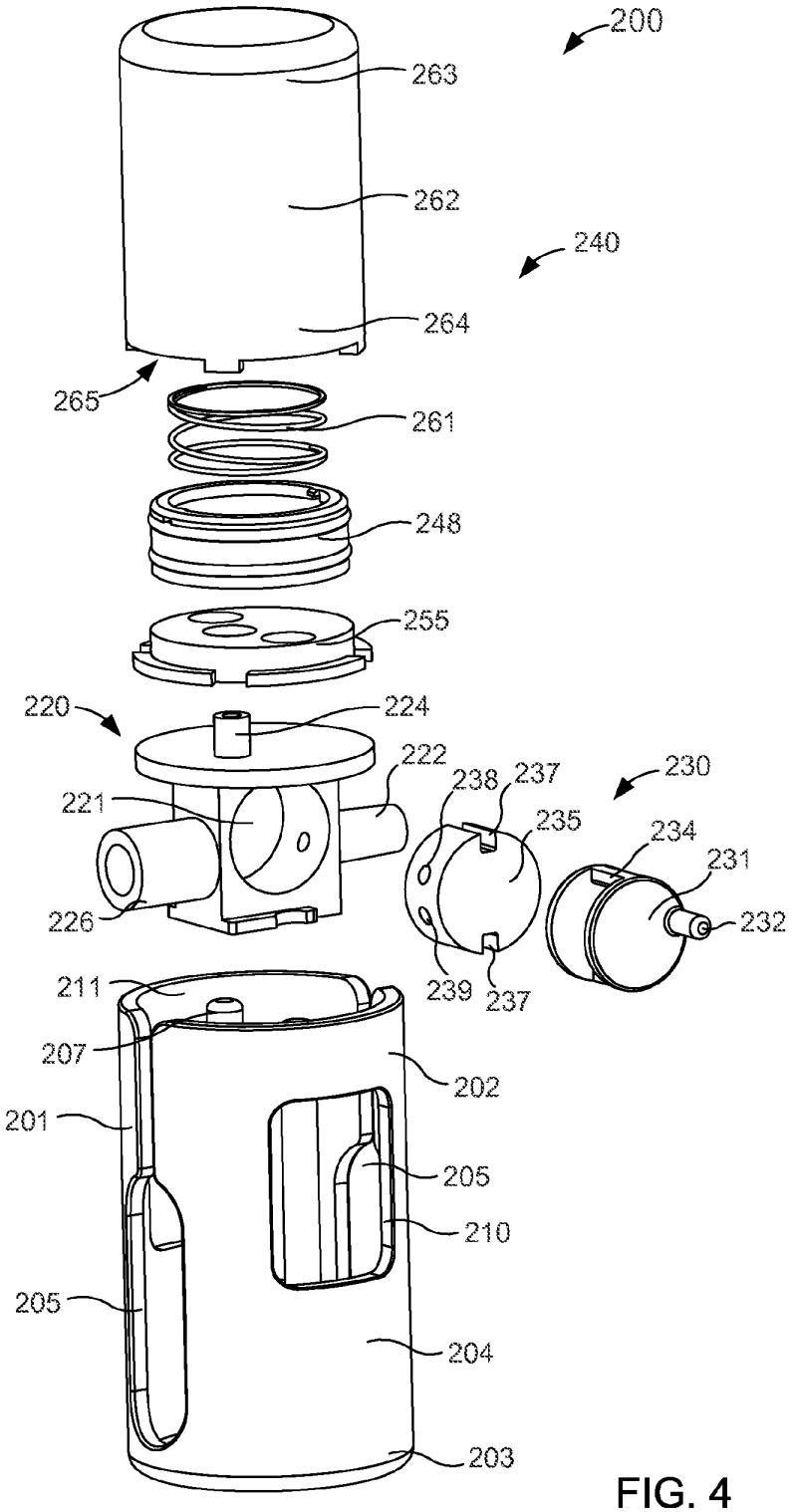

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FIG. 4

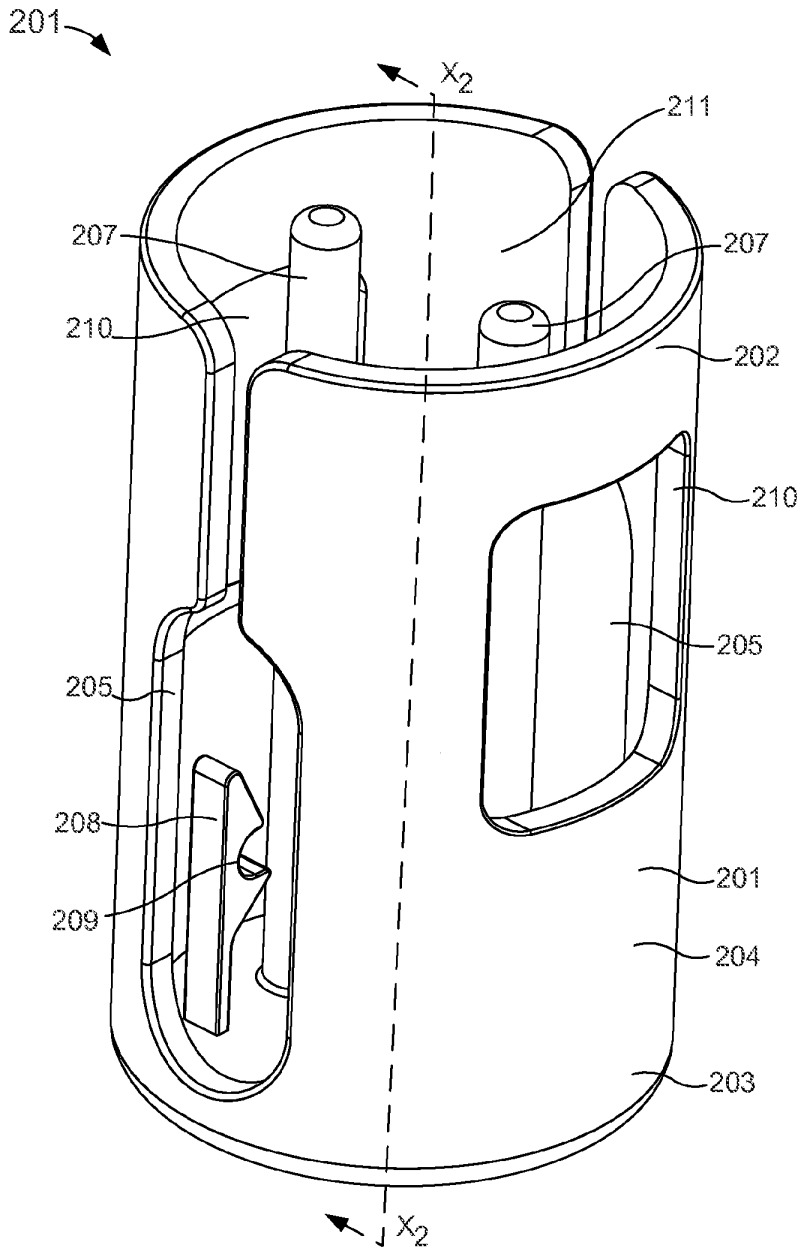


FIG. 5

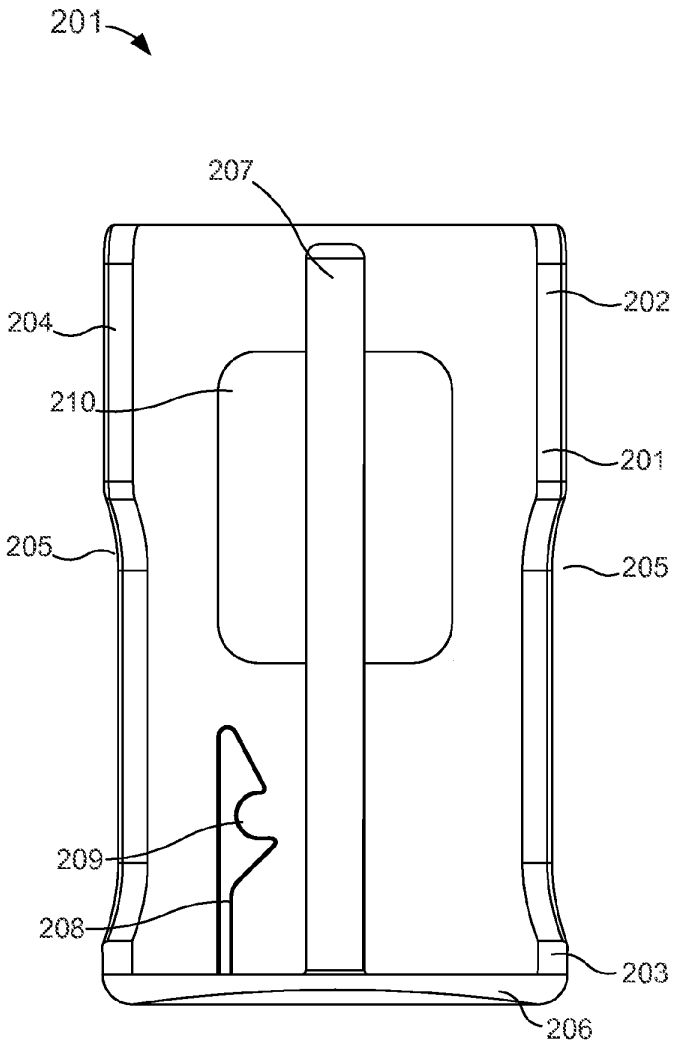


FIG. 6

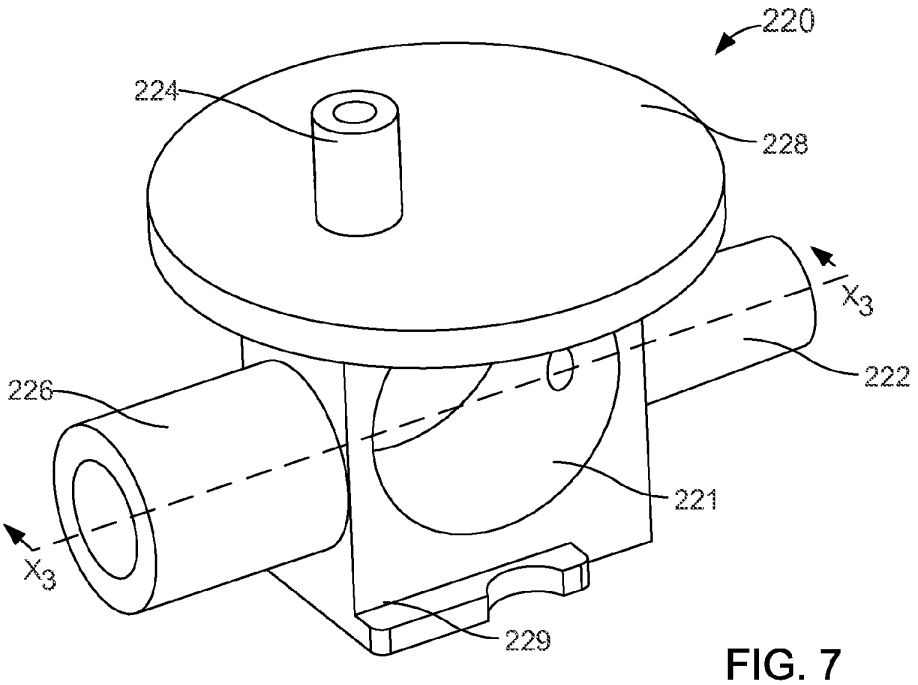

220
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228
X_3
222
226
221
X_3
229

FIG. 7

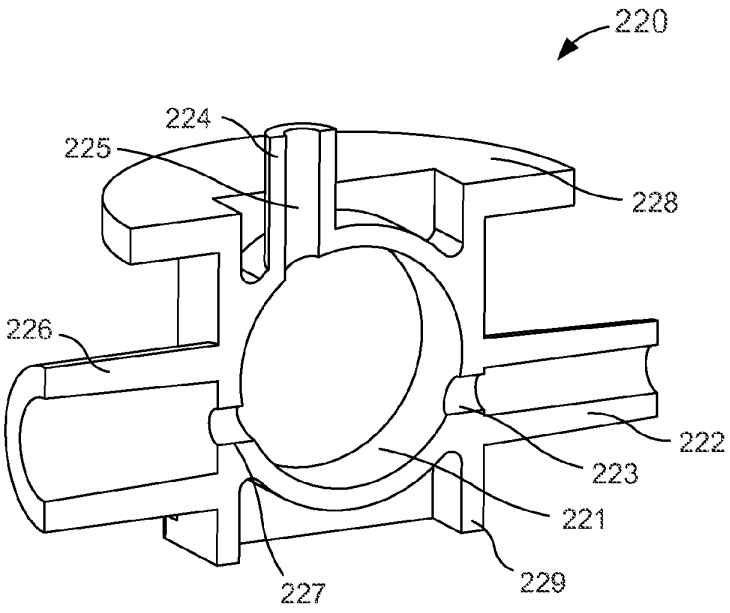

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FIG. 8

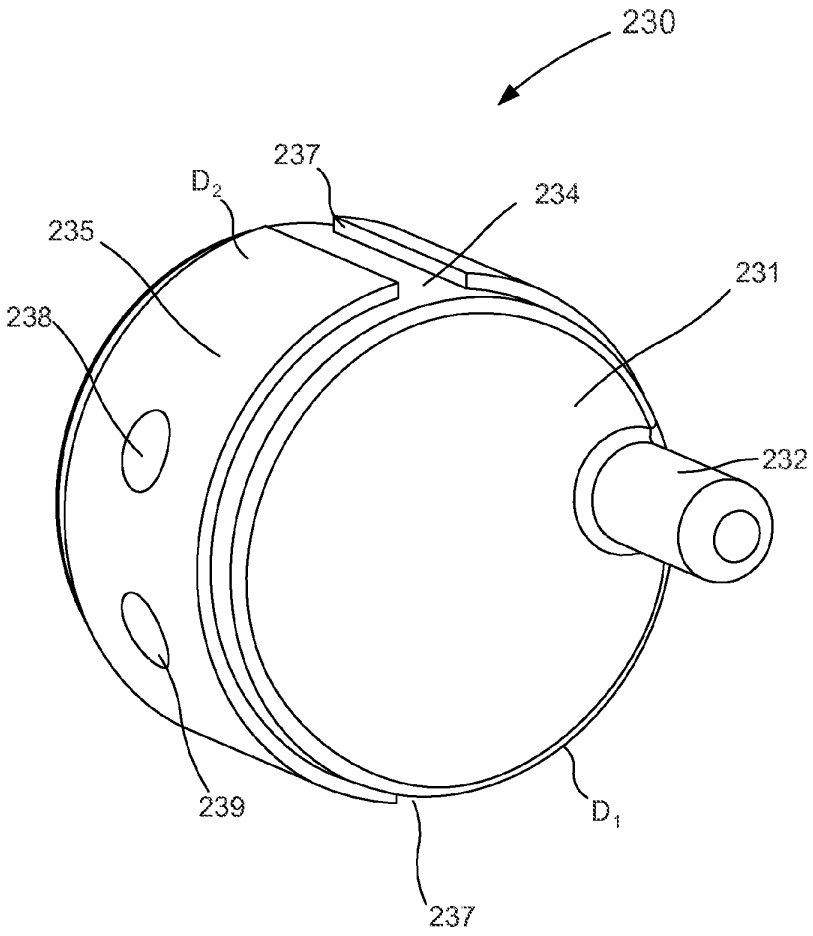


FIG. 9

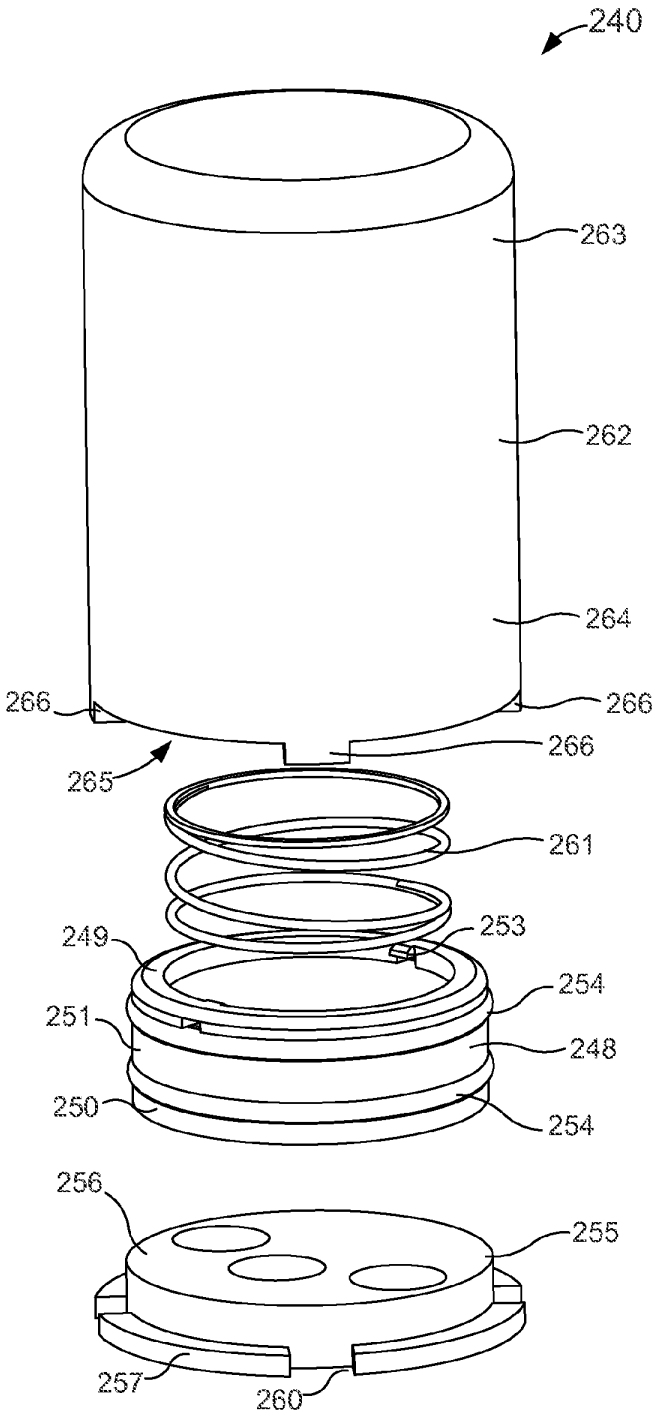

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FIG. 10

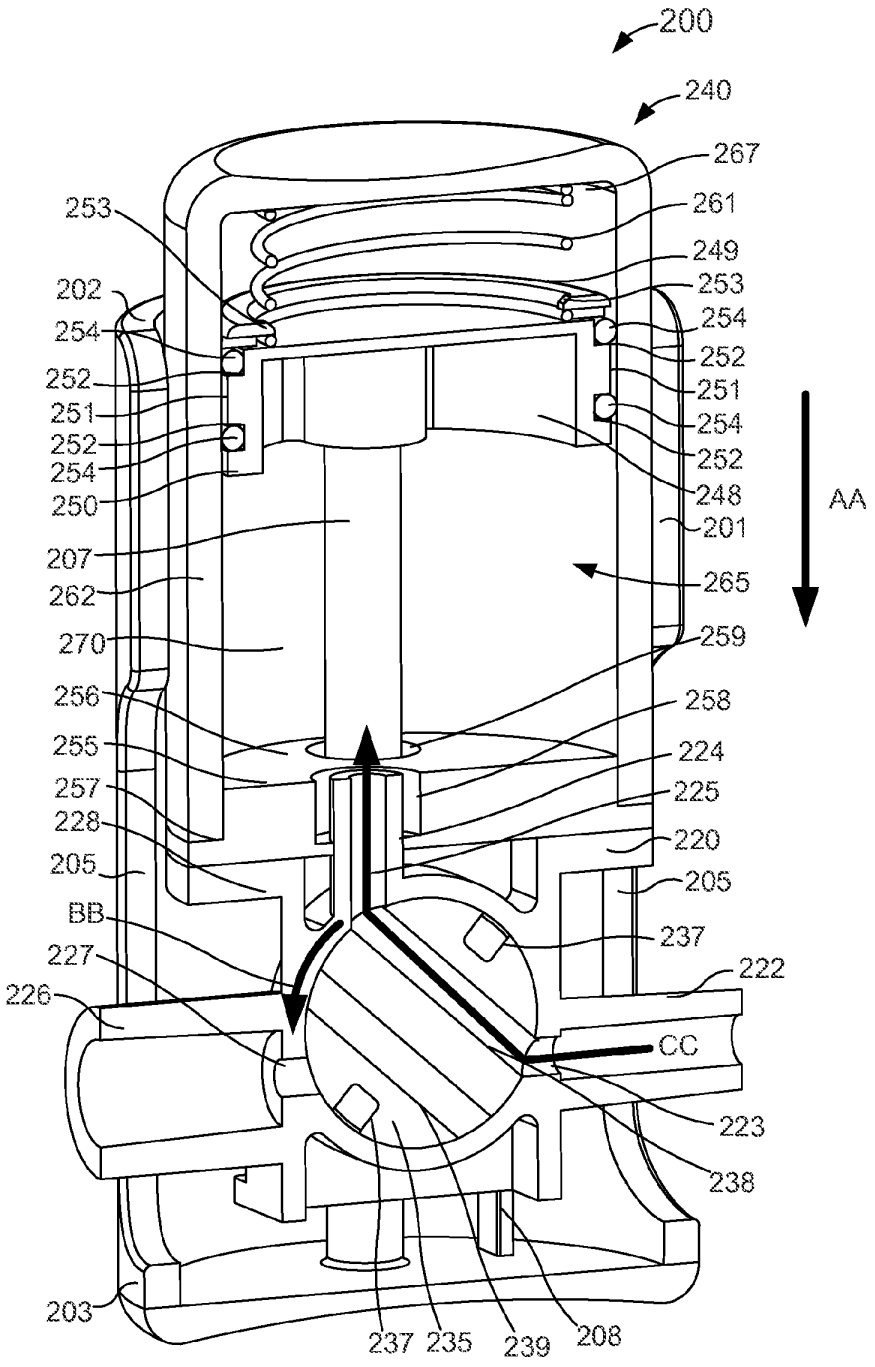

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265
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CC
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FIG. 11

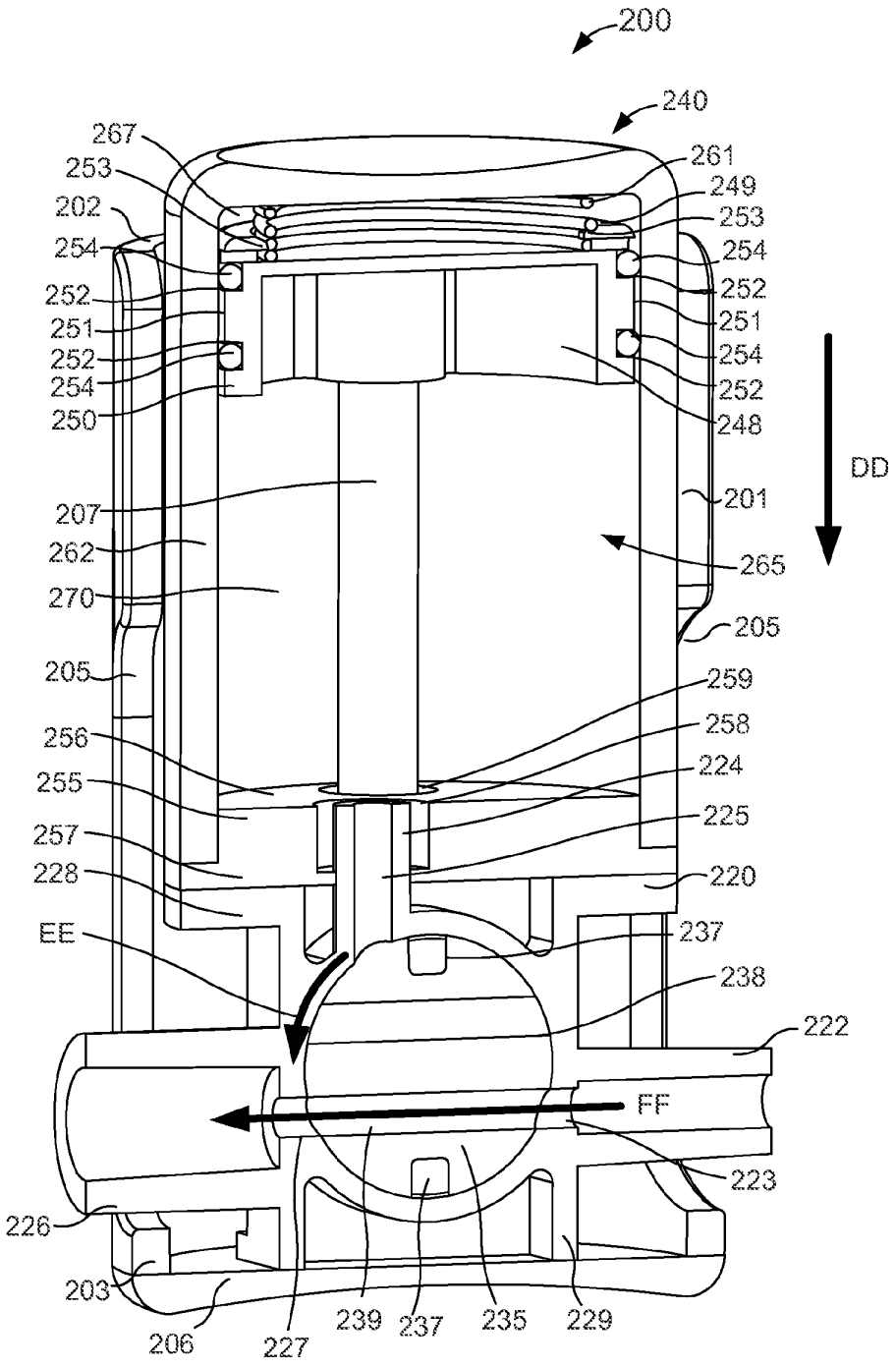

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DD
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FIG. 12

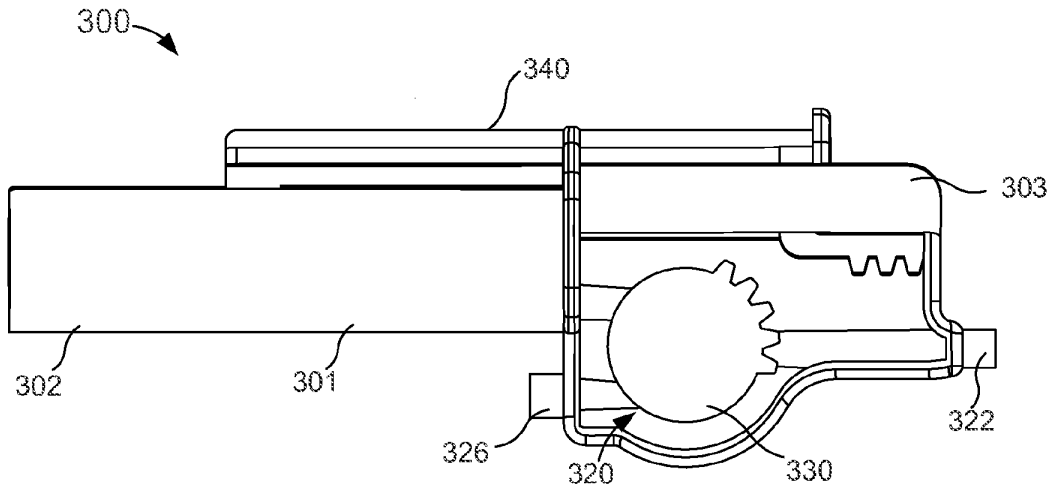

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FIG. 13

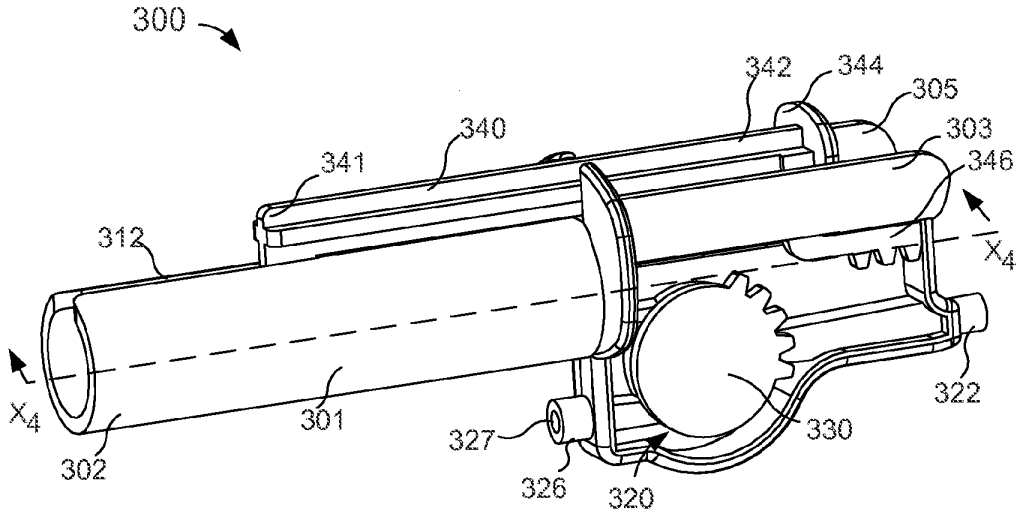

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X4
X4
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FIG. 14

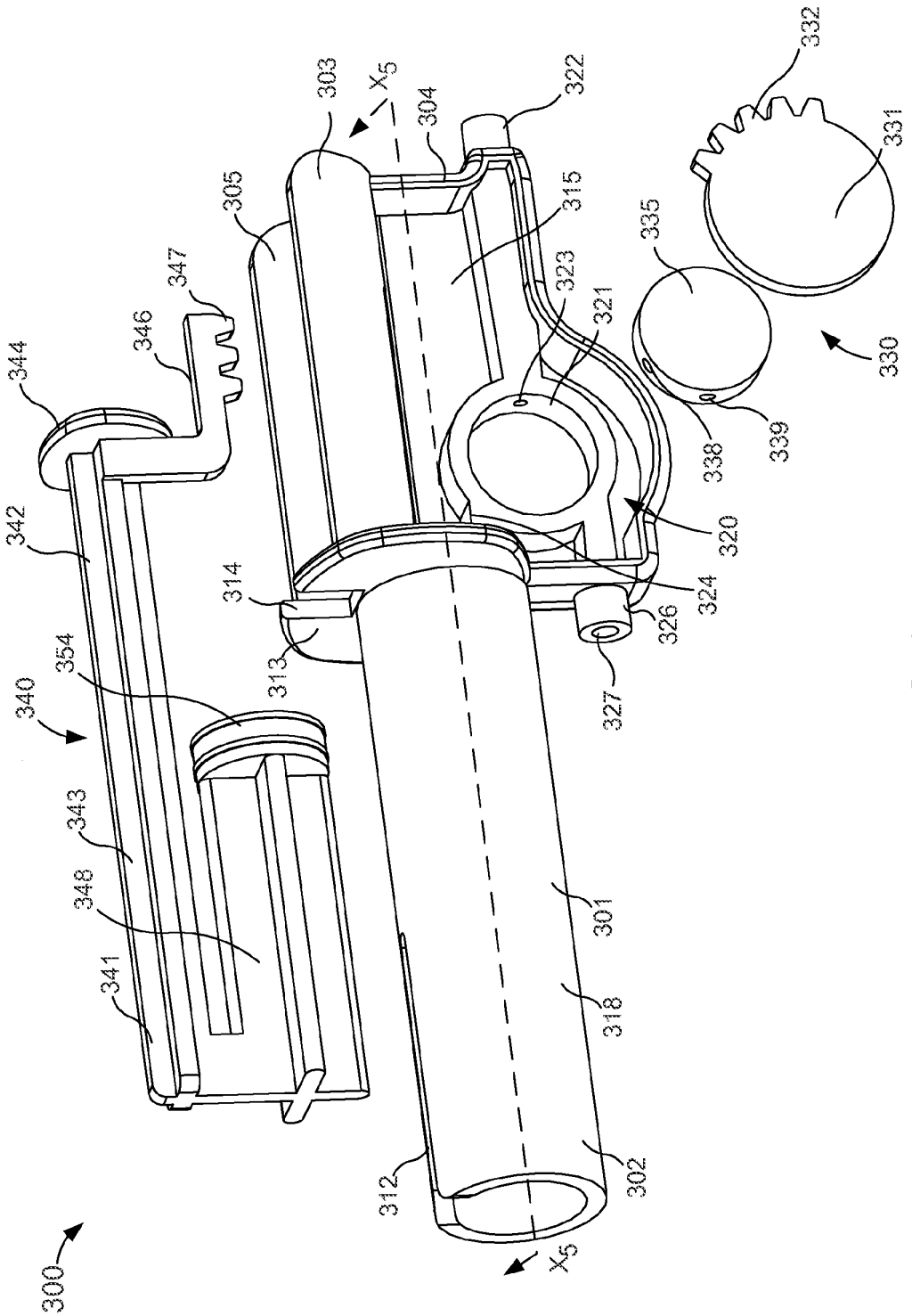

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X_5
X_5

FIG. 15

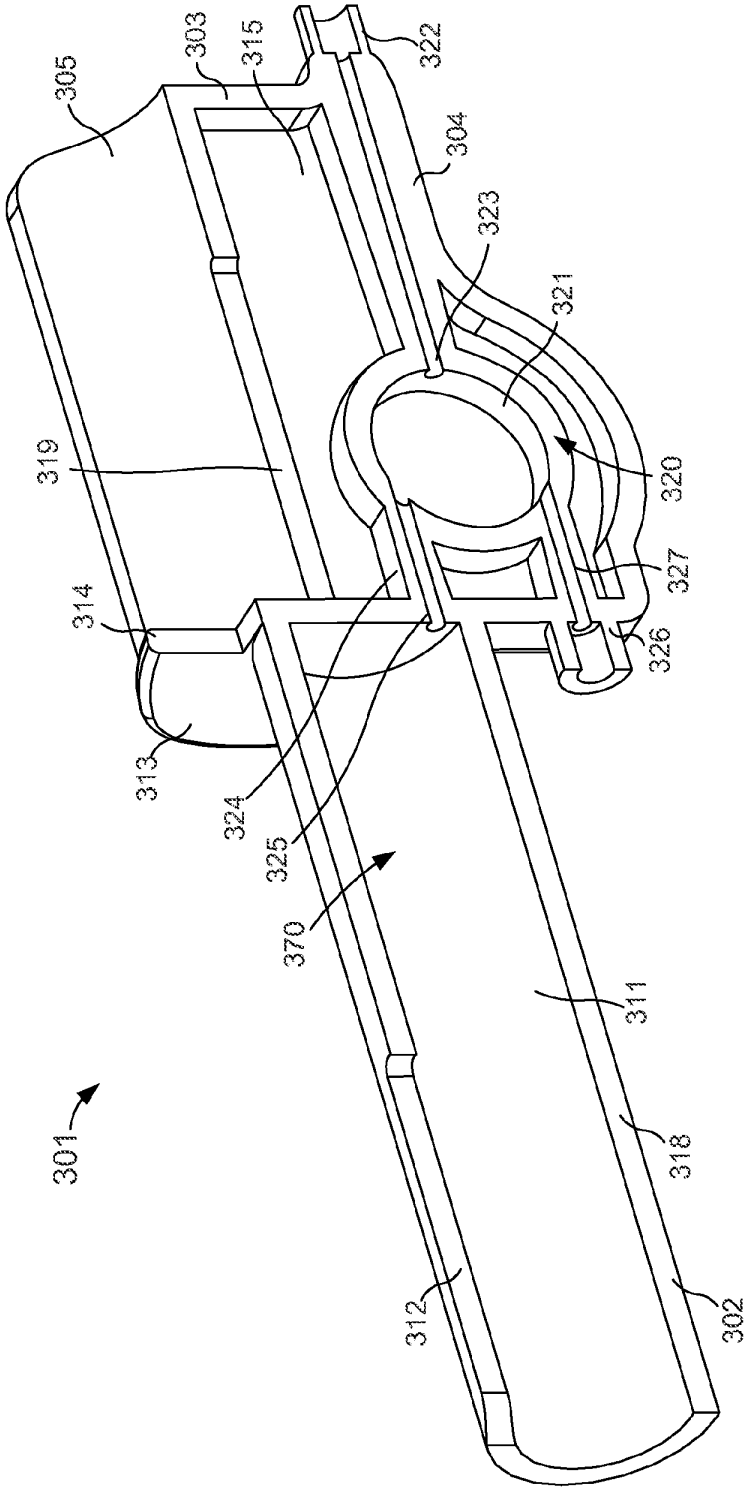

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FIG. 16

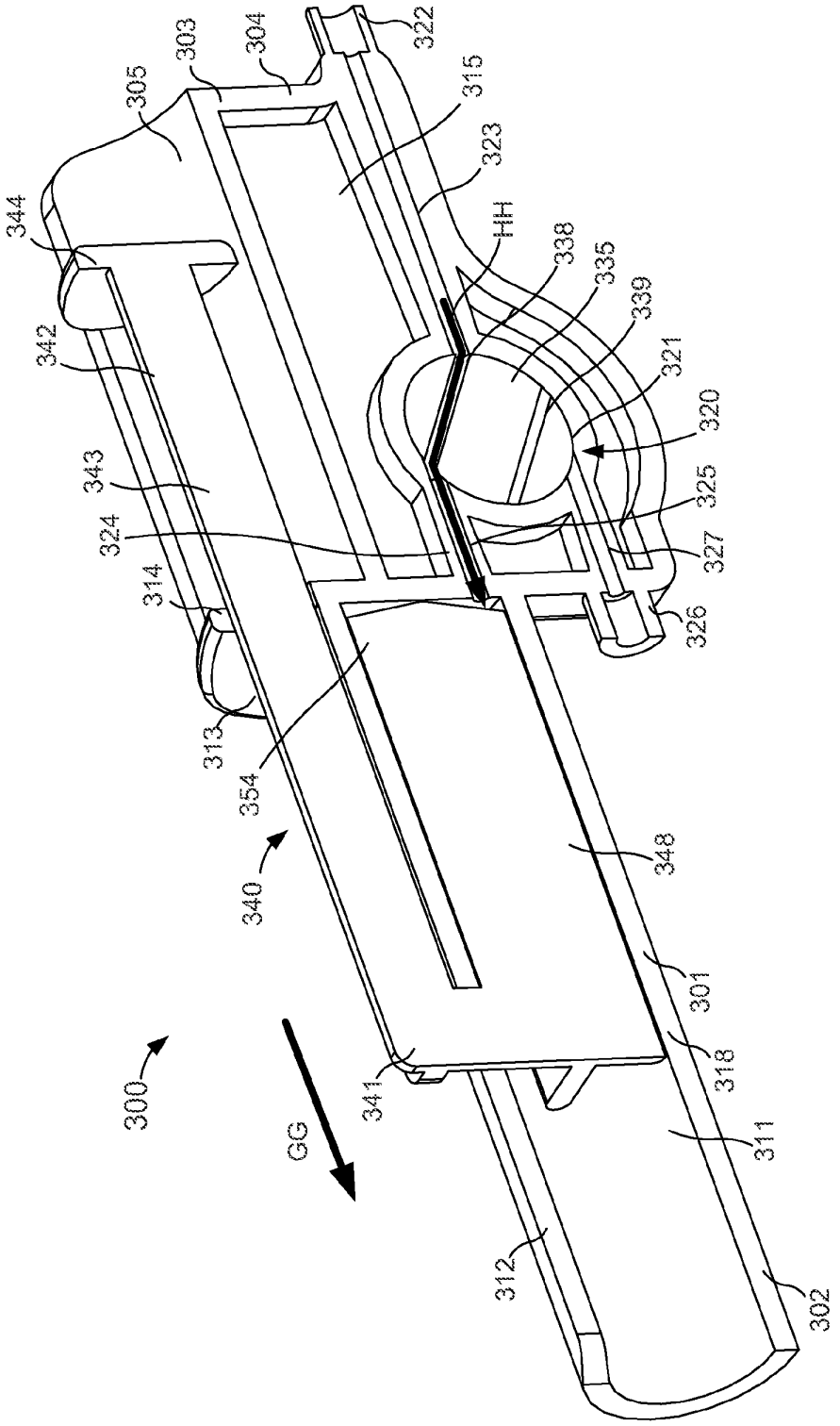

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FIG. 17

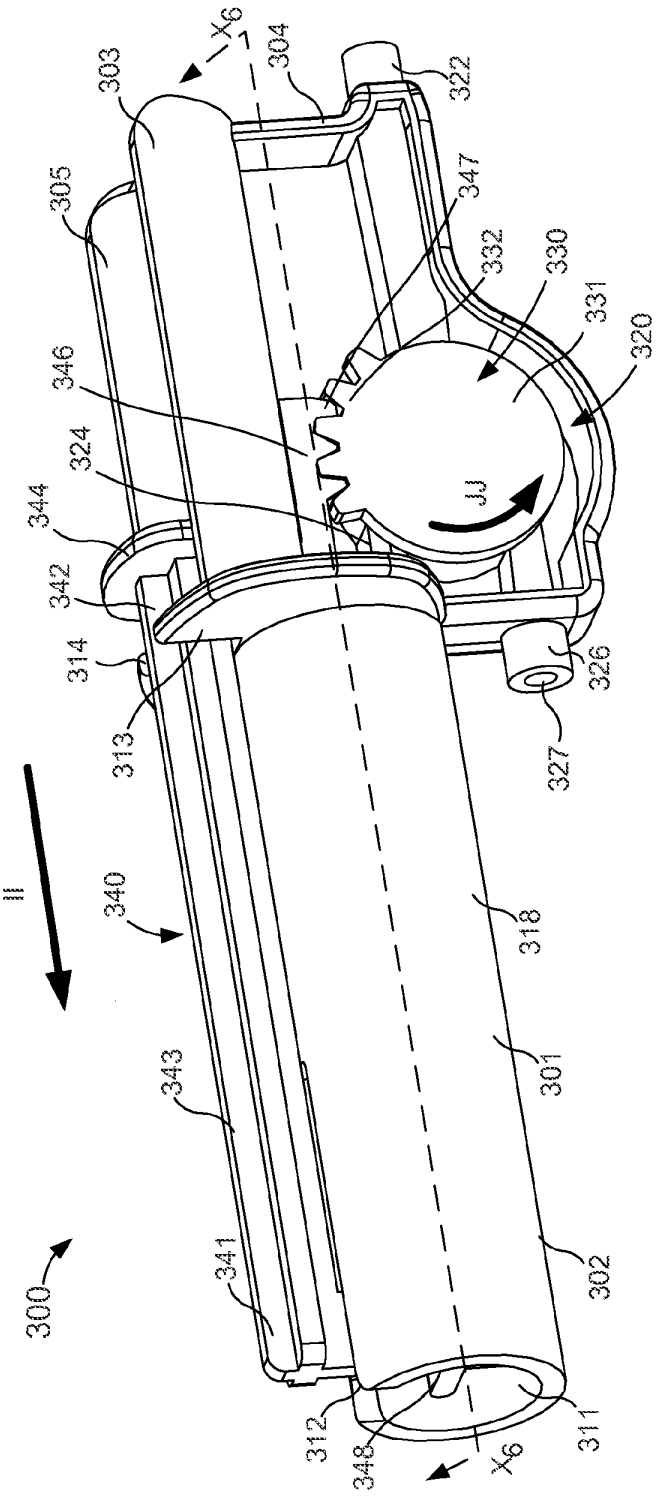

X6
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JJ
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343
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302
300
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348
311
X6

FIG. 18

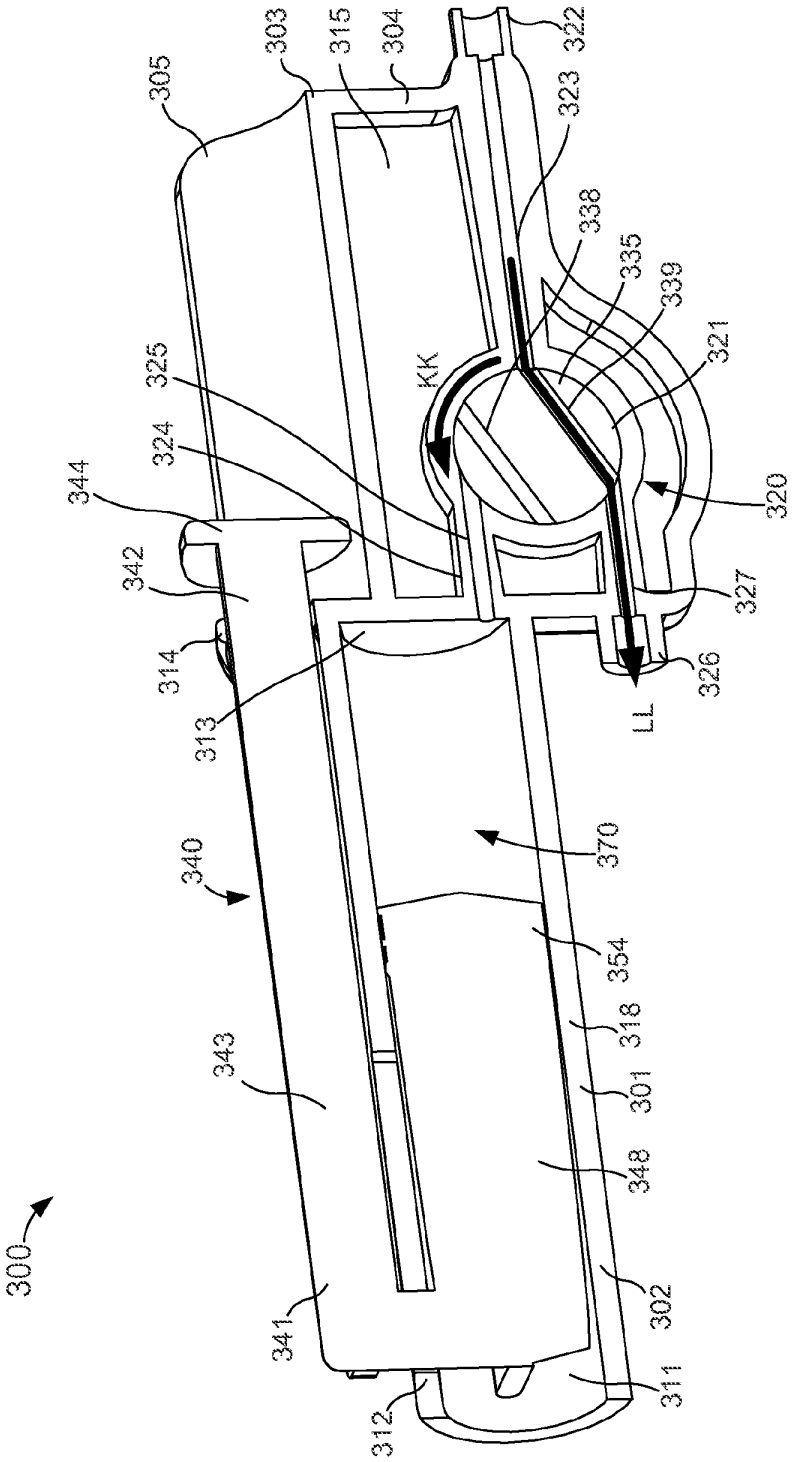

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FIG. 19

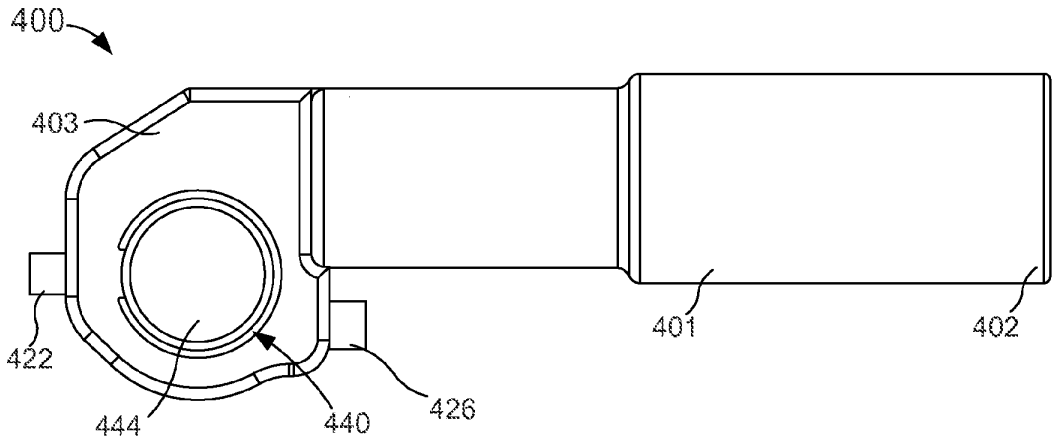

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FIG. 20

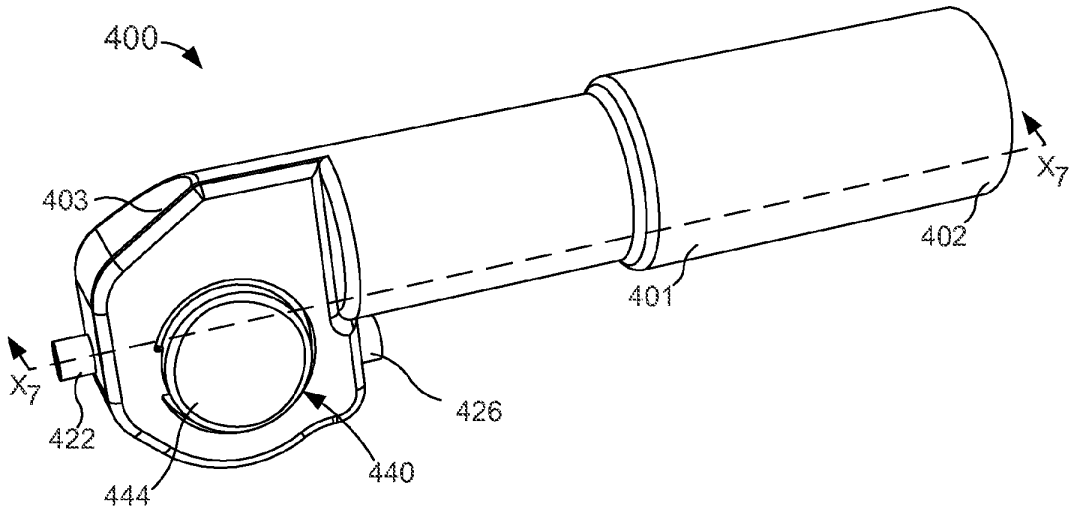

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X7
X7

FIG. 21

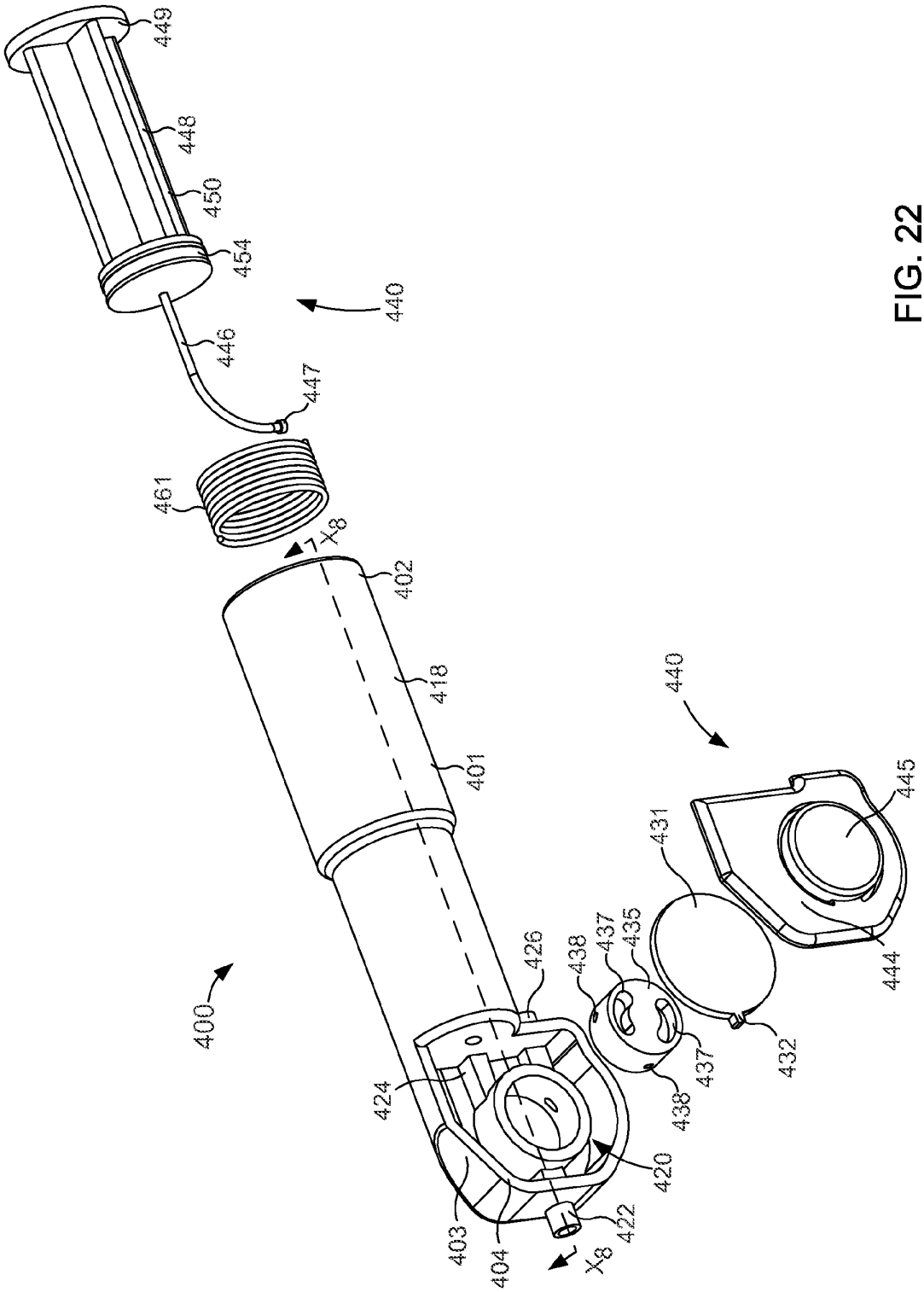

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404
X8

FIG. 22

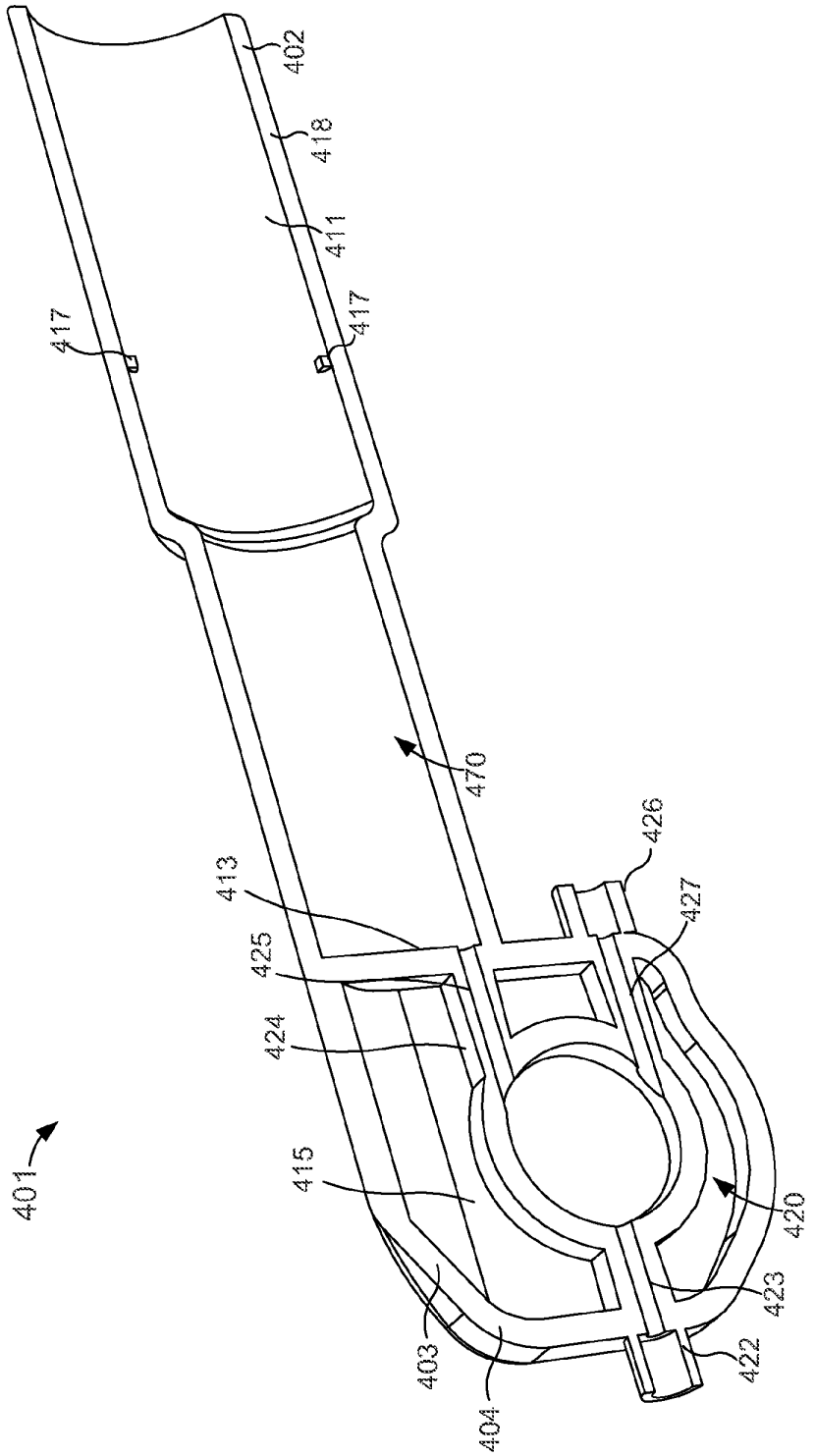

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FIG. 23

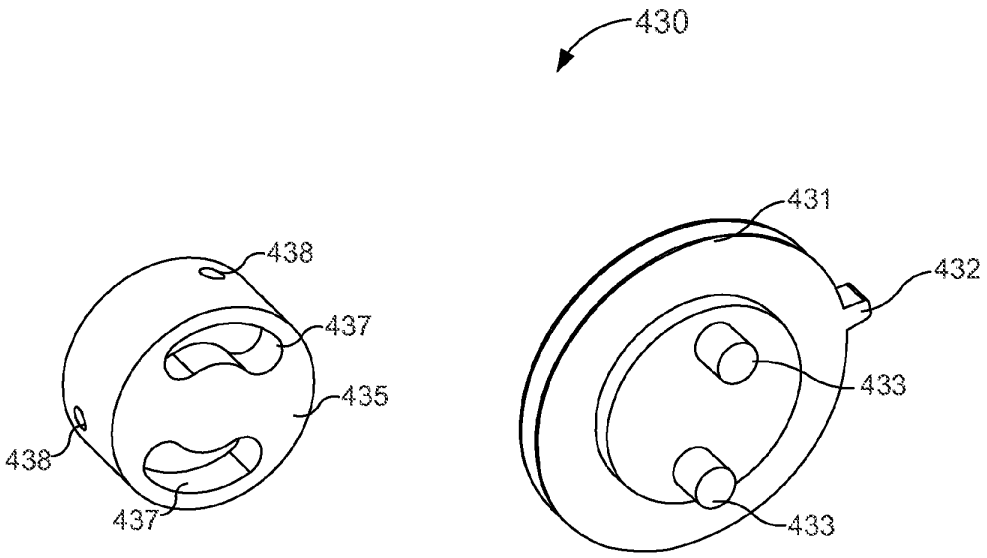


FIG. 24

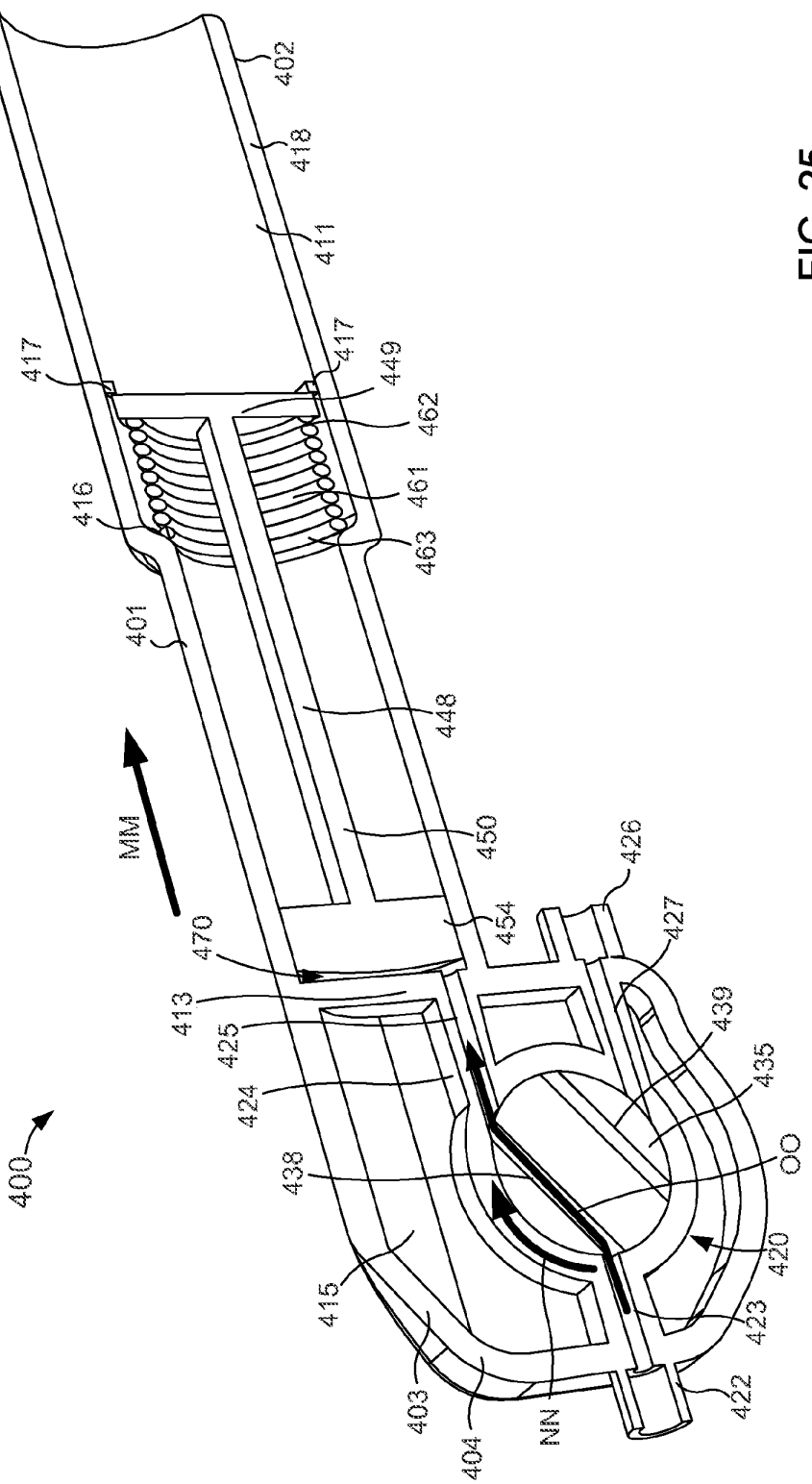

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MM

FIG. 25

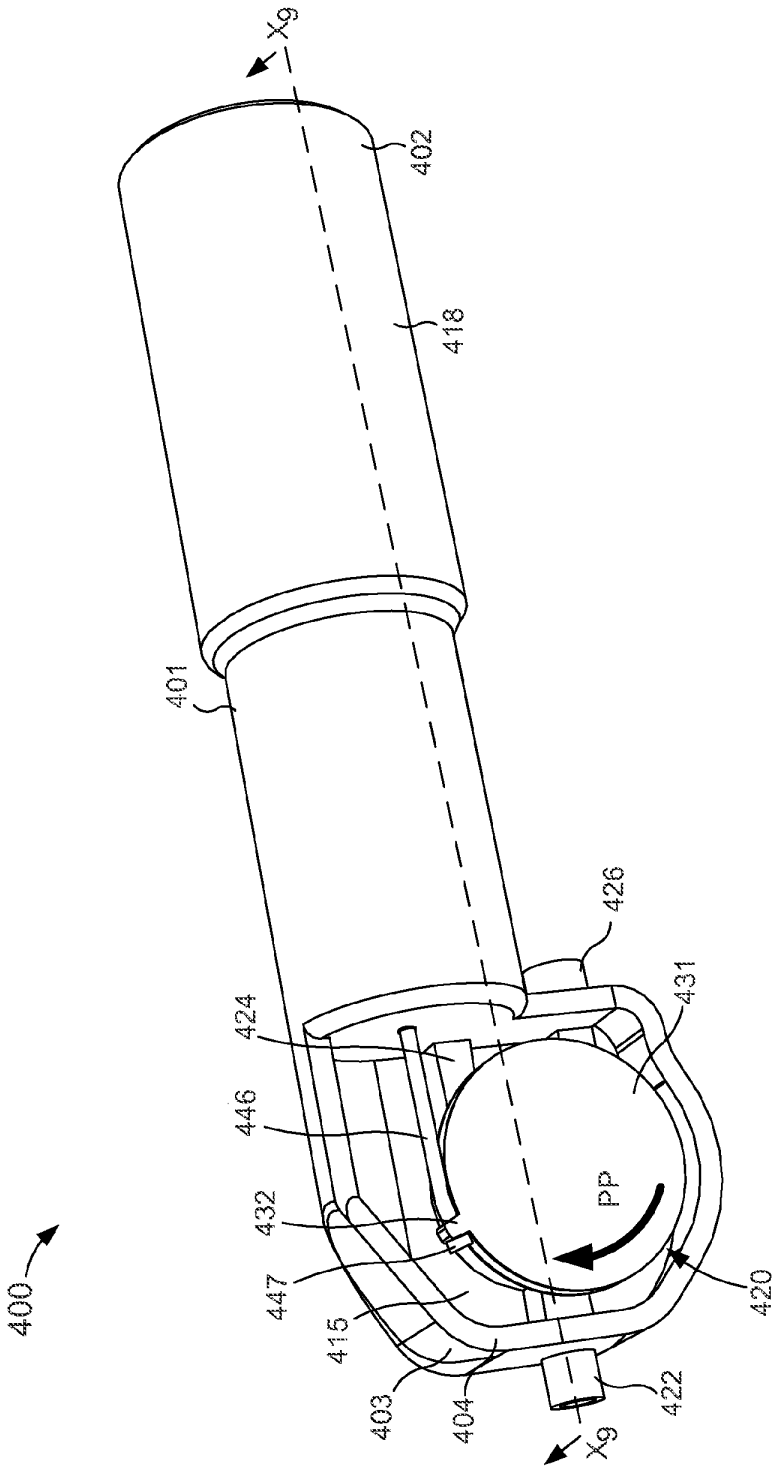

X9
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426
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X9
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FIG. 26

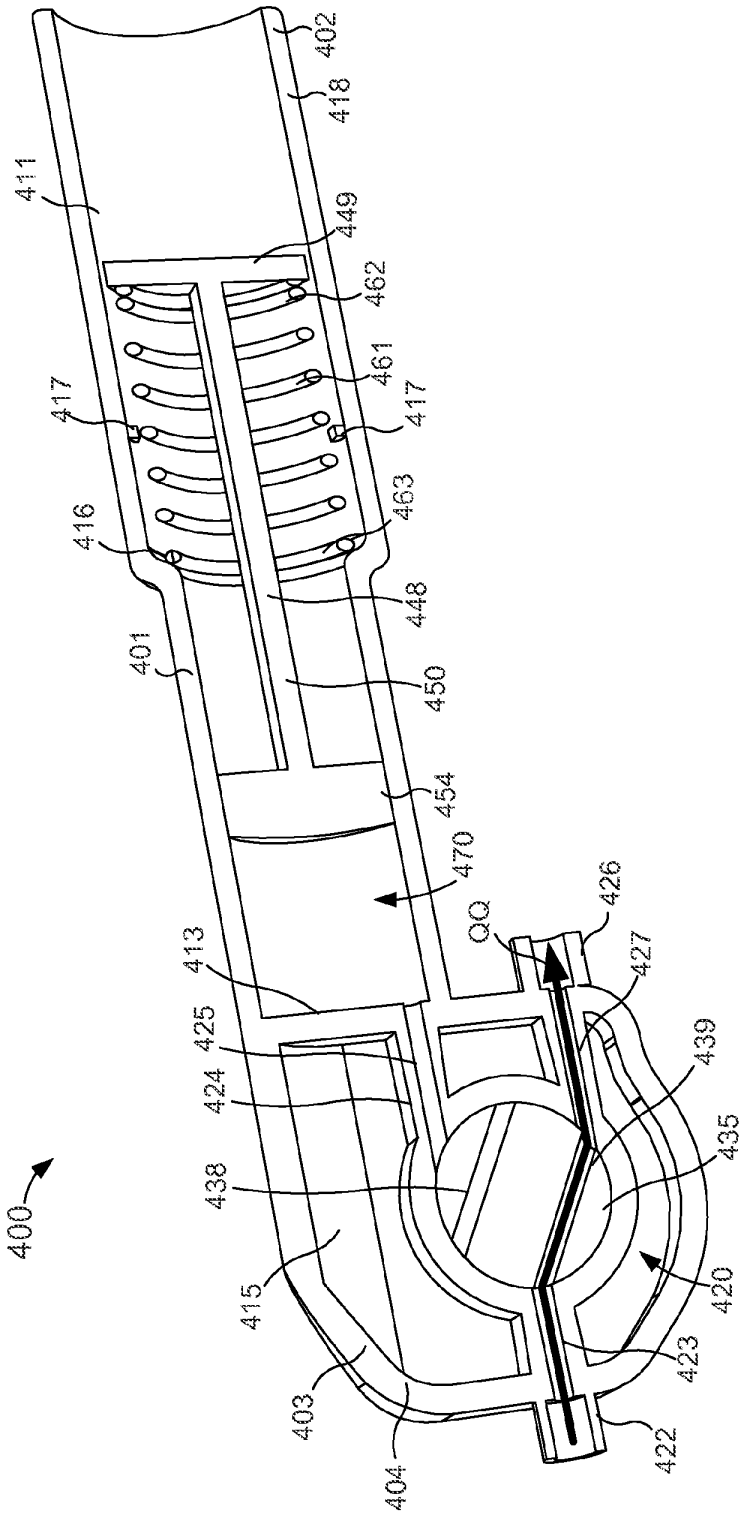

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FIG. 27

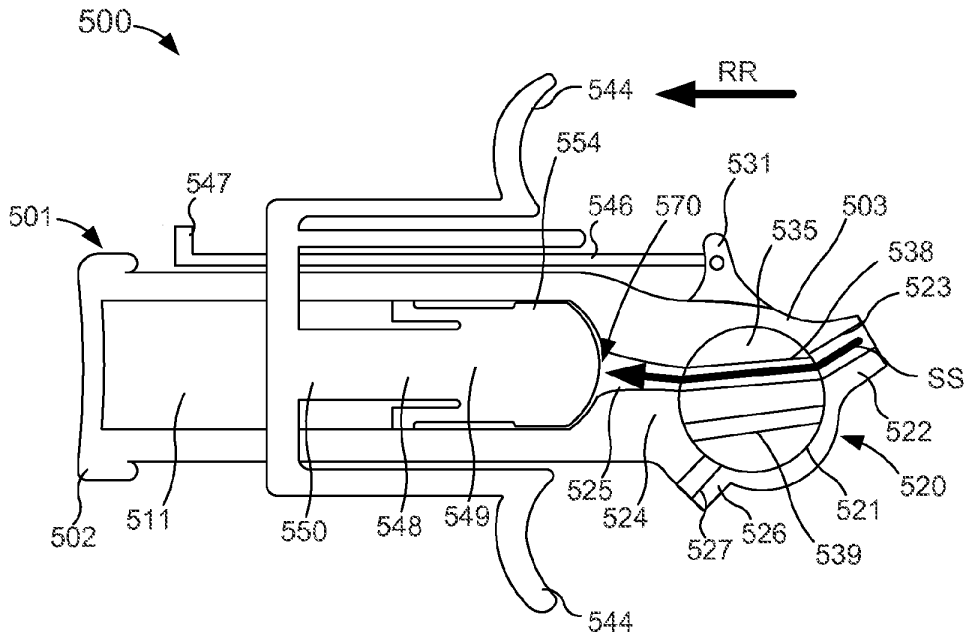

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FIG. 28

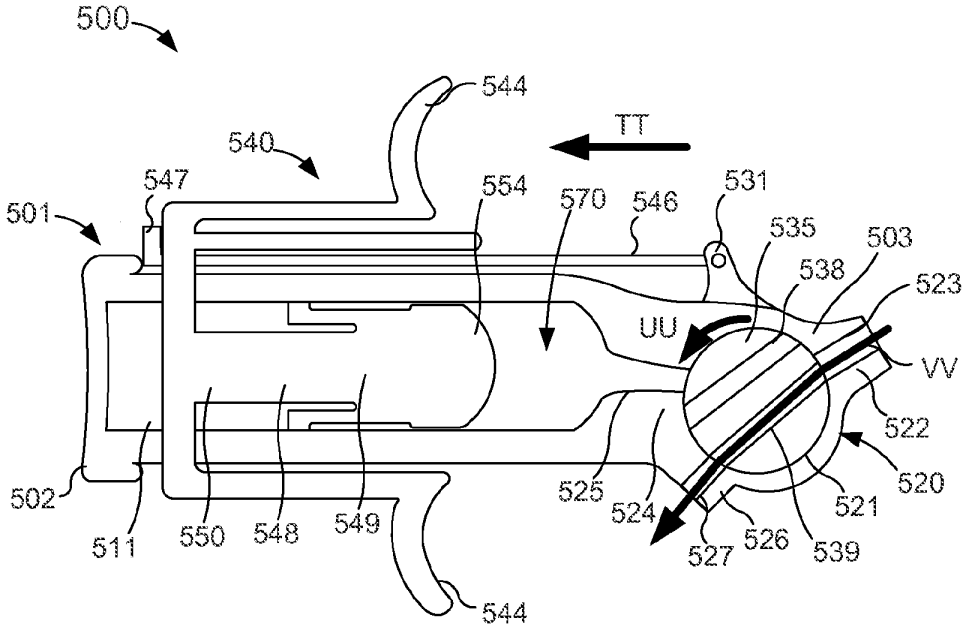

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FIG. 29

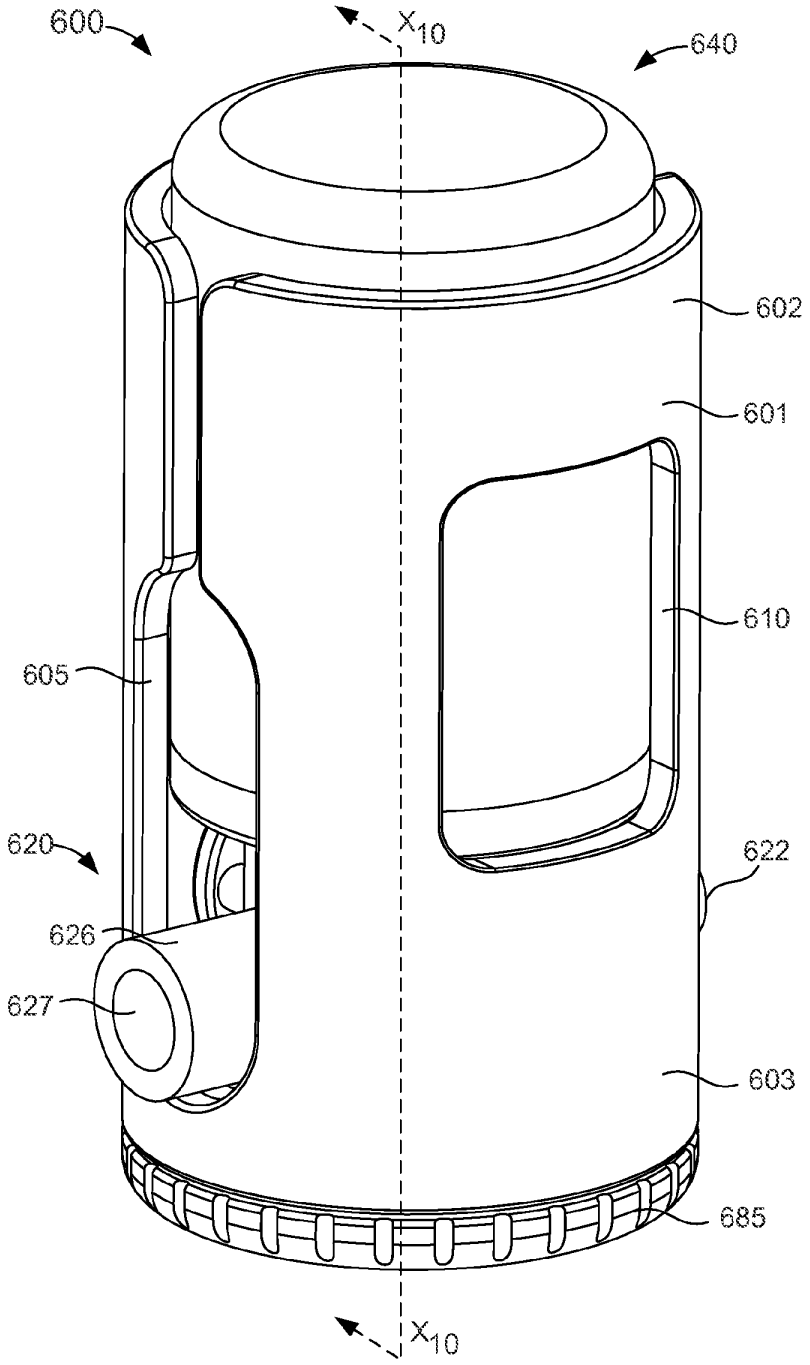


FIG. 30

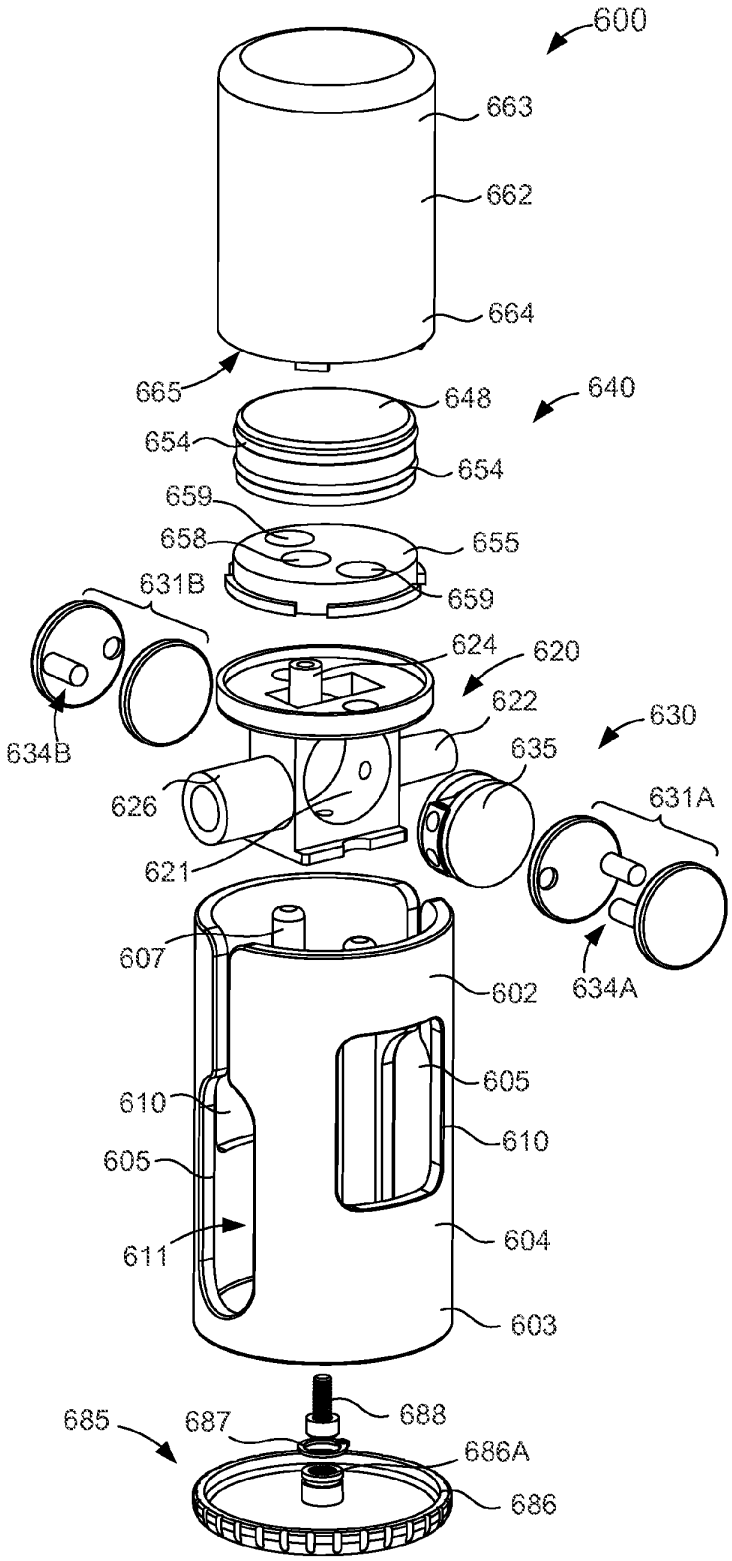

600
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658
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631B
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634B
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631A
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686A
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FIG. 31

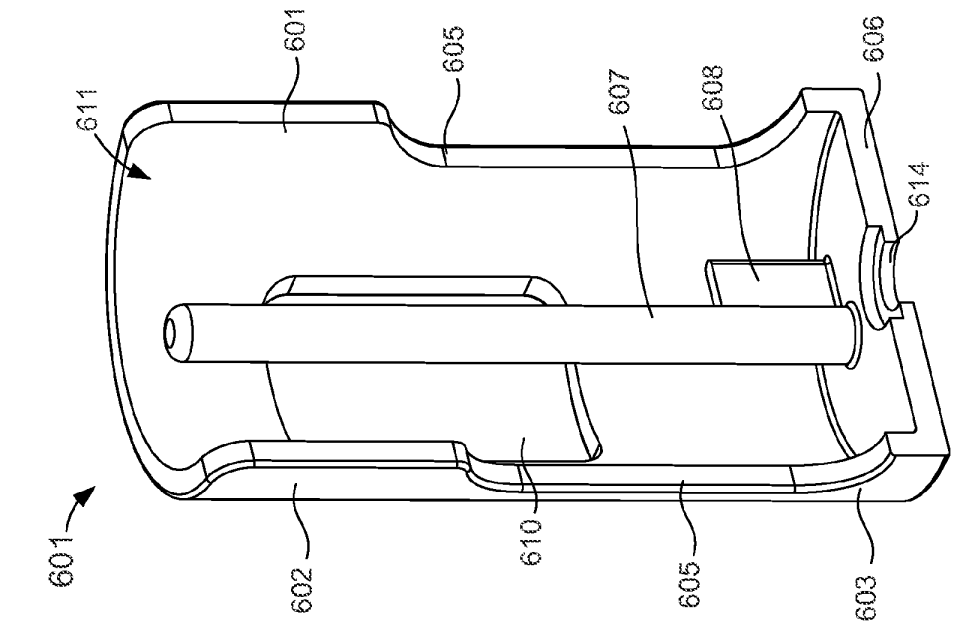

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FIG. 33

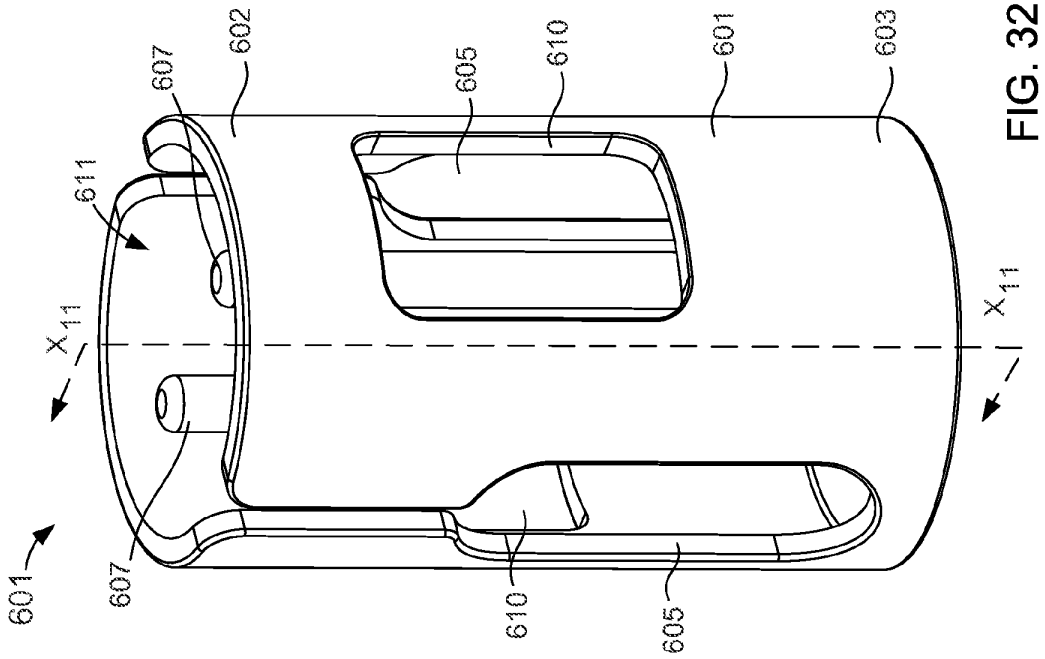

602
607
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603
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X11
X11
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607
610
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FIG. 32

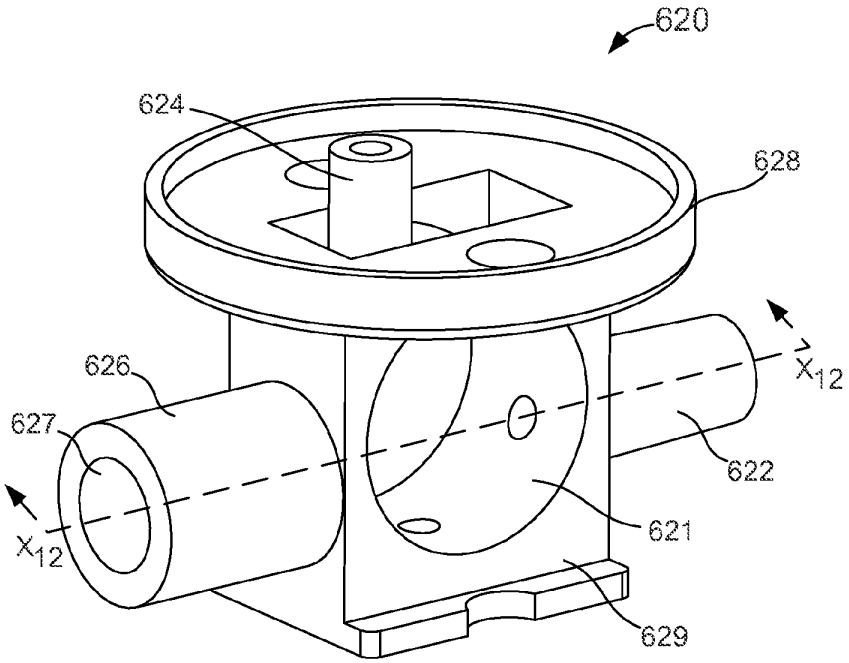

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624
628
626
627
X_{12}
622
621
X_{12}
629

FIG. 34

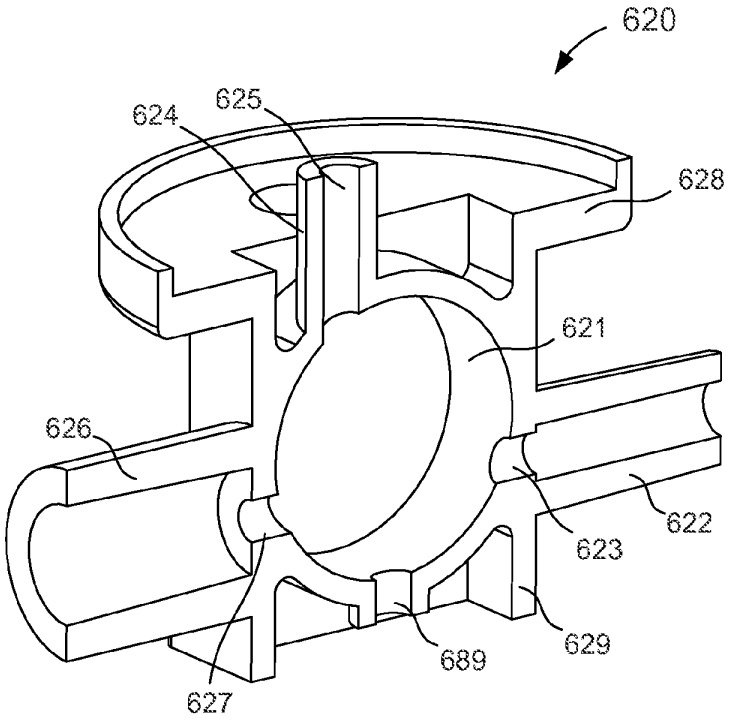

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689
627

FIG. 35

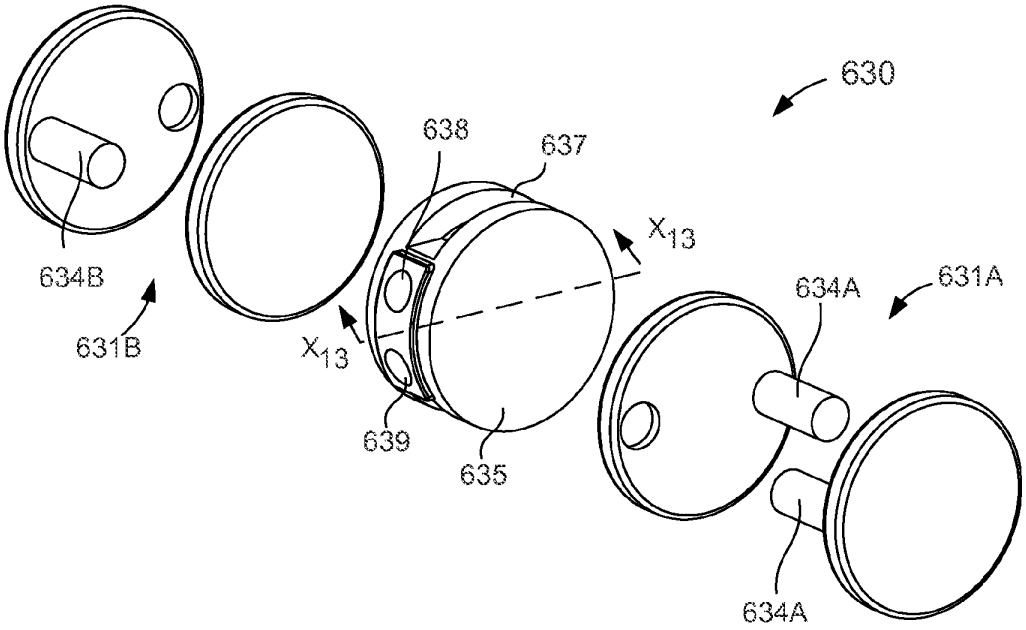

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631B
X_{13}
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634A

FIG. 36

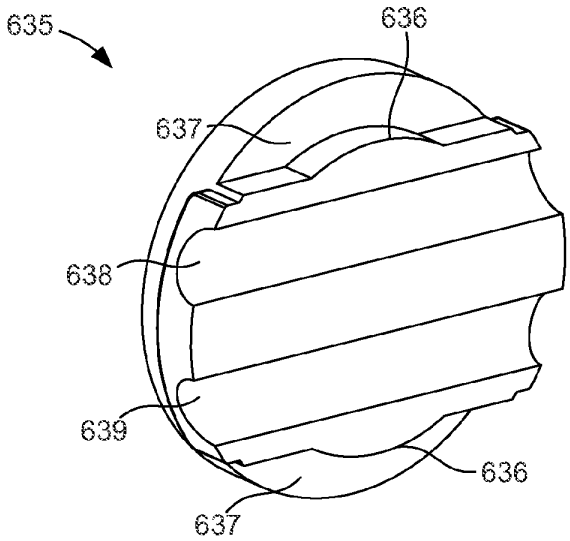

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FIG. 37

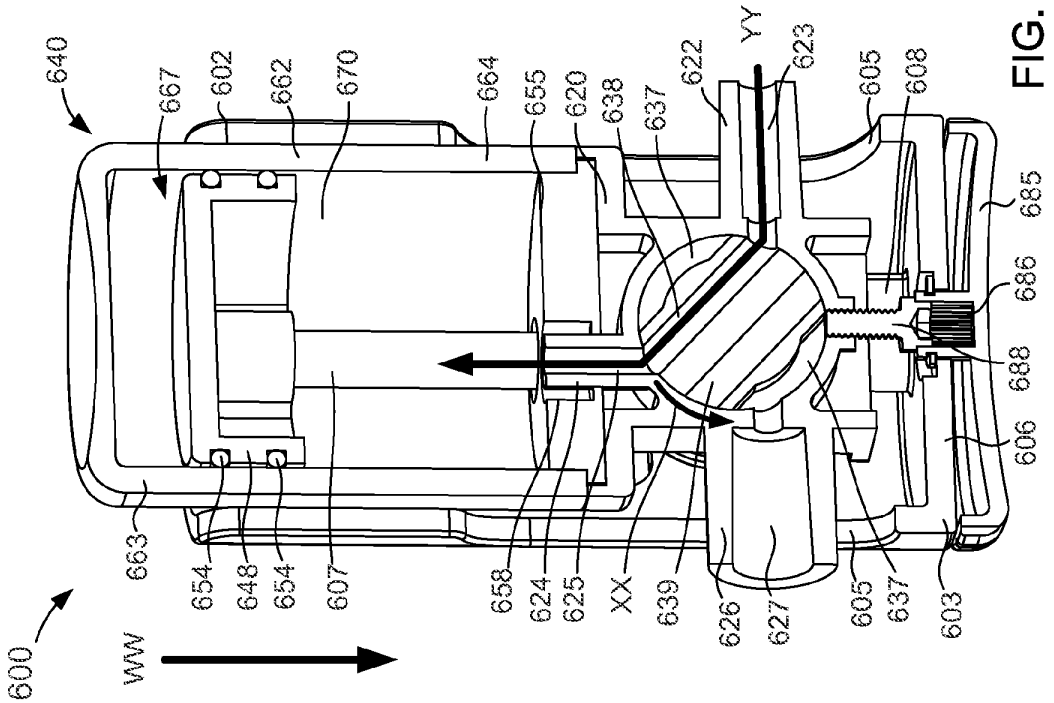

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FIG. 39

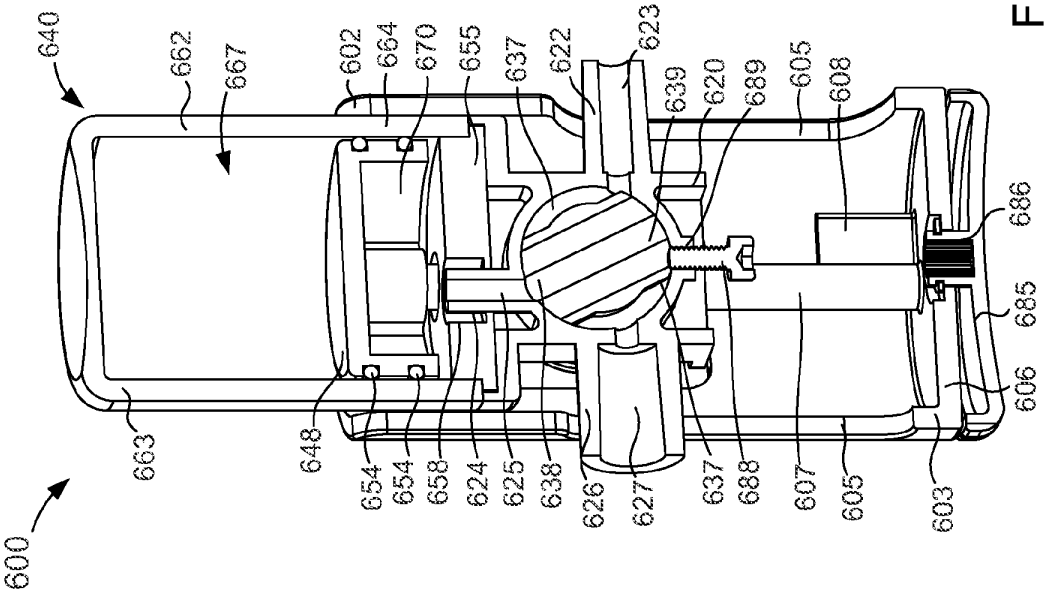

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FIG. 38

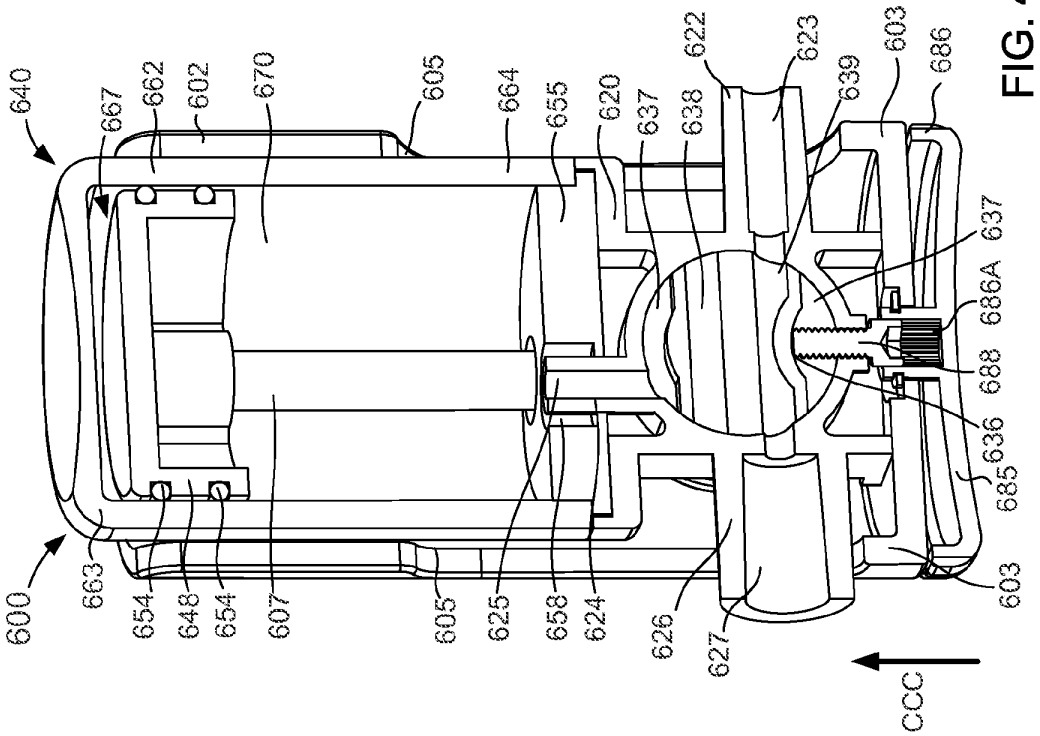

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FIG. 41

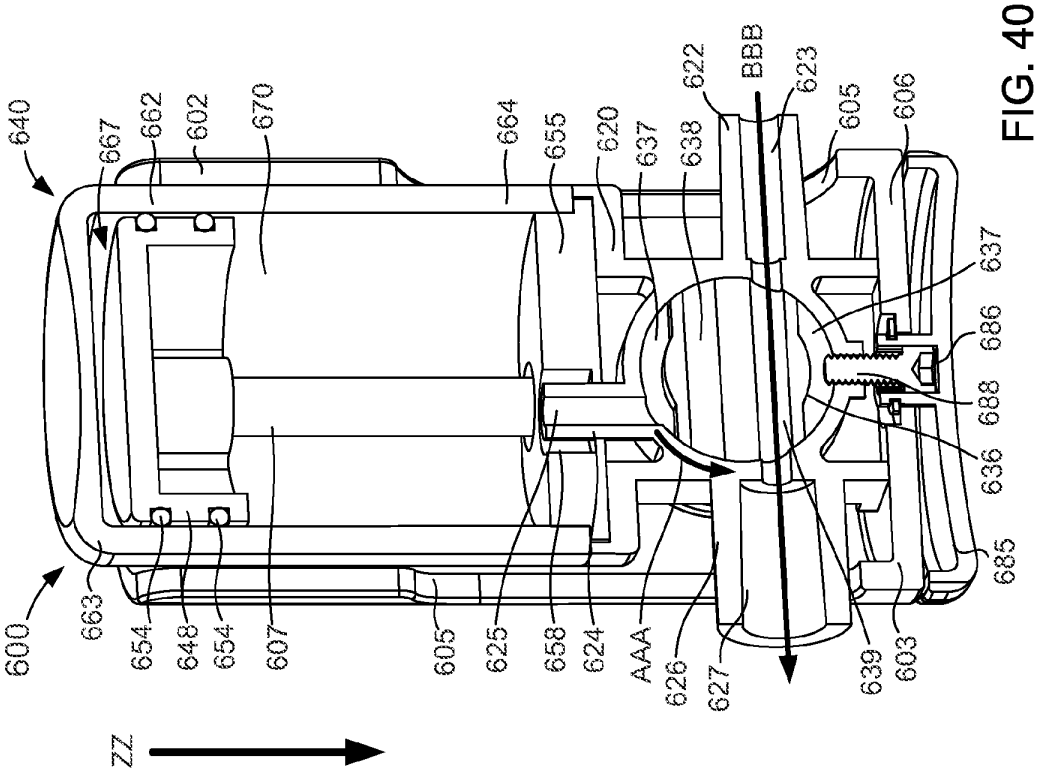

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FIG. 40

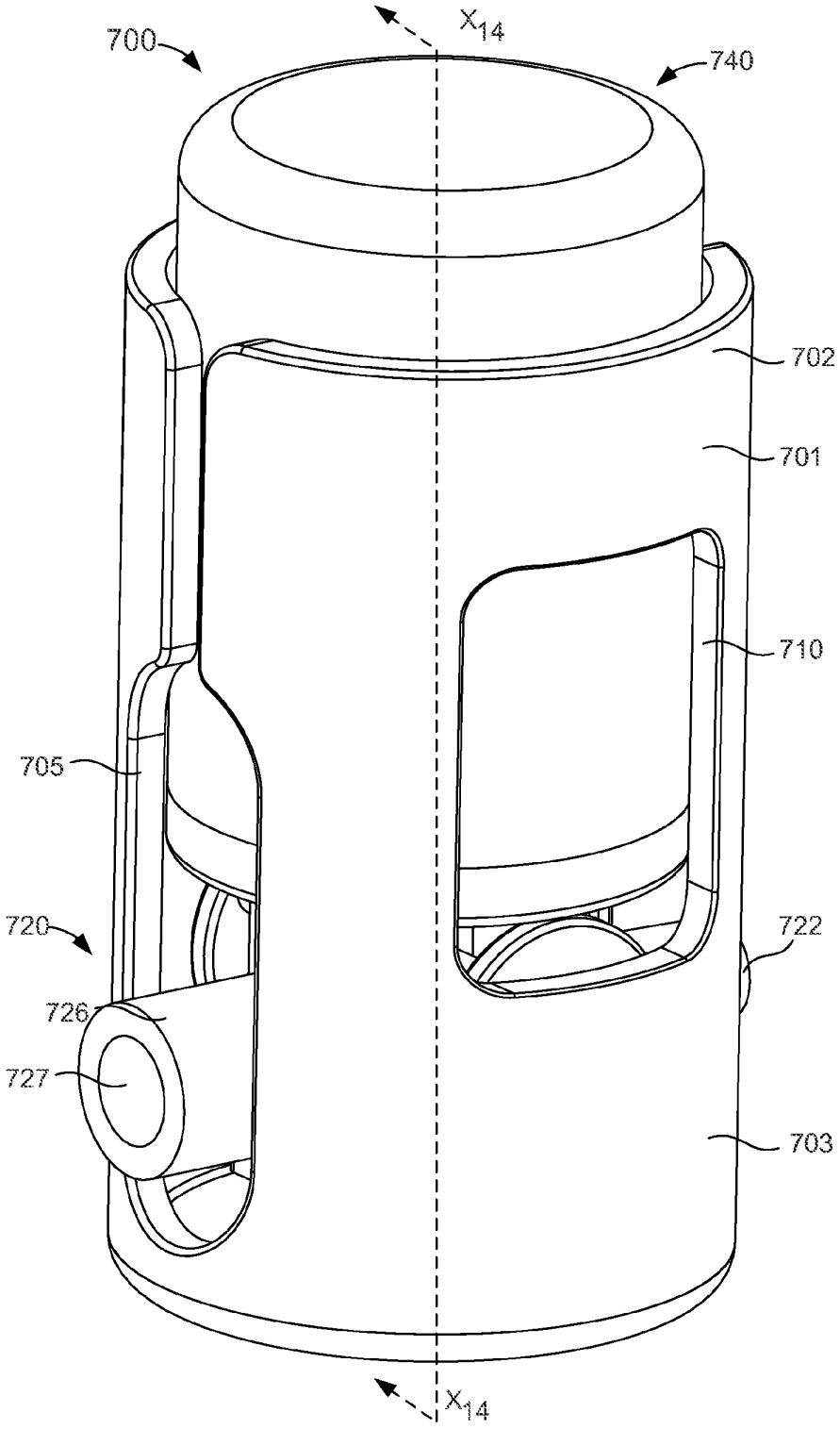


FIG. 42

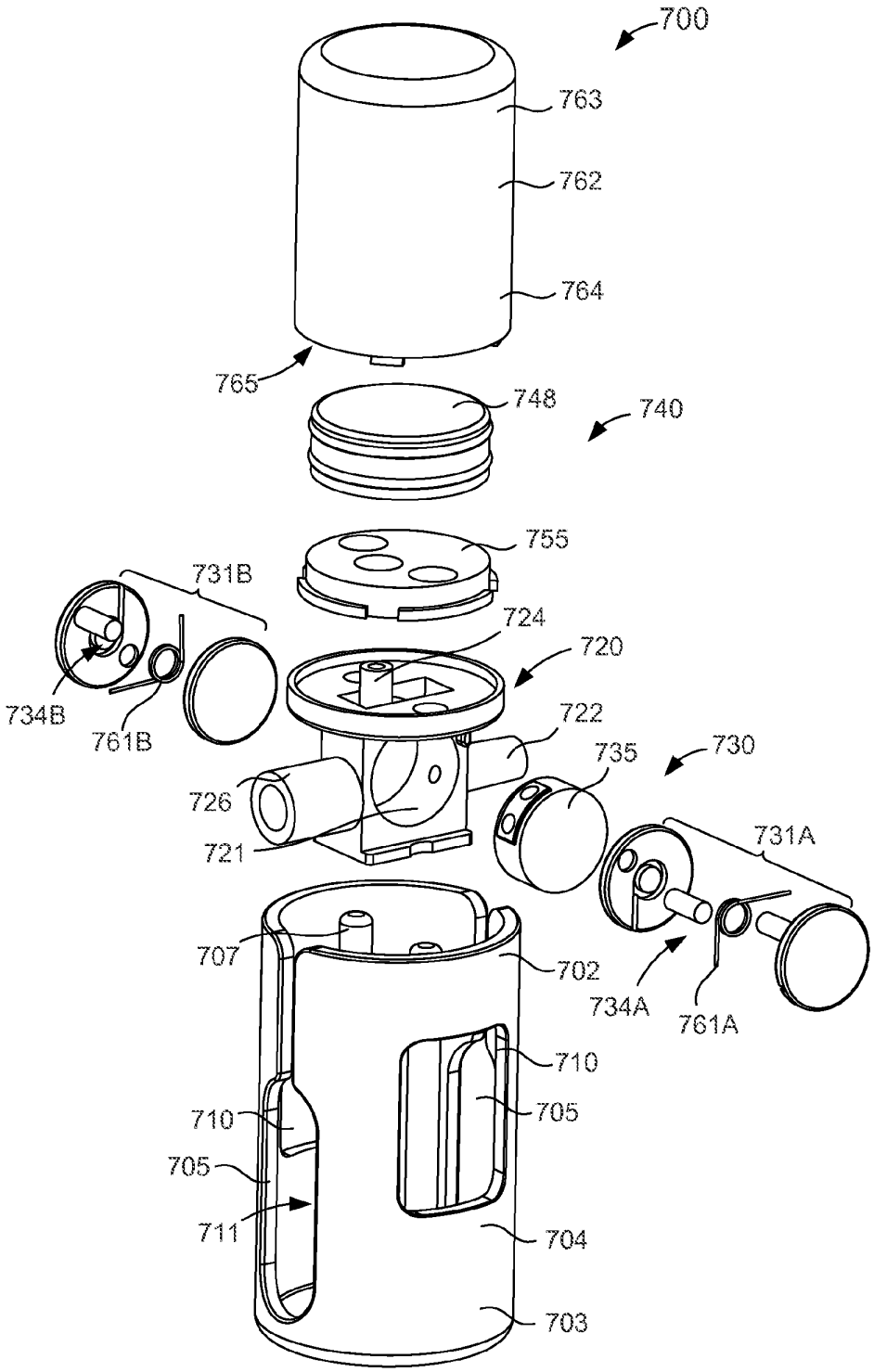

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763
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731B
724
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734B
761B
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702
734A
761A
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711
704
703

FIG. 43

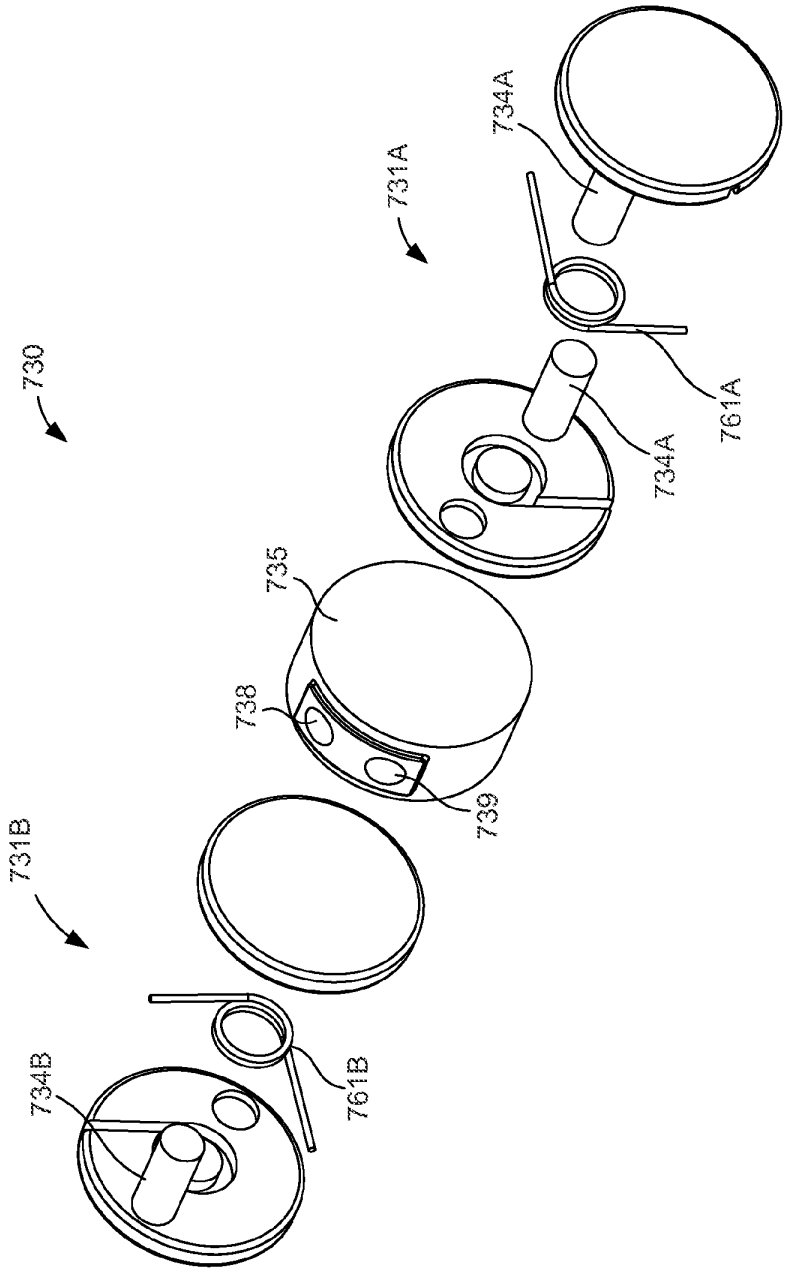


FIG. 44

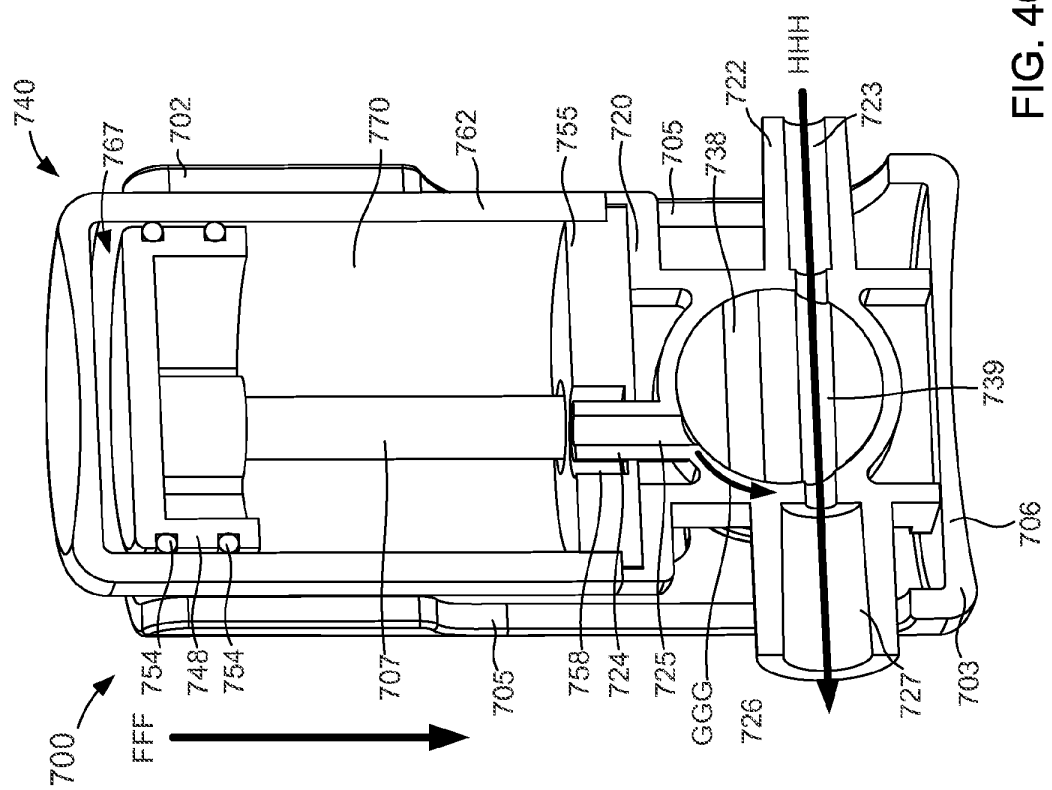

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FIG. 46

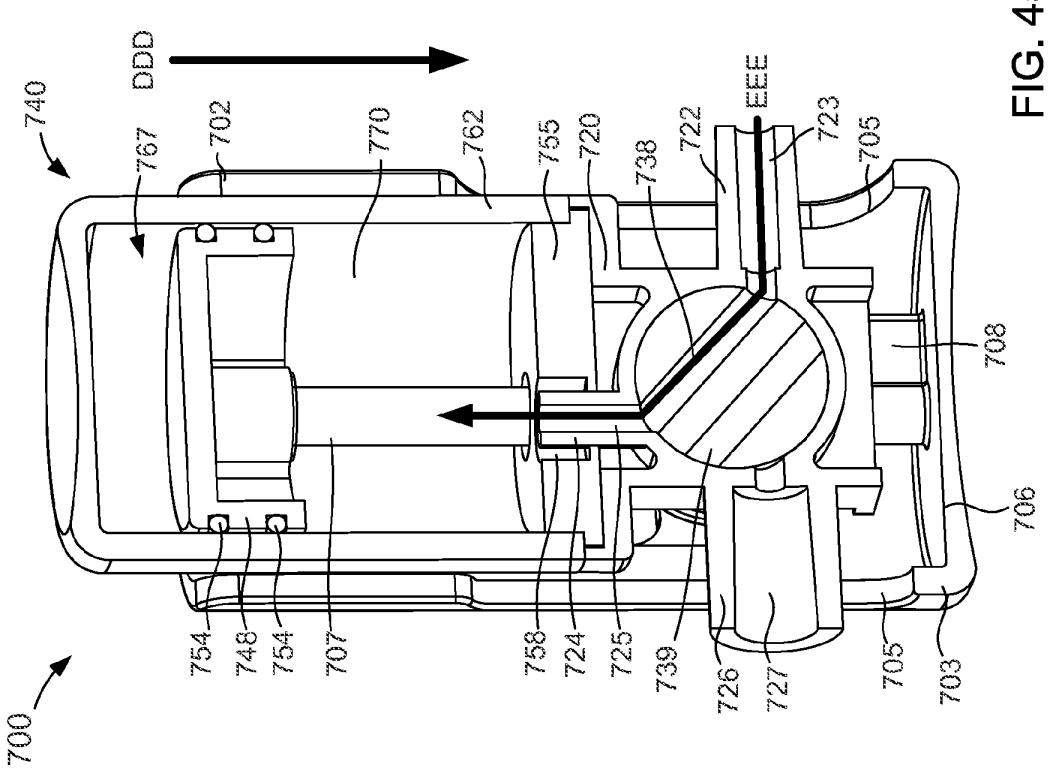

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FIG. 45

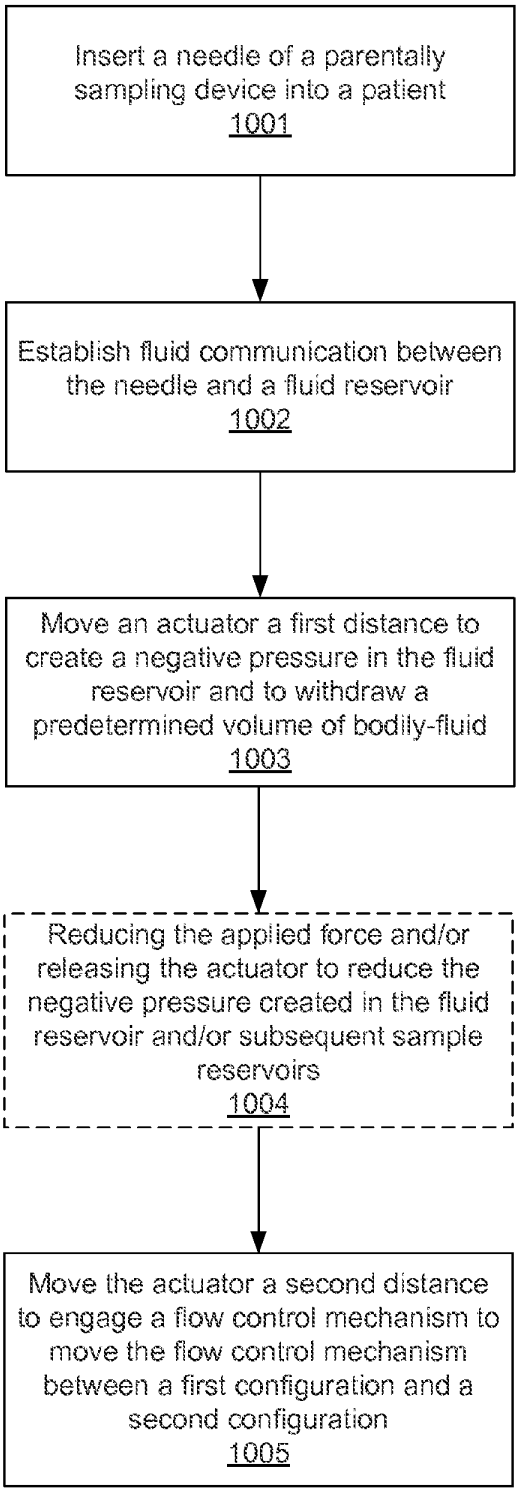

Insert a needle of a parentally sampling device into a patient
1001
Establish fluid communication between the needle and a fluid reservoir
1002
Move an actuator a first distance to create a negative pressure in the fluid reservoir and to withdraw a predetermined volume of bodily-fluid
1003
Reducing the applied force and/or releasing the actuator to reduce the negative pressure created in the fluid reservoir and/or subsequent sample reservoirs
1004
Move the actuator a second distance to engage a flow control mechanism to move the flow control mechanism between a first configuration and a second configuration
1005

FIG. 47

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US13/43289

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - A61B5/15; B01D43/00; B01L3/14; C12M1/00; C12N5/02; G01N33/49 (2013.01)
USPC - 210/516, 789; 422/918, 533; 600/573, 576, 579; 604/30, 33, 248
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC(8): A61B5/15; B01D43/00; B01L3/14; C12M1/00; C12N5/02; G01N33/49 (2013.01)
USPC: 210/516, 789; 422/918, 533; 600/573, 576, 579; 604/30, 33, 248

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
MicroPatent (US-G, US-A, EP-A, EP-B, WO, JP-bib, DE-C,B, DE-A, DE-T, DE-U, GB-A, FR-A); Public Patent Application Information Retrieval (PAIR); Google/Google Scholar; DialogPro; Pubmed/Medline: negative pressure, vacuum, contamination, sterile, low valve, rotating, actuator, inlet, outlet, reservoir, housing, body fluid, blood, semen, urine, sample, collection, specimen, assay, medical, diversion

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 4425235 A (CORNELL, WD et al.) January 10, 1984; figures 1-4; column 2, lines 56-67; column 3, lines 1-11, 18-36; column 4, lines 26-67; column 5, lines 1-13, 25-57	1-5, 14-19, 25-34
Y	US 2012/0095367 A1 (PATTON, RG) April 19, 2012; paragraphs [0041]-[0044]; claims 33, 38-41	1-5, 14-19, 25-34
Y	US 2008/0108954 A1 (MATHIAS, JM et al.) May 8, 2008; figures 6a-b; paragraph [0064]	16, 19, 29
E, X	US 2013/0116599 A1 (BULLINGTON, GJ et al.) May 9, 2013; figures 2-3; paragraphs [0037], [0068]-[0069]	1, 14, 25, 30

☐ Further documents are listed in the continuation of Box C. ☐

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
16 October 2013 (16.10.2013)	24 OCT 2013
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201	Authorized officer: Shane Thomas PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

Form PCT/ISA/210 (second sheet) (July 2009)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US13/43289

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I: Claims 1-5, 14-19 and 25-34 are directed toward a device and method for procuring bodily-fluid samples from a patient comprising an outlet port configured to be fluidically coupled to a sample reservoir; the fluid reservoir disposed in the inner volume and configured to receive and isolate a first volume of bodily-fluid withdrawn from the patient.

Group II: Claims 6-13 are directed toward a device for procuring bodily-fluid samples from a patient, the device comprising: a diverter.

Group III: Claims 20-24 are directed toward device for procuring bodily-fluid samples from a patient, the device comprising: a seal member.

-***-Continued Within the Next Supplemental Box-***-

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1-5, 14-19 and 25-34

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US13/43289

-***-Continued from Box No. III: Observations where unity of invention is lacking-***-

Group IV: Claims 35-39 are directed toward a method for procuring bodily-fluid samples using a parenteral sampling device, the device including a needle having a lumen configured for insertion into the patient, and a fluid reservoir fluidically coupleable to the needle, the method comprising: a first and second activation force.

The inventions listed as Groups I-IV do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: the special technical features of Group I include an outlet port configured to be fluidically coupled to a sample reservoir; a fluid reservoir disposed in the inner volume and configured to receive and isolate a first volume of bodily-fluid withdrawn from the patient; moving an actuator a first distance to create a negative pressure in the fluid reservoir and to withdraw a predetermined volume of bodily-fluid; moving the actuator a second distance to engage a flow control mechanism and rotate the flow control mechanism from a first configuration to a second configuration, the first configuration operable to allow bodily-fluid to flow through a first flow path from the needle to the fluid reservoir, the second configuration operable to allow bodily-fluid to flow through a second flow path from the needle to a sample reservoir, which are not present in Groups II-IV; the special technical features of Group II include a diverter disposed in the housing, the diverter having an inlet port configured to be fluidically coupled to the patient, a first outlet port configured to be fluidically coupleable to the fluid reservoir, and a second outlet port configured to be fluidically coupled to a sample reservoir, which are not present in Groups I and III-IV; the special technical features of Group III include a seal member movably disposed in the inner volume; a fluid reservoir disposed in the inner volume and at least partially defined by the seal member, the fluid reservoir configured to receive and isolate a first volume of bodily-fluid withdrawn from the patient, which are not present in Groups I-II and IV; the special technical features of Group IV include applying a first activation force to an actuator; reducing the first activation force applied to the actuator to reduce the negative pressure created in the fluid reservoir; and applying a second activation force to the actuator, which are not present in Groups I-III.

The common technical features of Groups I-III are a housing including a proximal end portion and a distal end portion and defining an inner volume therebetween, the housing having an inlet port configured to be fluidically coupled to the patient; the actuator configured to create a negative pressure in the fluid reservoir when actuated by a user; a flow control mechanism movably disposed in the housing, the flow control mechanism configured to move between a first configuration, in which the bodily-fluid can flow from the inlet port, through the flow control mechanism and to the fluid reservoir, and a second configuration, in which the fluid reservoir is fluidically isolated from the inlet port; create a negative pressure in the fluid reservoir, the actuator further configured to move the flow control mechanism from the first configuration to the second configuration after a first volume of bodily-fluid is received in the fluid reservoir from the patient.

The common technical features of Groups I and II further include an actuator movably disposed in the housing.

These common technical features are disclosed by the Cornell reference. Cornell discloses an actuator movably disposed in the housing (chamber 14 is a fluid reservoir configured to receive whole blood; figures 1-4; column 4, lines 26-37).

Since the common technical features are previously disclosed by the Cornell reference, the common features are not special and so Groups I and II lack unity.

The common technical features of Groups I and III further include an actuator operably coupled to the flow control mechanism.

These common technical features are disclosed by the Cornell reference. Cornell discloses an actuator operably coupled to the flow control mechanism (chamber 14 is a fluid reservoir configured to receive whole blood; figures 1-4; column 4, lines 26-37).

Since the common technical features are previously disclosed by the Cornell reference, the common features are not special and so Groups I and III lack unity.

The common technical features of Groups I and IV further include inserting the needle of the device into the patient; establishing fluid communication between the needle and the fluid reservoir.

These common technical features are disclosed by the Cornell reference. Cornell discloses inserting the needle of the device into the patient (distal end of cannula is inserted into vein of patient; column 4, lines 26-37); establishing fluid communication between the needle and the fluid reservoir (whole blood flows into container; column 4, lines 26-37).

Since the common technical features are previously disclosed by the Cornell reference, the common features are not special and so Groups I and IV lack unity.

The common technical features of Groups II and III further include a sealing member and a fluid reservoir defined at least in part by the sealing member.

These common technical features are disclosed by the Cornell reference. Cornell discloses a sealing member and a fluid reservoir defined at least in part by the sealing member (stopper 20 serves as a seal and is pierceable by a cannula which can be coupled to a patient; column 3, lines 1-11),

Since the common technical features are previously disclosed by the Cornell reference, the common features are not special and so Groups II and III lack unity.

Bibliographic data: EP0448795 (A2) — 1991-10-02

Compartmental body fluid collection tube.

Inventor(s): DUFRESNE CHRISTOPHER M [US] ± (DUFRESNE, CHRISTOPHER M)

Applicant(s): BECTON DICKINSON CO [US] ± (BECTON DICKINSON AND COMPANY)

Classification: **- international:** ***A61B5/15; A61B5/154; B01L3/14;*** (IPC1-7): B01L3/14
- cooperative: **A61B5/15003 (EP); A61B5/150251 (EP); A61B5/150351 (EP); A61B5/150389 (EP); A61B5/150473 (EP); A61B5/150732 (EP); A61B5/154 (EP); B01L3/5082 (EP)**

Application number: EP19900123434 19901206 Global Dossier

Priority number(s): US19900501214 19900329

Also published as: EP0448795 (A3) AU627387 (B2) AU6803590 (A) CA2031411 (A1) FI911489 (A) more

Abstract of EP0448795 (A2)

A compartmented body fluid specimen collection tube (10) is provided which allows the user to select a size compartment (14,16) depending upon the quantity of specimen required. Thus, the tube of the invention may be of the standard size which is much easier for the user to handle than very small tubes when taking a blood sample, but a selected size compartment (14,16) is available. The manufacturer of the tube itself may use a single mold for making tubes accommodating differing required specimen quantities, and, thereafter the vendor may select either size compartment (14,16) for imparting a vacuum and the other processing required into a final product. The invention allows the use of a single standard size laboratory equipment array for processing collected specimens of varying quantities, as well as a single standard stopper (28). Finally, reduced vacuum application or "partial draw" tubes are avoided, thus eliminating the problem of unpredictable specimen draw response because of varying atmospheric pressures at different locations of use.

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(12) **EUROPEAN PATENT APPLICATION**

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(51) Int. Cl.5: **B01L 3/14**

(22) Date of filing: **06.12.90**

(30) Priority: **29.03.90 US 501214**

(43) Date of publication of application:
02.10.91 Bulletin 91/40

(84) Designated Contracting States:
AT BE CH DE DK ES FR GB GR IT LI LU NL SE

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Franklin Lakes New Jersey 07417-1880(US)

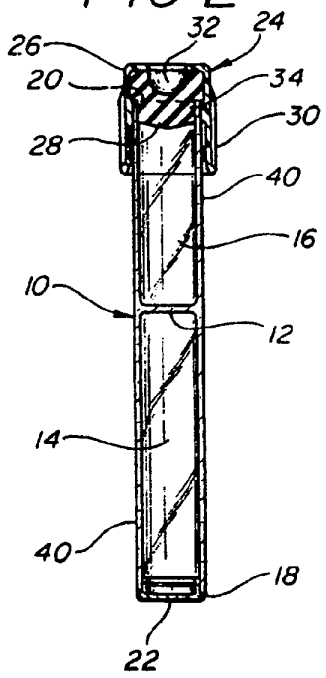
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Deichmannhaus am Hauptbahnhof
W-5000 Köln 1(DE)

(54) **Compartmental body fluid collection tube.**

(57) A compartmented body fluid specimen collection tube is provided which allows the user to select a size compartment depending upon the quantity of specimen required. Thus, the tube of the invention may be of the standard size which is much easier for the user to handle than very small tubes when taking a blood sample, but a selected size compartment is available. The manufacturer of the tube itself may use a single mold for making tubes accommodating differing required specimen quantities, and, thereafter the vendor may select either size compartment for imparting a vacuum and the other processing required into a final product. The invention allows the use of a single standard size laboratory equipment array for processing collected specimens of varying quantities, as well as a single standard stopper. Finally, reduced vacuum application or "partial draw" tubes are avoided, thus eliminating the problem of unpredictable specimen draw response because of varying atmospheric pressures at different locations of use.

FIG-2



EP 0 448 795 A2

BACKGROUND AND STATEMENT OF THE INVENTION

This invention relates to body fluid collection tubes for collecting a body fluid specimen from a patient for subsequent examination in a laboratory. More particularly, this invention relates to a blood collection tube for taking such specimens in which the tube has imparted thereto an internal vacuum with the vacuum being utilized for drawing the blood specimen from the vein of a patient.

Attempts have been made to overcome the problem of proliferation of a number of tubes for taking a plurality of specimens from a single venous entry into a patient. For example, Japanese Patent Application No. 62-51238, filed March 6, 1987 teaches a device in which a tube is divided axially into two chambers for taking two blood specimens simultaneously. However, there is no recognition for arranging different size compartments for taking different separate specimens of different size to accommodate subsequent laboratory testing of those specimens.

Other prior art arrangements, such as that taught in U.S. Patent 3,894,951, for example, provide for compartmentalized blood collection tubes in which the compartments have fluid connections for subsequent separation of a single blood sample into separate components.

In taking such specimens, differing quantities or volumes of specimens are required for certain applications. For this reason, larger and smaller tubes are manufactured for this purpose. As an alternative to making larger and smaller tubes, so-called "partial draw" tubes are provided in which the vacuum imparted to the tube is varied in order to accommodate differing quantities of specimen as required. All of these variations increase the cost of collecting blood specimens, and when it is understood that literally billions of such tubes are used and discarded after a single use each year the costs become substantial for medical applications.

This invention overcomes this problem by using a conventionally sized tube of, for example, 6cc in volume and incorporates an integral divider substantially centrally of the length of the tube to provide two compartments of differing size. Such compartments may be, for example, 2cc and 3cc. Thus, the manufacturer, rather than having to use two separate molds and two separate production lines, may manufacture a single tube having a selection of a 2cc and a 3cc compartment or chamber. Thereafter, the user or vendor may utilize or select one of the sizes of compartment and impart a vacuum thereto and place a stopper in the open end of the compartment size selected. The remaining compartment or chamber not being utilized for this particular series of tubes has a plug for closing the open end of the non-utilized chamber or compartment.

Conventional blood collection tubes have only one chamber, and volume in those conventional tubes is varied by using either larger or smaller diameter tubes, taller or shorter length tubes or varying the degree of vacuum imparted. As will be understood by practitioners-in-the-art, larger and smaller diameter tubes require specific dimensioned stoppers for accommodating those various sizes. Moreover, taller and shorter tubes require different packaging to accommodate tube length. If an accommodation is made to utilizing only a single size tube and imparting a partial vacuum for subsequent use in which only a small quantity of specimen is required in relatively large tubes, there is inconsistent draw over different areas of use because of differing atmospheric pressure gradients.

Finally, the users of tubes of different length and diameter must have varying size equipment, such as centrifuges, tube racks and like supporting arrangements to accommodate the varying sizes of tubes being utilized for collecting differing quantities of body fluid specimens for different applications.

With this invention, by contrast, a single size tube, as noted above is utilized. For this reason, the user, in the sometimes tense environment of taking a blood specimen from an individual, has a relatively large tube for handling during the collection activity Nevertheless the tube has a smaller compartment; for accommodating the actual size specimen required. Moreover, because only a single size tube relative to diameter is being utilized with the invention here, a single stopper size is required rather than a plurality of stopper sizes of differing diameters to accommodate differing diametered tubes. This reduces manufacturing requirements as well as storage requirements for such a variety of stopper sizes.

Moreover, because of the large size tubes having small compartmentalized areas, no "partial draw" vacuum applications are required. This eliminates the problem of inconsistency depending upon the atmospheric pressure gradients over many areas of use of such tubes. Finally, because of the uniformity of size of the tube, the hospital or clinical laboratory only needs to have one size equipment necessary for handling the tubes of a standard size.

A further feature of the invention may be the use of both compartments of a single tube by the phlebotomist. That is, the vendor or manufacturer of the tubes may, for example, impart vacuum to both a 3cc and a 2cc compartment or chamber in a single tube and place stoppers for sealing and

maintaining the vacuum. Thereafter, the phlebotomist, in requiring two separate blood sample volumes for different tests subsequently can first draw blood into one chamber followed by inversion of the tube and collection of blood into the second chamber. Two blood samples would then be contained in a single tube for subsequent examination in the clinical laboratory, and with only one venous entry.

Other objects and advantages of this invention will be apparent from the following description, the accompanying drawings and the appended claims.

DESCRIPTION OF THE DRAWINGS

Fig. 1 is longitudinal sectional view of the compartmentalized blood collection tube of the invention;

Fig. 2 is a longitudinal sectional view of one embodiment of the invention wherein a vacuum has been imparted to the smaller chamber or compartment of the tube of the invention and showing the sealing stopper arrangement for such a tube, together with a plug for the unused chamber;

Fig. 3 is a longitudinal sectional view of the tube of the invention reversed in its application from that shown in Fig. 2;

Fig. 4 is an enlarged partial cross-sectional view of one open end of the tube of the invention showing the mating configuration of a sealing plug applied to the open end for closing off the non-utilized chamber or compartment of the tube of the invention;

Fig. 5 is a longitudinal sectional view of a blood sample tube holder for taking a blood sample from a vein of a patient with the tube of the invention inserted therein; and

Fig. 6 is a longitudinal sectional view of a tube similar to that shown in Fig. 1, but both chambers being closed with a stopper closure for use in evacuating two chambers for collecting two specimens sequentially.

DETAILED DESCRIPTION OF THE INVENTION

Referring to the drawings in which like reference characters refer to like parts throughout the several views thereof, Fig. 1 illustrates the invention in the form of a conventionally sized blood collection tube compartmentalized in its formation to provide two chambers or compartments of differing size to accommodate differing blood sample requirements.

In Fig. 1, the device 10 is an elongated tube with walls 40 and having open ends 18, 20 at each end thereof. As can be seen in Fig. 1, tube 10 is divided by a wall 12 into compartments or chambers 14 and 16. Also, as will be seen in Fig. 1, chamber 14 is larger than chamber 16. For example, in a 6cc tube, chamber 14 may be, for example, 3cc in volume while chamber 16 may be 2cc in volume.

It will be understood that the volume amounts may be varied as use requirements dictate. Tube 10 may be comprised of a thermoplastic resin material, for example, formed in a mold to provide wall 12 integrally joined to wall 40 of tube 10.

Referring now to Fig. 2, tube 10 is shown in a prepared form for use by a vendor. In this case, the smaller dimensioned chamber 16 has had, for example, a vacuum applied thereto with a subsequent insertion of a stopper assembly 24 for maintaining the vacuum in chamber 16. The assembly 24 includes a rubber stopper for closing the open end, 20 of the tube, assembly 10. That is, the outer surface of lower portion of stopper 28 seals against the internal surface of walls 40 of the upper end of tube 10. The assembly 24 includes a plastic cap 26 connected to and surrounding elastomer stopper 28. This serves to accommodate removal of stopper 28 in a simple fashion, when required, to obtain access to the collected sample in chamber 16.

Stopper 28 includes a well 32 formed in the top surface thereof which has the purpose of reducing the vertical extent of stopper 28 in the center portion thereof to provide a diaphragm 34 of vertically smaller dimension through stopper 28 for receiving a needle such as needle 52 and the point 54 thereof, as shown in Fig. 5. The plastic portion 26 of stopper 24 assembly includes outer ridges 34 to provide an easier grip of the assembly 24 for removal thereof from the evacuated chamber 16, when required.

Referring to Fig. 4, the open end 18 of chamber 14, which in this case is not being utilized for fluid collection includes a plug 22 for stabilizing the open end 18 of the tube assembly 10 for subsequent use of the tube or for storing the tube prior to use.

In Fig. 4, an enlarged view of the open end 18 or 20 is shown to accommodate the snap-fit arrangement of plug 22 in the open end 18 or 20 of chamber 14 or 16, as the case may be, when they are not being utilized in a particular tube 10 assembly. That is, the lower end of wall 40 may include an annular indentation 36 for receiving in snap-fit engagement an annular abutment, 38 on plug 22.

Referring now to Fig. 3, a tube 10 is shown reversed from the Fig. 2 showing for accommodating use of the 3cc and/or larger compartment 14 as desired by the user. In this case, stopper assembly 24 closes the open end 18 rather than 20, while the open end 20 is closed with a plug 22. It will be understood by practitioners-in-the-art that both compartments or chambers 14, 16 may be utilized in a single tube 10 by imparting a vacuum to both chambers and using a stopper closure assembly

24 for closing both open ends 18 and 20. In such cases, a plug 22 is not utilized.

Such an arrangement is shown in Fig. 6 wherein a tube 60 similar to tube 10 is shown with chambers 64, 66 divided by wall 62. Tube 60 includes two open ends 68 and 70. In this case, a stopper assembly 24 is applied to both open ends after application of vacuum to chambers 64, 68, respectively. As discussed above, in such an application, the user collects two different volumes of specimen from a patient as required for subsequent testing purposes.

In use, the assembly 10 of the invention is inserted into a blood collection needle holder such as 42 shown in Fig. 5. Holders 42, for example, include at the closed end thereof a hub 46 with internal screw threads 48 for accommodating the screw threads of a needle holder hub 50. Thus, a plurality of needle holder hubs 50 may be, sequentially, screwed into hub 46 of needle holder 42 for repeated use. The needle 52 includes a sharpened end 56 which is inserted into the vein of a patient for collecting a blood Specimen.

Subsequent to insertion of the needle 56 into the vein of a patient, the laboratory technician, doctor or nurse inserts the tube assembly 10 into the blood collection holder 42 at the open end 43 thereof. In doing so, the technician holds onto the holder 42 utilizing the flange 44. Subsequently, the tube 10 is moved forward toward the closed end of the holder 42 until such time as the negative pressure needle point 54 passes through stopper 28. When this happens, access to the vacuum in chamber 16 takes place and the vacuum draws blood from the patient's vein through the needle 52 into chamber 16.

As will be understood by practitioners-in-the-art, the smaller chamber 16 may be, for example, of a volume of 2ccs which is all that is required for certain subsequent examinations of the specimen in the lab. A tube such as tube 60 shown in Fig. 6 may be used in holder 42 instead of tube 10. With such an arrangement, the double-ended needle assembly would include a sealing valve sleeve well known in the art so that the tube 60 may be pulled off needle point 54, and reversed for inserting the needle point 54 into the subsequent stopper 28 without blood loss, for collecting a second blood sample in chamber 66, for example.

Alternatively, the technician may use a standard size blood collection container and collect a subsequent larger blood sample, as required from the single insertion of point 56 of needle 52 in the patient's vein all as will be understood by the practitioner-in-the-art.

The blood collection tube of the invention may be comprised, preferably, from a clear molded thermoplastic material such as polyethylene, for example, or glass. Other materials which may be used, as will be appreciated by practitioners-in-the-art include various other thermoplastics such as polypropylene, polyethylene terephthalate, and polyvinyl chloride.

The evacuated chambers utilized for collection in the device of the invention here may have incorporated therein materials for reaction with the specimen being collected for providing a proper response to the collected specimen for subsequent examination in the clinical laboratory. The stopper may be comprised of an elastomer appropriate for providing the sealing required to maintain the imparted vacuum in the chamber selected for subsequent use by the laboratory technician. The plastic cover portion 26 of stopper assembly 24 may be comprised of polyethylene or other thermoplastic which may be molded into the proper shape for the assembly of the invention.

Whereas, as discussed above, specific embodiments of associated stoppers and caps have been shown, it should be understood that it is within the purview of this invention to provide other forms of closures for blood collection tubes of the kind discussed herein.

It will be understood that the invention here is most appropriate for medical applications because of the substantial reduced cost in accommodating a variety of different requirements for a body fluid specimen collection, and for reducing the number of molds required for providing an assembly which is nevertheless, much easier to handle than the miniaturized collection tubes presently being utilized for small volume specimen collection. Moreover, the arrangement herein eliminates the need for the application of "partial draw" tubes and the inconsistency apparent with the use of such partial draw tubes.

While the forms of apparatus herein described constitute preferred embodiments of the invention, it is to be understood that the invention is not limited to these precise forms of apparatus and that changes may be made therein without departing from the scope of the invention which is defined in the appended claims.

Claims

1. A blood collection tube; comprising
   (a) a tube body;
   (b) said tube body comprised of walls formed as a cylinder to define a tube body chamber;
   (c) said tube body chamber having a first open end at one end of said tube body chamber and a second open end at the end of said tube body chamber opposite said first open end;

(d) a divider wall positioned between said first and second open ends;
(e) said divider wall dividing said tube body chamber into a first and a second compartment; and
(f) said divider wall being formed integrally as one piece with said cylindrical tube body walls.

2. The blood collection tube of Claim 1, further comprising
(a) said first and second compartments being of different volume capacity.

3. The blood collection tube of Claim 1 further comprising
(a) a stopper closing one of said first and second open ends; and
(b) a plug closing the other of said open ends not closed by said stopper.

4. The blood collection tube of Claim 3, further comprising
(a) said compartment with the open end closed by said stopper being evacuated.

5. The blood collection tube of Claim 3, further comprising said stopper being comprised of
(a) a first elastomeric portion inserted into said open end in sealing engagement therewith;
(b) a plastic portion fitted over and surrounding said elastomeric portion;
(c) said plastic portion encompassing said tubular walls adjacent said open end into which said stopper is inserted;
(d) the top of said plastic portion having an opening adjacent the axis thereof for providing needle access to said elastomeric portion; and
(e) cooperating abutment means on said elastomeric portion and said plastic portion for holding said elastomeric portion and said plastic portion together.

6. The blood collection tube of Claim 3, further comprising
(a) said tube walls and said divider wall are comprised of a material selected from the group consisting of polyethylene, polypropylene, polyethylene terephthalate, polyvinyl chloride and glass.

7. A blood collection tube; comprising
(a) a tube body;
(b) said tube body comprised of walls formed as a cylinder to define a tube body chamber;
(c) said tube body chamber having a first open end at one end of said tube body chamber and a second open end at the end of said tube body chamber opposite said first open end;
(d) a divider wall positioned between said first and second open ends;
(e) said divider wall dividing said tube body chamber into a first and a second compartment;
(f) said divider wall being formed integrally as one piece with said cylindrical tube body walls;
(g) said first and second compartments being of different volume capacity;
(h) a first stopper closing said first open end; and
(i) a second stopper closing said second open end.

8. The blood collection tube of Claim 7, further comprising
(a) both said first and said second compartments being evacuated.

9. The blood collection tube of Claim 7, further comprising each of said first and second stoppers comprised of
(a) a first elastomeric portion inserted into said open end in sealing engagement therewith;
(b) a plastic portion fitted over and surrounding said elastomeric portion;
(c) said plastic portion encompassing said tubular walls adjacent said open end into which said stopper is inserted;
(d) the top of said plastic portion having an opening adjacent the axis thereof for providing needle access to said elastomeric portion; and
(e) cooperating abutment means on said elastomeric portion and said plastic portion for holding said elastomeric portion and said plastic portion together.

10. The blood collection tube of Claim 7, further comprising
(a) said tube walls and said divider wall are comprised of a material selected from the group consisting of polyethylene, polypropylene, polyethylene terephthalate, polyvinyl chloride and glass..

FIG-1

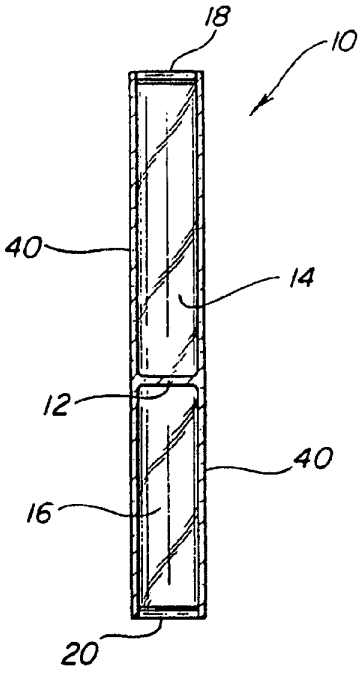


FIG-2

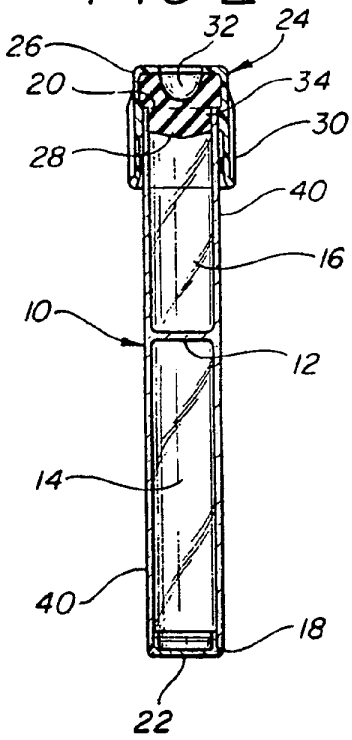


FIG-3

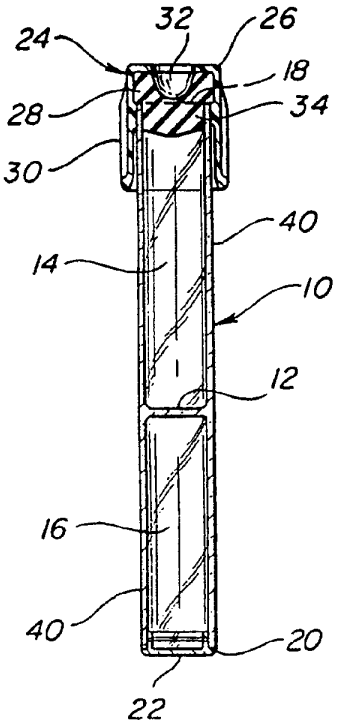


FIG-4

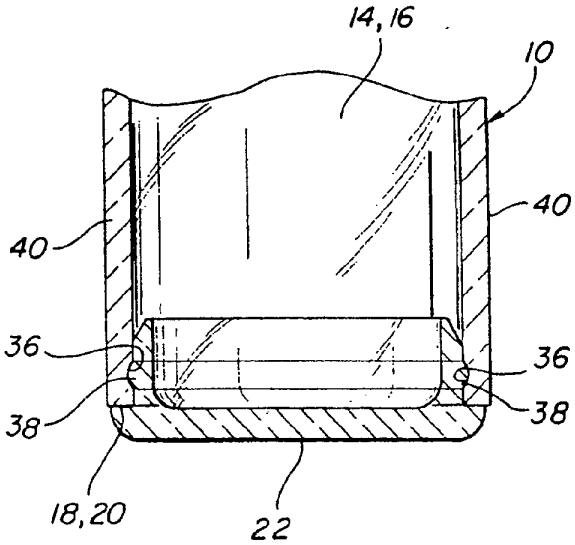


FIG-5

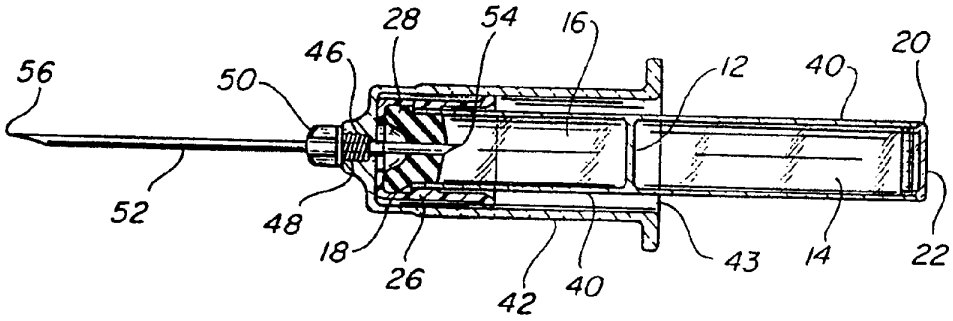
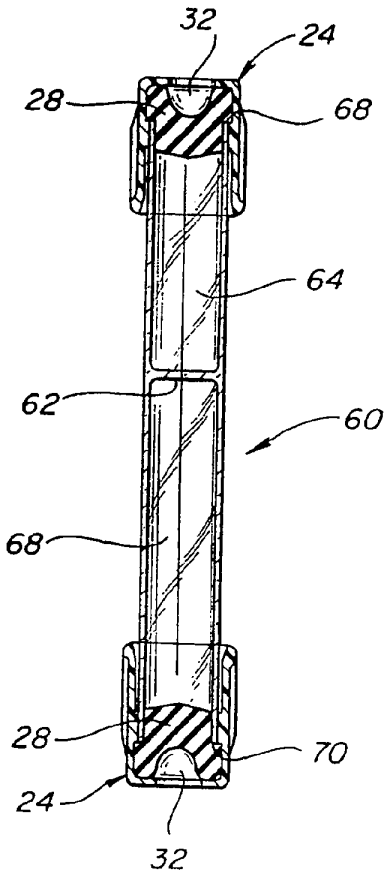

28
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FIG-6


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Patentanwälte PartG mbB
02. Dez. 2019
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Date
02.12.19

Reference	Application No./Patent No.
EPA-148 105	19200766.4 - 1132
Applicant/Proprietor	
Kurin, Inc.	

Communication

The extended European search report is enclosed.

The extended European search report includes, pursuant to Rule 62 EPC, the European search report (R. 61 EPC) or the partial European search report/ declaration of no search (R. 63 EPC) and the European search opinion.

Copies of documents cited in the European search report are attached.

☑ 0 additional set(s) of copies of such documents is (are) enclosed as well.

The following have been approved:

☐ Abstract ☑ Title

☑ The Abstract was modified and the definitive text is attached to this communication.

The following figure(s) will be published together with the abstract: 15C

Refund of search fee
If applicable under Article 9 Rules relating to fees, a separate communication from the Receiving Section on the refund of the search fee will be sent later.

Should you wish to further prosecute this application in the examination phase, your attention is drawn to the provisions of Rule 70a EPC. An invitation to respond to the extended European search report will be issued once the date of publication of the European search report has been mentioned in the European Patent Bulletin (R. 69(1), R. 70(2) EPC).

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EUROPEAN SEARCH REPORT

Application Number
EP 19 20 0766

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)
X	WO 96/05875 A1 (BAXTER INT [US]) 29 February 1996 (1996-02-29) * the whole document *	1-14	INV. A61B5/15 A61B5/153 A61B5/154
A	WO 2011/162772 A1 (CLEARVIEW PATIENT SAFETY TECHNOLOGIES LLC [US]; FISCHEL LLOYD [US]; BR) 29 December 2011 (2011-12-29) * paragraph [0070] * * figure 15 * * abstract *	1-14	
A	US 2009/227953 A1 (TAN CHEE LEONG [SG] ET AL) 10 September 2009 (2009-09-10) * the whole document *	1-14	
A	JP H08 257018 A (NISSHO KK) 8 October 1996 (1996-10-08) * abstract; figures *	1-14	
A	US 4 416 290 A (LUTKOWSKI LAWRENCE [US]) 22 November 1983 (1983-11-22) * abstract; figures *	1-14	TECHNICAL FIELDS SEARCHED (IPC) A61B
A	US 3 648 684 A (BARNWELL CLEORA W ET AL) 14 March 1972 (1972-03-14) * abstract; figures *	1-14	
A	EP 1 665 986 A1 (BECTON DICKINSON CO [US]) 7 June 2006 (2006-06-07) * figures 13,14 *	1-14	
A	US 4 056 101 A (GEISSLER ULRICH C ET AL) 1 November 1977 (1977-11-01) * abstract; figures *	1-14	

-/--

The present search report has been drawn up for all claims

Place of search	Date of completion of the search	Examiner
Berlin	18 November 2019	Schultz, Ottmar

CATEGORY OF CITED DOCUMENTS

X : particularly relevant if taken alone
Y : particularly relevant if combined with another document of the same category
A : technological background
O : non-written disclosure
P : intermediate document

T : theory or principle underlying the invention
E : earlier patent document, but published on, or after the filing date
D : document cited in the application
L : document cited for other reasons

& : member of the same patent family, corresponding document

EPO FORM 1503 03.82 (P04C01)

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EUROPEAN SEARCH REPORT

Application Number
EP 19 20 0766

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)
A	US 2013/317391 A1 (BULLINGTON GREGORY J [US] ET AL) 28 November 2013 (2013-11-28) * paragraphs [0084] - [0094] * * figures 16-18 *	1-14	

TECHNICAL FIELDS SEARCHED (IPC)

The present search report has been drawn up for all claims

Place of search	Date of completion of the search	Examiner
Berlin	18 November 2019	Schultz, Ottmar

CATEGORY OF CITED DOCUMENTS

X : particularly relevant if taken alone
Y : particularly relevant if combined with another document of the same category
A : technological background
O : non-written disclosure
P : intermediate document

T : theory or principle underlying the invention
E : earlier patent document, but published on, or after the filing date
D : document cited in the application
L : document cited for other reasons

& : member of the same patent family, corresponding document

EPO FORM 1503 03.82 (P04C01)

ANNEX TO THE EUROPEAN SEARCH REPORT ON EUROPEAN PATENT APPLICATION NO. EP 19 20 0766

This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report. The members are as contained in the European Patent Office EDP file on
The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

18-11-2019

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9605875 A1	29-02-1996	AT 208640 T	15-11-2001
		AU 686450 B2	05-02-1998
		CA 2173331 A1	29-02-1996
		DE 69523887 D1	20-12-2001
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		EP 0725658 A1	14-08-1996
		JP H09504726 A	13-05-1997
		US 5947932 A	07-09-1999
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WO 2011162772 A1	29-12-2011	NONE	
US 2009227953 A1	10-09-2009	US 2009227953 A1	10-09-2009
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EP 1665986 A1	07-06-2006	BR PI0505336 A	11-07-2006
		EP 1665986 A1	07-06-2006
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		JP 2006150083 A	15-06-2006
		US 2006129064 A1	15-06-2006
US 4056101 A	01-11-1977	NONE	
US 2013317391 A1	28-11-2013	US 2013317391 A1	28-11-2013
		US 2015099996 A1	09-04-2015
		US 2015351678 A1	10-12-2015
		US 2018092584 A1	05-04-2018
		US 2019209066 A1	11-07-2019

EPO FORM P0459

Information on Search Strategy - Pilot phase (see OJ 2015, A86)
The type of information contained in this sheet may change during the pilot for improving the usefulness of this new service.

Application Number
EP 19 20 0766

TITLE: BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE

APPLICANT: Kurin, Inc.

IPC CLASSIFICATION: A61B5/15, A61B5/153, A61B5/154

EXAMINER: Schultz, Ottmar

CONSULTED DATABASES: EPODOC, WPI, COMBI, TXT+

CLASSIFICATION SYMBOLS DEFINING EXTENT OF THE SEARCH:

IPC:

CPC: A61B5/15003, A61B5/150213, A61B5/150389, A61B5/150473, A61B5/150572, A61B5/153, A61B5/154

FI/F-TERMS:

KEYWORDS OR OTHER ELEMENTS FEATURING THE INVENTION:
See claims.

EPO FORM P0A42

ABSTRACT / ZUSAMMENFASSUNG / ABRÉGÉ

19200766.4

Blood sample optimization systems and methods are described that reduce or eliminate contaminates in collected blood samples, which in turn reduces or eliminates false positive readings in blood cultures or other testing of collected blood samples. A blood sample optimization system can include a blood sequestration device (1500) located between a patient needle and a sample needle. The blood sequestration device can include a sequestration chamber (1508) for sequestering an initial, potentially contaminated aliquot of blood, and may further include a sampling channel (1506) that bypasses the sequestration chamber to convey likely uncontaminated blood between the patient needle and the sample needle after the initial aliquot of blood is sequestered in the sequestration chamber.

The examination is being carried out on the **following application documents**

Description, Pages

1-43 as originally filed

Claims, Numbers

1-14 as originally filed

Drawings, Sheets

1/50-50/50 as originally filed

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Reference is made to the following document; the numbering will be adhered to in the rest of the procedure.

D1: WO 96/05875 A1 (BAXTER INT [US]) 29 February 1996.

1 The present application does not meet the requirements of Article 52(1) EPC, because the subject-matter of claims 1 and 6 are not new in the sense of Article 54(1) and (2) EPC.

The reasons are as follows:

1.1 Document D1 discloses (the references in parentheses applying to this document) all the features of claim 1, namely:

"A blood sequestration device (see figure 1: ref. sign 10 *"closed system blood sampling device"*) **comprising;**

an inlet port (see figure 1: ref. sign 14 *"cannula tip"*);

a junction (see fig. 1: the area where the bore 36 connects with bore 18) **connected with the inlet port;**

a sequestration chamber (see figure 1: ref. sign 22 *"blood disposal chamber"*) **having a vent** (see figure 1: ref. sign 30 *"liquid tight, air permeable hydrophobic membrane"*) **comprising an air permeable blood barrier;**

a sampling channel (see figure 1: ref. sign 36 *"bore"*) **having a proximal end connected with the inlet port via the junction and a distal end connected with an outlet port** (see fig. 1: ref. sign 42 *"luer"*); **and**

a housing (see fig. 1) **that houses and defines the inlet port, the junction, the sequestration chamber, and the sampling channel, and the outlet port,**

whereby the sequestration chamber (see figure 1: ref. sign 22 *"blood disposal chamber"*) **is connected** (see fig. 1) **with the inlet port via the junction which is configured to direct** (see page 3, lines 1 to 4: *"... It also feeds an initial fraction of withdrawn blood to a communicating blood disposal chamber which has an air permeable liquid sealed end ..."*) **the first portion of blood to the sequestration chamber** (see figure 1: ref. sign 22 *"blood disposal chamber"*), **and the air permeable blood barrier includes an air permeable material that seals at least partially upon contact with a portion of the first portion of blood"**.

Claim 1 is thus not novel (Art. 54(1)(2) EPC).

1.2 Document D1 also discloses (the references in parentheses applying to this document) all the features of claim 1, namely:

"A system of a blood sequestration device (see figures 1, 2: ref. sign 10 *"closed system blood sampling device"*), **a blood sampling pathway** (see figures 2: ref. sign 50 *"venipuncture device"*) **having a patient needle, and a sample collection device** (see figures 2: ref. sign 70 *"syringe"*), **the blood sequestration device comprising;**

an inlet port (see figure 1: ref. sign 14 *"cannula tip"*) **connected with the patient needle;**

a junction (see fig. 1: the area where the bore 36 connects with bore 18) **connected with the inlet port opposite the blood sampling pathway;**

a sequestration chamber (see figure 1: ref. sign 22 *"blood disposal chamber"*) **having a vent** (see figure 1: ref. sign 30 *"liquid tight, air permeable hydrophobic membrane"*) **comprising an air permeable blood barrier;**

a sampling channel (see figure 1: ref. sign 36 *"bore"*) **having a proximal end connected with the inlet port; and**

an outlet port (see fig. 1: ref. sign 42 *"luer"*) **connected with a distal end of the sampling channel and with the sample collection device; and**

a housing (see fig. 1) **that houses and defines the inlet port, the outlet port, the sequestration chamber, and the sampling channel,**

whereby the sequestration chamber is connected with the inlet port and the air permeable blood barrier includes an air permeable material that seals at least partially upon contact with blood".

Claim 6 is thus not novel (Art. 54(1)(2) EPC).

2 The dependent claims 2 to 5 and 7 to 14 do not appear to contain any features which, in combination with the features of any claim to which they refer, meet the requirements of the EPC with respect to novelty (Art. 54(1)(2), EPC) and/or inventive step (Article 56, EPC), the reasons being as follows:

Ad claims 2, 12, 13: Not novel, see D1, figure 1;

Ad claims 3, 4: Not novel, see D1, figures 1, 2;

Ad claims 5, 14: Not inventive to design the housing from two parts, see D1, figure 1;

Ad claims 7, 8, 9, 10, 11: Not novel, see D1, figures 2.

3 Further objections:

3.1 The closest prior art (see document D1) is not acknowledged in the description (Rule 42(1)(b) EPC).

3.2 Claim-like clauses appended at the end of the description (see pages 39 to 43) must also be deleted prior to grant, since they otherwise may lead to unclarity as to the actual scope of protection (Guidelines F-IV, 4.4).

3.3 "Incorporation by reference" is not an option in the European procedure since the concerned subject-matter does not fall within the scope of the claims (Article 84 EPC); the description thus requires amendment in this respect at paragraph [0001].

4 It is not at present apparent which part of the application could serve as a basis for a new, allowable claim.

5 If, however, filing an amended set of claims, **arguments in support of inventive step in the form of a problem-solution approach according to the Guidelines G-VII, 5 should be provided in an accompanying letter**.

6 Since the present description will not be consistent with the subject-matter as defined by such an amended set of claims, **to expedite the examining procedure** the applicant should then at the same time bring **all affected passages** of entire description into conformity with such an amended set of claims, i.e. the applicant should limit the application to the embodiment of the invention, namely as defined by an amended independent claim, and to the preferred embodiments, namely as defined by amended dependent claims.

In this respect, it is noted that terms like ***"... may ..."***, ***"... can ..."***, **etc.** as used throughout the description are not allowed if the related feature is part of the invention as defined by the independent claims. **Appropriate amendments are required.**

It is noted that anything denoted *"... embodiment ..."* and *"... invention ..."* must fall under the scope of protection sought, otherwise it is not an embodiment and not an invention.

Therefore, all the terms like *"... aspect of the invention ..."*, *"... embodiment ..."*, *"... invention ..."*, *"... variation of the invention ..."*, etc. related to all further inventions and further features or methods not covered by the amended set of claims should be replaced by the term *"... **example not being part of the invention** ..."*, if not then the remaining embodiments are to be excised from the amended set of claims, description and drawings or to be denoted not forming part of the present invention but represent background art that is useful for understanding the invention (see Guidelines F-IV, 4.3(iii)).

The subject-matter concerning the embodiments to be excised may be made the subject of one or more divisional applications according to Rule 36 EPC.

7 Care should then also be taken during revision of the description and the claims not to add subject-matter which extends beyond the content of the application as originally filed (Article 123(2) EPC).

Intermediate generalisations should also be avoided (Art. 123(2) EPC and Guidelines H-V, 3.2.1).

To make sure that the new set of claims meets the requirements of Art. 123(2) EPC and Guidelines H-V, 3.2.1, the applicant is requested to double check and provide basis for the amendments by references to the application as filed in the accompanying letter in his own interest.

+++++

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Application No.	Ref.	Date
17 840 467.9 - 1132	EPA-147 134	22.04.2020
Applicant Kurin, Inc.		

Communication under Rule 71(3) EPC

1. Intention to grant

You are informed that the examining division intends to grant a European patent on the basis of the above application, with the text and drawings and the related bibliographic data as indicated below.

A copy of the relevant documents is enclosed.

1.1 In the text for the Contracting States:
AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HR HU IE IS IT LI LT LU LV MC MK MT NL NO PL PT RO RS SE SI SK SM TR

Description, Pages

1, 2, 4-44	as published	
3, 3a	filed in electronic form on	16-12-2019

Claims, Numbers

1-14	filed in electronic form on	16-12-2019

Drawings, Sheets

1/69-69/69	as published

With the following amendments to the above-mentioned documents proposed by the division

Description, Pages	1, 20, 23, 27, 40

Comments

Registered letter
EPO Form 2004C 12.17CXP

DESCRIPTION
Page 1: Deletion of irrelevant and/or superfluous information (Rule 48(1)(c) EPC, Guidelines F-II, 7.4)
Pages 20, 23, 27, 40: Insertion of SI/metric units (Rule 49(10) EPC)
CLAIMS
Page 1: Deletion of irrelevant and/or superfluous information (Rule 48(1)(c) EPC, Guidelines F-II, 7.4)

1.2 Bibliographic data

The title of the invention in the three official languages of the European Patent Office, the international patent classification, the designated contracting states, the registered name(s) of the applicant(s) and the other bibliographic data are shown on **EPO Form 2056** (enclosed).

2. Invitation

You are invited, **within a non-extendable period of four months** of notification of this communication,

2.1 to EITHER approve the text communicated above and verify the bibliographic data (Rule 71(5) EPC)

(1) by filing a translation of the claim(s) in the other two official languages of the EPO

		Fee code	EUR
(2a)	by paying the fee for grant including the fee for publication:	**007**	960.00
	minus any amount already paid (Rule 71a(5) EPC):		0.00
		Total amount:	960.00
(3)	by paying additional claims fees under Rule 71(4) EPC; number of claims fees payable: 0	**016**	0.00
	minus any amount already paid (Rule 71a(5) EPC):		0.00
		Total amount:	0.00

Important: If the translations of the claims and fees have already been filed and paid respectively in reply to a previous communication under Rule 71(3) EPC, e.g. in the case of resumption of examination after approval (see Guidelines C-V, 6), **agreement as to the text to be granted** (Rule 71a(1) EPC) must be expressed within the same time limit (e.g. by approving the text and verifying the bibliographic data, by confirming that grant proceedings can go ahead with the documents on file and/or by stating which translations of the claims already on file are to be used).

Note 1: See "Notes concerning fee payments" below.
Note 2: Any overpaid "minus" amounts will be refunded when the decision to grant (EPO Form 2006A) has been issued.
Note 3: For the calculation of the grant fee under Article 2(2), No. 7, RFees (old fee structure), the number of pages is determined on the basis of a clean copy of the application documents, in which text deleted as a result of any amendments by the examining division is not shown. Such clean copy is made available via on-line file inspection only.

2.2 OR, in the case of disapproval, to request reasoned amendments or corrections to the text communicated above or keep to the latest text submitted by you (Rule 71(6) EPC).

In this case the translations of the claims and fee payments mentioned under point 2.1 above are NOT due.

The terms "amendment(s)" and "correction(s)" refer only to amendments or corrections of the application documents and not of other documents (e.g. bibliographic data, the designation of the inventor, etc.).

If filing amendments, you must identify them and indicate the basis for them in the application as filed. Failure to meet either requirement may lead to a communication from the examining division requesting that you correct this deficiency (Rule 137(4) EPC).

2.3 Bibliographic data

Where you request a change or correction of bibliographic data in response to the Rule 71(3) communication, this will **not** cause the sending of a further communication under Rule 71(3) EPC. You will still have to pay the fees and file translations in reply to the Rule 71(3) communication in the case of 2.1 above, unless you also file a reasoned request for amendments or corrections in response to the Rule 71(3) communication (see case 2.2 above).

3. Loss of rights

If neither of the two possible actions above (see points 2.1 or 2.2) is performed in due time, the European patent application will be deemed to be withdrawn (Rule 71(7) EPC).

4. Further procedure

4.1 In the case of point 2.1 above

4.1.1 The decision to grant the European patent will be issued, and the **mention of the grant** of the patent will be published in the European Patent Bulletin, if the requirements concerning the translation of the claims and the payment of all fees are fulfilled and there is agreement as to the text to be granted (Rule 71a(1) EPC).

Note on payment of the renewal fee:
If a renewal fee becomes due before the next possible date for publication of the mention of the grant of the European patent, publication will be effected only after the renewal fee and any additional fee have been paid (Rule 71a(4) EPC).

Under Article 86(2) EPC, the obligation to pay renewal fees to the European Patent Office terminates with the payment of the renewal fee due in respect of the year in which the mention of the grant of the European patent is published.

Note on payment of the designation fee(s):
If the designation fee(s) become(s) due after the communication under Rule 71(3) EPC, the mention of the grant of the European patent will not be published until these fees have been paid (Rule 71a(3) EPC).

4.1.2 After publication, the **European patent specification** can be downloaded free of charge from the EPO publication server https://data.epo.org/publication-server.

4.1.3 Filing of translations in the contracting states

As regards translation requirements prescribed by the contracting states under Article 65(1) EPC, please consult the website of the European Patent Office
www.epo.org →Law & practice →Legal texts, National law relating to the EPC
www.epo.org →Law & practice →All Legal texts →London Agreement

In the case of a valid extension or validation

As regards translation requirements prescribed by the extension or validation states, please consult the website of the European Patent Office

www.epo.org →Law & practice →Legal texts, National law relating to the EPC

Failure to supply a prescribed translation in a contracting state, or in an extension or validation state may result in the patent being deemed to be void *ab initio* in the state concerned (Art. 65(3) EPC).

4.2 In the case of 2.2 above

If the present communication under Rule 71(3) EPC is based on an auxiliary request and, within the time limit, you maintain the main request or a higher ranking request which is not allowable, the application will be refused (Art. 97(2) EPC).

If the examining division gives its consent to the requested amendments or corrections, it will issue a new communication under Rule 71(3) EPC; otherwise, it shall resume the examination proceedings (Rule 71(6) EPC).

5. Filing of a divisional application

Any divisional application relating to this European patent application must be filed directly with the European Patent Office in Munich, The Hague or Berlin and will be in the language of the proceedings for the present application, or if the latter was not in an official language of the EPO, the divisional application may be filed in the language of the present application as filed (see Article 76(1) and Rule 36(2) EPC). Any such divisional application must be filed while the present application is still pending (Rule 36(1) EPC; Guidelines A-IV, 1.1.1).

6. Notes concerning fee payments

6.1 Making payments

For payments made via deposit account, please note that as from 1 December 2017 debit orders will only be carried out if filed in an electronically processable format (xml), using an accepted means of filing as laid down in the Arrangements for deposit accounts (ADA), published in the Supplementary publication in the Official Journal.

All relevant information related to the modes of payment of fees to the EPO can be retrieved from the EPO website at "**Making Payments**".

6.2 Information concerning fee amounts

Procedural fees are usually adjusted every two years, on even years, with effect from 1 April. Therefore, before making a payment, parties should verify the amounts actually due on the date of payment using the applicable version of the Schedule of fees and expenses, published as a Supplement to the Official Journal of the EPO, available on the EPO website (**www.epo.org**) at **www.epo.org/schedule-of-fees**. The "Schedule of fees" table allows the viewing, downloading and searching of individual fee amounts, both current and previous.

6.3 Note to users of the automatic debiting procedure

The fee for grant, including the fee for publication, and any additional claims fees due under Rule 71(4) EPC will be debited automatically on the date of filing of the translations of the claims, or on the last day of the period of this communication. However, if the designation fee(s) become(s) due as set out in Rule 71a(3) EPC and/or a renewal fee becomes due as set out in Rule 71a(4) EPC, these should be paid separately by another permitted way of payment in order not to delay the publication of the mention of the grant. The same applies in these circumstances to the payment of extension and validation fees. The same applies in these circumstances to the payment of extension and validation fees.

Note: If a waiver is expressed in response to a Rule 71(3) communication (see OJ EPO 2015, A52), the fee for grant, including the fee for publication/printing, and any additional claims fees will not be debited automatically. These fees must be paid separately by another means of payment allowed under the Rules relating to Fees.

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Enclosures: Text intended for grant

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Annex to EPO Form 2004, Communication pursuant to Rule 71(3) EPC

Bibliographical data of European patent application No. 17 840 467.9

For the intended grant of the European patent, the bibliographical data are set out below, for information:

Title of invention:
- BLUTPROBENOPTIMIERUNGSSYSTEM SOWIE VORRICHTUNG ZUR SEQUESTRIERUNG VON BLUTKONTAMINANTEN
- BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE
- SYSTÈME D'OPTIMISATION D'ÉCHANTILLON DE SANG ET DISPOSITIF DE SÉQUESTRATION DE CONTAMINANT DU SANG

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*)	If the time limit for the payment of designation fees according to Rule 39(1) EPC has not yet expired and the applicant has not withdrawn any designation, **all Contracting States/Extension States/Validation States** are currently still deemed to be designated. See also Rule 71a(3) EPC and, if applicable, the above Note to users of the automatic debiting procedure.
**)	If two or more applicants have designated different Contracting States, this is indicated here.

~~BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE AND METHOD~~

BACKGROUND

[0001] Bacteraemia is the presence of microorganisms in the blood. Sepsis, on the other hand, is bacteraemia in the presence of clinical symptoms and signs such as fever, tachycardia, tachypnea and hypotension. Bacteraemia and sepsis are associated with a high mortality and an increased incidence and duration of hospital stay and associated costs. Many bacteraemias, sepsis, fungaemias and other pathogens actually occur within a hospital or other healthcare settings with catheters and venipunctures being a source of contamination as potential carriers of these pathogens.

[0002] Blood cultures are the standard test used to detect microbial pathogens related to bacteraemia and sepsis in a patient's blood. The term blood culture refers to a single venipuncture, either from a peripheral site or central or arterial line, with the blood inoculated into one or more blood culture bottles or containers. One bottle is considered a blood culture where two or more are considered a set. Multiple sets may be obtained from multiple venipunctures and are associated with different sites on the patient.

[0003] These methods allow for microbial identification and susceptibility testing to be performed, which is a critical component to managing sepsis, however the lack of rapid results and decreased sensitivity for fastidious pathogens has led to the development of improved systems and adjunctive molecular or proteomic testing.

[0004] Collection of blood samples for conducting blood cultures is a critical component of modern patient care and can either positively affect the patient outcome by providing an accurate diagnosis, or can adversely affect the outcome by prolonging unnecessary antimicrobial therapy, the length of hospital stays, and increasing costs.

[0005] One outcome of collection of blood cultures is contamination. Blood culture contamination can lead to a false positive culture result and/or significant increase in healthcare related costs. Sources of blood culture contamination include improper skin antisepsis, improper collection tube disinfection, and contamination of the initial blood draw which may then skew results.

[0006] Blood culture collection kits generally consist of a "butterfly" set, infusion set, or other type of venipuncture device as offered by companies like BD, Smiths, B. Braun and others, and aerobic and anaerobic blood culture bottles. Various different bottles are also available depending on the test requirements. These bottles are specifically designed to optimize recovery of both aerobic and anaerobic organisms. In conventional kits, a bottle used is known generally as a "Vacutainer," which is a blood collection tube formed of a sterile glass or plastic tube with a closure that is evacuated to create a vacuum inside the tube to facilitate the draw of a predetermined volume of liquid such as blood.

[0007] False positive blood cultures are typically a result of poor sampling techniques. They cause the use of antibiotics when not needed, increasing hospital costs and patient anxiety. Blood cultures are drawn from a needlestick into the skin, and then a Vacutainer is attached to capture a sample of blood. Contamination may occur from improper or incomplete disinfection of the skin area in and around the puncture site. It may also occur from the coring of the skin by the needle during insertion, with the cored skin cells and any associated contamination being pulled into the sample.

[0008] Blood flow through a hypodermic needle is laminar, and as such, a velocity gradient can be developed over the flow tube as a pressure drop is applied to the hypodermic needle. Either forceful aspiration of blood, or using a very small hypodermic needle, can cause lysis and a release of potassium from the red blood cells, thereby rendering the blood samples abnormal.

[0009] In other instances, some patients have delicate veins that can collapse under a pressure drop or vacuum, particularly as applied by a syringe's plunger that is drawn too quickly for the patient's condition. Since such condition is impossible to know beforehand, such vein collapses are a risk and very difficult to control.

[0010] Various strategies have been implemented to decrease blood culture contamination rates, e.g. training staff with regard to aseptic collection technique, feedback with regard to contamination rates and implementation of blood culture collection kits. Although skin antisepsis can reduce the burden of contamination, 20% or more of skin organisms are located deep within the dermis and are unaffected by

antisepsis. Changing needles before bottle inoculation is not advisable as it increases the risk to acquire needle stick injuries without decreasing contamination rates.

[0011] Some conventional systems and techniques for reducing blood culture contamination include discarding the initial aliquot of blood taken from central venous catheters, venipunctures, and other vascular access systems. However, these systems require the user to mechanically manipulate an intravascular device, or require a complex series of steps that are difficult to ensure being followed.

US 2014/039348 A1 discloses a device including a pre-sample reservoir, an actuator mechanism and a diverter. The pre-sample reservoir can be fluidically coupled to a delivery member to receive and isolate a predetermined volume of bodily-fluid withdrawn from a patient. US 2014/107564 A1 discloses an apparatus including a cannula assembly, a housing, a fluid reservoir, a flow control mechanism and an actuator. US 4 813 433 A discloses a syringe for withdrawing fluids which consists of one-handed operated syringe. The syringe comprises a double compartmented housing, a piston disposed in one of said compartments, a piston rod connected to said piston controlling the movement of said piston in a barrel, and vent means. US 2013/317391 A1 discloses an apparatus including a housing, a flow control mechanism and an actuator. At least a portion of the flow control mechanism is movably disposed within the housing.

SUMMARY

[0012] This document presents systems and methods for reducing blood culture contamination, lysing of cells, and vein collapse. In some implementations, a system and method can eliminate user variability in disinfection, and also eliminate the risk of skin cells getting into the blood culture sample. The systems and methods disclosed herein do not require a change in existing clinical processes, other than to potentially indicate when a vacutainer or other blood collection device (i.e., syringe) should be attached for drawing contaminant-free blood samples.

[0013] In some implementations of the systems and methods disclosed herein the withdrawal of blood is accomplished passively by use of the patient's own blood pressure, thereby reducing the risk of vein collapse and eliminating any additional user steps over current practice. The systems and methods can be applied to accommodate

short-path direct stick or butterfly venipuncture systems. They can also be used with samples drawn through a catheter.

[0014] In one aspect, a blood sequestration device is presented. The blood sequestration device includes an inlet port and an outlet port. The blood sequestration device further includes a sequestration chamber connected with the inlet port, the sequestration chamber having a vent comprising an air permeable blood barrier. The blood sequestration device further includes a sampling channel having a proximal end connected with the inlet port and a distal end connected with the outlet port.

[0015] In another aspect, a blood sequestration device connected with a blood sampling pathway is described. The blood sampling pathway has a patient needle and a sample collection device. The blood sequestration device includes an inlet port connected

with the patient needle, and a sequestration chamber connected with the inlet port, the sequestration chamber having a vent comprising an air permeable blood barrier. The blood sequestration device further includes a sampling channel having a proximal end connected with the inlet port, and an outlet port connected with a distal end of the sampling channel and with the sample collection device.

[0016] In yet another aspect, a blood sequestration device connected with a blood sampling system is described. The blood sampling system includes a patient needle for accessing a blood sample from a patient, and a sample needle that is sealed and adapted for receiving an evacuated blood collection tube. The blood sequestration device includes an inlet port connected with the patient needle to receive the blood sample from the patient. The blood sequestration device further includes a sequestration chamber connected with the inlet port and having a vent comprising an air permeable blood barrier, the sequestration chamber for receiving and sequestering a first portion of the blood sample prior to the sample needle being unsealed by the evacuated blood collection tube. The blood sequestration device further includes a sampling channel having a proximal end connected with the inlet port, the sampling channel for conveying a subsequent portion of the blood sample once the sample needle is unsealed by the evacuated blood collection tube. The blood sequestration device further includes an outlet port connected with a distal end of the sampling channel for conveying the subsequent portion of the blood sample to the sample needle.

[0017] In yet another aspect, a blood sample optimization system is disclosed and described. The blood sample optimization system includes a blood sampling system for accessing and acquiring one or more samples of a patient's blood, and a blood sequestration device for receiving and sequestering a first portion of the one or more samples of the patient's blood which might be contaminated by a venipuncture process and which could result in a false positive identification of a pathogen in the patient's blood.

[0018] The blood sampling system includes a patient needle configured for a venipuncture of a patient to access a sample of blood of a patient, a blood sampling pathway connected with the patient needle for conveying the sample of blood, and a sample needle configured for receiving an evacuated blood collection container to collect and contain a subsequent portion of the sample of blood.

[0019] In yet another aspect, a blood sequestration device is disclosed and described. In some implementations, the blood sequestration device can include an inlet port, an outlet port connected with the inlet port, and a sequestration chamber connected with the inlet port. The sequestration chamber can have a vent comprising an air permeable blood barrier.

[0020] The blood sequestration device, in one aspect can include an inlet port, an outlet port, a sequestration chamber connected with the inlet port via a junction, the sequestration chamber having a vent that includes an air permeable blood barrier, the vent being defined by an outer wall that at least partially circumscribes the air permeable blood barrier and includes one or more air vents, the vent further includes a cap that at least partially covers the wall and a one-way seal abutting the air permeable blood barrier that inhibits air from entering the sequestration chamber, and a sampling channel having a proximal end connected with the inlet port via the junction, and a distal end connected with the outlet port. In certain related aspects, the sequestration chamber, the sampling channel and the junction are sized and configured such that a first portion of blood flows into the sequestration chamber toward the air permeable blood barrier for sequestration therein, and a second portion of blood bypasses the sequestration chamber and the first portion of blood sequestered therein and is directed into the sampling channel toward the outlet port.

[0021] In another aspect, the sampling channel and the junction is sized and configured such that a first portion of blood flows into and fills the sequestration chamber to displace air therein through the vent, and such that a second portion of blood bypasses the sequestration chamber and the first portion of blood sequestered therein and is directed into the sampling channel toward the outlet port.

[0022] The blood sequestration and sampling system sequestration device, in certain aspects can include a blood sampling pathway having a patient needle on a proximal end and a sample collection device on a distal end; and a blood sequestration device attached on the blood sampling pathway between the proximal end and distal end of the blood sampling pathway. The blood sequestration device in one aspect can include an inlet port coupled with the blood sampling pathway toward the patient needle, an outlet port coupled with the blood sampling pathway toward the sample collection device, a sequestration chamber connected with the inlet port via a junction, which chamber has a

vent that includes an air permeable blood barrier, the vent being defined by an outer wall that at least partially circumscribes the air permeable blood barrier and includes one or more air vents, the vent further including a cap that at least partially covers the wall and a one-way seal abutting the air permeable blood barrier that inhibits air from entering the sequestration chamber; and a sampling channel having a proximal end connected with the inlet port via the junction, and a distal end connected with the outlet port. In a certain related aspect, the sequestration chamber, the sampling channel and the junction can be sized and configured such that a first portion of blood flows into the sequestration chamber toward the air permeable blood barrier for sequestration therein, and a second portion of blood bypasses the sequestration chamber and the first portion of blood sequestered therein and is directed into the sampling channel toward the outlet port.

[0023] The blood sequestration device is connected along the blood sampling pathway between the patient needle and the sample needle, and includes an inlet port for receiving the sample of blood. The blood sequestration device further includes a sequestration chamber connected with the inlet port for receiving a first amount of the sample of blood, the sequestration chamber having a vent comprising an air permeable blood barrier for sequestering at least a first portion of the first amount of the sample of blood. The blood sequestration device may further include a sampling channel having a proximal end connected with the inlet port, the sampling channel conveying a subsequent amount of the sample of blood to the evacuated blood collection container upon the sequestration chamber sequestering at least the first portion of the first amount of the sample of blood. The blood sequestration device further includes an outlet port connected with a distal end of the sampling channel, the outlet port for outputting the subsequent amount of the sample of blood.

[0024] The details of one or more embodiments are set forth in the accompanying drawings and the description below. Other features and advantages will be apparent from the description and drawings, and from the claims.

BRIEF DESCRIPTION OF THE DRAWINGS

[0025] These and other aspects will now be described in detail with reference to the following drawings.

[0026] FIG. 1 illustrates a blood sample optimization system.

[0027] FIG. 2 illustrates a blood sample optimization system in accordance with an alternative implementation.

[0028] FIG. 3 illustrates a blood sample optimization system in accordance with another alternative implementation.

[0029] FIG. 4 illustrates a blood sample optimization system in accordance with another alternative implementation.

[0030] FIG. 5 illustrates a blood sample optimization system in accordance with another alternative implementation.

[0031] FIG. 6 illustrates a blood sample optimization system in accordance with an alternative implementation.

[0032] FIG. 7 is a flowchart of a method for optimizing a quality of a blood culture.

[0033] FIGS. 8A – 8E illustrate a blood sequestration system for non-contaminated blood sampling, in accordance with some implementations.

[0034] FIG. 9 illustrates a pathway splitter for use in a blood sequestrations system.

[0035] FIGS. 10A – 10D illustrate a blood sequestration system for non-contaminated blood sampling, in accordance with alternative implementations.

[0036] FIGS. 11A – 11E illustrate a blood sequestration system for non-contaminated blood sampling, in accordance with other alternative implementations.

[0037] FIGS. 12A-12D illustrate a blood sample optimization system including a blood sequestration device in accordance with yet other alternative implementations.

[0038] FIGS. 13A-13D illustrate a blood sample optimization system 1300 in accordance with yet another alternative implementations.

[0039] FIGS. 14A-14E illustrate yet another implementation of a blood sampling system to sequester contaminates of an initial aliquot or sample to reduce false positives in blood cultures or tests performed on a patient's blood sample.

[0040] FIGS. 15A-15G illustrate a blood sequestration device and method of using the same, in accordance with yet another implementation.

[0041] FIGS. 16A-16D illustrate a blood sequestration device in accordance with yet another implementation.

[0042] FIGS. 17A – 17E illustrate a bottom member of a housing for a blood sequestration device.

[0043] FIGS. 18A – 18F illustrate a top member of a housing for a blood sequestration device.

[0044] FIGS. 19A and 19B illustrate a blood sequestration device having a top member mated with a bottom member.

[0045] FIG. 20 shows a blood sample optimization system including a blood sequestration device.

[0046] FIG. 21 illustrates a non-vented blood sequestration device using a wicking material chamber.

[0047] FIGS. 22A and 22B illustrate a material makeup of a filter for sequestering blood in a sequestration chamber of a blood sequestration device.

[0048] FIGS. 23A – 23E illustrate another implementation of a blood sequestration device that uses a vacuum force from a blood collection device.

[0049] FIGS. 24A – 24D illustrate another implementation of a blood optimization system and blood sequestration device.

[0050] FIGS. 25A – 25D illustrate another implementation of a blood optimization system and blood sequestration device.

[0051] FIGS. 26A – 26E illustrate another implementation of a blood optimization system and blood sequestration device.

[0052] FIGS. 27A – 27D illustrate another implementation of a blood optimization system and blood sequestration device.

[0053] FIGS. 28A – 28F illustrate another implementation of a blood optimization system and blood sequestration device.

[0054] FIGS. 29A – 29C illustrate another implementation of a blood optimization system and blood sequestration device.

[0055] FIGS. 30A – 30G illustrate another implementation of a blood optimization system and blood sequestration device.

[0056] Like reference symbols in the various drawings indicate like elements.

DETAILED DESCRIPTION

[0057] This document describes blood sample optimization systems and methods for reducing or eliminating contaminates in collected blood samples, which in turn reduces or eliminates false positive readings in blood cultures or other testing of collected blood samples. In some implementations, a blood sample optimization system includes a patient needle for vascular access to a patient's bloodstream, a sample needle for providing a blood sample to a blood collection container, such as an evacuated blood collection container or tube like a Vacutainer™ or the like, or other sampling device, and a blood sequestration device located between the patient needle and the sample needle. The blood sequestration device includes a sequestration chamber for sequestering an initial, potentially contaminated aliquot of blood, and may further include a sampling channel that bypasses the sequestration chamber to convey likely uncontaminated blood between the patient needle and the sample needle after the initial aliquot of blood is sequestered in the sequestration chamber.

[0058] FIG. 1 illustrates a blood sample optimization system in accordance with some implementations. The system includes a patient needle 1 to puncture the skin of a patient to access the patient's vein and blood therein. The system further includes a sample needle (i.e., a resealably closed needle for use with Vacutainers™ or the like) 5, which may be contained within and initially sealed by a resealable boot 10, a Luer activated valve, or another collection interface or device. The resealable boot 10 can be

pushed aside or around the sample needle 5 by application of a Vacutainer™ bottle (not shown) for drawing the patient's blood. The system can further include a low volume chamber 30 that leads to the sample needle 5, but also includes an orifice or one or more channels 45 that lead to a sequestration chamber 55 formed by a housing 50.

[0059] The sequestration chamber 55 is a chamber, channel, pathway, lock, or other structure for receiving and holding a first aliquot of the patient's blood, which may be in a predetermined or measured amount, depending on a volume of the sequestration chamber 55. The first draw of blood typically contains or is more susceptible to containing organisms that cause bacteraemia and sepsis or other pathogens than subsequent blood draws. The sequestration chamber 55 can be a vessel encased in a solid housing, formed in or defined by the housing itself, or can be implemented as tubing or a lumen. The sequestration chamber 55, regardless how formed and implemented, may have a predetermined volume. In some implementations, the predetermined volume may be based on a volume of the patient needle, i.e. ranging from less than the volume of the patient needle to any volume up to or greater than 20 times or more of the volume of the patient needle. The predetermined volume of the sequestration chamber 55 may also be established to economize or minimize an amount of blood to be sequestered and disposed of.

[0060] The sequestration chamber 55 can be formed, contained or housed in a chamber housing 50, and can be made of plastic, rubber, steel, aluminum or other suitable material. For example, the sequestration chamber 55 could be formed of flexible tubing or other elastomeric materials. The sequestration chamber 55 further includes an air permeable blood barrier 20 that allows air to exit the sequestration chamber 55. As used herein the term "air permeable blood barrier" means an air permeable but substantially blood impermeable substance, material, or structure. Examples may include hydrophobic membranes and coatings, a hydrophilic membrane or coating combined with a hydrophobic membrane or coating, mesh, a filter, a mechanical valve, antimicrobial material, or any other means of allowing air to be displaced from the sequestration chamber 55 as it is filled with blood. In various exemplary embodiments, an air permeable blood barrier may be formed by one or more materials that allow air to pass through until contacted by a liquid, such material then becomes completely or partially sealed to prevent or inhibit the passage of air and/or liquid. In other words, prior to contact with liquid, the material forms a barrier that is air permeable. After contact with a

liquid, the material substantially or completely prevents the further passage of air and/or liquid.

[0061] The orifice or channel 45 can be any desired length, cross-sectional shape or size, and/or can be formed to depart from the low volume chamber 30 at any desired angle or orientation. The orifice or channel 45 may also include a one-way flap or valve 60 that maintains an initial aliquot of blood sample within the sequestration chamber 55. In some specific implementations, the orifice or channel 45 can include a "duck bill" or flapper valve 60, or the like, for one-way flow of blood from low volume chamber 30 to the sequestration chamber 55. The air permeable blood barrier 20 can also be constructed of a material that allows air to exit but then seals upon contact with blood, thereby not allowing external air to enter sequestration chamber 55. This sealing would eliminate the need for a valve.

[0062] Valve 60 can be any type of valve or closing mechanism. Chamber 30 is designed to hold virtually no residual blood, and can be designed to be adapted to hold or allow pass-through of a particular volume or rate of blood into sequestration chamber 55. Likewise, sequestration chamber 55 may also include any type of coating, such as an anti-microbial coating, or a coating that aids identification and/or diagnosis of components of the first, sequestered blood draw.

[0063] Housing 50 and 40 can be formed of any suitable material, including plastic, such as acrylonitrile butadiene styrene (ABS) or other thermoplastic or polymeric material, rubber, steel, or aluminum. The air permeable blood barrier 20 can include a color-providing substance, or other signaling mechanism, that is activated upon contact with blood from the initial blood draw, or when air displacement is stopped, or any combination of events with blood in the sequestration chamber 55. The air permeable barrier may also include an outer layer such as a hydrophobic membrane or cover that inhibits or prevents the inadvertent or premature sealing of the filter by an external fluid source, splash etc. Sequestration chamber 55 can also be translucent or clear to enable a user to visually confirm the chamber is filled.

[0064] FIG. 2 illustrates a blood sample optimization system in accordance with some alternative implementations. In the implementation shown in FIG. 2, a sequestration chamber 55, or waste chamber, surrounds the patient needle 1, with an

open-ended cuff or housing connected with the waste chamber and encircling the sample needle housing base and housing. The patient needle 1 and sample needle 5 are connected together by a boot 56, which forms a continuous blood draw channel therethrough. The boot 56 includes a single orifice or channel leading from the blood draw channel into sequestration chamber 55. The device can include more than one single orifice or channel, in other implementations. Each orifice or channel can include a one-way valve, and can be sized and adapted for predetermined amount of blood flow.

[0065] The sequestration chamber 55 includes an air permeable blood barrier. The filter can further include a sensor or indicator to sense and/or indicate, respectively, when a predetermined volume of blood has been collected in the sequestration chamber 55. That indication will alert a user to attach an evacuated blood collection tube or bottle, such as a Vacutainer™ to the sample needle 5. The housing for the sequestration chamber 55 can be any size or shape, and can include any type of material to define an interior space or volume therein. The interior space is initially filled only with air, but can also be coated with an agent or substance, such as a decontaminate, solidifying agent, or the like. Once evacuated blood collection tube is attached to the sample needle 5, blood will flow automatically into the patient needle 1, through the blood draw channel and sample needle 5, and into the bottle. The sample needle 5 is covered by a resealable boot, coating or membrane that seals the sample needle when a blood collection bottle is not attached thereon or thereto.

[0066] FIG. 3 illustrates a blood sample optimization system in accordance with some alternative implementations. In the implementation shown, a sample needle 5 is surrounded by a resealable boot or membrane, and is further connected with a patient needle 1. A blood flow channel is formed through the sample needle and the patient needle. The connection between the sample needle and patient needle includes a "T" or "Y" connector 102, which includes a channel, port or aperture leading out from the main blood flow channel to a sequestration chamber 104.

[0067] The T or Y connector 102 may include a flap or one-way valve, and have an opening that is sized and adapted for a predetermined rate of flow of blood. The sequestration chamber 104 can be formed from tubing, or be formed by a solid housing, and is initially filled with air. The sequestration chamber 104 will receive blood that flows out of a patient automatically, i.e. under pressure from the patient's own blood

pressure. The sequestration chamber 104 includes an air permeable blood barrier 106, preferably at the distal end of tubing that forms the sequestration chamber 104, and which is connected at the proximal end to the T or Y connector 102. The T or Y connector 102 can branch off at any desired angle for most efficient blood flow, and can be formed so as to minimize an interface between the aperture and channel and the main blood flow channel, so as to minimize or eliminate mixing of the initial aliquot of blood with main blood draw samples.

[0068] In some alternative implementations, the sample needle may be affixed to a tubing of any length, as shown in FIG. 4, connecting at its opposite end to the T or Y connector 102. The sequestration chamber 104 can be any shape or volume so long as it will contain a predetermined amount of blood sample in the initial aliquot. The T or Y connector 102 may also include an opening or channel that is parallel to the main blood flow channel. The air permeable blood barrier may further include an indicator 107 or other mechanism to indicate when a predetermined amount of blood has been collected in the sequestration chamber, or when air being expelled reaches a certain threshold, i.e. to zero. The tubing can also include a clip 109 that can be used to pinch off and prevent fluid flow therethrough.

[0069] Once the air permeable blood barrier and primary chamber are sealed the initial aliquot of blood is trapped in the sequestration chamber 104, an evacuated blood collection tube, such as a Vacutainer™ bottle may be attached to the sample needle 5 to obtain the sample. The blood collection tube can be removed, and the sample needle 5 will be resealed. Any number of follow-on blood collection tubes can then be attached for further blood draws or samples. Upon completion of all blood draws, the system can be discarded, with the initial aliquot of blood remaining trapped in the sequestration chamber 104.

[0070] FIG. 5 illustrates a blood sample optimization system in accordance with some alternative implementations. In the implementation shown, a sample needle 5 is connected with a patient needle by tubing. A “T” or “Y” connector 120 is added along the tubing at any desired location, and includes an aperture, port or channel leading to a sequestration chamber 204, substantially as described above.

[0071] FIG. 6 illustrates a blood sample optimization system in accordance with some alternative implementations, in which a sequestration chamber 304, formed as a primary collection channel, receives an initial aliquot of blood, and is provided adjacent to the blood sampling channel. The sequestration chamber 304 can encircle the blood sampling channel, the patient needle 1, and/or the sample needle 5. The primary collection channel can include a T or Y connector 120, or other type of aperture or channel. The sequestration chamber 304 includes an air permeable blood barrier, which can also include an indicator of being contacted by a fluid such as blood, as described above.

[0072] In some implementations, either the patient needle 1 or the sample needle 5, or both, can be replaced by a Luer lock male or female connector. However, in various implementations, the connector at a sample needle end of the blood sample optimization system is initially sealed to permit the diversion of the initial aliquot of blood to the sequestration chamber, which is pressured at ambient air pressure and includes the air outlet of the air permeable blood barrier. In this way, the system passively and automatically uses a patient's own blood pressure to overcome the ambient air pressure of the sequestration chamber to push out air through the air permeable blood barrier and displace air in the sequestration chamber with blood.

[0073] FIG. 7 is a flowchart of an exemplary method for optimizing the quality of a blood culture. At 702, a clinician places a needle into a patient's vein. At 704, blood then flows into a sequestration chamber, pushing the air in the sequestration chamber out of the sequestration chamber through an air permeable blood barrier. In some implementations, the volume of the sequestration chamber is less than 0.1 to more than 5 cubic centimeters (cc's), or more. The sequestration chamber is sized and adapted to collect a first portion of a blood sample, which is more prone to contamination than secondary and other subsequent portion of the blood sample or subsequent draws. Since the sequestration chamber has an air-permeable blood barrier through which air can be displaced by blood pushed from the patient's vein, such blood will naturally and automatically flow into the sequestration chamber before it is drawn into or otherwise enters into a Vacutainer or other bottle for receiving and storing a blood sample.

[0074] When the sequestration chamber fills, the blood will gather at or otherwise make contact with the air permeable blood barrier, which will inhibit or prevent blood

from passing therethrough. At 706, when the blood comes into contact with the entire internal surface area of the air permeable blood barrier, the air permeable blood barrier is then closed and air no longer flows out or in. At 708, the clinician may be provided an indictor or can see the full chamber, to indicate the evacuated blood collection tube, such as a Vacutainer™ can be attached. The indicator can include visibility into the primary chamber to see whether it is full, the blood barrier changing color, for example, or other indicator. The fill time of the sequestration chamber may be substantially instantaneous, so such indicator, if present, may be only that the sequestration chamber is filled.

[0075] Prior to an evacuated blood collection tube being attached, communication between the needle, sampling channel, and the sequestration chamber is restricted by the sealing of the sequestration chamber blood barrier thereby not permitting air to reenter the system through the sequestration. Sealing the communication path could also be accomplished with a mechanical twist or other movement, a small orifice or tortuous pathway, eliminating the need for a separate valve or mechanical movement or operation by the clinician. At 710, once the evacuated blood collection tube is removed, the self-sealing membrane closes the sample needle, and at 712, additional subsequent evacuated blood collection tubes may be attached. Once samples have been taken, at 714 the device is removed from the patient and discarded.

[0076] FIGS. 8A – 8E illustrate an exemplary blood sample optimization system 800 for non-contaminated blood sampling, in accordance with some implementations. The blood sample optimization system 800 includes an inlet port 802 that can be connected to tubing, a patient needle (or both), or other vascular or venous access device, and a pathway splitter 804 having a first outlet to a sequestration chamber tubing 806 and a second outlet to sample collection tubing 808. One or both of the sequestration chamber tubing 806 and the sample collection tubing 808 can be formed of tubing. In some implementations, the sequestration chamber tubing 806 is sized so as to contain a particular volume of initial blood sample. The sample collection tubing 808 will receive a blood sample once the sequestration chamber tubing 806 is filled. The sample collection tubing 808 can be connected to a Vacutainer™ base or housing 810, or other blood sample collection device.

[0077] The blood sequestration system 800 further includes a blood sequestration device 812 which, as shown in more detail in FIGS. 8B – 8D, includes a housing 818 that

includes a sampling channel 820 defining a pathway for the non-contaminated sample collection tubing 808 or connected at either end to the non-contaminated sample collection tubing 808. The sampling channel 820 can be curved through the housing 818 so as to better affix and stabilize the housing 818 at a location along the non-contaminated sample collection tubing 808.

[0078] The blood sequestration device 812 further includes a sequestration chamber 822 connected with the sequestration chamber tubing 806 or other chamber. The sequestration chamber 822 terminates at an air permeable blood barrier 824. The air permeable blood barrier 824 can also include a coloring agent that turns a different color upon full contact with blood, as an indicator that the regular collection of blood samples (i.e. the non-contaminated blood samples) can be initiated. Other indicators may be used, such as a small light, a sound generation mechanism, or the like. In some implementations, the air permeable blood barrier is positioned at a right angle from the direction of sequestration chamber 822, but can be positioned at any distance or orientation in order to conserve space and materials used for the housing 818. The housing 818 and its contents can be formed of any rigid or semi-rigid material or set of materials.

[0079] FIG. 9 illustrates a pathway splitter 900 for use in a blood sequestrations system, such as those shown in FIGS. 8A – 8E, for example. The pathway splitter 900 includes an inlet port 902, a main line outlet port 904, and a sequestration channel outlet port 906. The inlet port 902 can be connected to main tubing that is in turn connected to a patient needle system, or directly to a patient needle. The main line outlet port 904 can be connected to main line tubing to a blood sampling system, such as a vacutainer base or housing, or directly to such blood sampling system. The sequestration channel outlet port 906 can be connected to sequestration tubing for receiving and sequestering a first sample of blood, up to a measured amount or predetermined threshold. Alternatively, the sequestration channel outlet port 906 can be connected to a sequestration chamber. The sequestration channel outlet port 906 is preferably 20-70 degrees angled from the main line outlet port 904, which in turn is preferably in-line with the inlet port 902. Once the predetermined amount of initial blood sample is sequestered in the sequestration tubing or chamber, in accordance with mechanisms and techniques described herein, follow-on blood samples will flow into the inlet port 902 and directly out the main line outlet port 904, without impedance.

[0080] FIGS. 10A – 10D illustrate a blood sequestration device 1000 in accordance with alternative implementations. The blood sequestration device 1000 includes an inlet port 1002, a main outlet port 1004, and a sequestration channel port 1006. The inlet port 1002 can be connected to a patient needle or related tubing. The main outlet port 1004 can be connected to a blood sample collection device such as a Vacutainer, associated tubing, or a Luer activated valve, or the like. The sequestration channel port 1006 splits off from the main outlet port 1004 to a sequestration chamber 1008. In some implementations, the sequestration chamber 1008 is formed as a helical channel within a housing or other container 1001.

[0081] The sequestration chamber 1008 is connected at the distal end to an air permeable blood barrier 1010, substantially as described above. Air in the sequestration chamber 1008 is displaced through the air permeable blood barrier 1010 by an initial aliquot of blood that is guided into the sequestration channel port 1006. Once the sequestration chamber 1008 is filled, further blood draws through the main outlet port 1004 can be accomplished, where these samples will be non-contaminated.

[0082] FIGS. 11A – 11E illustrate a blood sequestration device 1100 in accordance with other alternative implementations. The blood sequestration device 1100 includes an inlet port 1102, similar to the inlet ports described above, a main outlet port 1104, and a sequestration channel port 1106 that splits off from the main outlet port 1104 and inlet port 1102. The sequestration channel port is connected to a sequestration chamber 1108. In the implementation shown in FIGS. 11A – 11E, the blood sequestration device includes a base member 1101 having a channel therein, which functions as the sequestration chamber 1108. The channel can be formed as a tortuous path through the base member 1101, which is in turn shaped and formed to rest on a limb of a patient.

[0083] A portion of the sequestration chamber 1108 can protrude from the base member or near a top surface of the base member, just before exiting to an air permeable blood barrier 1110, to serve as a blood sequestration indicator 1109. The indicator 1109 can be formed of a clear material, or a material that changes color when in contact with blood.

[0084] In some implementations, the blood sequestration device 1100 can include a blood sampling device 1120 such as a normally closed needle, Vacutainer™ shield or other collection device. The blood sampling device 1120 can be manufactured and sold with the blood sequestration device 1100 for efficiency and convenience, so that a first aliquot of blood that may be contaminated by a patient needle insertion process can be sequestered. Thereafter, the blood sampling device 1120 can draw non-contaminated blood samples to reduce the risk of false positive testing and ensure a non-contaminated sample.

[0085] FIGS. 12A-12D illustrate a blood sample optimization system 1200 in accordance with yet other alternative implementations. The system 1200 includes a blood sequestration device 1202 for attaching to a blood sampling device 1204, such as a Vacutainer™ or other collection and sampling device. The blood sequestration device 1202 is configured and arranged to receive, prior to a Vacutainer™ container or vial being attached to a collection needle of the blood sampling device 1204, a first aliquot or amount of blood, and sequester that first aliquot or amount in a sequestration channel of the blood sequestration device 1202.

[0086] In some implementations, the blood sequestration device 1202 can include an inlet port 1212, a main outlet port, and a sequestration channel port. The inlet port 1212 can be connected to a patient needle or related tubing. The main outlet port 1214 can be connected to a normally closed needle or device to enable connection with an evacuated blood collection container or other collection device such as a Vacutainer™, associated tubing, luer connectors, syringe, a Luer activated valve, or the like. The sequestration channel port splits off from the main outlet port to a sequestration chamber 1218.

[0087] In some implementations, the sequestration chamber 1218 is formed as a channel within the body of a sequestration device 1202. The sequestration chamber 1218 can be a winding channel, such as a U-shaped channel, an S-shaped channel, a helical channel, or any other winding channel. The sequestration device 1202 can include a housing or other containing body, and one or more channels formed therein. As shown in FIGS. 12A and 12B, the sequestration device 1202 includes a main body 1206 and a cap 1208. The main body 1206 is formed with one or more cavities or channels, which are further formed with one or more arms 1210 that extend from the cap 1208, and which

abut the cavities or channels in the main body 1206 to form the primary collection port and main outlet port.

[0088] FIGS. 13A-13D illustrate a blood sample optimization system 1300 in accordance with yet other alternative implementations. The system 1300 includes a blood sequestration device 1302 for attaching to a blood sampling device 1304, such as a Vacutainer or other bodily fluid collection and sampling device. The blood sequestration device 1302 is configured and arranged to receive, prior to a Vacutainer container or vial being attached to a collection needle of the blood sampling device 1304, a first aliquot or amount of blood, and to sequester that first aliquot or amount of blood or other bodily fluid in a sequestration channel of the blood sequestration device 1302.

[0089] The blood sequestration device 1302 includes a housing 1301 having an inlet port 1314, a main outlet port 1312, and a sequestration channel port 1316. The inlet port 1314 can be connected to a patient needle or associated tubing. The main outlet port 1312 can be connected to a normally closed needle or device to enable connection with an evacuated blood collection container or other collection device such as a Vacutainer™, associated tubing, luer connectors, syringe, a Luer activated valve, or the like. The sequestration channel port 1316 splits off from the main inlet port 1314 to a sequestration chamber 1318.

[0090] In the implementation shown in FIGS. 13A-D, the sequestration chamber 1318 is formed as a cavity or chamber within housing 1301 or formed by walls that define housing 1301. The sequestration chamber 1318 can be a winding channel, such as a U-shaped channel, an S-shaped channel, a helical channel, or any other winding channel, that is defined by the cooperation and connection of housing 1301 with cap 1307 which cap 1307 can include a protrusion 1305 that provides one or more walls or directors for the winding channel in the sequestration chamber 1318. The protrusion 1305 from the cap 1307 can be straight or curved, and may have various channels, apertures or grooves embedded therein, and can extend from the cap 1307 any angle or orientation. When the cap 1307 is connected with the housing 1301 to complete the formation of the sequestration chamber 1318, the protrusion 1305 forms at least part of the winding channel to sequester a first aliquot or amount of blood or other bodily fluid in a sequestration channel formed in the sequestration chamber 1318 and by the winding channel.

[0091] The sequestration chamber 1318 includes an air permeable blood barrier 1310, substantially as described above. Air in the sequestration chamber 1318 is displaced through the air permeable blood barrier 1310 by an initial aliquot of blood that is provided into the sequestration chamber 1318 by the blood pressure of the patient. Once the sequestration chamber 1318 is filled and the air in the sequestration chamber 1318 displaced, the blood pressure of the patient will be insufficient to drive or provide further blood into the blood sequestration device 1302, and in particular the outlet port 1312, until a force such as a vacuum or other pressure, such as provided by the blood sample collection device like Vacutainer is provided to draw out a next aliquot or amount of blood or bodily fluid. Further blood draws through the main outlet port 1312 can be accomplished, where these samples will be non-contaminated since any contaminants would be sequestered in the sequestration chamber 1318 with the first aliquot of blood.

[0092] FIGS. 14A-14E illustrate yet another implementation of a blood sampling system 1400 to sequester contaminates of an initial aliquot or sample to reduce false positives in blood cultures or tests performed on a patient's blood sample. The blood sampling system 1400 includes a blood sequestration device 1401 that can be connected between a blood sample collection device 1403 and a patient needle (not shown). The blood sample collection device 1403 can be a Vacutainer or the like. The blood sequestration device 1401 includes an inlet port 1402 that can be connected with a patient needle that is inserted into a patient's vascular system for access to and withdrawing of a blood sample. The inlet port 1402 may also be connected with tubing or other conduit that is in turn connected with the patient needle.

[0093] The inlet port 1402 defines an opening into the blood sequestration device 1401, which opening can be the same cross sectional dimensions as tubing or other conduit connected with the patient needle or the patient needle itself. For instance, the opening can be circular with a diameter of approximately ≥ 0,1143 cm (0,045 inches), ≥ ~~0.045 inches,~~ but can have a diameter of between ≥ 0,0254 cm (0,01 inches) ≥ ~~0.01 inches~~ or less to ≥ 0,508 cm (0,2 inches) ≥ ~~0.2 inches~~ or more. The blood sequestration device 1401 further includes an outlet port 1404, which defines an opening out of the blood sequestration device 1401 and to the blood sample collection device 1403. The outlet port 1404 may also be connected with tubing or other conduit that is in turn connected with the blood sequestration device 1403. The outlet port 1404 can further include a connector device such as a threaded cap, a Luer connector (male or female), a

non threaded interference or glue joint fitting for attachment of various devices including but not limited to tubing, or the like.

[0094] The blood sequestration device 1401 further includes a sampling channel 1406 between the inlet port 1402 and the outlet port 1404, and which functions as a blood sample pathway once a first aliquot of blood has been sequestered. The sampling channel 1406 can be any sized, shaped or configured channel, or conduit. In some implementations, the sampling channel 1406 has a substantially similar cross sectional area as the opening of the inlet port 1402. In other implementations, the sampling channel 1406 can gradually widen from the inlet port 1402 to the outlet port 1404.

[0095] The blood sequestration device 1401 further includes a sequestration chamber 1408 that is connected to and split off or diverted from the sampling channel 1406 at any point between the inlet port 1402 and the outlet port 1404, but preferably from a proximal end of the sampling channel 1406 near the inlet port 1402. The sequestration chamber 1408 is at first maintained at atmospheric pressure, and includes an air outlet 1412 at or near a distal end of the sequestration chamber 1408 opposite the diversion point from the sampling channel 1406. The air outlet 1412 includes an air permeable blood barrier 1412. As shown in FIG. 14B, the air permeable blood barrier 1412 can be overlaid with a protective cover 1416. The protective cover 1416 can be sized and configured to inhibit a user from touching the air permeable blood barrier 1412 with their finger or other external implement, while still allowing air to exit the air permeable blood barrier 1412 as the air is displaced from the sequestration chamber 1408 by blood being forced into the sequestration chamber 1408 by a patient's own blood pressure. In addition the protective cover 1416 can be constructed to inhibit or prevent accidental exposure of the air permeable blood barrier to environmental fluids or splashes. This can be accomplished in a variety of mechanical ways including but not limited to the addition of a hydrophobic membrane to the protective cover.

[0096] As shown in FIGS. 14C and 14D, the sampling channel 1406 can be cylindrical or frusto-conical in shape, going from a smaller diameter to a larger diameter, to minimize a potential to lyse red blood cells. Likewise, the sampling channel 1406 is formed with a minimal amount of or no sharp turns or edges, which can also lyse red blood cells. The sampling channel 1406 splits off to the sequestration chamber 1408 near the inlet port 1402 via a diversion pathway 1409. The diversion pathway 1409 can have

any cross-sectional shape or size, but is preferably similar to the cross-sectional shape of at least part of the inlet port 1402.

[0097] In some implementations, the sampling channel 1406 and the sequestration chamber 1408 are formed by grooves, channels, locks or other pathways formed in housing 1414. The housing 1414 can be made of plastic, metal or other rigid or semi-rigid material. The housing 1414 can have a bottom member that sealably mates with a top member. One or both of the bottom member and the top member can include the sampling channel 1406 and the sequestration chamber 1408, as well as the diversion pathway 1409, the inlet port 1402, and the outlet port 1404. In some other implementations, one or more of the diversion pathway 1409, the inlet port 1402, and/or the outlet port 1404 can be at least partially formed by a cap member that is connected to either end of the housing 1414. In some implementations, the top member and the bottom member, as well as the cap member(s), can be coupled together by laser welding, heat sealing, gluing, snapping, screwing, bolting, or the like. In other implementations, some or all of the interior surface of the diversion pathway 1409 and/or sequestration chamber 1408 can be coated or loaded with an agent or substance, such as a decontaminate, solidifying agent, or the like. For instance, a solidifying agent can be provided at the diversion pathway 1409 such that when the sequestration chamber 1408 is filled and the initial aliquot of blood backs up to the diversion pathway 1409, that last amount of sequestered blood could solidify, creating a barrier between the sequestration chamber 1408 and the sampling channel 1406.

[0098] FIGS. 15A-15G illustrate a blood sequestration device 1500. The blood sequestration device 1500 can be connected to a normally closed needle or device to enable connection with an evacuated blood collection container or other collection device such as a Vacutainer™, associated tubing, luer connectors, syringe, a Luer activated valve, or the like.

[0099] The blood sequestration device 1500 includes an inlet port 1502 that can be connected with a patient needle that is inserted into a patient's vascular system for access to and withdrawing of a blood sample. The inlet port 1502 may also be connected with tubing or other conduit that is in turn connected with the patient needle. The inlet port 1502 defines an opening into the blood sequestration device 1500, which opening may be the same cross sectional dimensions as tubing or other conduit connected with the

patient needle or the patient needle itself. For instance, the opening can be circular with a diameter of approximately ~~2~~ 0,1143 cm (0,045 inches), ~~2 0.045 inches,~~ but can have a diameter of between ~~2~~ 0,0254 cm (0,01 inches) ~~2 0.01 inches~~ or less to ~~2~~ 0,508 cm (0,2 inches) ~~2 0.2 inches~~ or more.

[00100] The inlet port 1502 can also include a sealing or fluid-tight connector or connection, such as threading or Luer fitting, or the like. In some implementations, tubing or other conduit associated with the patient needle can be integral with the inlet port 1502, such as by co-molding, gluing, laser weld, or thermally bonding the parts together. In this manner, the blood sequestration device 1500 can be fabricated and sold with the patient needle as a single unit, eliminating the need for connecting the patient needle to the blood sequestration device 1500 at the time of blood draw or sampling.

[00101] The blood sequestration device 1500 further includes an outlet port 1504, which defines an opening out of the blood sequestration device 1500 and to the blood sample collection device. The outlet port 1504 may also be connected with tubing or other conduit that is in turn connected with the blood sequestration device, and may also include a sealing or fluid-tight connector or connection, such as threading or Luer fitting, or the like. Accordingly, as discussed above, the blood sequestration device 1500 can be fabricated and sold with the patient needle and/or tubing and the blood sample collection device as a single unit, eliminating the need for connecting the patient needle and the blood sample collection device to the blood sequestration device 1500 at the time of blood draw or sampling.

[00102] The blood sequestration device 1500 further includes a sampling channel 1506 between the inlet port 1502 and the outlet port 1504, and which functions as a blood sample pathway once a first aliquot of blood has been sequestered. The sampling channel 1506 can be any sized, shaped or configured channel or conduit. In some implementations, the sampling channel 1506 has a substantially similar cross sectional area as the opening of the inlet port 1502. In other implementations, the sampling channel 1506 can gradually widen from the inlet port 1502 to the outlet port 1504.

[00103] The blood sequestration device 1500 further includes a sequestration chamber 1508 that is connected to and split off or diverted from the sampling channel 1506 at any point between the inlet port 1502 and the outlet port 1504, but preferably from a proximal end of the sampling channel 1506 near the inlet port 1502. In some

implementations, the diversion includes a Y-shaped junction. The sequestration chamber 1508 is preferably maintained at atmospheric pressure, and includes a vent 1510 at or near a distal end of the sequestration chamber 1508. The vent 1510 includes an air permeable blood barrier 1512. FIG. 15C illustrates the blood sequestration device 1500 with the sequestration chamber 1508 filled with a first aliquot or sample of blood from the patient.

[00104] The air permeable blood barrier 1512 can be covered with a protective cover 1516. The protective cover 1516 can be sized and configured to inhibit a user from touching the air permeable blood barrier 1512 with their finger or other external implement, while still allowing air to exit the air permeable blood barrier 1512 as the air is displaced from the sequestration chamber 1508 by blood being forced into the sequestration chamber 1508 by a patient's own blood pressure. The protective cover 1516 can be constructed to inhibit or prevent accidental exposure of the filter to environmental fluids or splashes. This can be accomplished in a variety of mechanical ways including but not limited to the addition of a hydrophobic membrane to the protective cover.

[00105] FIG. 15B is a perspective view of the blood sequestration device 1500 from the outlet port 1504 and top side of a housing 1501 of the blood sequestration device 1500 that includes the vent 1510, and illustrating an initial aliquot of blood filling sequestration chamber 1508 while the sampling channel 1506 is empty, before a sample collection device is activated. FIG. 15G is a perspective view of the blood sequestration device 1500 from the outlet port 1504 and bottom side of the housing 1501 of the blood sequestration device 1500, and illustrating the initial aliquot of blood filling sequestration chamber 1508 while the sampling channel 1506 is empty, before the sample collection device is activated. FIG. 15C is another perspective view of the blood sequestration device 1500 from the inlet port 1502 and top side of a housing 1501 of the blood sequestration device 1500 that includes the vent 1510, and illustrating blood now being drawn through sampling channel 1506 while the sequestered blood remains substantially in the sequestration chamber 1508.

[00106] FIG. 15D is a cross section of the blood sequestration device 1500 in accordance with some implementations, showing the housing 1501 that defines the sampling channel 1506 and the sequestration chamber 1508. FIGS. 15E and 15F

illustrate various form factors of a housing for a blood sequestration device, in accordance with one or more implementations described herein.

[00107] The sequestration chamber 1508 can have a larger cross-sectional area than the sampling channel 1506, and the cross-sectional area and length can be configured for a predetermined or specific volume of blood to be sequestered or locked. The sampling channel 1506 can be sized to be compatible with tubing for either or both of the patient needle tubing or the blood collection device tubing.

[00108] The housing 1501 can be formed of multiple parts or a single, unitary part. In some implementations, and as illustrated in FIG. 15D, the housing 1501 includes a top member 1520 and a bottom member 1522 that are mated together, one or both of which having grooves, channels, locks, conduits or other pathways pre-formed therein, such as by an injection molding process or by etching, cutting, drilling, etc. The top member 1520 can be connected with the bottom member 1522 by any mating or connection mechanism, such as by laser welding, thermal bonding, ultrasonic welding, gluing, using screws, rivets, bolts, or the like, or by other mating mechanisms such as latches, grooves, tongues, pins, flanges, or the like.

[00109] In some implementations, such as shown in FIG. 15D, the top member 1520 can include the grooves, channels, locks, conduits or other pathways, while the bottom member 1522 can include a protrusion 1524 that is sized and adapted to fit into at least one of the grooves, channels, locks or other pathways of the top member 1520. The protrusion 1524 can provide a surface feature, such as a partial groove or channel, for instance, to complete the formation of either the sampling channel 1506 and/or the sequestration chamber 1508. In some implementations, the protrusion 1524 can be formed with one or more angled sides or surfaces for a tighter fit within the corresponding groove, channel, lock or other pathway. In yet other implementations, both the top member 1520 and the bottom member can include grooves, channels, locks or other pathways, as well as one or more protrusions 1524.

[00110] In some implementations, the sampling channel 1506 and the sequestration chamber 1508 are formed by grooves, channels, locks or other pathways formed in housing 1501. The housing 1501 can be made of any suitable material, including rubber, plastic, metal or other material. The housing 1501 can be formed of a clear or translucent

material, or of an opaque or non-translucent material. In other implementations, the housing 1501 can be mostly opaque or non-translucent, while the housing surface directly adjacent to the sampling channel 1506 and/or the sequestration chamber 1508 is clear or translucent, giving a practitioner a visual cue or sign that the sequestration chamber 1508 is first filled to the extent necessary or desired, and/or then a visual cue or sign that the sequestered blood remains sequestered while a clean sample of blood is drawn through the sampling channel 1506. Other visual cues or signs of the sequestration can include, without limitation: the air permeable blood barrier 1512 turning a different color upon contact, saturation, or partial saturation with blood; a color-coded tab or indicator at any point along or adjacent to the sequestration chamber; an audible signal; a vibratory signal; or other signal.

[00111] After a venipuncture by a patient needle of a patient (not shown), which could gather a number of pathogens from the patient's skin, a first amount of the patient's blood with those pathogens will make its way into the inlet port 1502 blood sequestration device 1500 and flow into the sequestration chamber 1508 by following the path of least resistance, as the patient's own blood pressure overcomes the atmospheric pressure in the sequestration chamber 1508 to displace air therein through the air permeable blood barrier 1512. The patient's blood pressure will not be sufficient to overcome the air pressure that builds up in the sealed sampling channel 1506. Eventually, the sequestration chamber 1508, which has a predetermined volume, is filled with blood that displaces air through the air permeable blood barrier 1512. Once the blood hits the air permeable blood barrier, the blood interacts with the air permeable blood barrier 1512 material to completely or partially seal the vent 1510. A signal or indication may be provided that the practitioner can now utilize the Vacutainer capsule or other blood sample collection device to acquire a next amount of the patient's blood for sampling. The blood in the sequestration chamber 1508 is now effectively sequestered in the sequestration chamber.

[00112] Upon filling the blood sequestration pathway 1508 but prior to use of the Vacutainer or other blood sample collection device, the patient's blood pressure may drive compression of the air in the sampling channel 1506, possibly resulting in a small amount of blood moving past the diversion point to the sequestration chamber 1508 and into the sampling channel 1506, queuing up the uncontaminated blood to be drawn through the sampling channel 1506.

[00113] In some instances, as shown in FIG. 15H, an inlet port 1532 can include a male luer connector for connecting to a removable patient needle, and an outlet port 11534 can include a female luer connector for connecting with a syringe. This implementation of the inlet port and outlet port can be used with any device described herein, for avoiding a propensity of a Vacutainer-type device collapsing a patient's vein. In this implementation, a clinician can use the syringe in a modulated fashion to obtain a blood sample. In operation, the syringe is attached to the outlet port 1004, and the needle is attached to the inlet port 1002. A venipuncture is performed with the needle, and without the clinician pulling on the syringe. An initial aliquot of blood fills a sequestration chamber, and then the syringe can be used to draw a sample of blood through the collection channel, bypassing the sequestered blood in the sequestration chamber.

[00114] FIGS. 16-19 illustrate yet another implementation of a blood sequestration device. FIGS. 16A-16D illustrate a blood sequestration device 1600 that can be connected between a blood sample collection device, such as an evacuated blood collection container like a Vacutainer™ (not shown), and a patient needle (not shown) and/or associated tubing. FIG. 17 illustrates a bottom member of the blood sequestration device, and FIG. 18 illustrates a top member of the blood sequestration device, which top member and bottom member can be mated together to form an inlet port, and outlet port, a sequestration chamber and a sampling channel, as explained more fully below. FIGS. 19A and B show the top member and bottom member mated together. It should be understood that FIGS. 16-19 illustrate one exemplary manner of constructing a blood sequestration device as described herein, and other forms of construction are possible.

[00115] Referring to FIGS. 16A – D, the blood sequestration device 1600 includes an inlet port 1602 that can be connected with a patient needle that is inserted into a patient's vascular system for access to and withdrawing of a blood sample. The inlet port 1602 may also be connected with tubing or other conduit that is in turn connected with the patient needle. The inlet port 1602 defines an opening into the blood sequestration device 1600, which opening can be the same cross sectional dimensions as tubing or other conduit connected with the patient needle or the patient needle itself. For instance, the opening can be circular with a diameter of approximately ≥ 0,1143 cm (0,045 inches), ≥ ~~0.045 inches,~~ but can have a diameter of between ≥ 0,0254 cm (0,01 inches) ≥ ~~0.01 inches~~ or less to ≥ 0,508 cm (0,2 inches) ≥ ~~0.2 inches~~ or more.

[00116] The inlet port 1602 can also include a sealing or fluid-tight connector or connection, such as threading or Luer fitting, or the like. In some implementations, tubing or other conduit associated with the patient needle can be integral with the inlet port 1602, such as by co-molding, gluing, laser weld, or thermally bonding the parts together. In this manner, the blood sequestration device 1600 can be fabricated and sold with the patient needle and/or tubing as a single unit, eliminating the need for connecting the patient needle to the blood sequestration device 1600 at the time of blood draw or sampling.

[00117] The blood sequestration device 1600 further includes an outlet port 1604, which defines an opening out of the blood sequestration device 1600 and to the blood sample collection device. The outlet port 1604 may also be connected with tubing or other conduit that is in turn connected with the blood sequestration device, and may also include a sealing or fluid-tight connector or connection, such as threading or Luer fitting, or the like. Accordingly, as discussed above, the blood sequestration device 1600 can be fabricated and sold with the patient needle and/or tubing and the blood sample collection device as a single unit, eliminating the need for connecting the patient needle and the blood sample collection device to the blood sequestration device 1600 at the time of blood draw or sampling.

[00118] The blood sequestration device 1600 further includes a sampling channel 1606 between the inlet port 1602 and the outlet port 1604, and a sequestration chamber 1608 that is connected to and split off or diverted from the sampling channel 1606 at any point between the inlet port 1602 and the outlet port 1604. The sampling channel 1606 functions as a blood sampling pathway once a first aliquot of blood has been sequestered in the sequestration chamber 1608. The sampling channel 1606 can be any sized, shaped or configured channel, or conduit. In some implementations, the sampling channel 1606 has a substantially similar cross sectional area as the opening of the inlet port 1602. In other implementations, the sampling channel 1606 can gradually widen from the inlet port 1602 to the outlet port 1604. The sequestration chamber 1608 may have a larger cross section to form a big reservoir toward the sequestration channel path so that the blood will want to enter the reservoir first versus entering a smaller diameter on the sampling channel 1606, as is shown more fully in FIGS. 17 and 19.

[00119] In some exemplary implementations, the diversion between the sampling channel 1606 and the sequestration chamber 1608 is by diverter junction 1607. Diverter junction 1607 may be a substantially Y-shaped, T-shaped, or U-shaped. In some preferred exemplary implementations, and as shown in FIG. 17A – 17B, the diverter junction 1607 is configured such that the flow out of the inlet port 1602 is preferentially directed toward the sequestration chamber 1608. The sequestration chamber 1608 may also include or form a curve or ramp to direct the initial blood flow toward and into the sequestration chamber 1608.

[00120] The sequestration chamber 1608 is preferably maintained at atmospheric pressure, and includes a vent 1610 at or near a distal end of the sequestration chamber 1608. The vent 1610 may include an air permeable blood barrier 1612 as described above.

[00121] The blood sequestration device 1600 can include a housing 1601 that can be formed of multiple parts or a single, unitary part. In some implementations, and as illustrated in FIGS. 17A – 17E and FIGS. 18A – 18F, the housing 1601 includes a top member 1620 and a bottom member 1622 that are mated together. The blood sequestration device 1600 can also include a gasket or other sealing member (not shown) so that when the top member 1620 is mechanically attached with the bottom member 1622, the interface between the two is sealed by the gasket or sealing member. The FIGS. 17A – 17E illustrate a bottom member 1622 of a housing for a blood sequestration device 1600. The bottom member 1622 can include grooves, channels, locks, conduits or other pathways pre-formed therein, such as by an injection molding process or by etching, cutting, drilling, etc., to form the sampling channel 1606, the sequestration chamber 1608, and diverter junction 1607.

[00122] The sequestration chamber 1608 may have a larger cross section than the sampling channel 1606 so that the blood will preferentially move into the sequestration chamber first versus entering a smaller diameter on the sampling channel 1606.

[00123] FIGS. 18A – 18F illustrate the top member 1620, which can be connected with the bottom member 1622 by any mating or connection mechanism, such as by laser welding, thermal bonding, gluing, using screws, rivets, bolts, or the like, or by other mating mechanisms such as latches, grooves, tongues, pins, flanges, or the like. The top

member 1620 can include some or all of the grooves, channels, locks, conduits or other pathways to form the sampling channel 1606, the sequestration chamber 1608, and the diverter junction 1607. In yet other implementations, both the top member 1620 and the bottom member 1622 can include the grooves, channels, locks or other pathways.

[00124] In some implementations, the sampling channel 1606 and the sequestration chamber 1608 are formed by grooves, channels, locks or other pathways formed in housing 1601. The housing 1601 can be made of rubber, plastic, metal or any other suitable material. The housing 1601 can be formed of a clear or translucent material, or of an opaque or non-translucent material. In other implementations, the housing 1601 can be mostly opaque or non-translucent, while the housing surface directly adjacent to the sampling channel 1606 and/or the sequestration chamber 1608 may be clear or translucent, giving a practitioner a visual cue or sign that the sequestration chamber 1608 is first filled to the extent necessary or desired, and/or then a visual cue or sign that the sequestered blood remains sequestered while a clean sample of blood is drawn through the sampling channel 1606. Other visual cues or signs of the sequestration can include, without limitation: the air permeable blood barrier 1612 turning a different color upon contact, saturation, or partial saturation with blood; a color-coded tab or indicator at any point along or adjacent to the sequestration chamber; an audible signal; a vibratory signal; or other signal.

[00125] As shown in FIGS. 18A – 18F, the air permeable blood barrier 1612 can be covered with, or surrounded by, a protective member 1616. The protective member 1616 can be sized and configured to inhibit a user from touching the air permeable blood barrier 1612 with their finger or other external implement, while still allowing air to exit the air permeable blood barrier 1612 as the air is displaced from the sequestration chamber 1608. In some implementations, the protective member 1616 includes a protrusion that extends up from a top surface of the top member 1620 and around the air permeable blood barrier 1612. The protective member 1616 can be constructed to inhibit or prevent accidental exposure of the filter to environmental fluids or splashes. This can be accomplished in a variety of mechanical ways including but not limited to the addition of a hydrophobic membrane to the protective cover.

[00126] In use, the blood sequestration device 1600 includes a sampling channel 1606 and a sequestration chamber 1608. Both pathways are initially air-filled at

atmospheric pressure, but the sampling channel 1606 is directed to an outlet port 1604 that will be initially sealed by a Vacutainer or other such sealed blood sampling device, and the sequestration chamber 1608 terminates at a vent 1610 to atmosphere that includes an air permeable blood barrier 1612.

[00127] After a venipuncture by a patient needle of a patient (not shown), which could gather a number of pathogens from the patient's skin, a first amount of the patient's blood with those pathogens will pass through inlet port 1602 of blood sequestration device 1600. This initial volume of potentially contaminated blood will preferentially flow into the sequestration chamber 1608 by finding the path of least resistance. The patient's own blood pressure overcomes the atmospheric pressure in the vented sequestration chamber 1608 to displace air therein through the air permeable blood barrier 1612, but is not sufficient to overcome the air pressure that builds up in the sealed sampling channel 1606. In various exemplary embodiments, the sequestration chamber 1608 and sampling channel 1606 can be configured such that the force generated by the patient's blood pressure is sufficient to overcome any effect of gravity, regardless of the blood sequestration device's orientation.

[00128] Eventually, the sequestration chamber 1608 fills with blood that displaces air through the air permeable blood barrier 1612. Once the blood contacts the air permeable blood barrier, the blood interacts with the air permeable blood barrier 1612 material to completely or partially seal the vent 1610. A signal or indication may be provided that the practitioner can now utilize the Vacutainer or other blood sampling device.

[00129] Upon filling the blood sequestration pathway 1608 but prior to use of the Vacutainer or other blood sample collection device, the patient's blood pressure may drive compression of the air in the sampling channel 1606, possibly resulting in a small amount of blood moving past the diversion point into the sampling channel 1606, queuing up the uncontaminated blood to be drawn through the sampling channel 1606.

[00130] FIG. 19A is a side view, and FIG. 19B is a cross-sectional view, of the blood sequestration device 1600, illustrating the top member 1620 mated with the bottom member 1622.

[00131] FIG. 20 shows a blood sample optimization system 2000 that includes a patient needle 2002 for vascular access to a patient's bloodstream, a blood sample collection device 2004 to facilitate the collecting of one or more blood samples, and a conduit 2006 providing a fluid connection between the patient needle 2002 and the blood sample collection device 2004. In some implementations, the blood sample collection device 2004 includes a protective shield that includes a sealed collection needle on which a sealed vacuum-loaded container is placed, which, once pierced by the collection needle, draws in a blood sample under vacuum pressure or force through the conduit 2006 from the patient needle 2002.

[00132] The blood sample optimization system 2000 further includes a blood sequestration device 2008, located at any point on the conduit 2006 between the patient needle 2002 and the blood sample collection device 2004 as described herein.

[00133] FIG. 21 illustrates a non-vented blood sequestration device 2100 using a wicking material chamber. The blood sequestration device 2100 includes a housing 2101 that has a sampling channel 2104 that is at least partially surrounded or abutted by a sequestration chamber 2102 that is filled with a wicking material. An initial aliquot of blood is drawn in from the patient needle into the sampling channel 2104 where it is immediately wicked into the wicking material of the sequestration chamber 2102. The wicking material and/or sequestration chamber 2102 is sized and adapted to receive and hold a predetermined amount of blood, such that follow-on or later blood draws pass by the wicking material and flow straight through the sampling channel 2104 to a sampling device such as a Vacutainer. The wicking material can include a substance such as a solidifier, a decontaminate, or other additive.

[00134] As described herein, an air permeable blood barrier may be created using a wide variety of different structures and materials. As shown in FIGS. 22A and B, an air permeable blood barrier 2202 of a blood sequestration device 2200 can include a polymer bead matrix 2204, in which at least some beads are treated to make them hydrophilic. The air permeable blood barrier 2202 further includes a self-sealing material 2206, such as carboxymethyl cellulose (CMC) or cellulose gum, or other sealing material. The air permeable blood barrier 2202 can further include voids 2208 that permit air flow before contact or during partial contact with a fluid such as blood. As shown in FIG. 22B,

contact with a fluid causes the self-sealing material 2206 to swell and close off the voids 2208, occluding air flow through the voids 2208 and creating a complete or partial seal.

[00135] FIGS. 23A and B illustrate yet another implementation of a blood sequestration device 2300, having an inlet port 2302 to connect with a patient needle, an outlet port 2304 to connect with a blood sample collection device, a sequestration chamber 2306, and a sampling channel 2308 that bypasses the sequestration chamber 2306 once the sequestration chamber is filled to an initial aliquot of potentially contaminated blood to be sequestered. The sequestration chamber 2306 includes a hydrophobic plug 2312 at a distal end of the sequestration chamber 2306 that is farthest from the inlet port 2302. A vacuum or other drawing force applied from the outlet port 2304, such as from a Vacutainer or the like, draws in blood into the inlet port 2302 and directly into the sequestration chamber 2306, where the initial aliquot of blood will contact the hydrophobic plug 2312 and cause the initial aliquot of blood to back up into the sequestration chamber 2306 and be sequestered there. A small amount of blood may make its way into the sampling channel 2308, which is initially closed off by valve 2308. Upon release of the valve 2308, and under further force of the vacuum or other force, follow-on amounts of blood will flow into inlet port 2302, bypass the sequestration chamber 2306, and flow into and through sampling channel 2308 toward the outlet port 2304 and to the collection device.

[00136] The sampling channel 2308 can have any suitable geometry and can be formed of plastic tubing or any other suitable material. Valve 2308 can be a clip or other enclosing device to pinch, shunt, bend or otherwise close off the sampling channel 2308 before the initial aliquot of blood is sequestered in the sequestration chamber 2306. For instance, valve 2308 can also be formed as a flap, door or closable window or barrier within the sampling channel 2308.

[00137] FIGS. 23C – 23E illustrate an alternative implementation of the blood sequestration device 2300', in which a sequestration chamber 2320 branches off from a main collection channel 2322 between an inlet port 2316 to connect with a patient needle and an outlet port 2318 to connect with a blood sample collection device, such as a Vacutainer, a syringe, or the like. The sequestration chamber 2320 includes an air-permeable, blood impermeable blood barrier 2324, such as a hydrophobic plug of material, or a filter formed of one or more layers, for example. A valve 2324 closes off

and opens the collection channel 2322, and the device 2300' can be used similarly as described above.

[00138] FIG. 24A – 24D illustrate a blood sample optimization system 2400 that includes a patient needle 2402 for vascular access to a patient's bloodstream, a blood sample collection device 2404 to facilitate the collecting of one or more blood samples for blood testing or blood cultures, and a conduit 2406 providing a fluid connection between the patient needle 2402 and the blood sample collection device 2404. In some implementations, the blood sample collection device 2404 includes a protective shield that includes a sealed collection needle on which a sealed vacuum-loaded container is placed, which, once pierced by the collection needle, draws in a blood sample under vacuum pressure or force through the conduit 2006 from the patient needle 2402.

[00139] The blood sample optimization system 2400 further includes a blood sequestration device 2408, located at any point on the conduit 2406 between the patient needle 2402 and the blood sample collection device 2404. The location of the blood sequestration device 2408 can be based on a length of the conduit between the blood sequestration device 2408 and the patient needle 2402, and the associated volume that length provides.

[00140] The blood sequestration device 2408 includes an inlet port 2412 for being connected to the conduit 2406 toward the patient needle 2402, and an outlet port 2414 for being connected to the conduit 2406 toward the blood sample collection device 2404, and a housing 2416. The housing 2416 can be any shape, although it is shown in FIGS. 24A – D as being substantially cylindrical, and includes the inlet port 2412 and outlet port 2414, which can be located anywhere on the housing although shown as being located on opposite ends of the housing 2416.

[00141] The blood sequestration device 2408 further includes a blood sequestration chamber 2418 connected with the inlet port 2412. The blood sequestration chamber 2418 is defined by an inner chamber housing 2419 that is movable from a first position to receive and sequester a first aliquot of blood, to a second position to expose one or more apertures 2424 at a proximal end of the inner chamber housing 2419 to allow blood to bypass and/or flow around the inner chamber housing 2419 and through a blood sample channel 2422 defined by the outer surface of the inner chamber housing 2419 and the

inner surface of the housing 2416. The blood sequestration chamber 2418 includes an air permeable blood barrier 2420 at a distal end of the blood sequestration chamber 2418.

[00142] In operation, the inner chamber housing 2419 is in the first position toward the inlet port 2412, such that the one or more apertures 2424 are closed, and the blood sequestration chamber 2418 is in a direct path from the patient needle. Upon venipuncture of a patient, and drawing of blood by way of a syringe or Vacutainer, or other blood collection device 2404, the initial aliquot of blood flows into the blood sequestration chamber 2418. As the initial aliquot of blood flows into the blood sequestration chamber, it displaces air therein and eventually the blood contacts the blood barrier 2420, forcing the inner chamber housing to the second position. The inner chamber housing 2419 and/or housing 2416 can include a locking mechanism of one or more small tabs, grooves, detents, bumps, ridges, or the like, to maintain the inner chamber housing 2419 in the first position until the blood sequestration chamber 2418 is filled, providing force to overcome the locking mechanism to enable movement of the inner chamber housing 2419 to the second position. Once in the second position, the initial aliquot of blood is sequestered in the blood sequestration chamber 2418 and the one or more apertures 2424 are opened to create a pathway from the inlet port 2412 to the blood sampling channel 2422, bypassing and/or flowing around the blood sequestration chamber 2418.

[00143] As described above, the housing 2416 and/or inner chamber housing 2419 can be formed as cylindrical and concentric, but can be any shape, such as squared, rectangular, elliptical, oval, or other cross-sectional shape. The outer surface of the distal end of the inner chamber housing 2419 can have one or more outwardly projecting tangs 2421with gaps therebetween. The tangs 2421 contact the inner surface of the housing 2416 to help define the blood sampling channel 2422 therebetween, and to help stop the inner chamber housing 2419 in the second position. The gaps between the tangs 2421 enable blood to flow through the blood sampling channel 2422 and to the outlet port 2414. When the inner chamber housing 2419 is in the second position and the blood sequestration chamber 2418 is filled with the first aliquot of blood, further blood samples will automatically flow through the inlet port 2412, through the one or more apertures 2424, through the blood sampling channel 2422, through the gaps between the tangs 2421, and ultimately through the outlet port 2414 to be collected by a blood sampling device 2404.

[00144] FIGS. 25A – D show a blood optimization system 2500 and blood sequestration device 2502, formed substantially as described in FIGS. 15, 16, 17, 18 and 19, but being formed to inhibit a user or other object from touching or blocking an air venting mechanism from a blood sequestration chamber 2520. Air initially in the blood sequestration chamber 2520 is displaced by an initial aliquot of blood upon venipuncture, where a patient's blood pressure overcomes the ambient air pressure in the blood sequestration chamber 2520. The air venting mechanism includes an air permeable blood barrier 2506, such as a porous material or set of materials that allows air to escape but blocks blood from leaving the blood sequestration chamber 2520.

[00145] The air venting mechanism includes an inner wall 2516 that at least partially circumscribes or surrounds the air permeable blood barrier 2506, and an outer wall 2504 spaced apart from the inner wall 2516. The outer wall 2504 can have one or more air vents 2514 formed therein. The outer wall 2504 extends higher upward than the inner wall 2516, such that a lid 2510, such as a cap, plug, cover, etc., can be attached to the outer wall 2504 and be displaced by a small distance from the top of the inner wall 2516. A seal 2508 in the form of a silicone wafer, or other elastomeric material, fits within the outer wall 2504 to cover the air permeable blood barrier 2506 and abut the top of the inner wall 2516. The seal 2508 covers and seals the air permeable blood barrier 2506 and inhibits air from entering the blood sequestration chamber 2520 through the air permeable blood barrier 2506. A fulcrum 2512 on an underside of the lid 2510 allows the seal 2508 to flexibly disconnect from the top of the inner wall 2516 when pushed by air displaced from the blood sequestration chamber 2520, to allow air to vent from the air permeable blood barrier 2506 and through the one or more air vents 2514 in the outer wall 2504.

[00146] FIG. 26A – E illustrate a blood sample optimization system 2600 that includes a patient needle 2602 for vascular access to a patient's bloodstream, a blood sample collection device 2604 to facilitate the collecting of one or more blood samples for blood testing or blood cultures, and a conduit 2606 providing a fluid connection between the patient needle 2602 and the blood sample collection device 2604. The conduit 2606 can include flexible tubing. In preferred implementations, the blood sample collection device 2604 includes a protective shield 2605 that includes a sealed collection needle on which a sealed vacuum-loaded container is placed, which, once pierced by the

collection needle, draws in a blood sample under vacuum pressure or force through the conduit 2006 from the patient needle 2602.

[00147] The blood sample optimization system 2600 further includes a blood sequestration device 2608, located at any point on the conduit 2606 between the patient needle 2602 and the blood sample collection device 2604. The location of the blood sequestration device 2608 can be based on a length of the conduit between the blood sequestration device 2608 and the patient needle 2602, and the associated volume that length provides.

[00148] The blood sequestration device 2608 includes an inlet port 2612 for being connected to the conduit 2606 toward the patient needle 2602, and an outlet port 2614 for being connected to the conduit 2606 toward the blood sample collection device 2604. The blood sequestration device 2608 includes an outer housing 2616 and an inner housing 2617, both having a cylindrical form, and being connected concentrically. The outer housing 2616 includes an outer wall 2618 and an inner conduit 2620 that defines a blood sampling channel 2622 to convey blood through the conduit 2606 to the blood sampling device 2604. The inner housing 2617 fits snugly between the inner conduit 2620 and the outer wall 2618 of the outer housing, and is rotatable in relation to the outer housing 2616. The fit between the outer housing 2616 and the inner housing 2617 can be a friction fit that maintains the housings in a particular position. The inner housing 2617 defines a blood sequestration chamber 2624, preferably a helical or corkscrew channel around the outer surface of inner conduit 2620 of the outer housing 2616, and which terminates at an air vent 2628 having an air permeable blood barrier, as shown in FIG. 26E.

[00149] The blood sequestration chamber 2624 is connected with the blood sampling channel 2622 via diversion junction 2624 formed in the inner conduit 2620, when the blood sequestration device in a first state, illustrated in FIG. 26C. The protective shield 2606 on the collection needle 2604 provides a block for air or blood, enabling a diversion of an initial aliquot of blood into the blood sequestration chamber 2624 as the patient's blood pressure overcomes the ambient air pressure in the blood sequestration channel 2624 to displace air therefrom through air vent 2628.

[00150] When the inner housing 2617 is rotated relative to the outer housing 2616, or vice versa, to a second state, as illustrated in FIG. 26D, the blood sequestration chamber 2624 is shut off from diversion junction 2624, enabling a direct path from the patient needle through the conduit 2606 to the collection needle 2604, via blood sampling channel 2622. The outer housing 2616 and/or inner housing 2617 can include ridges or grooves formed within a portion of their surfaces, to facilitate relative rotation from the first state to the second state.

[00151] FIGS. 27A – D illustrate a blood optimization system 2700 and blood sequestration device 2702, formed substantially as described with reference to at least FIGS. 15, 16, 17, 18, 19, and 25, but being formed to inhibit a user or other object from touching or blocking an air venting mechanism from a blood sequestration chamber 2720. Air initially in the blood sequestration chamber 2720 is displaced by an initial aliquot of blood upon venipuncture, where a patient's blood pressure overcomes the ambient air pressure in the blood sequestration chamber 2720. The air venting mechanism includes an air permeable blood barrier 2706, such as a porous material or set of materials that allows air to escape but blocks blood from leaving the blood sequestration chamber 2720.

[00152] The air venting mechanism includes an inner wall 2716 that at least partially circumscribes or surrounds the air permeable blood barrier 2706, and an outer wall 2704 spaced apart from the inner wall 2716. A cap 2722 is positioned on the air venting mechanism, preferably by having a lower cap wall 2728 that fits between the inner wall 2716 and the outer wall 2704 of the air venting mechanism, and frictionally abutting either the the inner wall 2716 or the outer wall 2704 or both. The cap 2722 further includes one or more vent holes 2724 or slits, apertures, openings, or the like, which extend through an upper surface of the cap 2722 around a downwardly extending plug 2726. The plug 2726 is sized and adapted to fit snugly within the space defined by inner wall 2716.

[00153] In a first position, as illustrated in FIG. 27C, the cap 2722 is extended from the air venting mechanism to allow air from the blood sequestration chamber 2720 to exit through the air permeable blood barrier 2706 and through the one or more vent holes 2724. Once the air from the blood sequestration chamber 2720 has been displaced, i.e., when the blood sequestration chamber 2720 is filled with the first aliquot of potentially tainted blood from the patient, then the cap 2722 can be pushed down on the air venting

mechanism in a second position as shown in FIG. 27D, so that the plug 2726 fits within the inner wall 2716 over the air permeable blood barrier 2706 to seal the air venting mechanism. In either the first position or the second position, the cap 2722 protects the air permeable blood barrier 2706 from outside air or from being touched by a user.

[00154] FIGS. 28A – F illustrate a blood optimization system 2800 and blood sequestration device 2802, formed substantially as described with reference to at least FIGS. 15, 16, 17, 18, 19, 25 and 26, but utilizing a multi-layered filter, and in some implementations, a filter with trapped reactive material, for an air permeable blood barrier. As shown in FIGS. 28C and D, an air permeable blood barrier 2803 includes a first layer 2804 of an air permeable but blood impermeable material, and a second layer 2806 that includes a reactive material, such as a hydrophobic material, for repelling blood while still allowing air to pass through both layers. As shown in FIGS. 28E and F, the air permeable blood barrier 2803 can include any number of layers, such as a third layer 2808 formed of the same air permeable but blood impermeable material as first layer 2804, while a second layer 2806 includes trapped or embedded blood reactive material.

[00155] FIGS. 29A – C illustrate a blood optimization system 2900 and blood sequestration device 2902, formed substantially as described with reference to at least FIGS. 15, 16, 17, 18, 19, 25 and 26, but in which a blood sequestration chamber 2904 is at least partially filled with a blood-absorptive material 2906. The blood-absorptive material 2906 can act as a wicking material to further draw in blood to be sequestered upon venipuncture of the patient, and prior to use of a blood drawing device such as a Vacutainer™ or a syringe, or the like.

[00156] FIGS. 30A – G illustrate a blood optimization system 3000 and blood sequestration device 3002, formed substantially as described with reference to at least FIGS. 15, 16, 17, 18, 19, 25 and 26. The blood sequestration device 3000 includes an inlet port 3002 that can be connected with a patient needle that is inserted into a patient's vascular system for access to and withdrawing of a blood sample. The inlet port 3002 may also be connected with tubing or other conduit that is in turn connected with the patient needle. The inlet port 3002 defines an opening into the blood sequestration device 3000, which opening can be the same cross sectional dimensions as tubing or other conduit connected with the patient needle or the patient needle itself. For instance, the

opening can be circular with a diameter of approximately ≥ ≤ 0,1143 cm (0,045 inches), ≤ ≥ ~~0.045 inches,~~ but can have a diameter of between ≥ ≤ 0,0254 cm (0,01 inches) ≤ ≥ ~~0.01 inches~~ or less to ≥ ≤ 0,508 cm (0,2 inches) ≤ ≥ ~~0.2 inches~~ or more.

[00157] The inlet port 3002 can also include a sealing or fluid-tight connector or connection, such as threading or Luer fitting, or the like. In some implementations, tubing or other conduit associated with the patient needle can be integral with the inlet port 3002, such as by co-molding, gluing, laser weld, or thermally bonding the parts together. In this manner, the blood sequestration device 3000 can be fabricated and sold with the patient needle and/or tubing as a single unit, eliminating the need for connecting the patient needle to the blood sequestration device 3000 at the time of blood draw or sampling.

[00158] The blood sequestration device 3000 further includes an outlet port 3004, which defines an opening out of the blood sequestration device 3000 and to the blood sample collection device. The outlet port 3004 may also be connected with tubing or other conduit that is in turn connected with the blood sequestration device, and may also include a sealing or fluid-tight connector or connection, such as threading or Luer fitting, or the like. Accordingly, as discussed above, the blood sequestration device 3000 can be fabricated and sold with the patient needle and/or tubing and the blood sample collection device as a single unit, eliminating the need for connecting the patient needle and the blood sample collection device to the blood sequestration device 3000 at the time of blood draw or sampling.

[00159] The blood sequestration device 3000 further includes a sampling channel 3006 between the inlet port 3002 and the outlet port 3004, and a sequestration chamber 3008 that is connected to and split off or diverted from the sampling channel 3006 at any point between the inlet port 3002 and the outlet port 3004. The sampling channel 3006 functions as a blood sampling pathway once a first aliquot of blood has been sequestered in the sequestration chamber 3008. The sampling channel 3006 can be any sized, shaped or configured channel, or conduit. In some implementations, the sampling channel 3006 has a substantially similar cross sectional area as the opening of the inlet port 3002. In other implementations, the sampling channel 3006 can gradually widen from the inlet port 3002 to the outlet port 3004. The sequestration chamber 3008 may have a larger cross section to form a big reservoir toward the sequestration channel path so that the

blood will want to enter the reservoir first versus entering a smaller diameter on the sampling channel 3006.

[00160] In some exemplary implementations, the diversion between the sampling channel 3006 and the sequestration chamber 3008 is by diverter junction 3007. Diverter junction 3007 may be a substantially Y-shaped, T-shaped, or U-shaped. In some preferred exemplary implementations, and as shown in FIG. 17A – 17B, the diverter junction 3007 is configured such that the flow out of the inlet port 3002 is preferentially directed toward the sequestration chamber 3008. The sequestration chamber 3008 may also include or form a curve or ramp to direct the initial blood flow toward and into the sequestration chamber 3008.

[00161] The sequestration chamber 3008 is preferably maintained at atmospheric pressure, and includes a vent 3010 at or near a distal end of the sequestration chamber 3008. The vent 3010 may include an air permeable blood barrier 3012 as described above.

[00162] The blood sequestration device 3000 can include a housing 3001 that can be formed of multiple parts or a single, unitary part. In some implementations, and as illustrated FIG. 30F, the housing 3001 includes a top member 3020 and a bottom member 3022 that are mated together. The blood sequestration device 3000 can also include a gasket or other sealing member (not shown) so that when the top member 3020 is mechanically attached with the bottom member 3022, the interface between the two is sealed by the gasket or sealing member. The bottom member 3022 can include grooves, channels, locks, conduits or other pathways pre-formed therein, such as by an injection molding process or by etching, cutting, drilling, etc., to form the sampling channel 3006, the sequestration chamber 3008, and diverter junction 3007.

[00163] The sequestration chamber 3008 may have a larger cross section than the sampling channel 3006 so that the blood will preferentially move into the sequestration chamber first versus entering a smaller diameter on the sampling channel 3006.

[00164] In some implementations, the sampling channel 3006 and the sequestration chamber 3008 are formed by grooves, channels, locks or other pathways formed in housing 3001. The housing 3001 can be made of rubber, plastic, metal or any other suitable material. The housing 3001 can be formed of a clear or translucent material, or

of an opaque or non-translucent material. In other implementations, the housing 3001 can be mostly opaque or non-translucent, while the housing surface directly adjacent to the sampling channel 3006 and/or the sequestration chamber 3008 may be clear or translucent, giving a practitioner a visual cue or sign that the sequestration chamber 3008 is first filled to the extent necessary or desired, and/or then a visual cue or sign that the sequestered blood remains sequestered while a clean sample of blood is drawn through the sampling channel 3006. Other visual cues or signs of the sequestration can include, without limitation: the air permeable blood barrier 3012 turning a different color upon contact, saturation, or partial saturation with blood; a color-coded tab or indicator at any point along or adjacent to the sequestration chamber; an audible signal; a vibratory signal; or other signal.

[00165] The air permeable blood barrier 3012 can be covered with, or surrounded by, a cap 3032. The cap 3032 can be sized and configured to inhibit a user from touching the air permeable blood barrier 3012 with their finger or other external implement, while still allowing air to exit the air permeable blood barrier 3012 as the air is displaced from the sequestration chamber 3008. The cap 3032 can be constructed to inhibit or prevent accidental exposure of the filter to environmental fluids or splashes. This can be accomplished in a variety of mechanical ways including but not limited to the addition of a hydrophobic membrane to the protective cover.

[00166] The air venting mechanism includes a wall 3030 that at least partially circumscribes or surrounds the air permeable blood barrier 3012. The wall 3030 can have one or more air vents formed therein. The cap 3032 covers wall 3030 and can be snapped, glued, or otherwise attached in place. A seal 3017 in the form of a silicone wafer, or other elastomeric material, fits within the wall 3030 to cover the air permeable blood barrier 3012 and abut the top of the wall 3030. The seal 3017 covers and seals the air permeable blood barrier 3012 and inhibits air from entering the blood sequestration chamber 3008 through the air permeable blood barrier 3012. A fulcrum 3012 on an underside of the cap 3032 allows the seal 3008 to flexibly disconnect from the top of the inner wall 3016 when pushed by air displaced from the blood sequestration chamber 3008, to allow air to vent from the air permeable blood barrier 3012 and through the one or more air vents in the wall 3030 and/or cap 3032.

[00167] In use, the blood sequestration device 3000 includes a sampling channel 3006 and a sequestration chamber 3008. Both pathways are initially air-filled at atmospheric pressure, but the sampling channel 3006 is directed to an outlet port 3004 that will be initially sealed by a Vacutainer or other such sealed blood sampling device, and the sequestration chamber 3008 terminates at a vent 3010 to atmosphere that includes an air permeable blood barrier 3012.

[00168] After a venipuncture by a patient needle of a patient (not shown), which could gather a number of pathogens from the patient's skin, a first amount of the patient's blood with those pathogens will pass through inlet port 3002 of blood sequestration device 3000. This initial volume of potentially contaminated blood will preferentially flow into the sequestration chamber 3008 by finding the path of least resistance. The patient's own blood pressure overcomes the atmospheric pressure in the vented sequestration chamber 3008 to displace air therein through the air permeable blood barrier 3012, but is not sufficient to overcome the air pressure that builds up in the sealed sampling channel 3006. In various exemplary embodiments, the sequestration chamber 3008 and sampling channel 3006 can be configured such that the force generated by the patient's blood pressure is sufficient to overcome any effect of gravity, regardless of the blood sequestration device's orientation.

[00169] Eventually, the sequestration chamber 3008 fills with blood that displaces air through the air permeable blood barrier 3012. Once the blood contacts the air permeable blood barrier, the blood interacts with the air permeable blood barrier 3012 material to completely or partially seal the vent 3010. A signal or indication may be provided that the practitioner can now utilize the Vacutainer or other blood sampling device.

[00170] Upon filling the blood sequestration pathway 3008 but prior to use of the Vacutainer or other blood sample collection device, the patient's blood pressure may drive compression of the air in the sampling channel 3006, possibly resulting in a small amount of blood moving past the diversion point into the sampling channel 3006, queuing up the uncontaminated blood to be drawn through the sampling channel 3006.

[00171] In yet another aspect, the blood sequestration chamber and/or blood sampling channel, or other component, of any of the implementations described herein,

can provide a visually discernable warning or result in a component adapted for operative fluid communication with the flash chamber of an introducer for an intravenous catheter into a blood vessel of a patient. The device and method provides a visually discernable alert when blood from the patient communicates with a test component reactive to communicated blood plasma, to visually change. The reaction with the blood or the plasma occurs depending on one or a plurality of reagents positioned therein configured to test for blood contents, substances or threshold high or low levels thereof, to visually change in appearance upon a result.

[00172] In yet other aspects, the blood sequestration chamber and/or blood sampling channel can be sized and adapted to provide a particular volumetric flow of blood, either during the sequestration process and/or the sampling process.

[00173] Although a variety of embodiments have been described in detail above, other modifications are possible. Other embodiments may be within the scope of the following claims.

~~Amended~~ claims

1. A blood sequestration device (812, 1000, 1100, 1202, 1302, 1401, 1500, 1600, 2008, 2100, 2200, 2300, 2408, 2502, 2608, 2702, 2802, 2902, 3000) comprising;

an inlet port (802, 902, 1002, 1102, 1212, 1314, 1402, 1502, 1532, 1602, 2302, 2316, 2412, 2612, 3002);

an outlet port (904, 1004, 1104, 1214, 1312, 1404, 1504, 1534, 1604, 2304, 2318, 2414, 2614, 3004) ;

a sequestration chamber (55, 104, 204, 304, 822, 1008, 1108, 1218, 1318, 1408, 1508, 1608, 2102, 2306, 2320, 2418, 2520, 2624, 2720, 2904, 3008) connected with the inlet port via a junction, the sequestration chamber having a vent (1510, 1610, 2628, 3010) that includes an air permeable blood barrier (20, 106, 824, 1010, 1110, 1310, 1412, 1512, 1612, 2202, 2420, 2506, 2706, 2803, 3012), the vent being defined by an outer wall (2504, 2618, 2704) that at least partially circumscribes the air permeable blood barrier and includes one or more air vents (2514), the vent further including a cap (1208, 1307, 2722, 3032), that at least partially covers the wall and a one-way seal abutting the air permeable blood barrier that inhibits air from entering the sequestration chamber; and

a sampling channel (820, 1406, 1508, 1606, 2104, 2308, 2422, 2622, 3006) having a proximal end connected with the inlet port via the junction, and a distal end connected with the outlet port;

the sequestration chamber, the sampling channel and the junction being sized and configured such that a first portion of blood flows into the sequestration chamber toward the air permeable blood barrier for sequestration therein, and a second portion of blood bypasses the sequestration chamber and the first portion of blood sequestered therein and is directed into the sampling channel toward the outlet port.

2. The blood sequestration device in accordance with claim 1, further comprising a housing (40, 50, 818, 1301, 1414, 1501, 1601, 2101, 2416, 2616, 3001) that houses and defines the inlet port, the outlet port, the sequestration chamber, and the sampling channel.

3. The blood sequestration device in accordance with claim 1, wherein the vent further includes an inner wall (2516, 2716, 3016) within the outer wall and that contains the air permeable blood barrier.

4. The blood sequestration device in accordance with claim 1, wherein the one-way seal is positioned over the inner wall and within the outer wall of the vent.

5. The blood sequestration device in accordance with claim 4, wherein the cap includes an inner surface that faces the air permeable blood barrier, the inner surface of the cap including a fulcrum (2512, 3012) against which the seal can flexibly unseal from the air permeable blood barrier to allow air to escape the sequestration chamber.

6. The blood sequestration device in accordance with claim 1, wherein the air permeable blood barrier includes a sealing material that seals the vent upon contact with blood.

7. The blood sequestration device in accordance with claim 1, wherein the air permeable blood barrier includes a filter having a first layer and a second layer, the second layer of the filter having a hydrophobic material to repel blood.

8. A blood sequestration and sampling system (800, 1200, 1300, 1400, 2000, 2400, 2500, 2600, 2700, 2800, 2900, 3000) comprising;

a blood sampling pathway having a patient needle on a proximal end and a sample collection device on a distal end; and

a blood sequestration device in accordance with any of claims 1 to 7 attached on the blood sampling pathway between the proximal end and distal end of the blood sampling pathway, wherein the inlet port is coupled with the blood sampling pathway toward the patient needle;

the outlet port is coupled with the blood sampling pathway toward the sample collection device.

9. The blood sequestration system in accordance with claim 8, wherein the blood sequestration device further comprises a housing that houses and defines the inlet port, the outlet port, the sequestration chamber, and the sampling channel.

10. The blood sequestration system in accordance with claim 8, wherein the vent of the blood sequestration device further includes an inner wall within the outer wall and that contains the air permeable blood barrier.

11. The blood sequestration system in accordance with claim 8, wherein the one-way seal of the vent is positioned over the inner wall and within the outer wall of the vent.

12. The blood sequestration system in accordance with claim 11, wherein the cap includes an inner surface that faces the air permeable blood barrier, the inner surface of the cap including a fulcrum against which the seal can flexibly unseal from the air permeable blood barrier to allow air to escape the sequestration chamber.

13. The blood sequestration system in accordance with claim 8, wherein the air permeable blood barrier of the blood sequestration device includes a sealing material that seals the vent upon contact with blood.

14. The blood sequestration system in accordance with claim 8, wherein the air permeable blood barrier of the blood sequestration device includes a filter having a first layer and a second layer, the second layer of the filter having a hydrophobic material to repel blood.

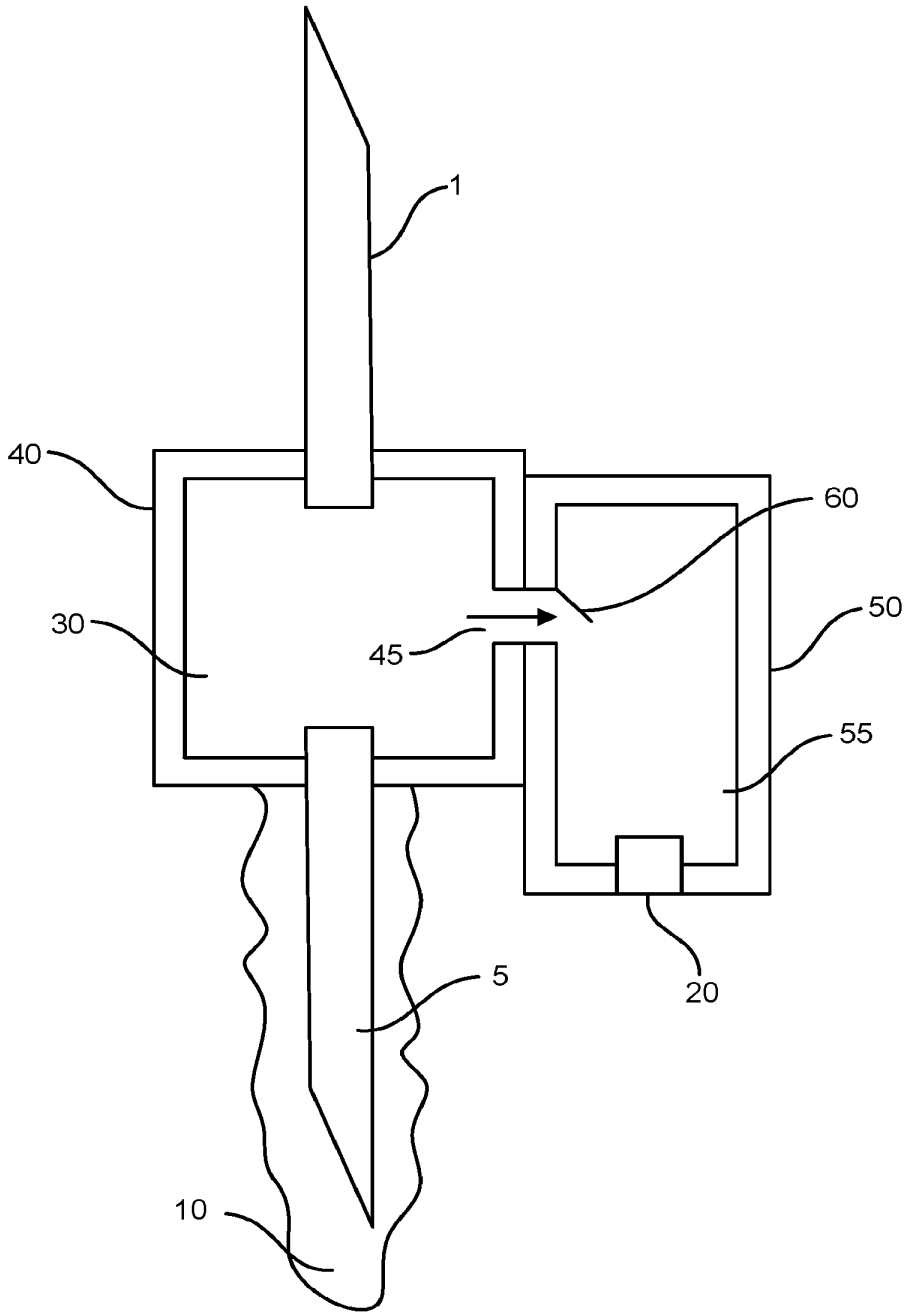


FIG. 1

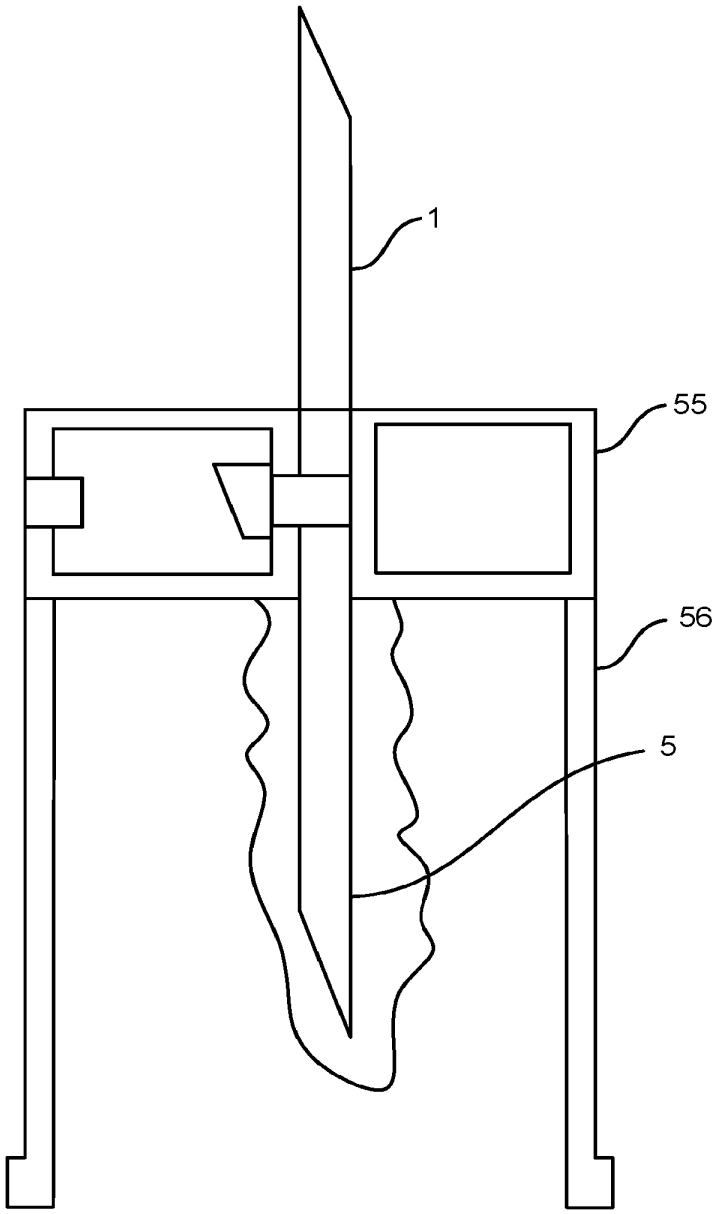


FIG. 2

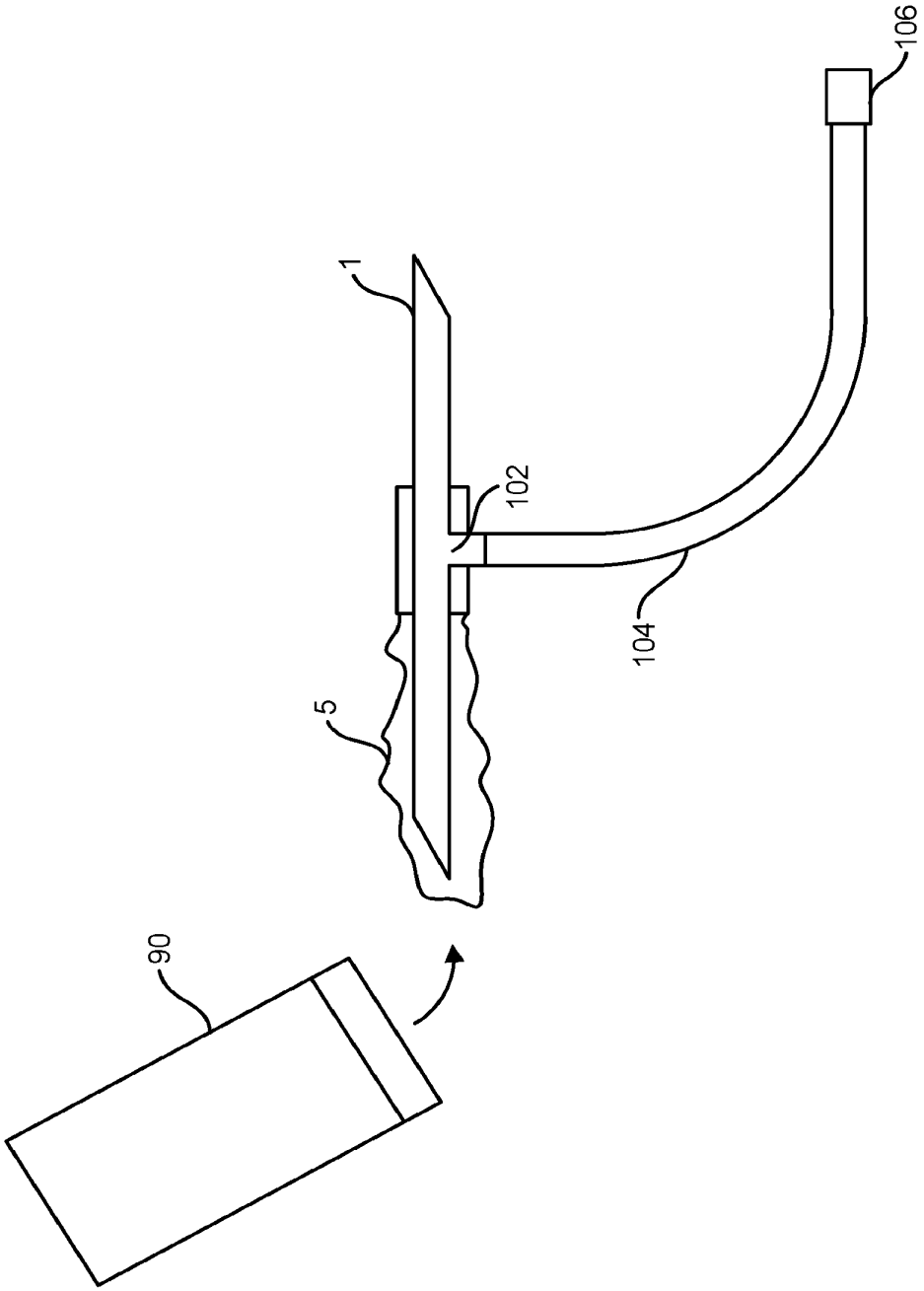


FIG. 3

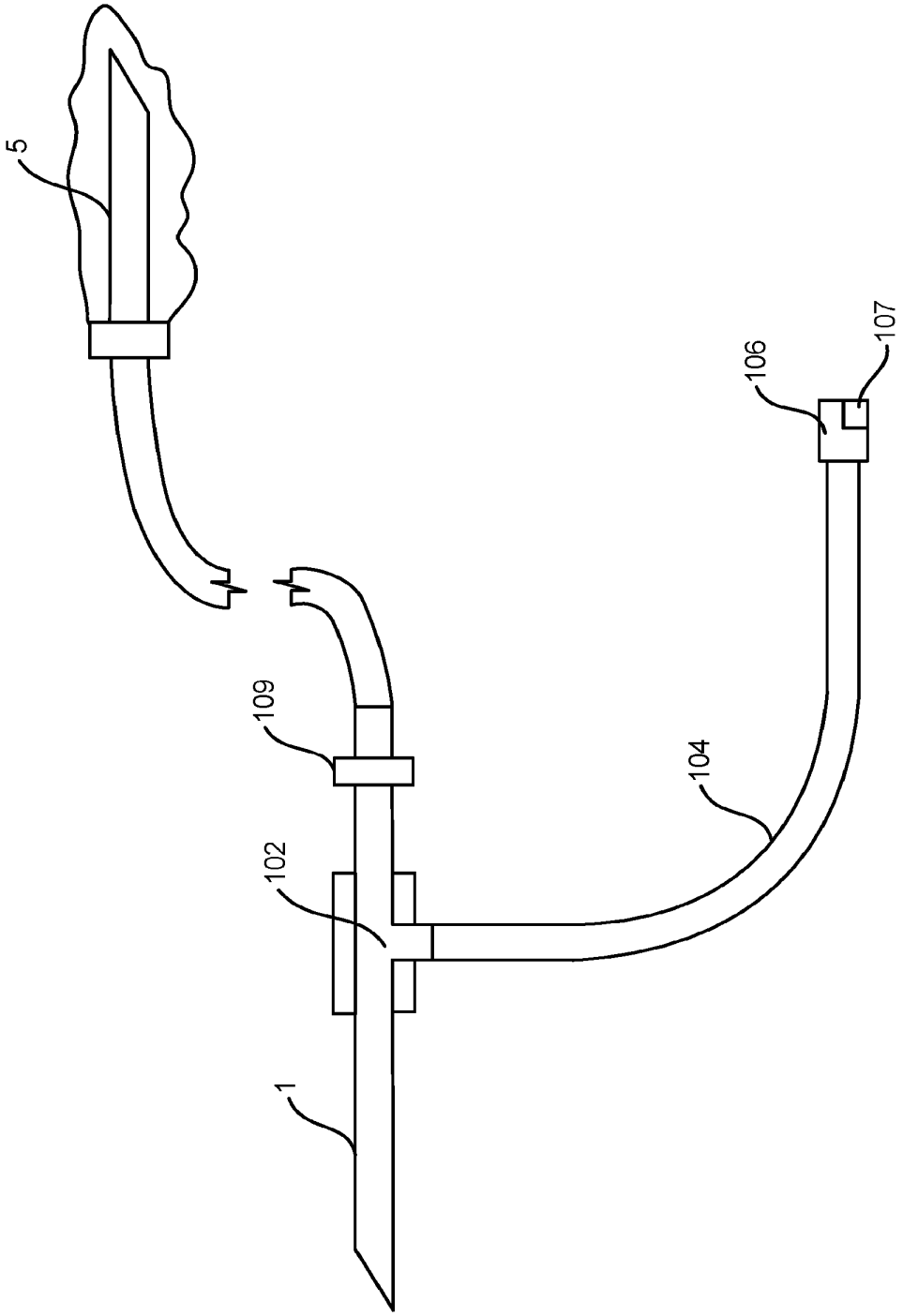


FIG. 4

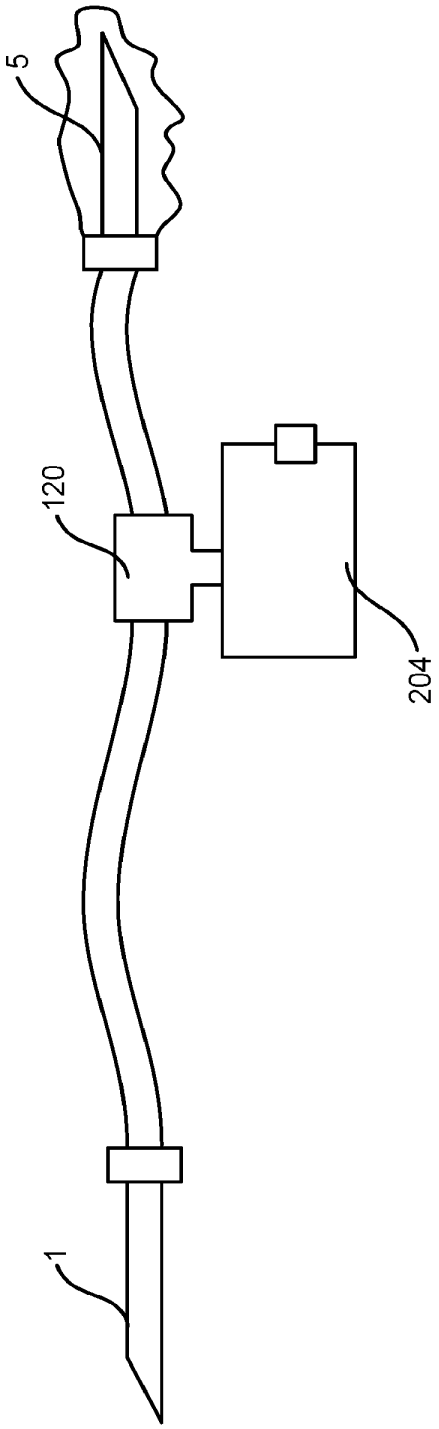


FIG. 5

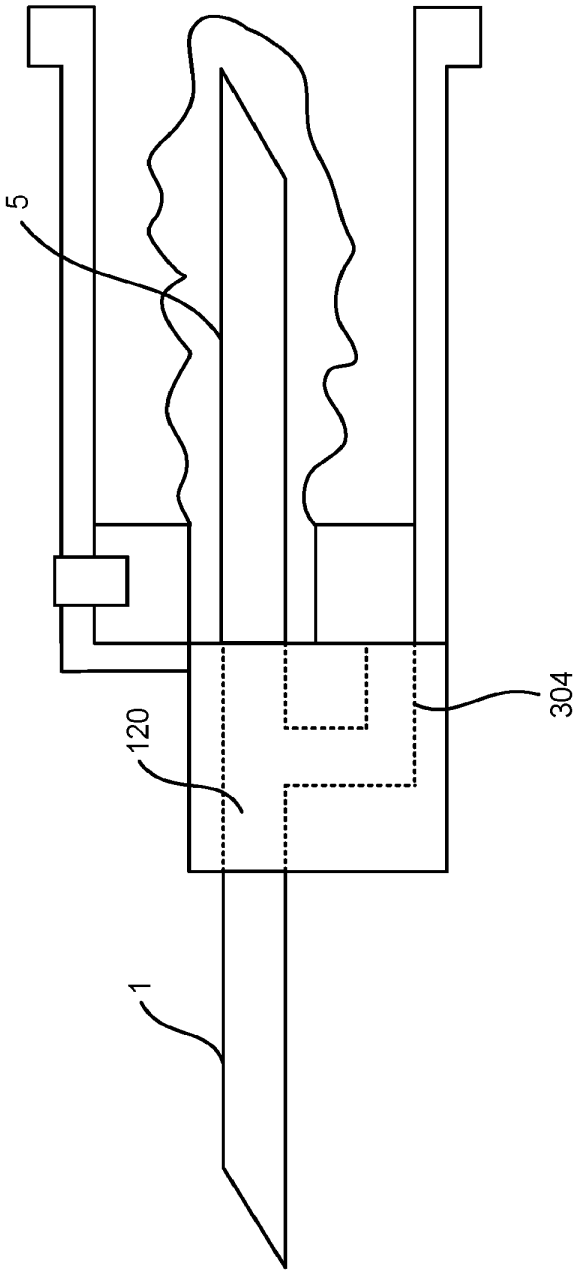


FIG. 6

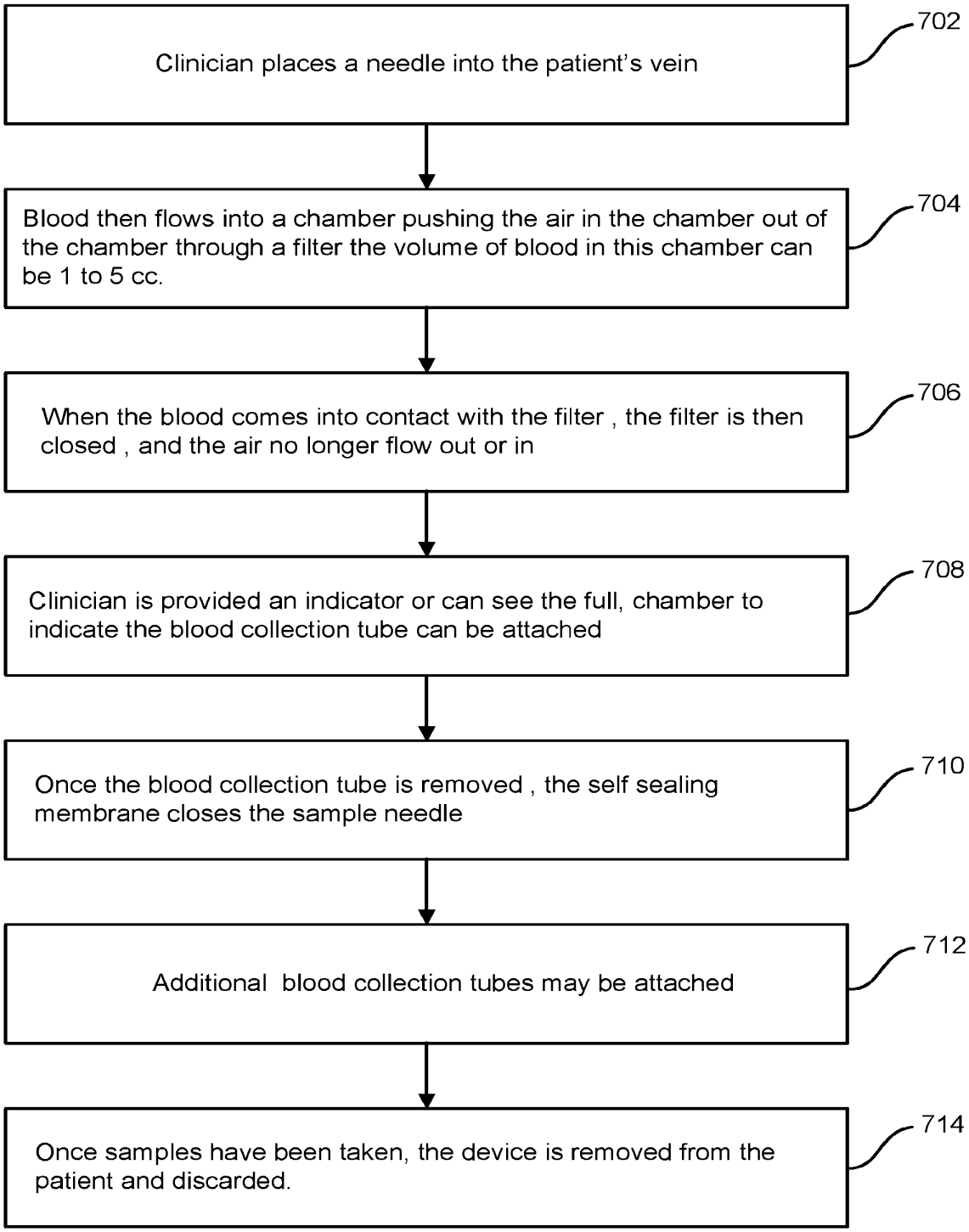
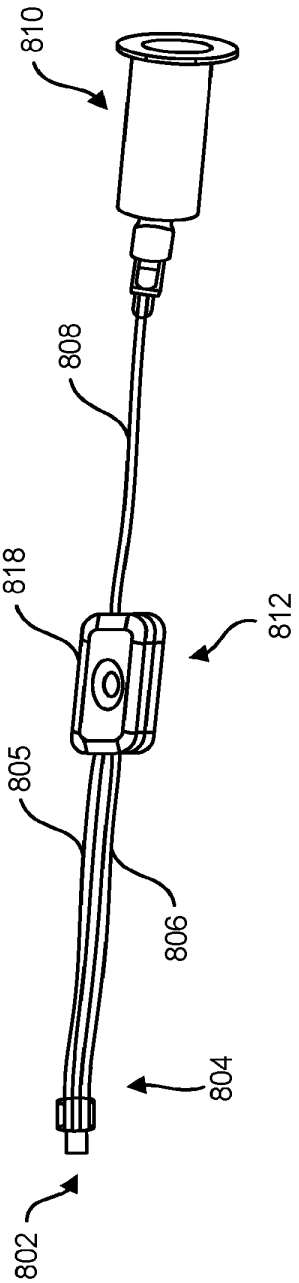

Clinician places a needle into the patient's vein
702
Blood then flows into a chamber pushing the air in the chamber out of the chamber through a filter the volume of blood in this chamber can be 1 to 5 cc.
704
When the blood comes into contact with the filter , the filter is then closed , and the air no longer flow out or in
706
Clinician is provided an indicator or can see the full, chamber to indicate the blood collection tube can be attached
708
Once the blood collection tube is removed , the self sealing membrane closes the sample needle
710
Additional blood collection tubes may be attached
712
Once samples have been taken, the device is removed from the patient and discarded.
714

FIG. 7



800

FIG. 8A

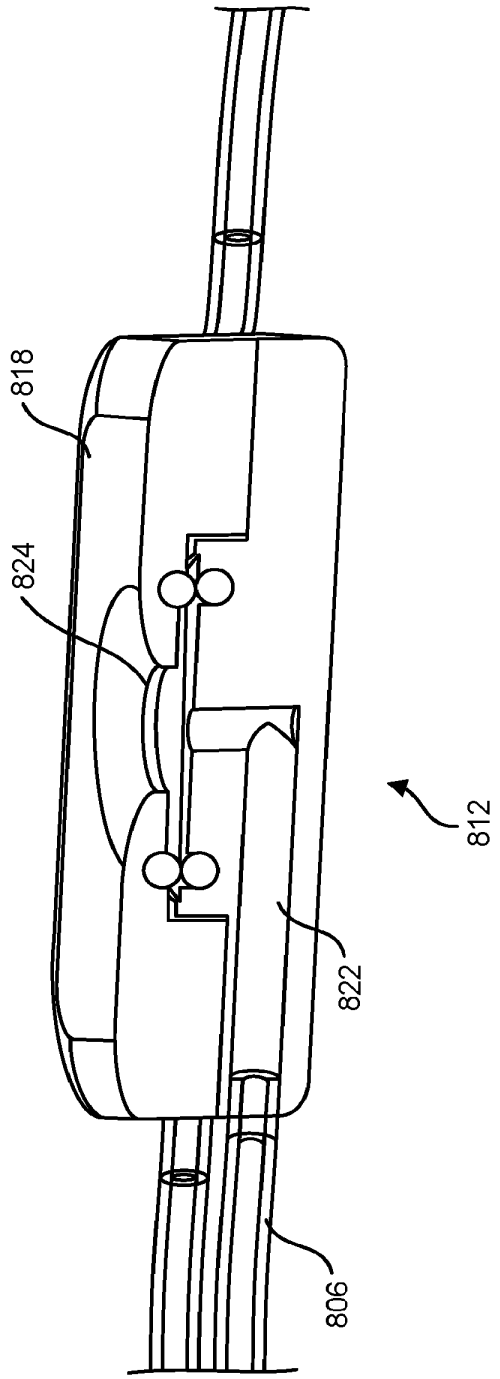


FIG. 8B

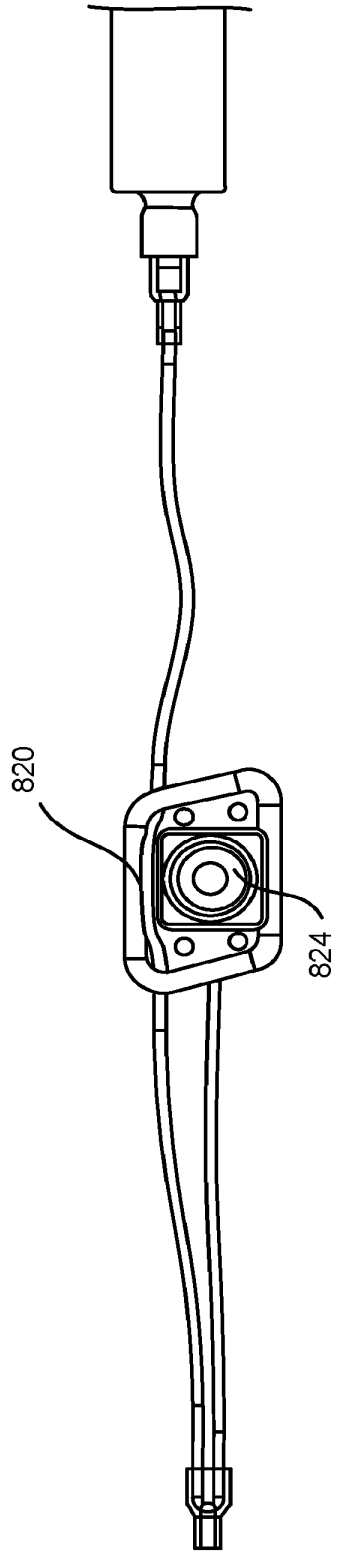


FIG. 8C

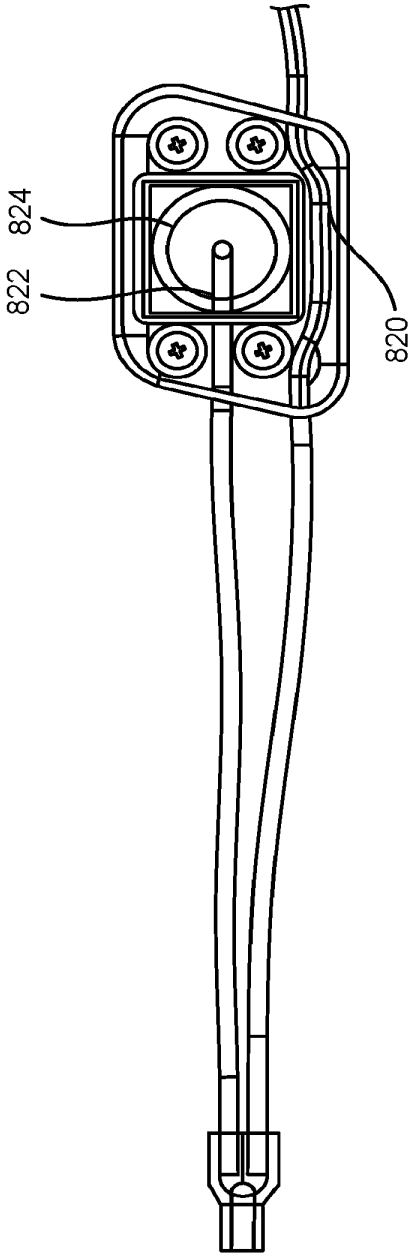


FIG. 8D

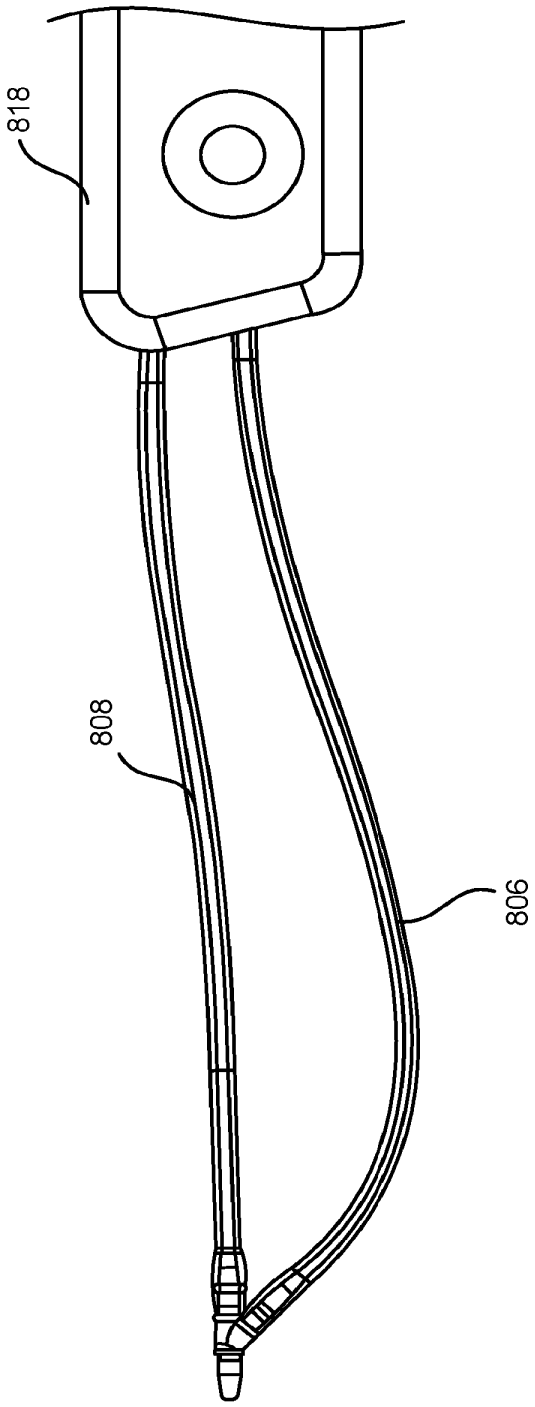


FIG. 8E

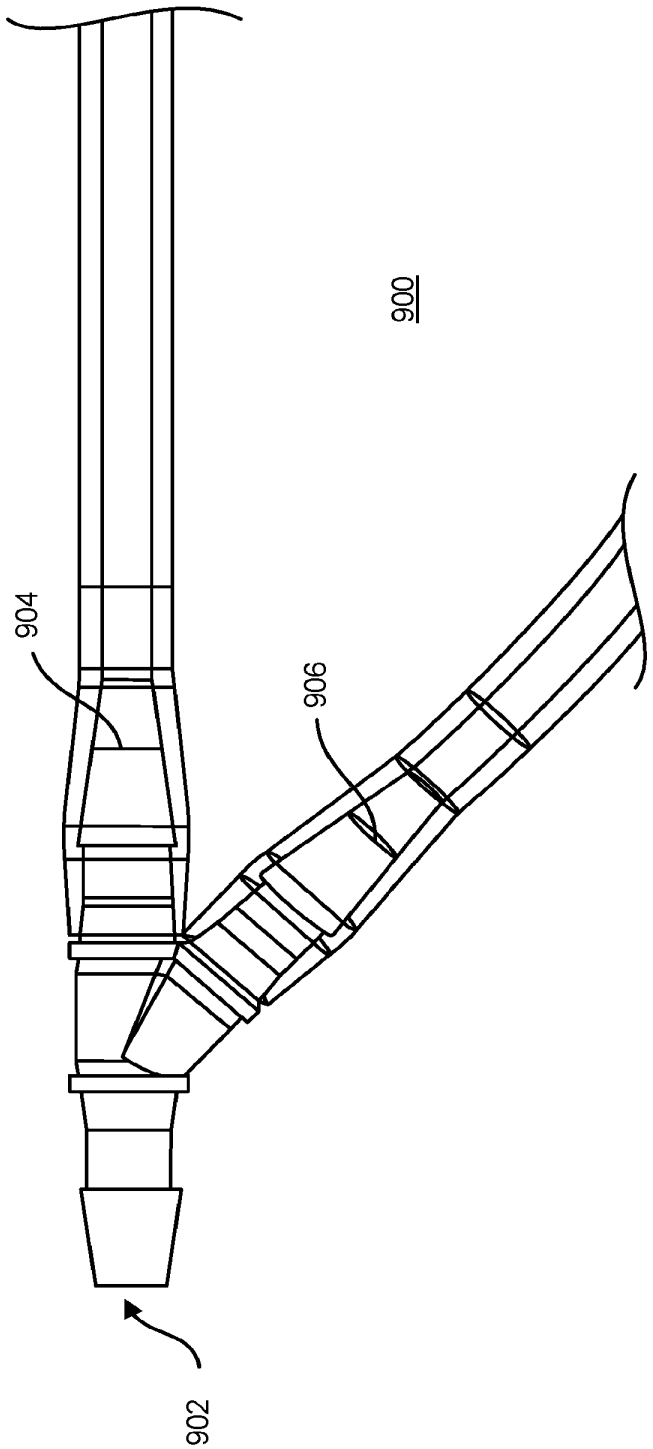


FIG. 9

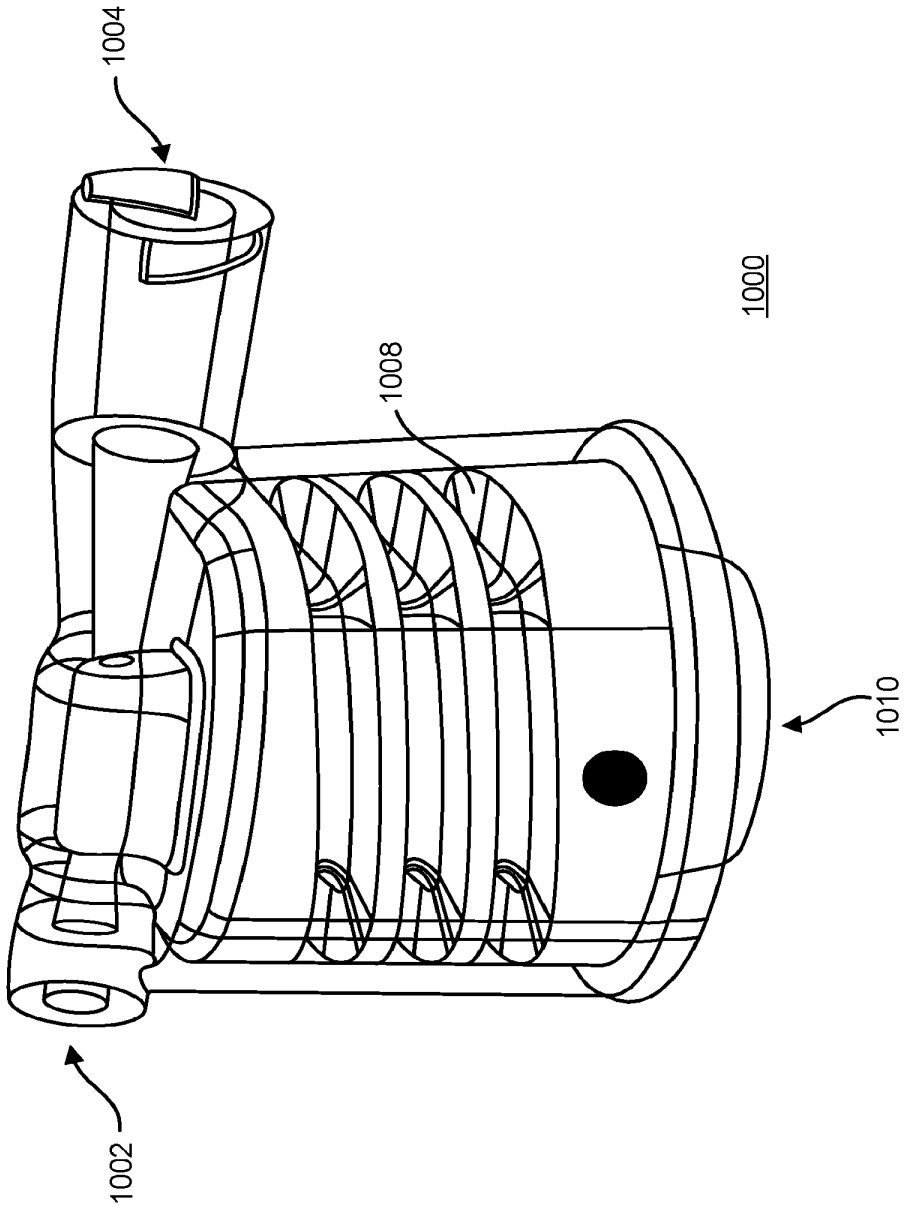


FIG. 10A

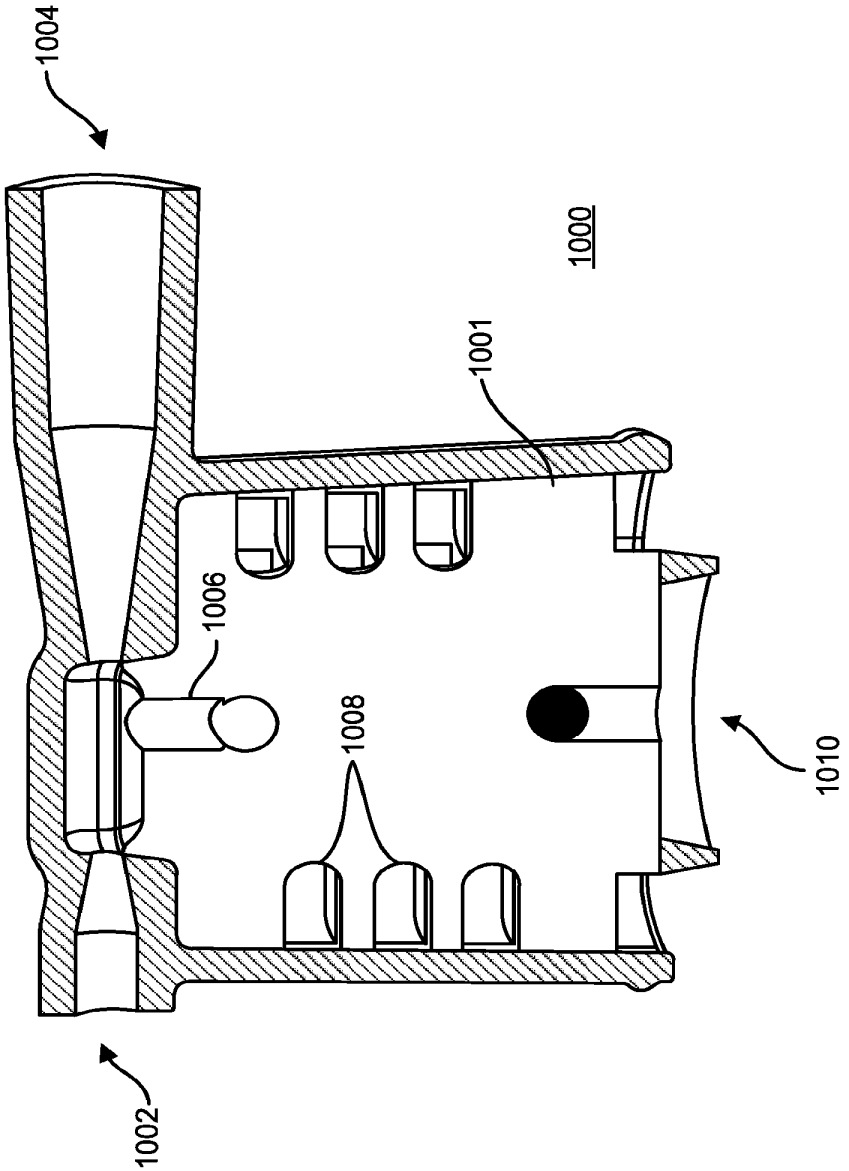


FIG. 10B

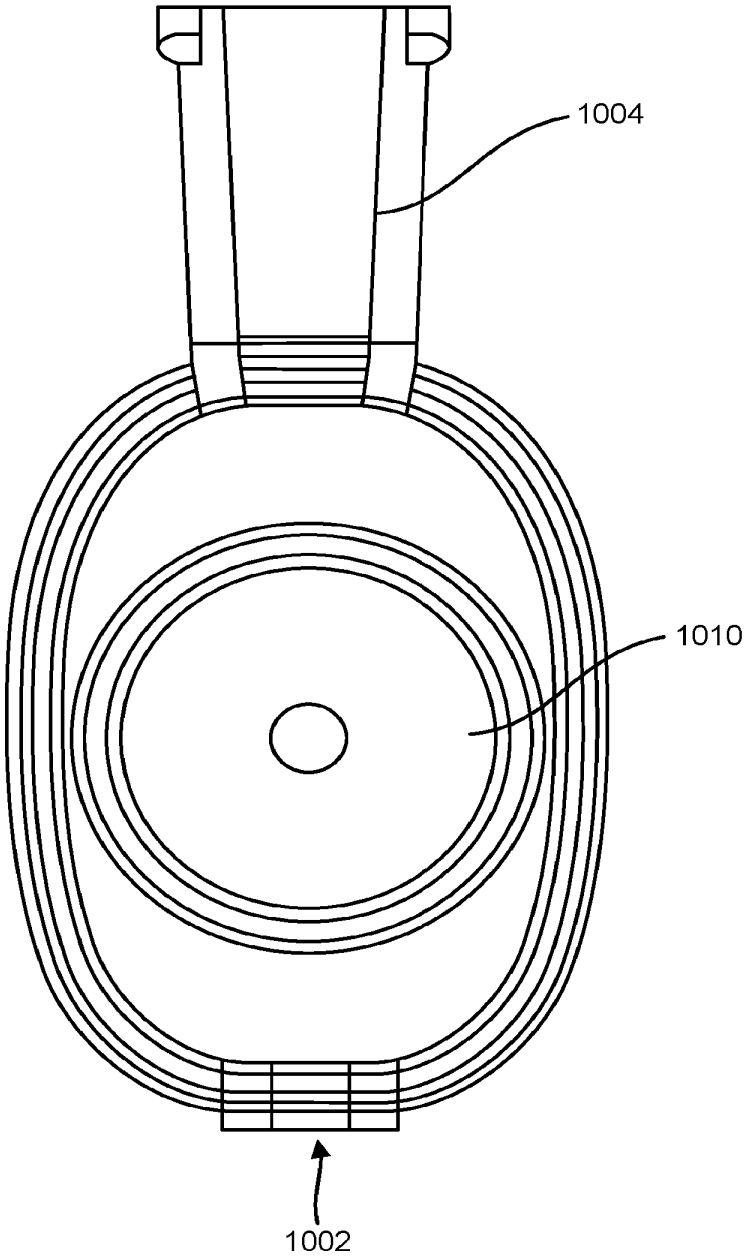


FIG. 10C

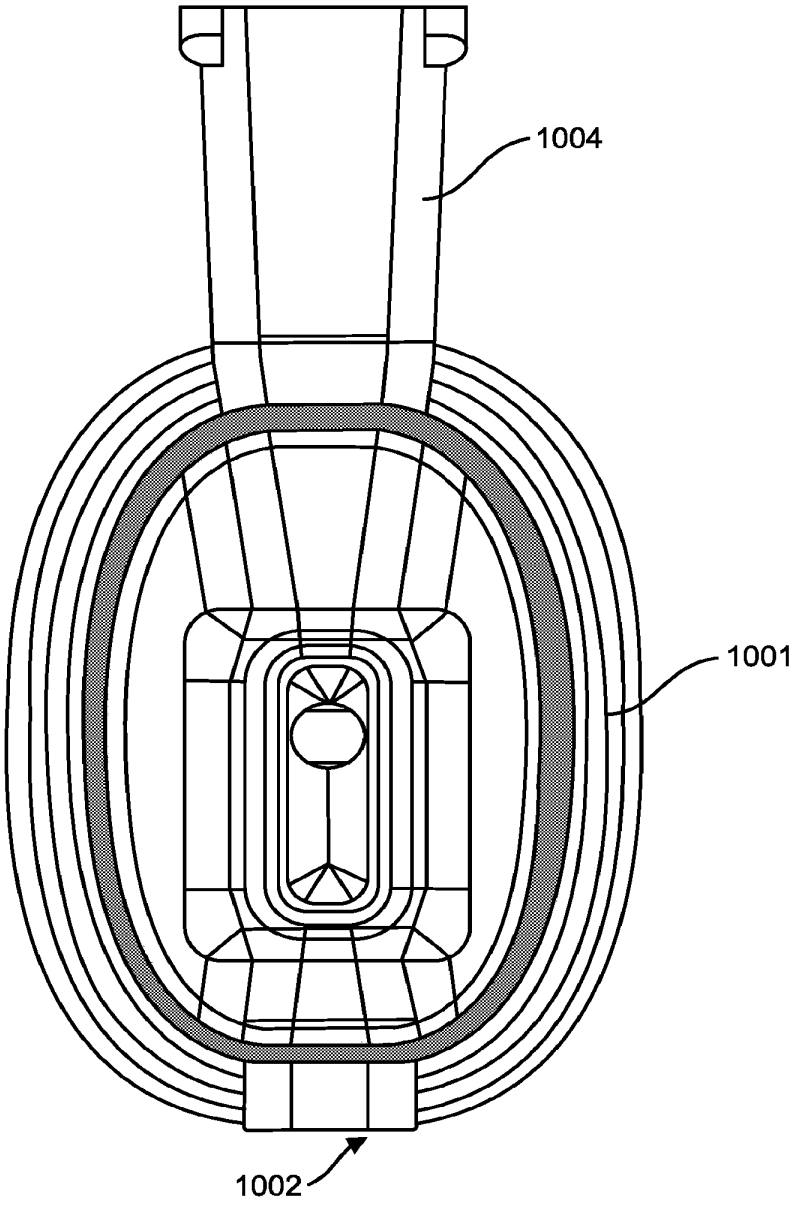


FIG. 10D

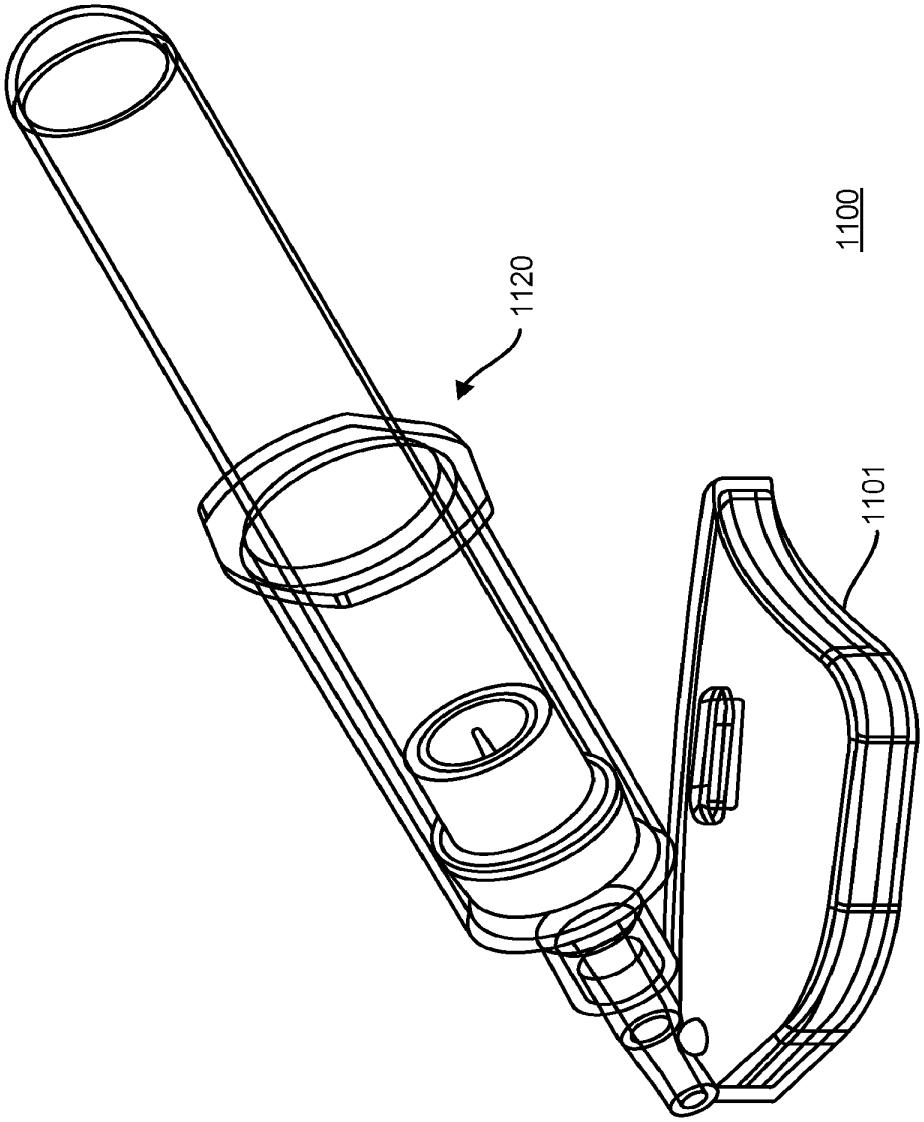


FIG. 11A

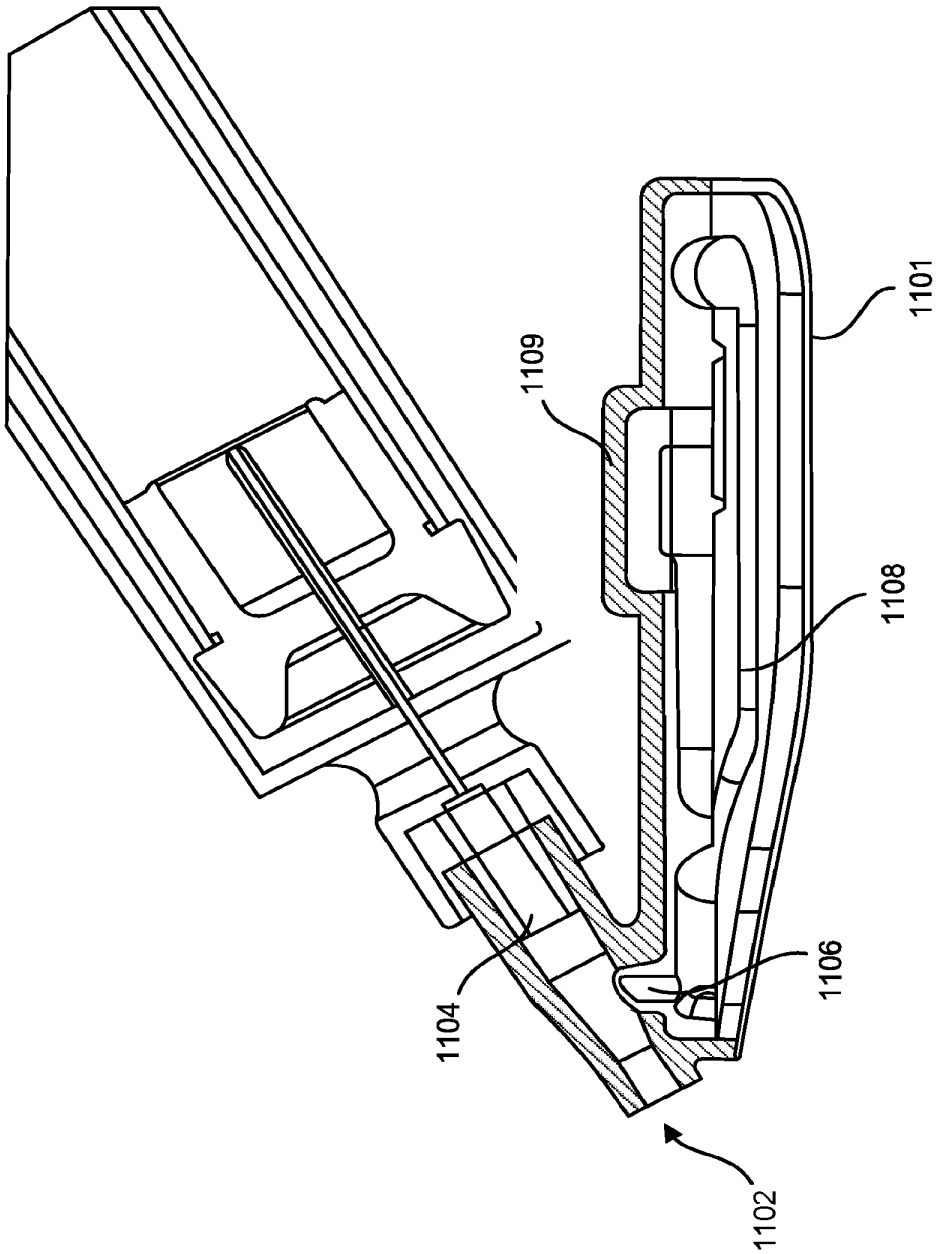


FIG. 11B

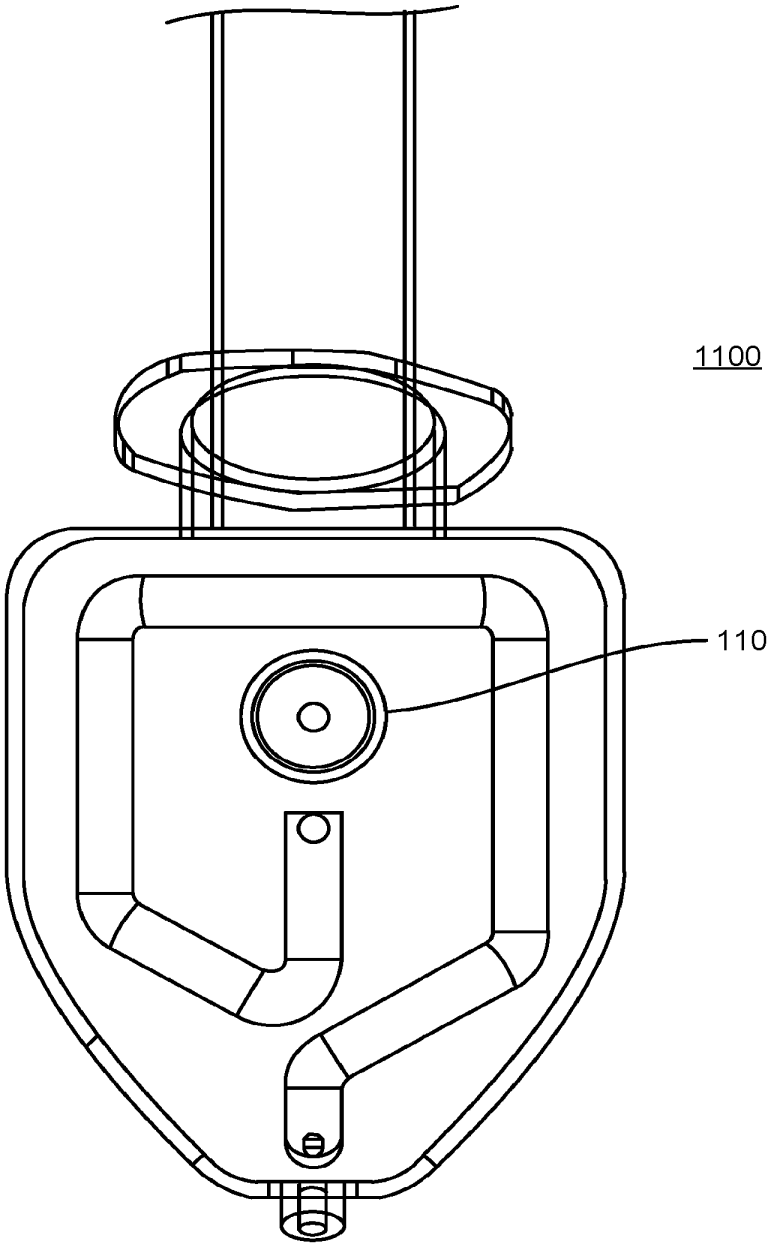


FIG. 11C

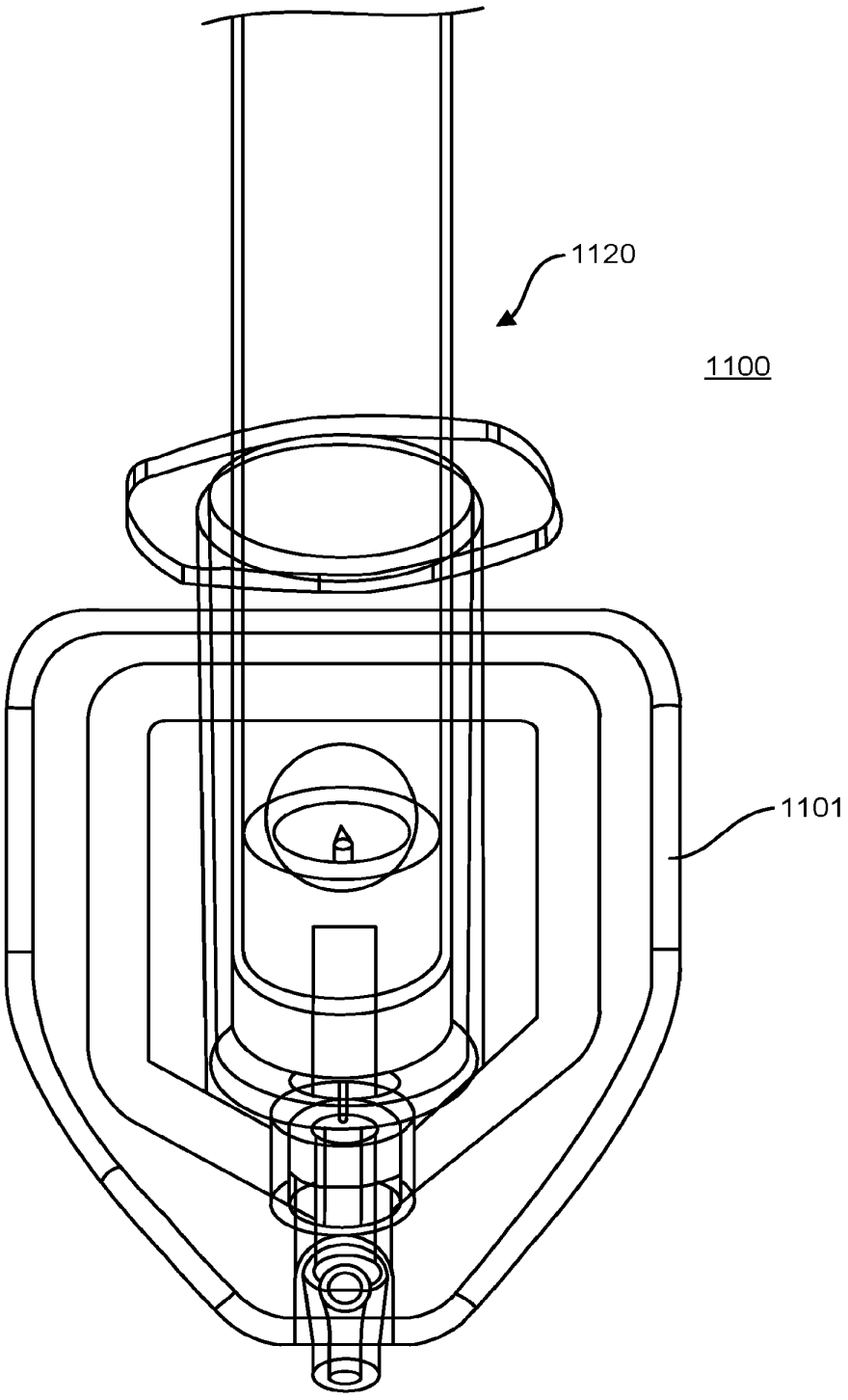


FIG. 11D

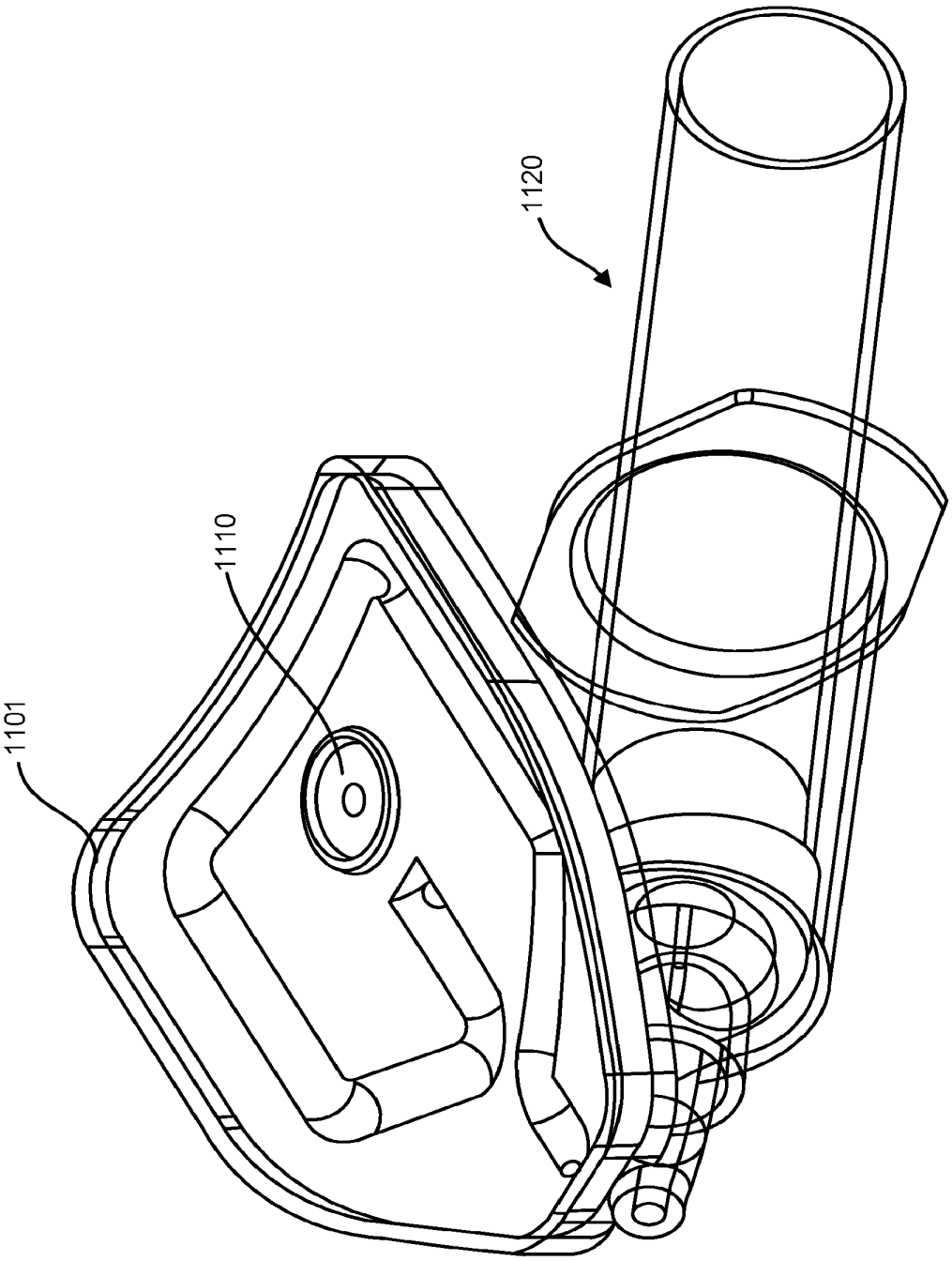


FIG. 11E

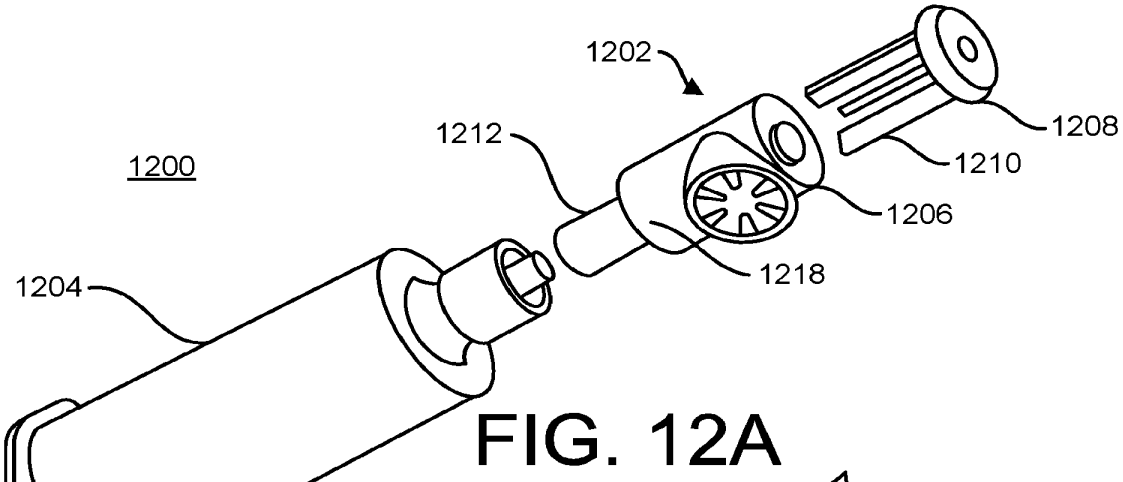


FIG. 12A

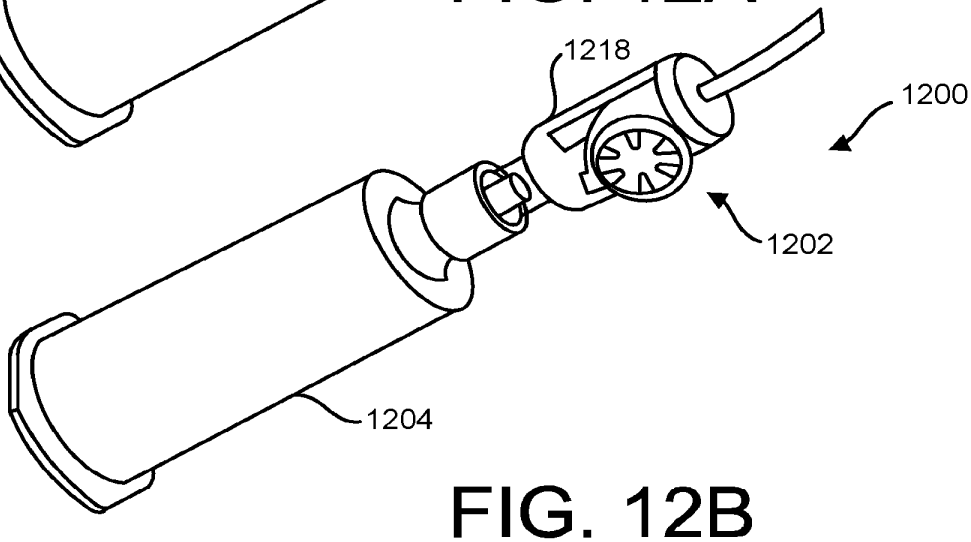


FIG. 12B

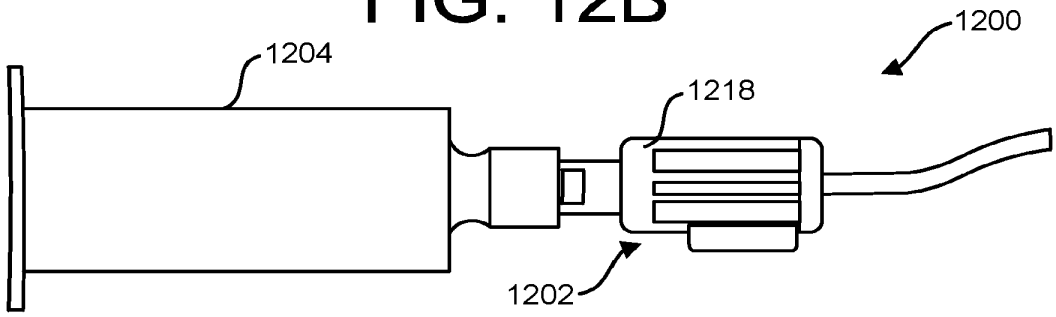


FIG. 12C

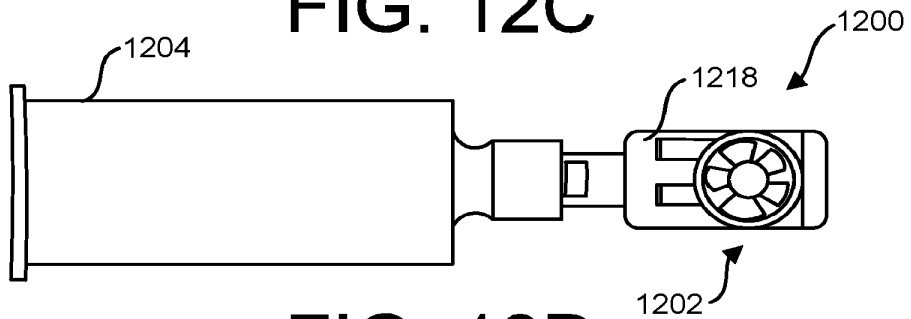


FIG. 12D

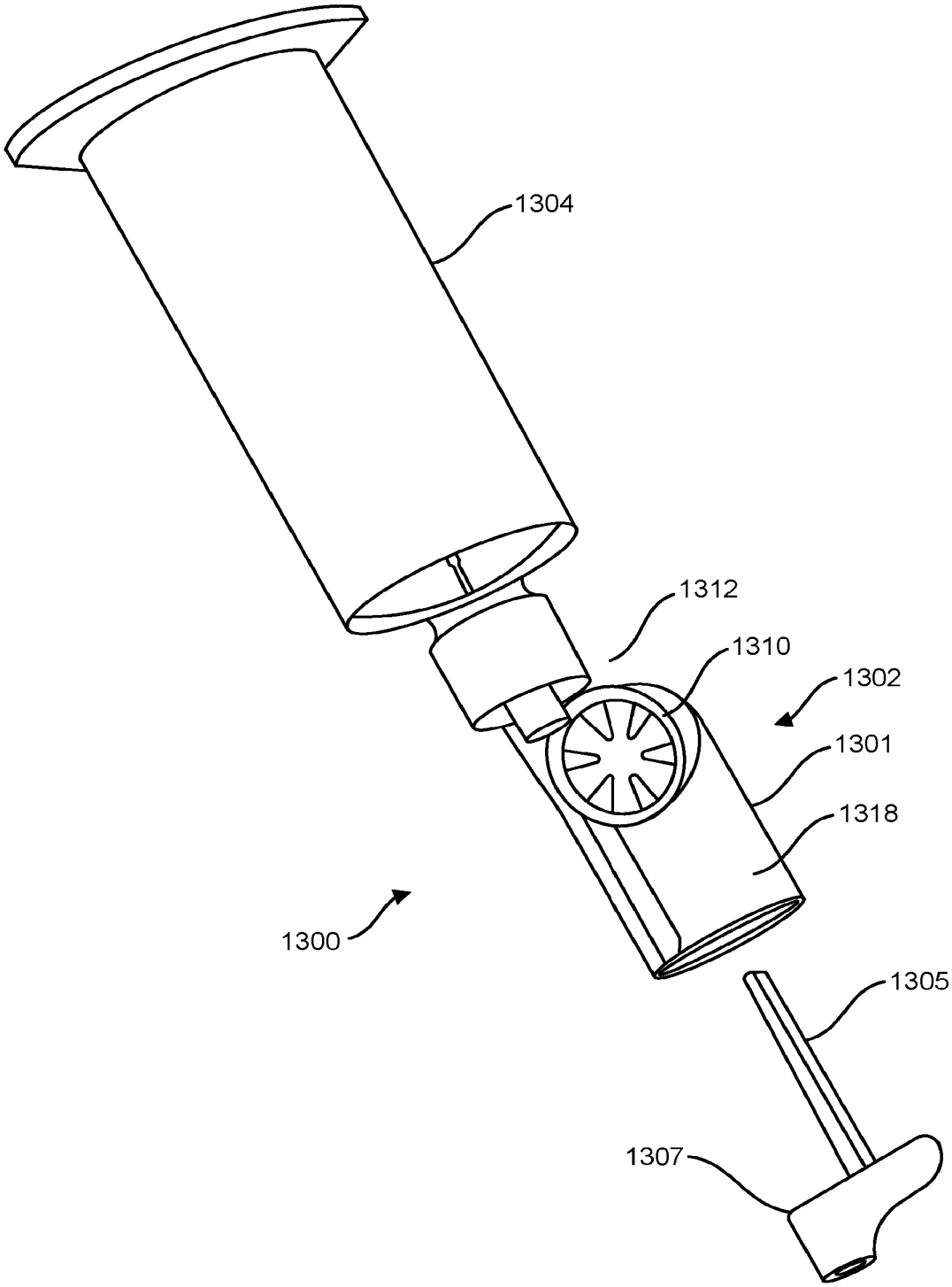


FIG. 13A

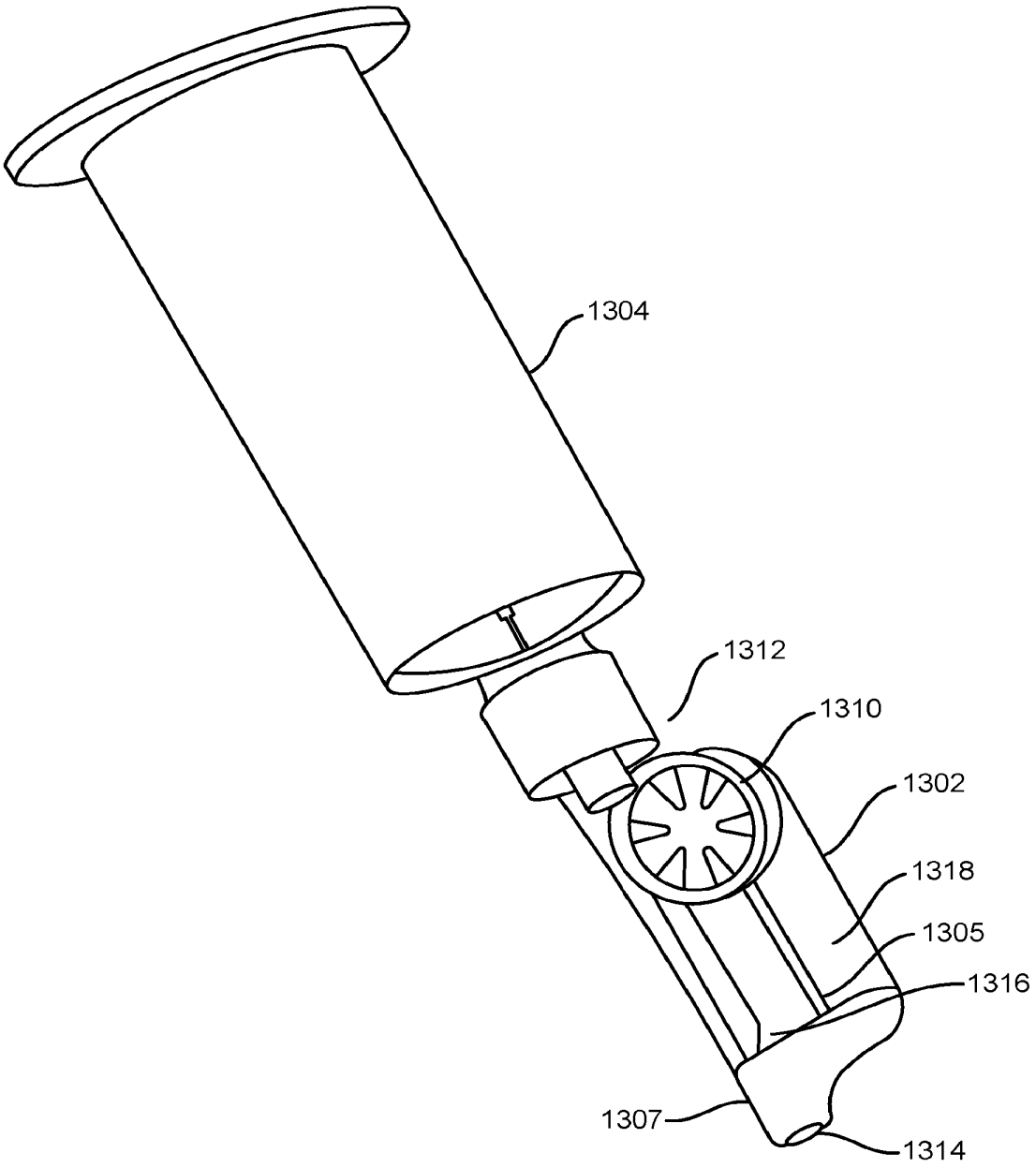


FIG. 13B

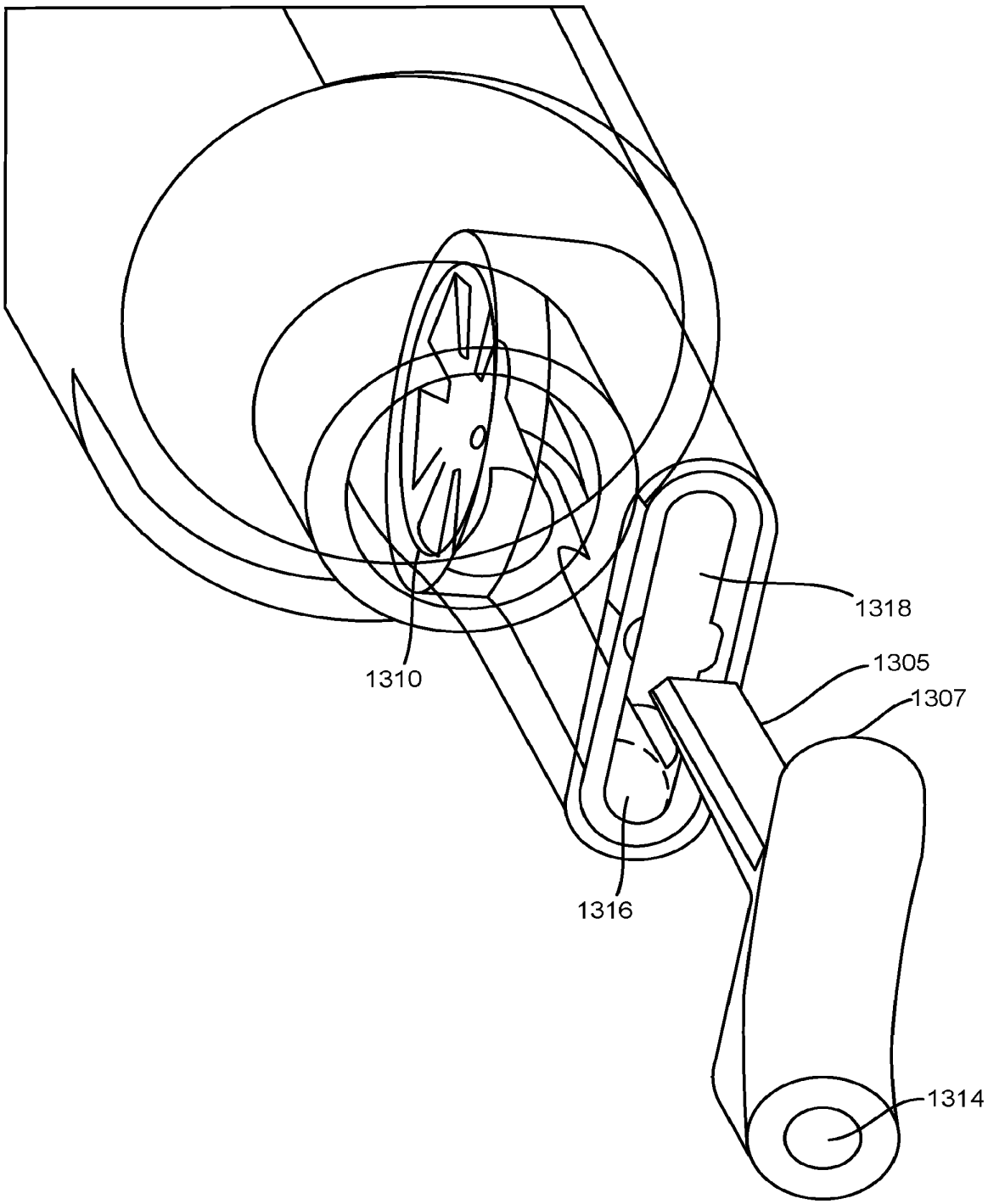


FIG. 13C

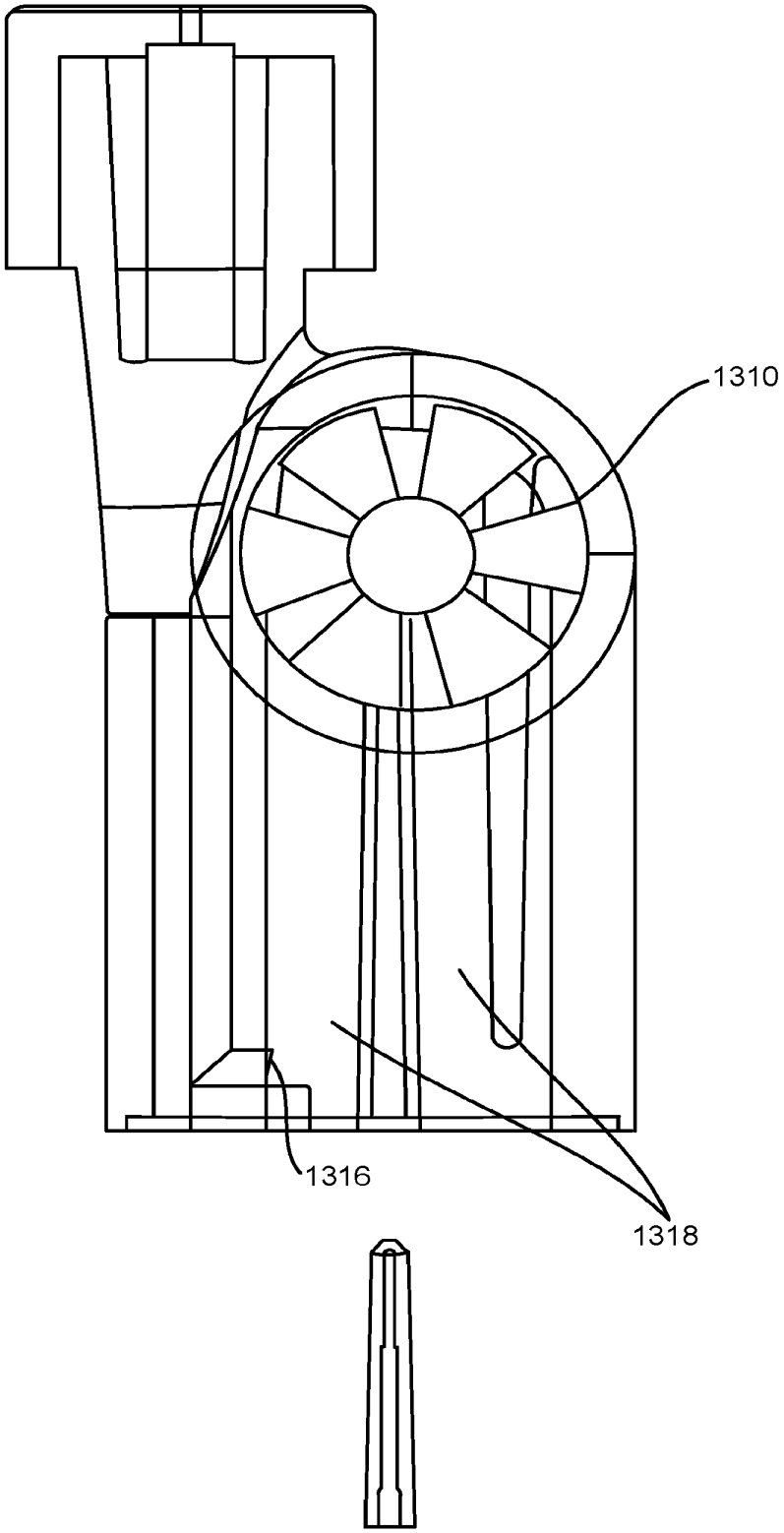


FIG. 13D

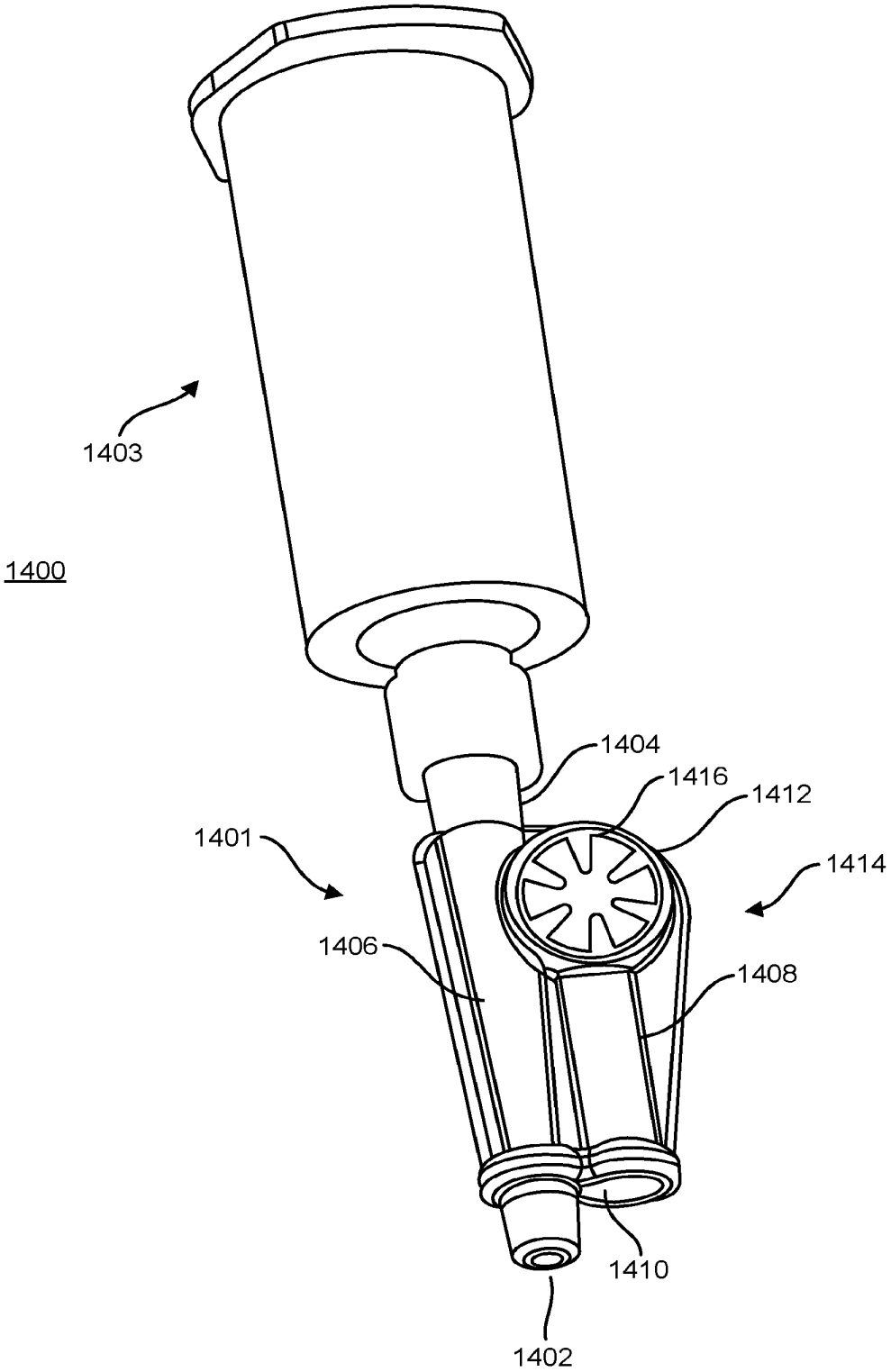


FIG. 14A

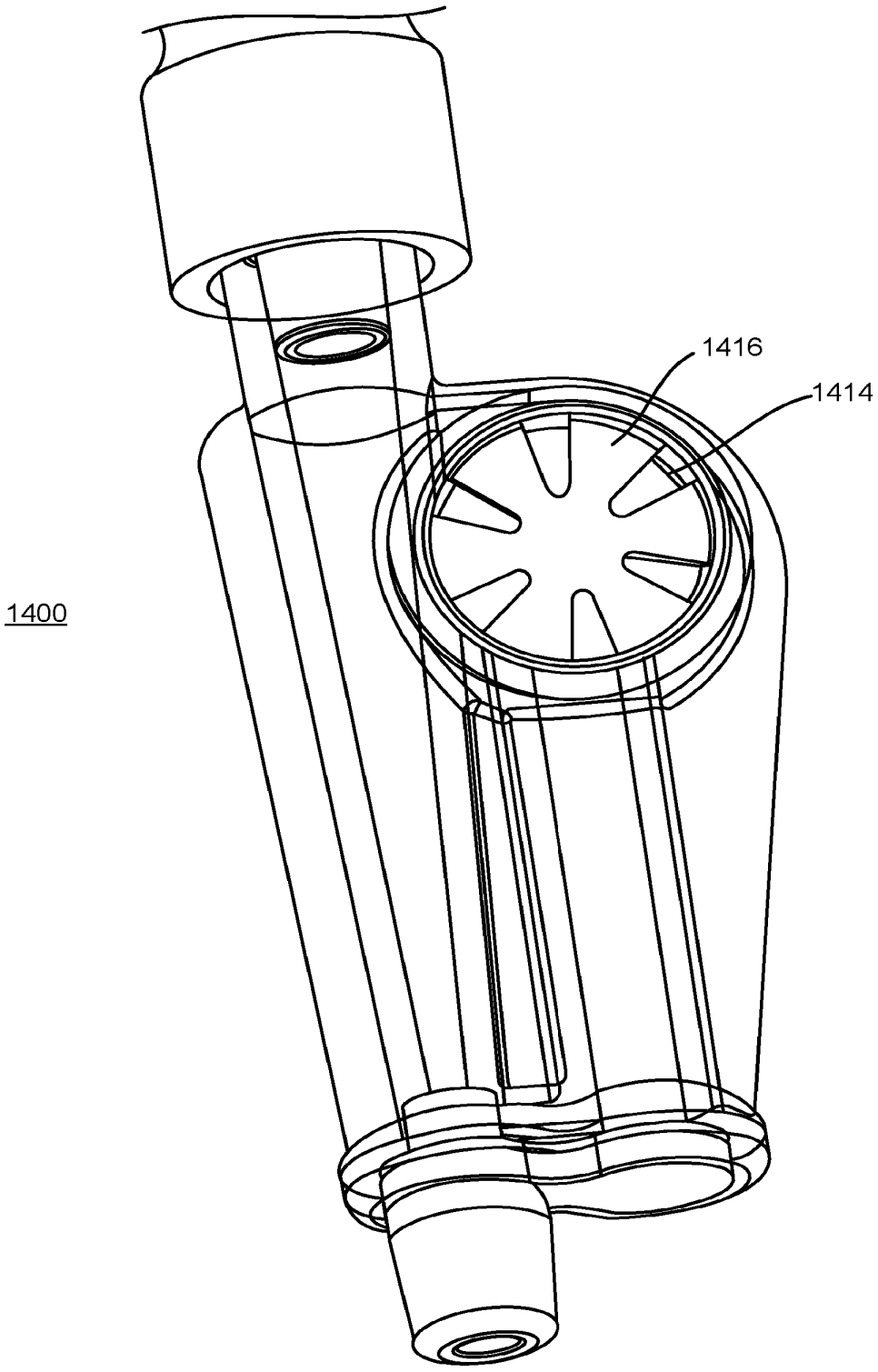


FIG. 14B

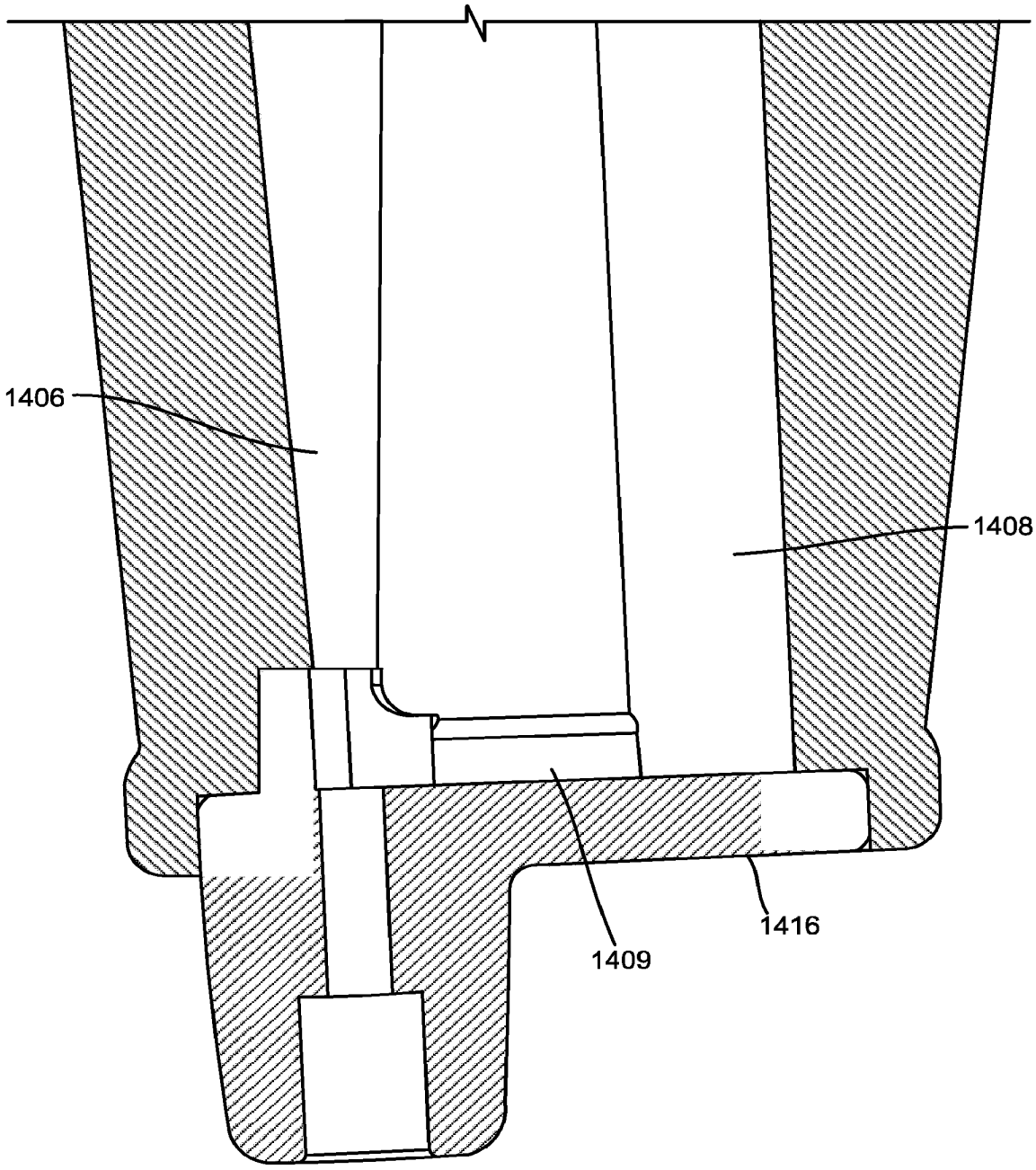


FIG. 14C

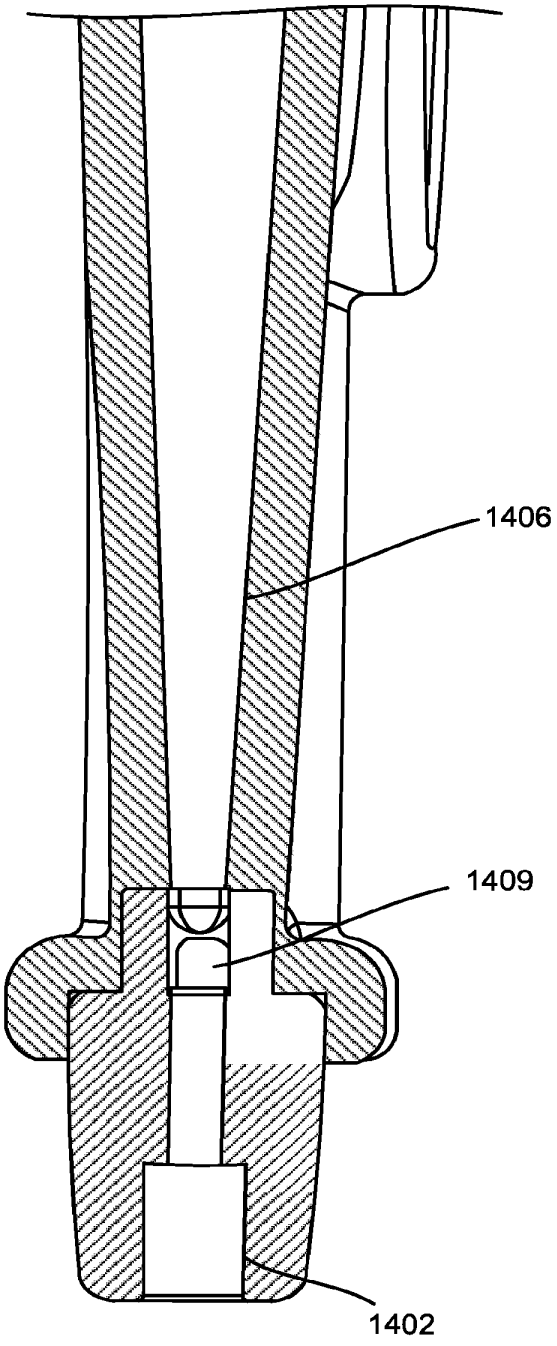


FIG. 14D

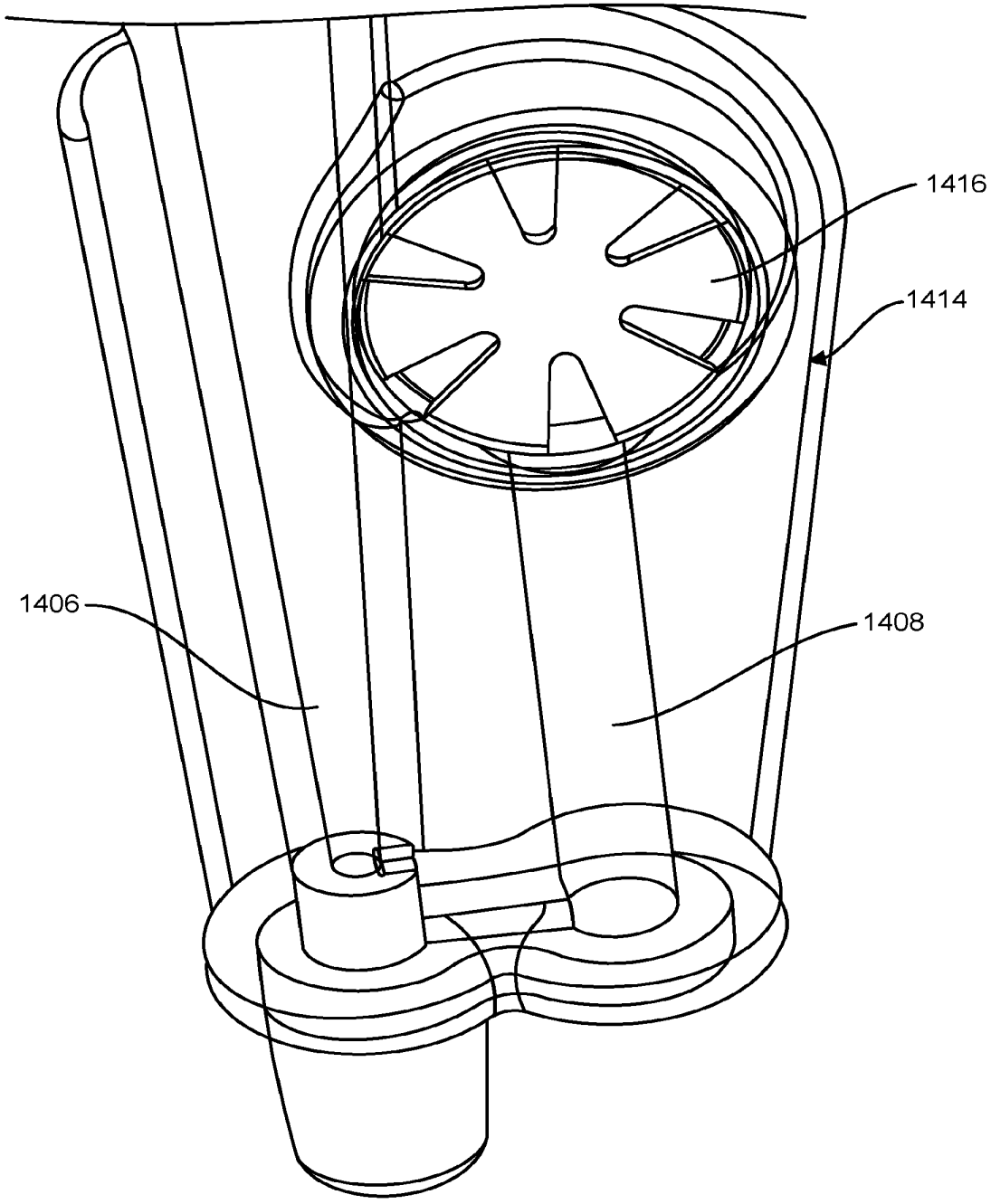


FIG. 14E

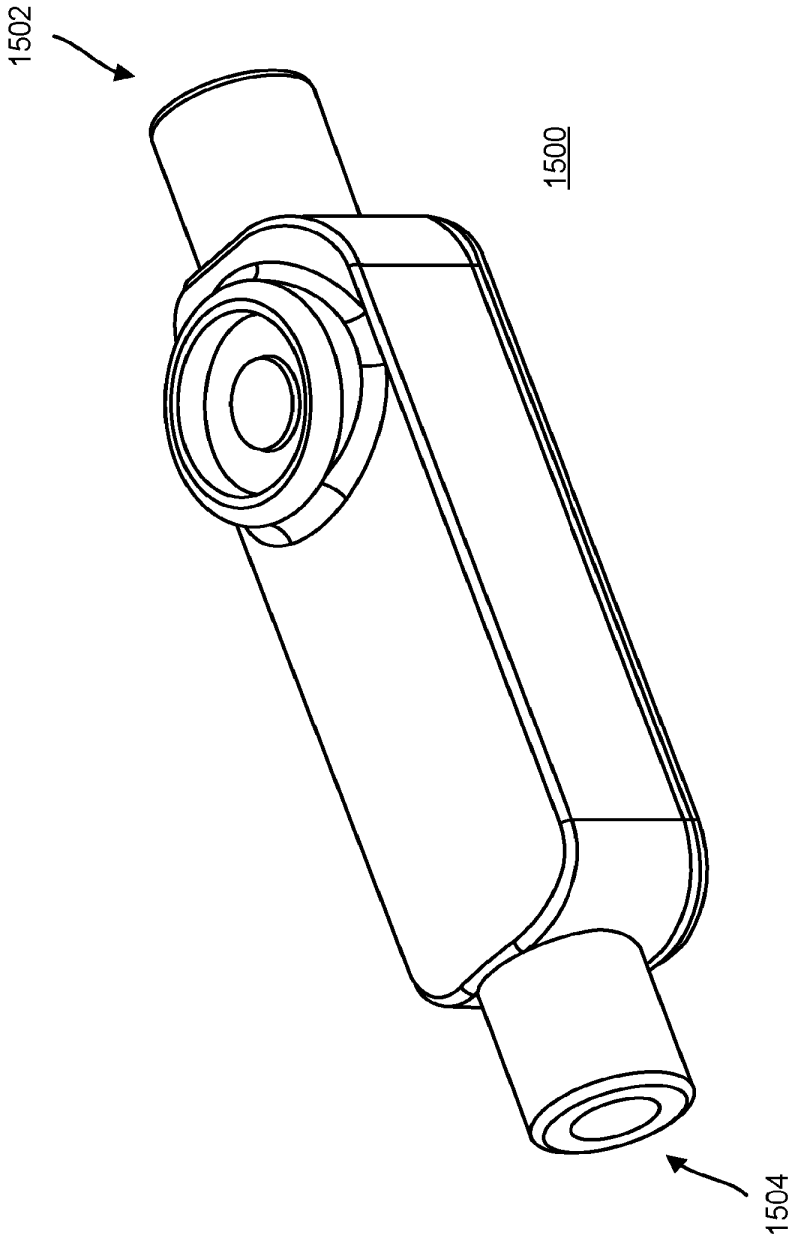


FIG. 15A

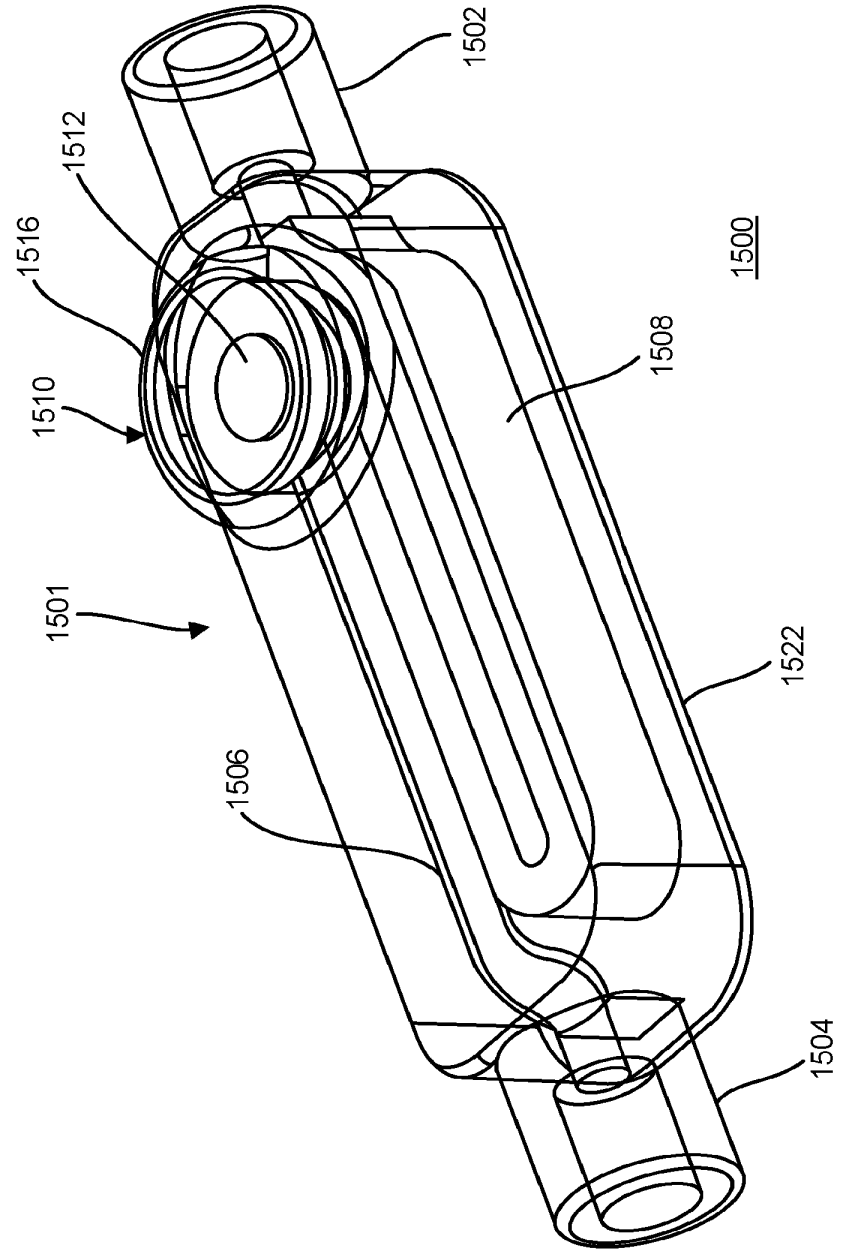


FIG. 15B

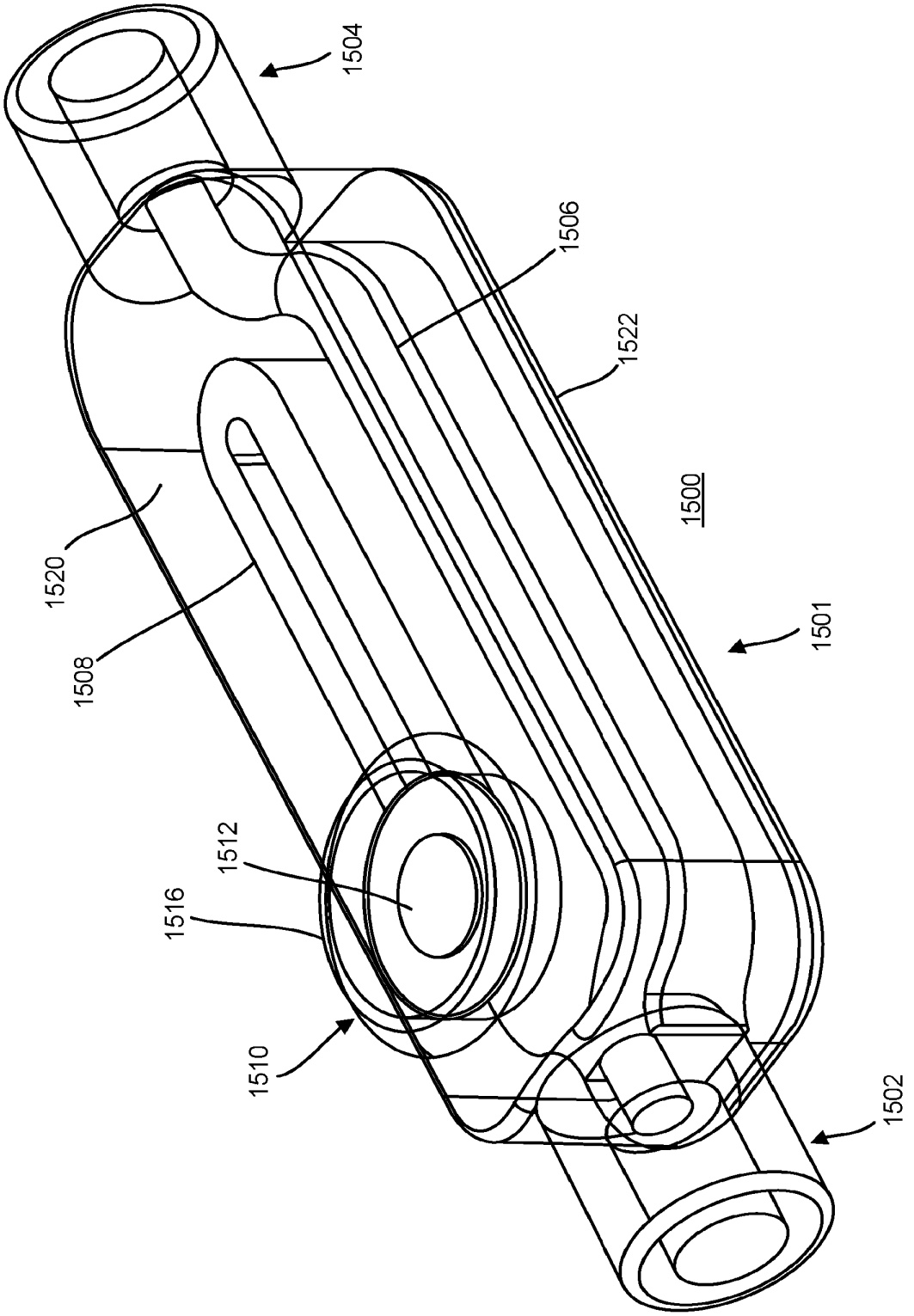


FIG. 15C

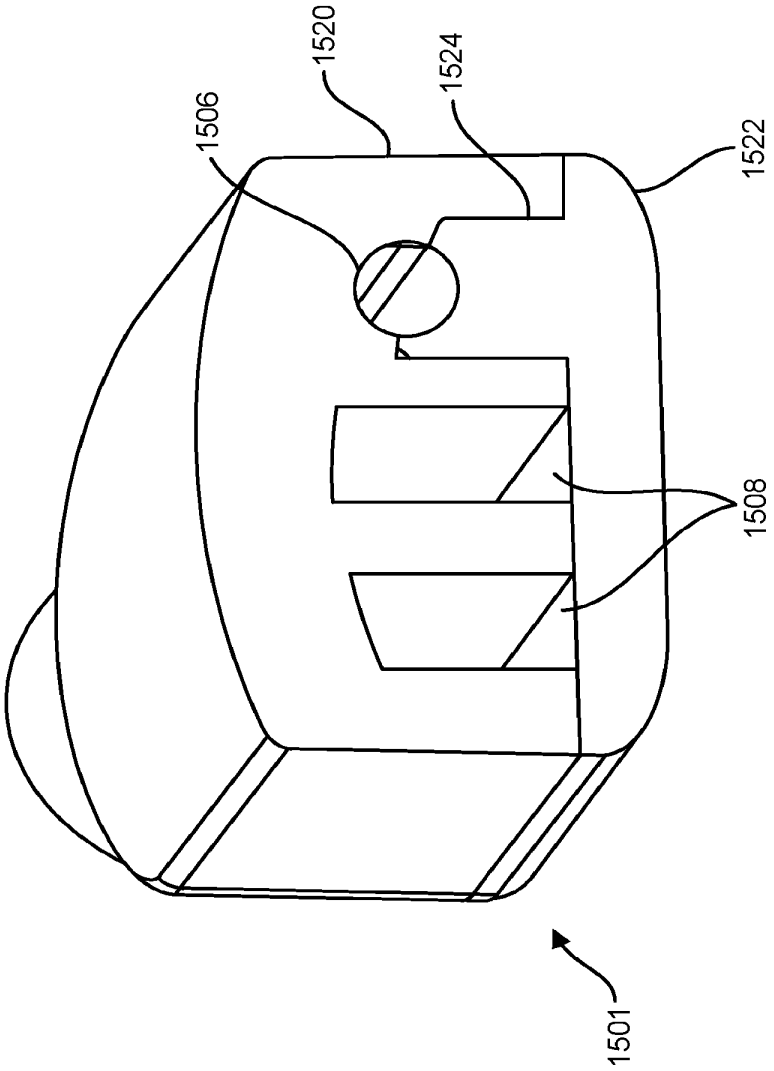


FIG. 15D

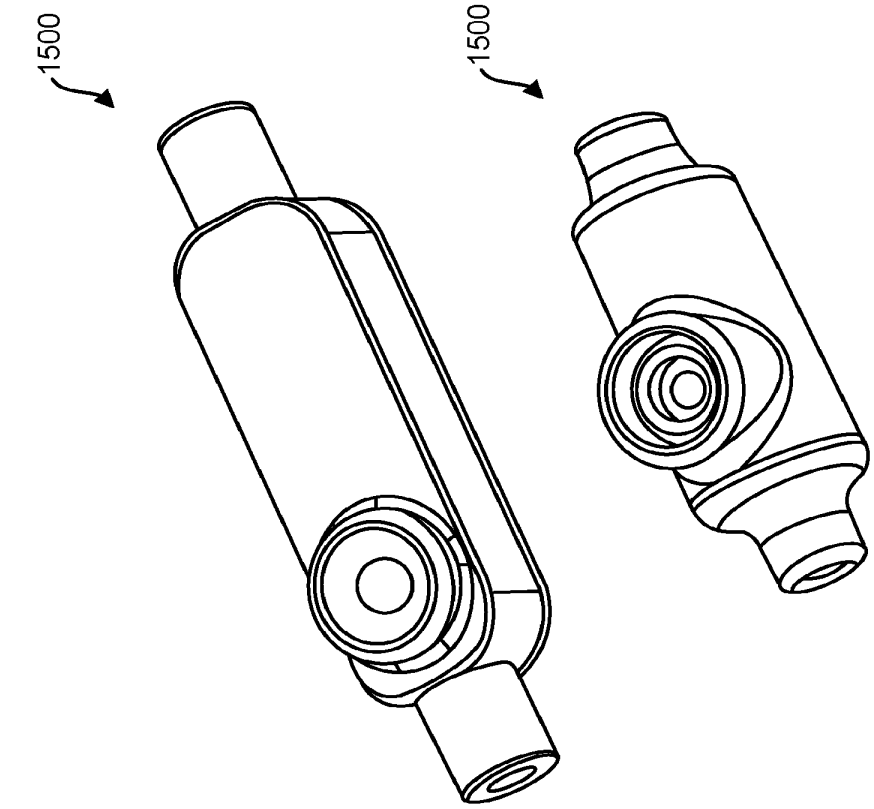


FIG. 15F

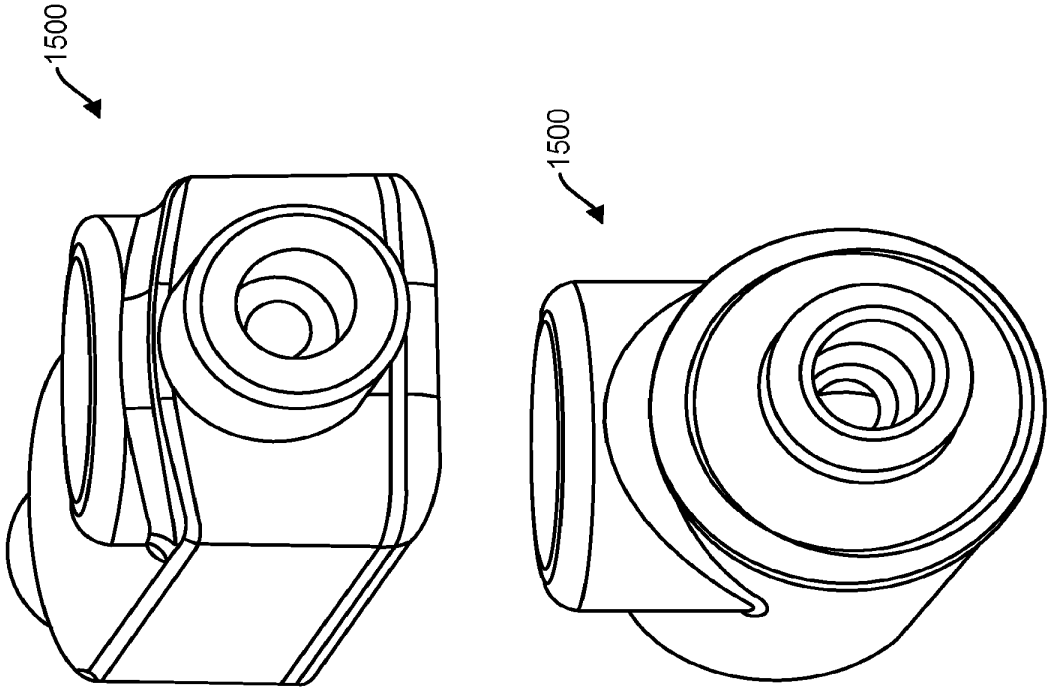


FIG. 15E

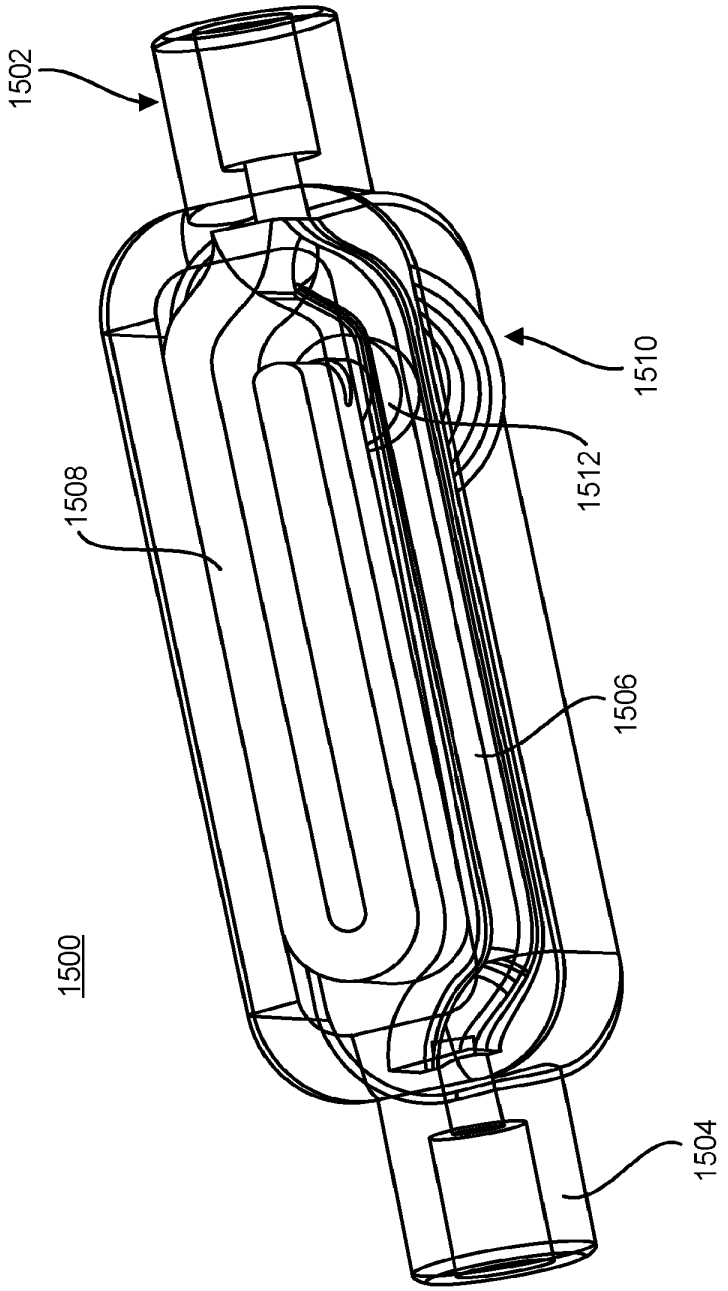


FIG. 15G

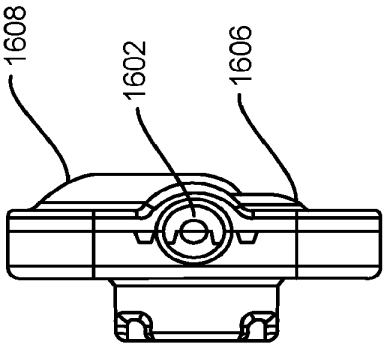


FIG. 16C

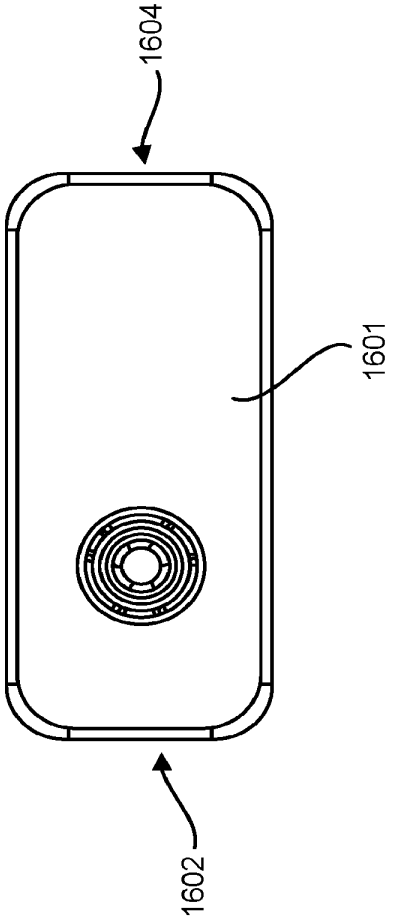


FIG. 16A

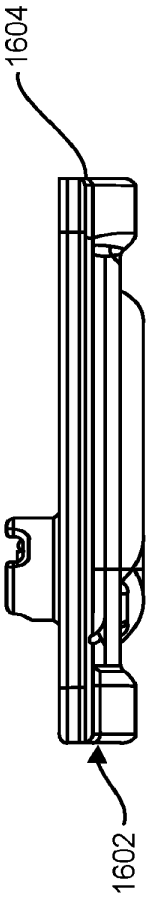


FIG. 16B

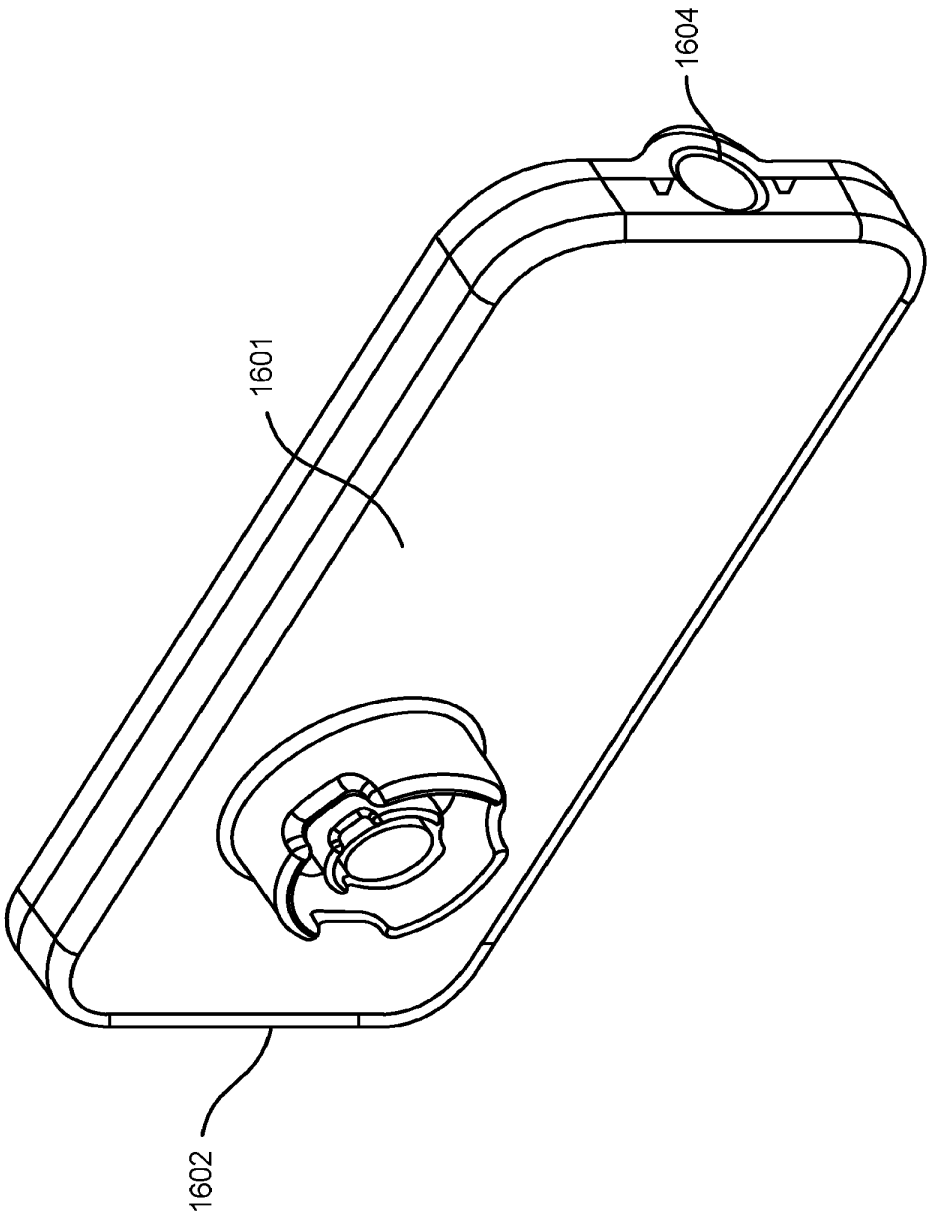


FIG. 16D

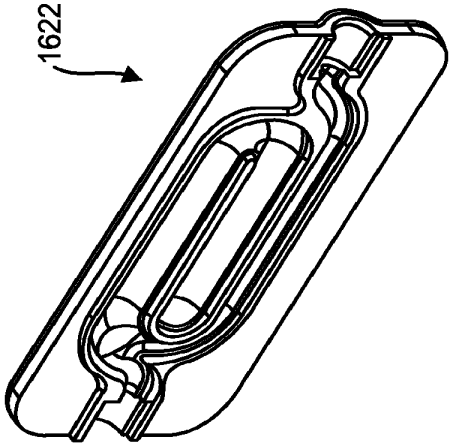


FIG. 17B



FIG. 17E

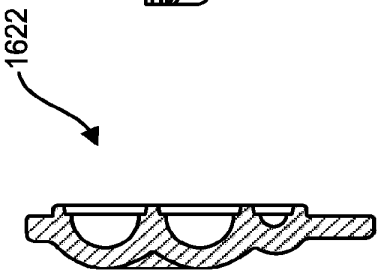


FIG. 17D

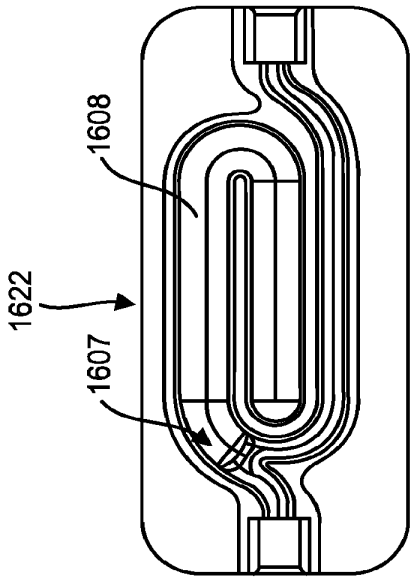


FIG. 17A

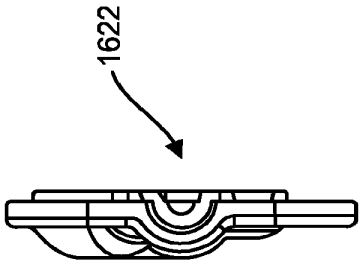


FIG. 17C

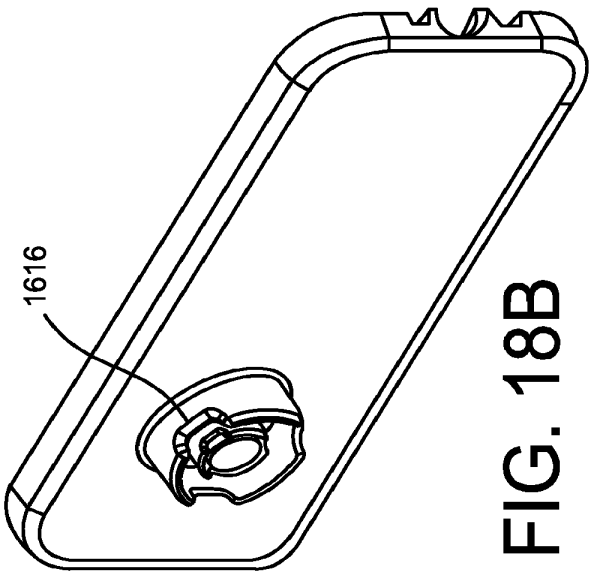


FIG. 18B

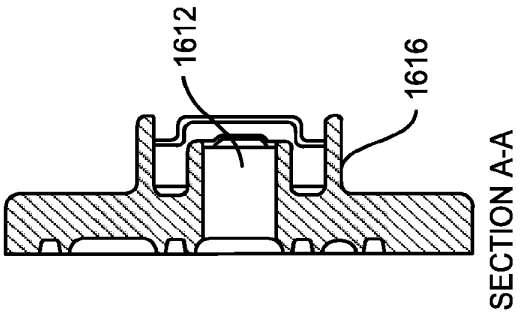


FIG. 18F

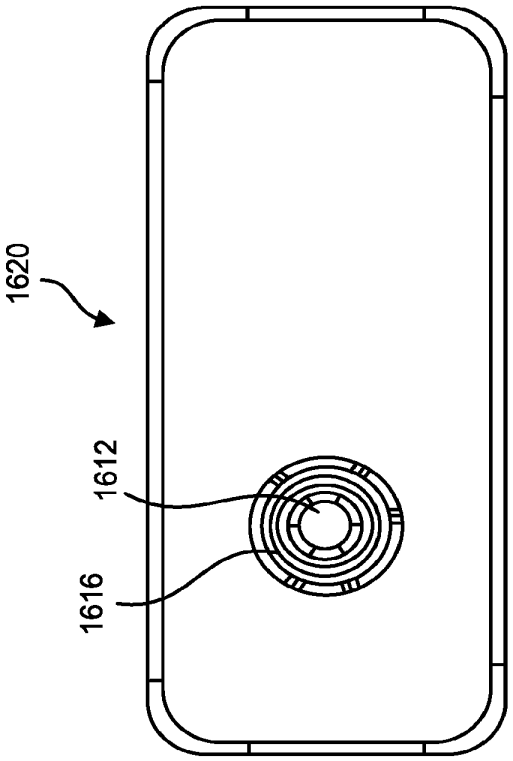


FIG. 18A

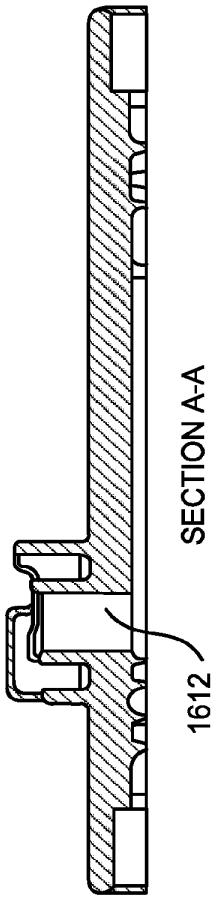


FIG. 18D

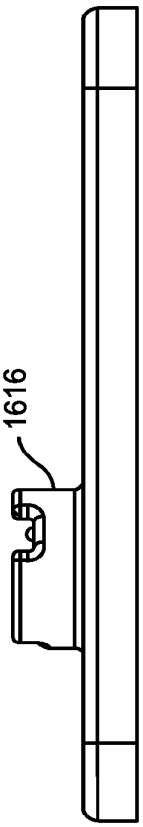


FIG. 18E

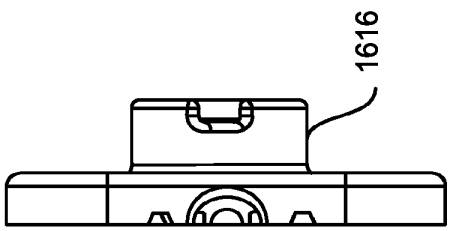


FIG. 18C

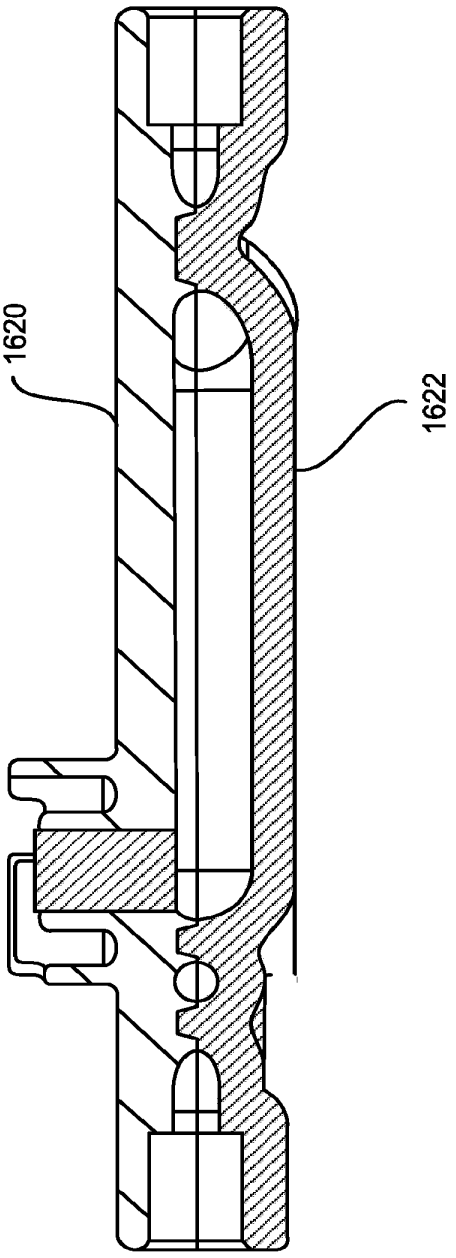


FIG. 19A

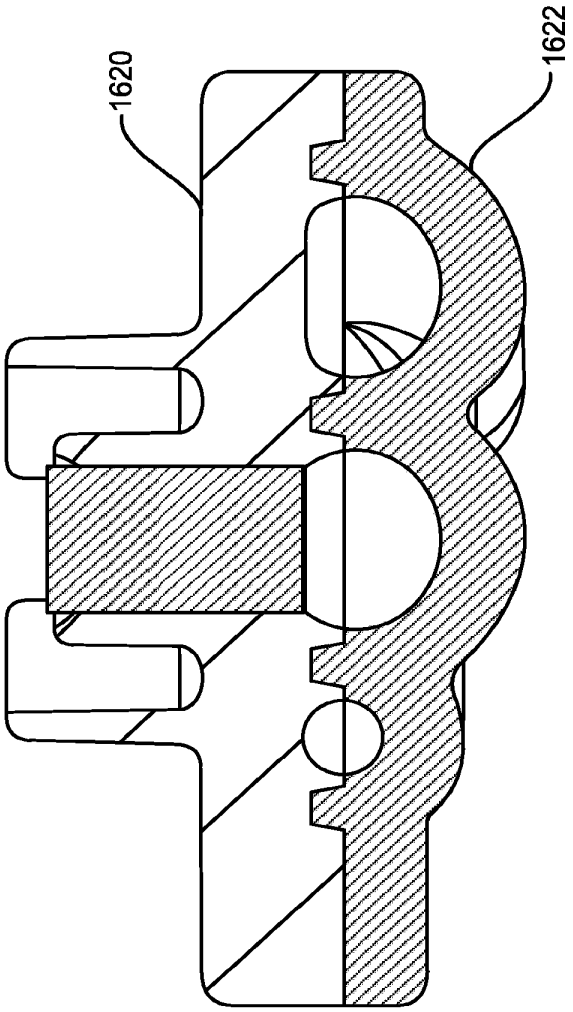


FIG. 19B

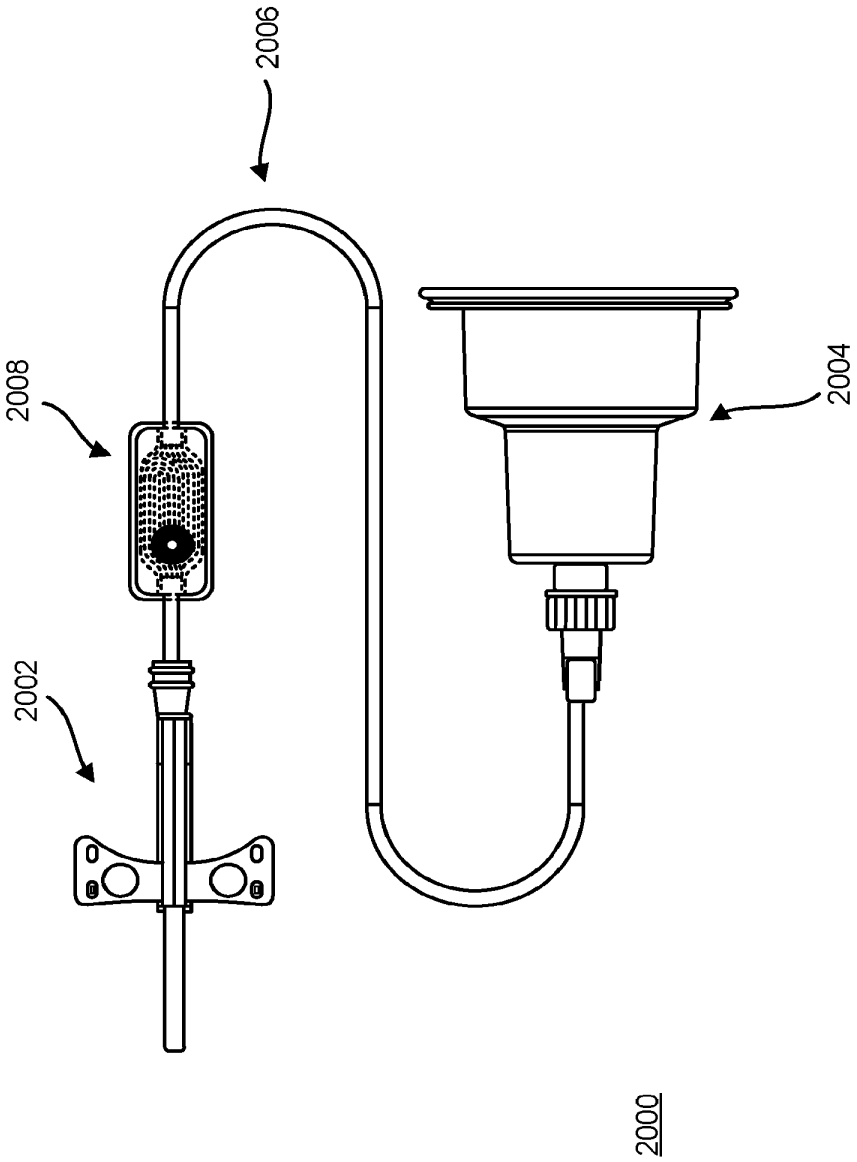


FIG. 20

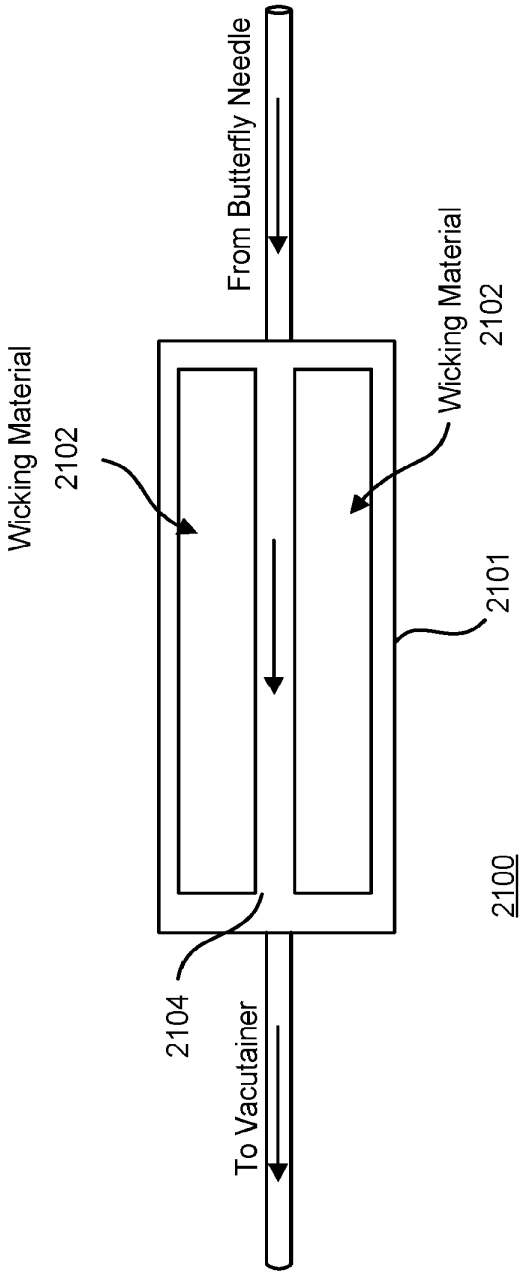

From Butterfly Needle
Wicking Material
2102
Wicking Material
2102
2101
2100
2104
To Vacutainer

FIG. 21

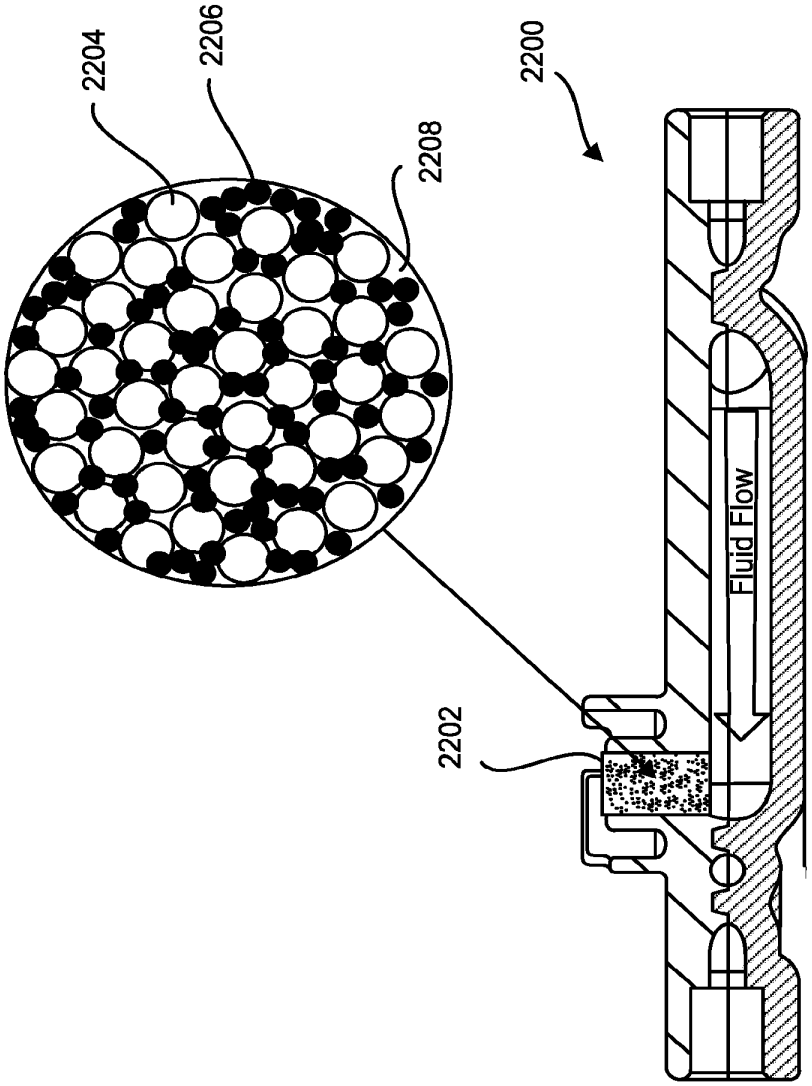


FIG. 22A

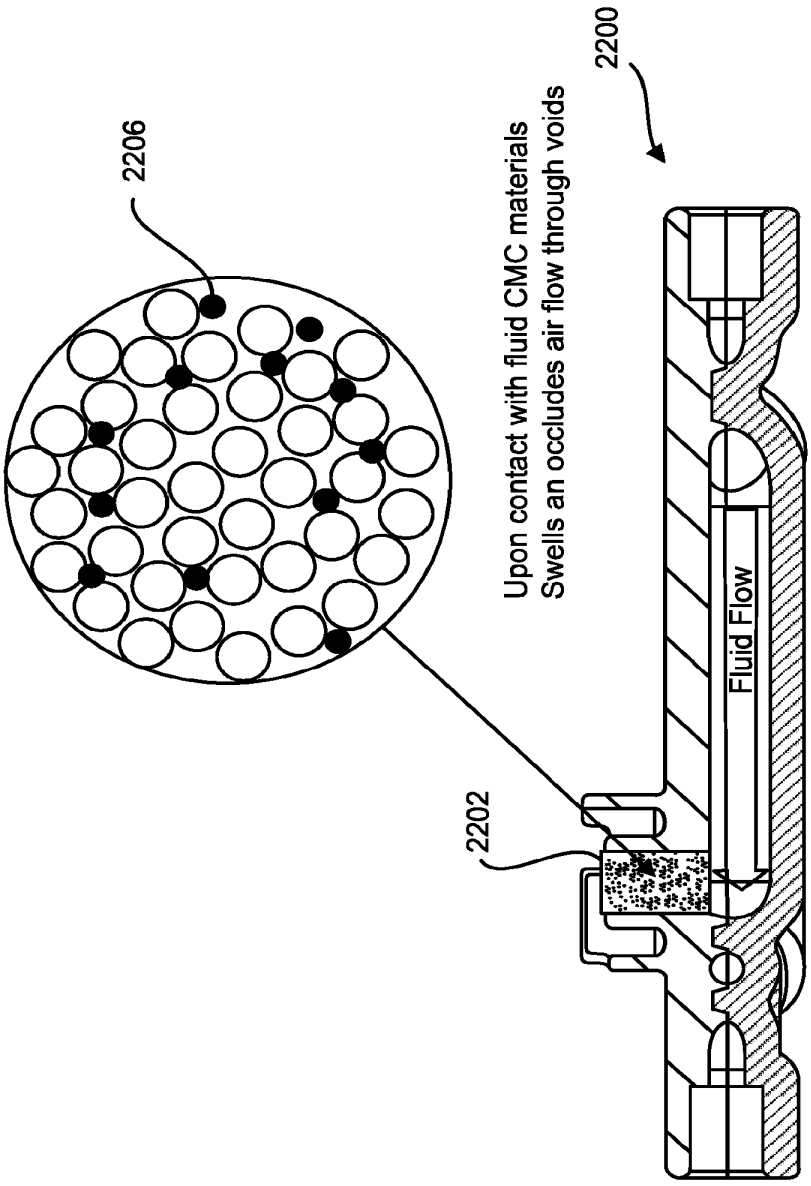

2200
2206
Upon contact with fluid CMC materials
Swells an occludes air flow through voids
Fluid Flow
2202

FIG. 22B

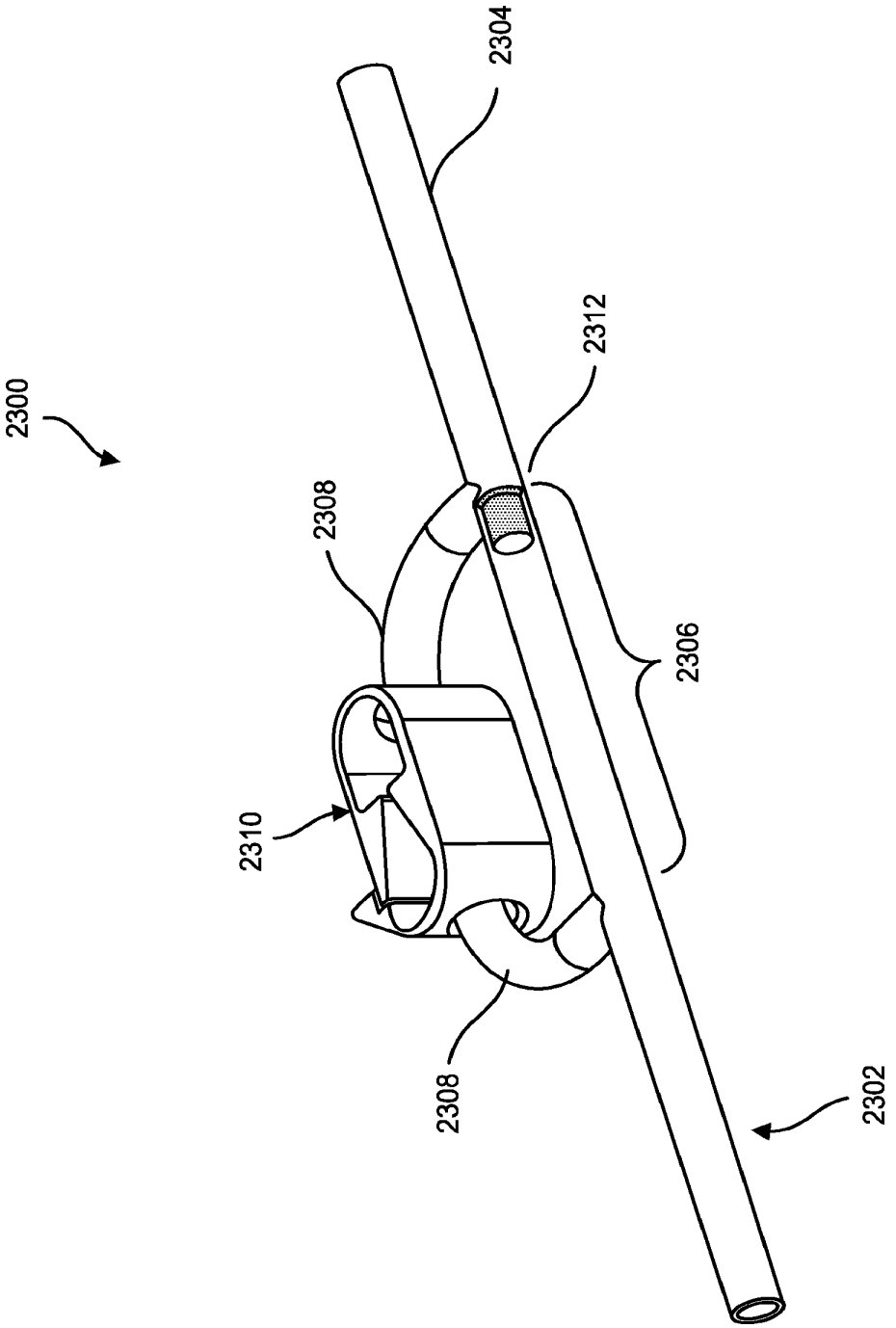


FIG. 23A

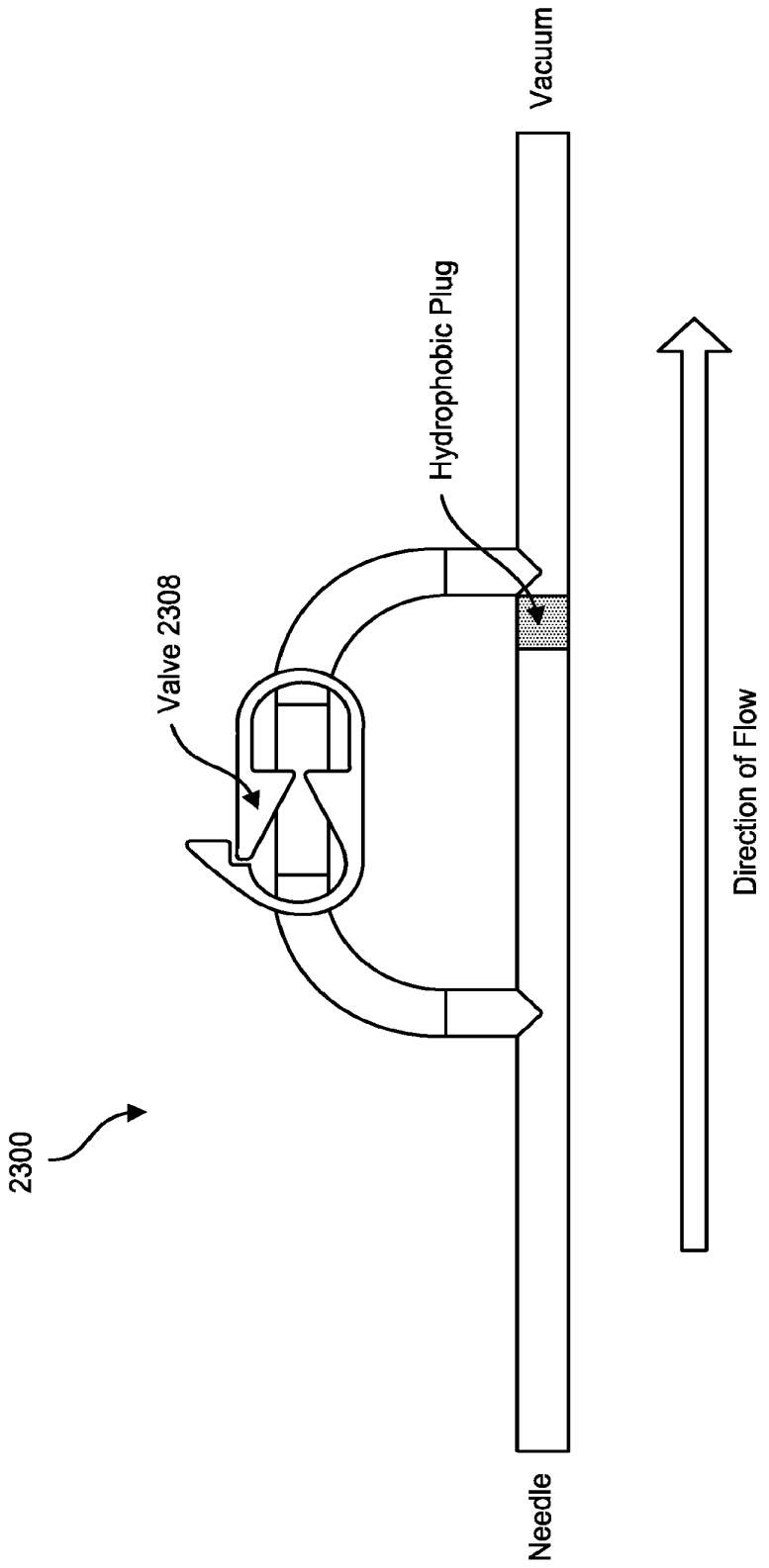

Vacuum
Hydrophobic Plug
Valve 2308
Direction of Flow
2300
Needle

FIG. 23B

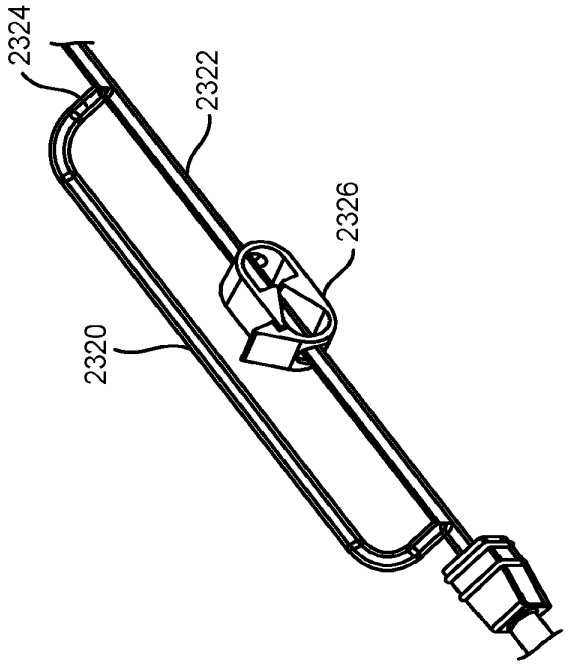


FIG. 23D

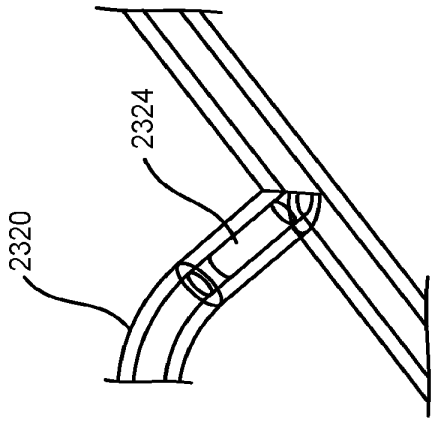


FIG. 23E

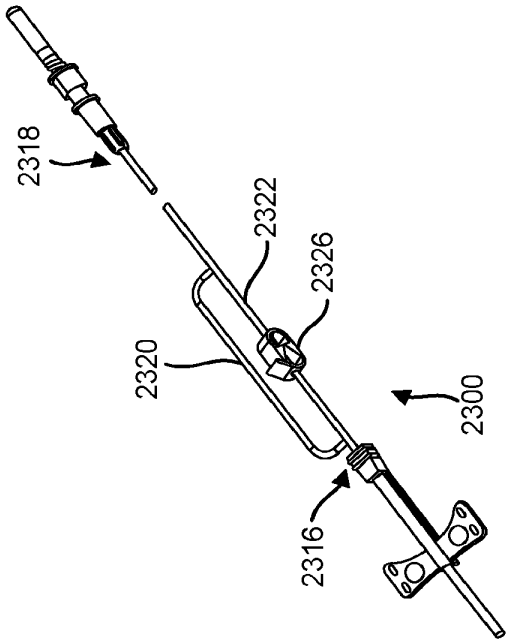


FIG. 23C

Replacement Sheet
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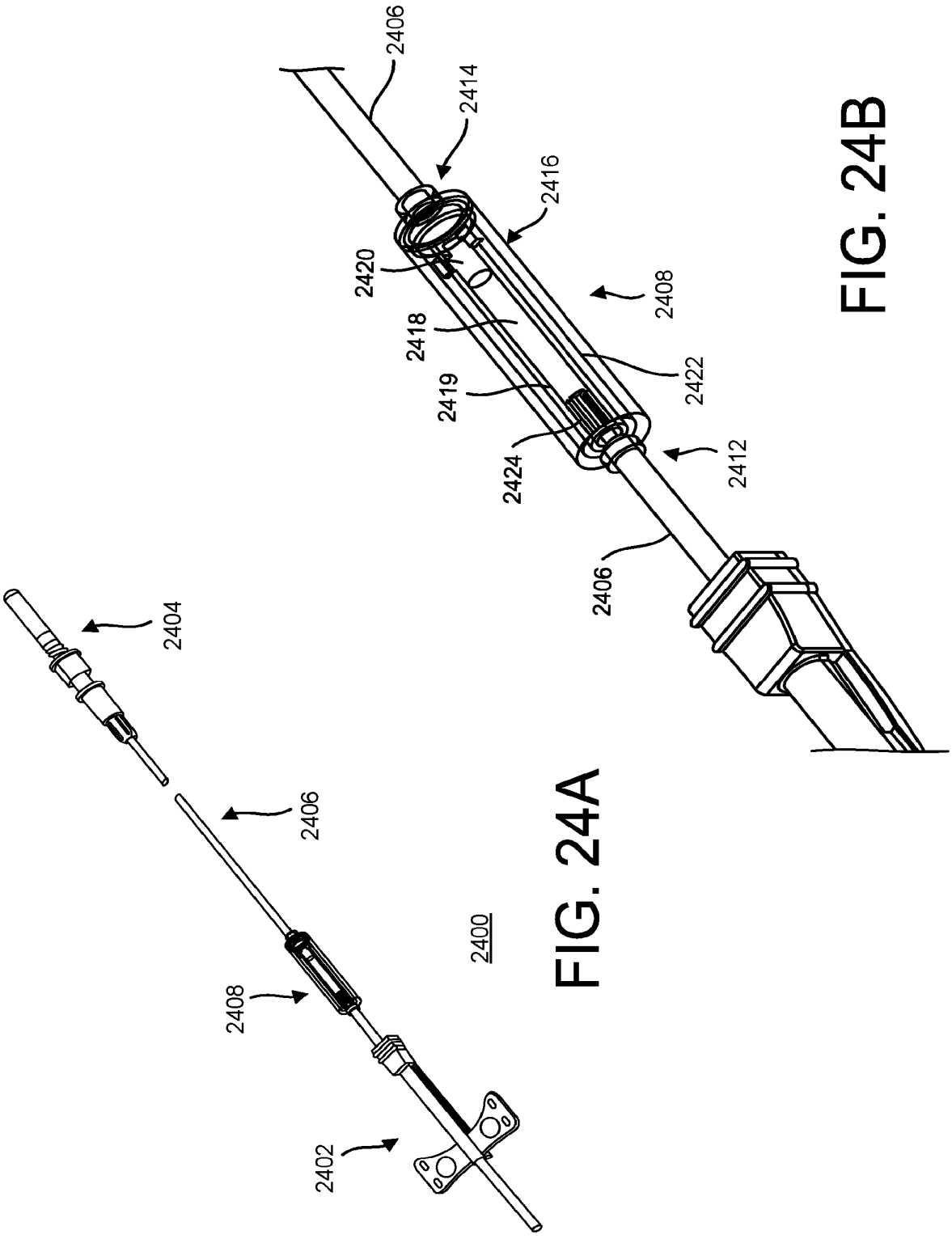


FIG. 24B

FIG. 24A

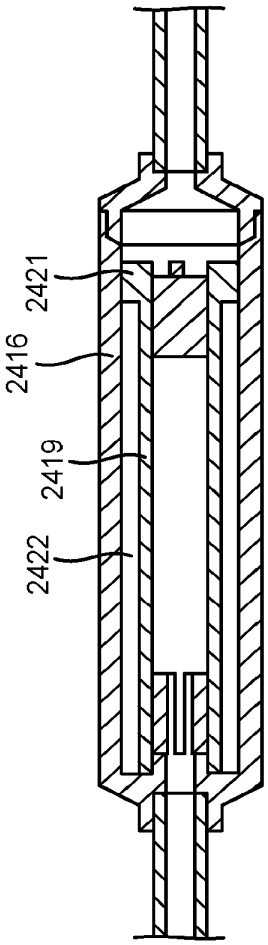


FIG. 24C

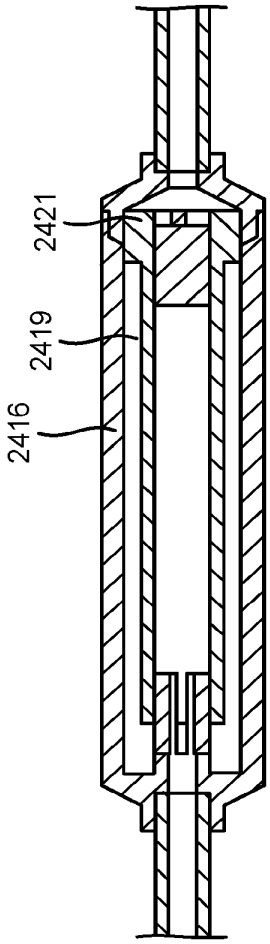


FIG. 24D

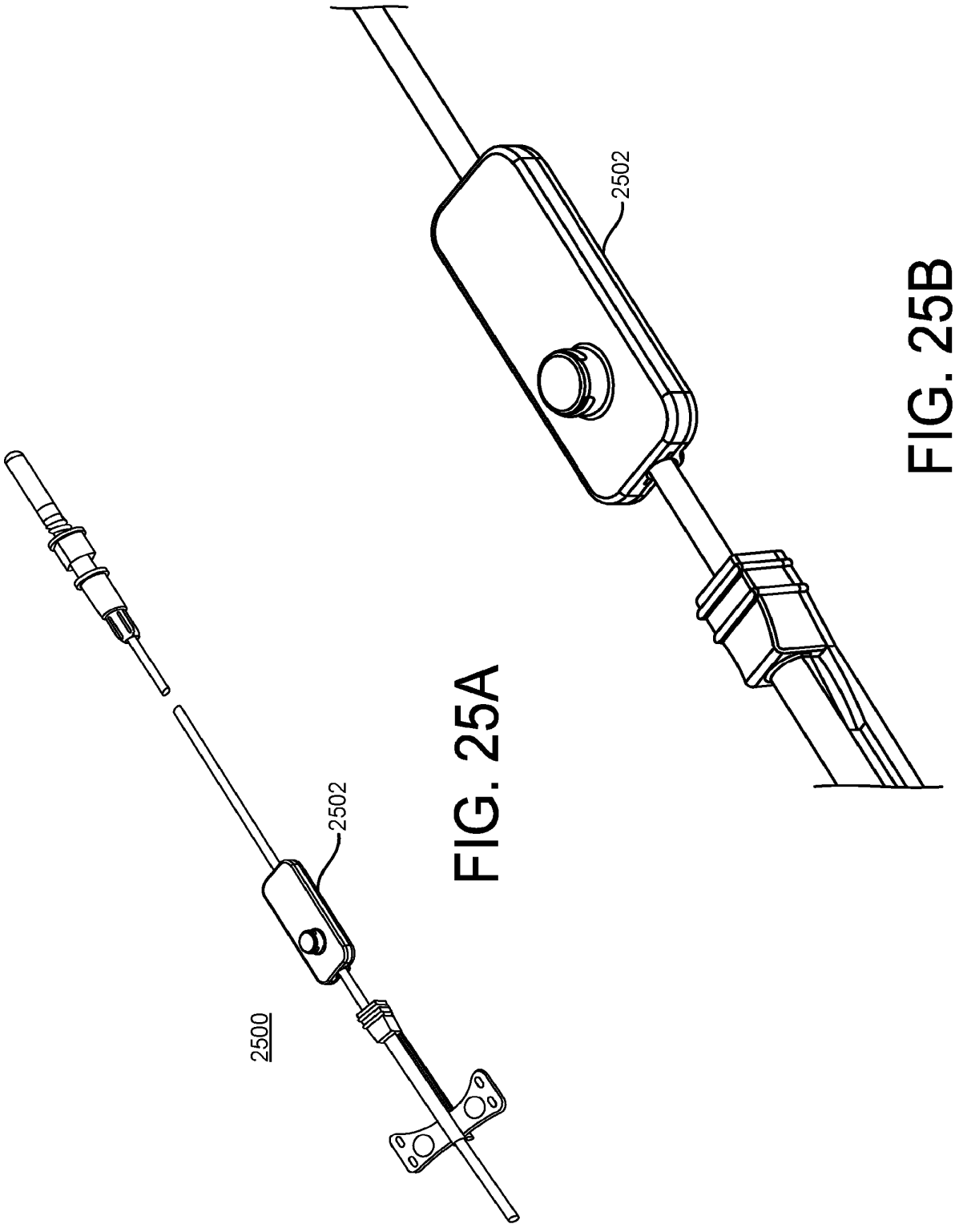


FIG. 25A

FIG. 25B

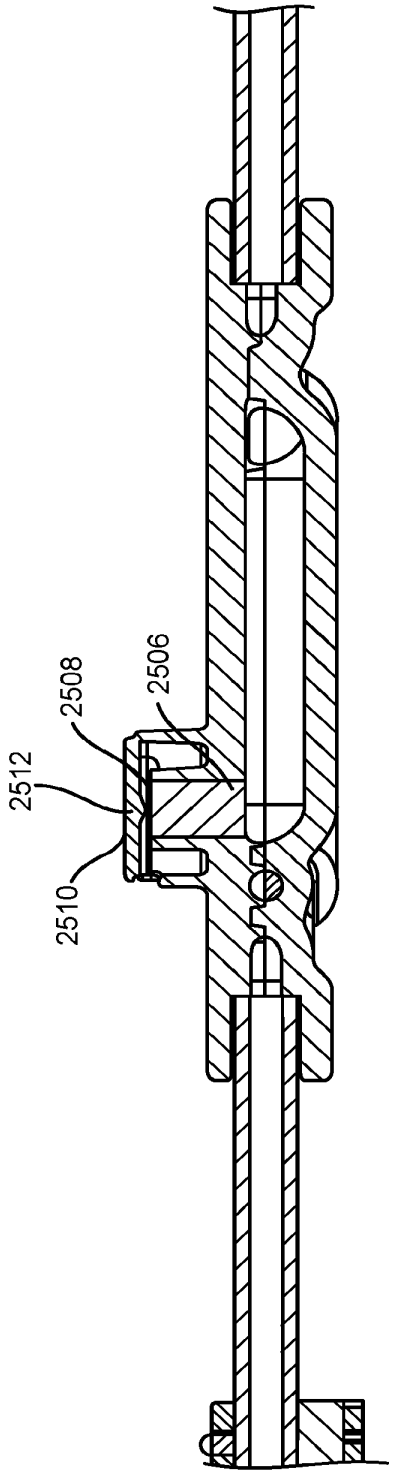


FIG. 25C

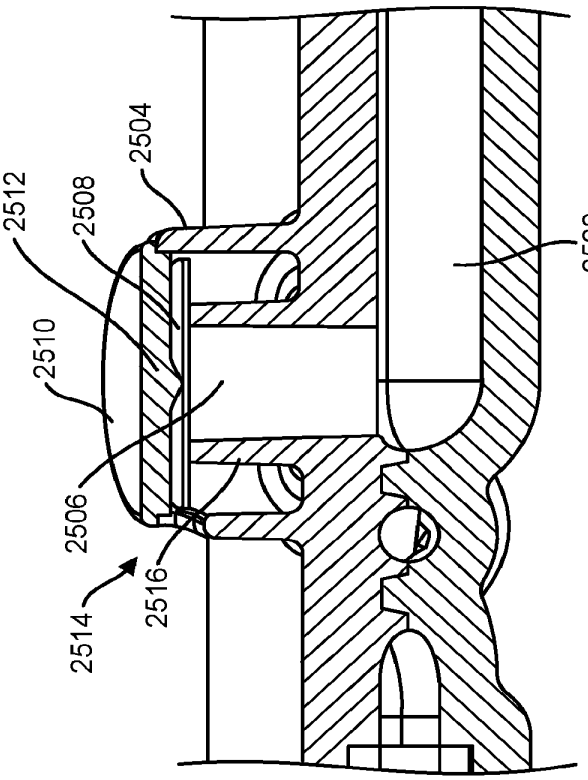


FIG. 25D

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Docket No. KURIN3PCT
PCT/US2017/068569

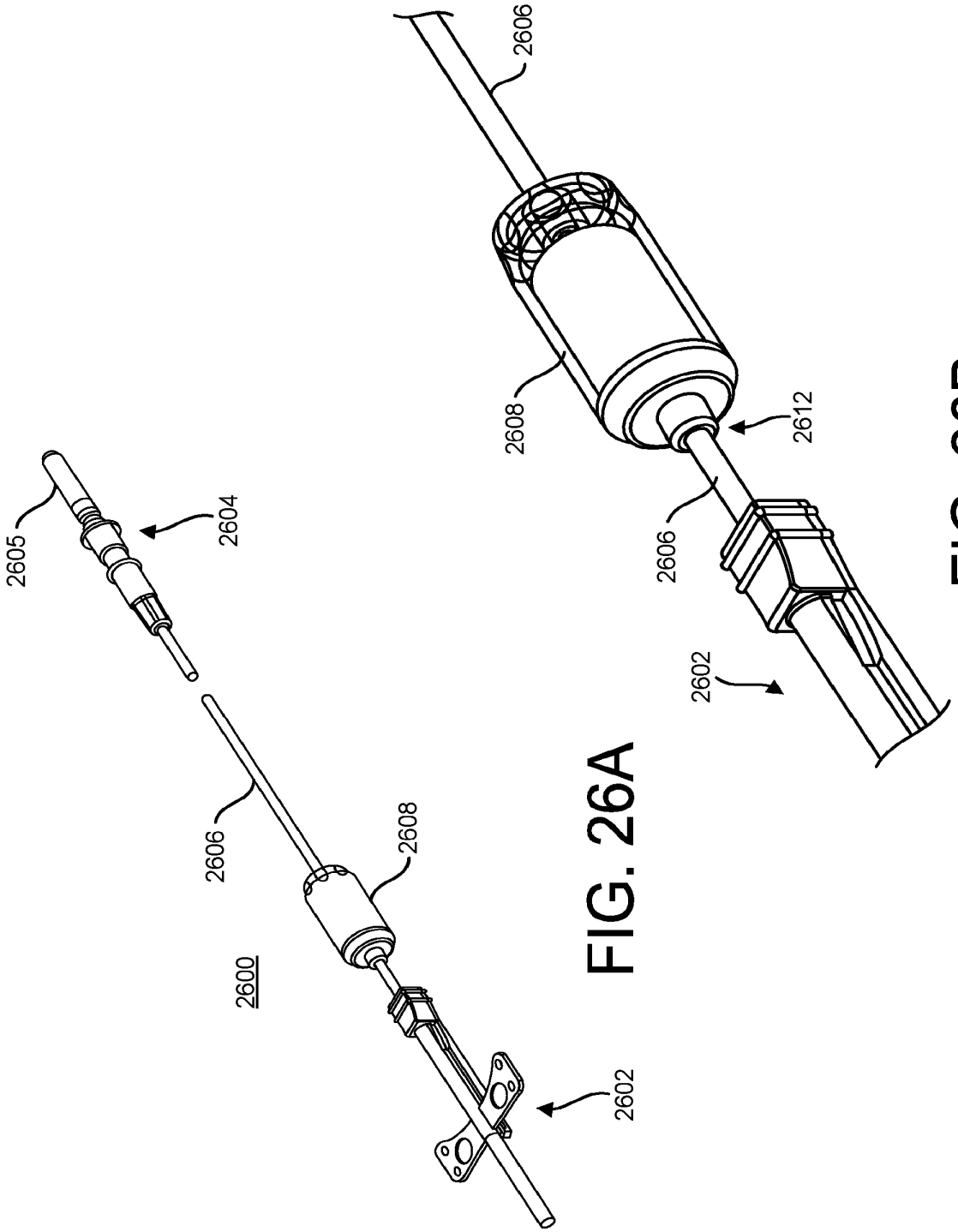


FIG. 26B

FIG. 26A

Replacement Sheet
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Docket No. KURIN3PCT
PCT/US2017/068569

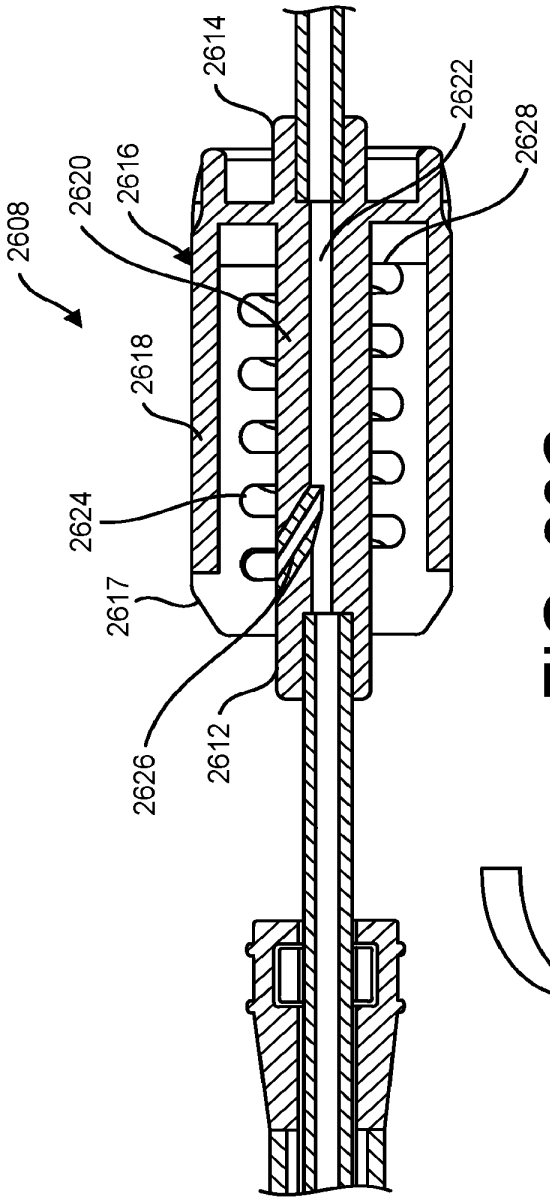


FIG. 26C

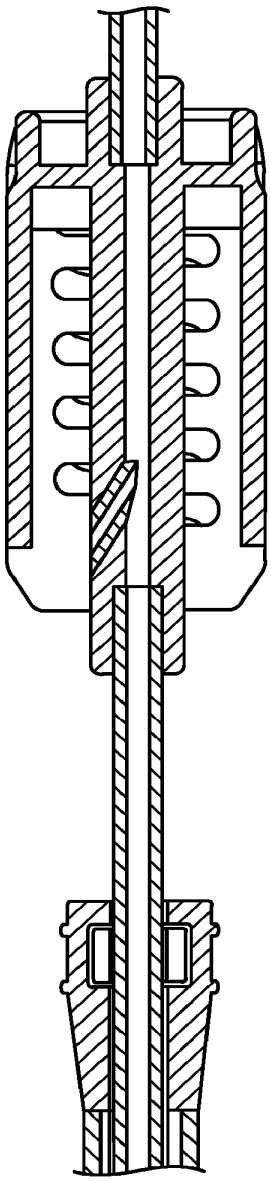


FIG. 26D

Replacement Sheet
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Docket No. KURIN3PCT
PCT/US2017/068569

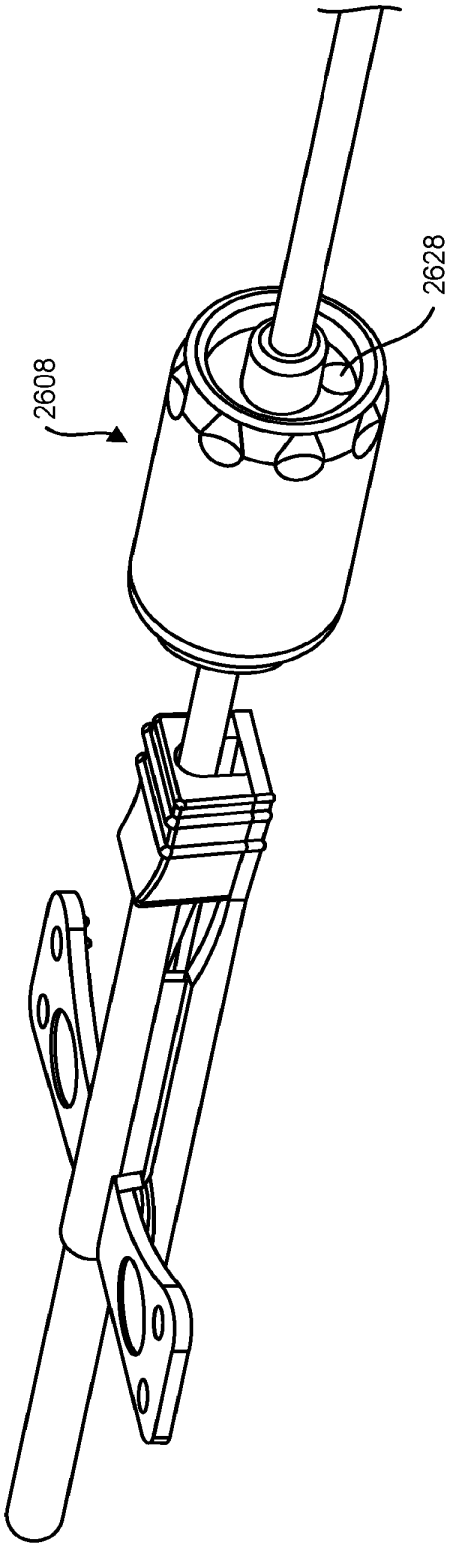


FIG. 26E

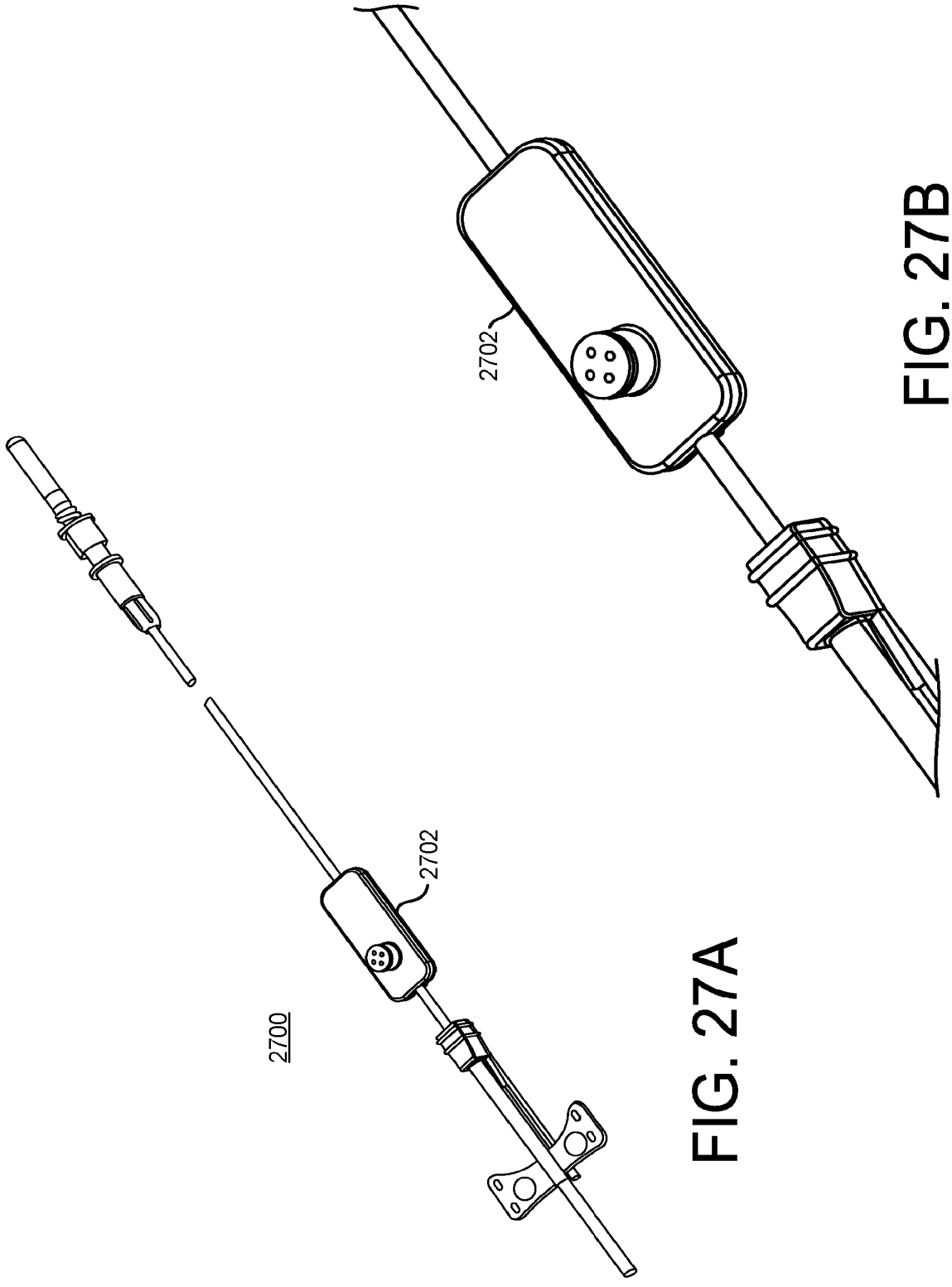


FIG. 27B

FIG. 27A

Replacement Sheet
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Docket No. KURIN3PCT
PCT/US2017/068569

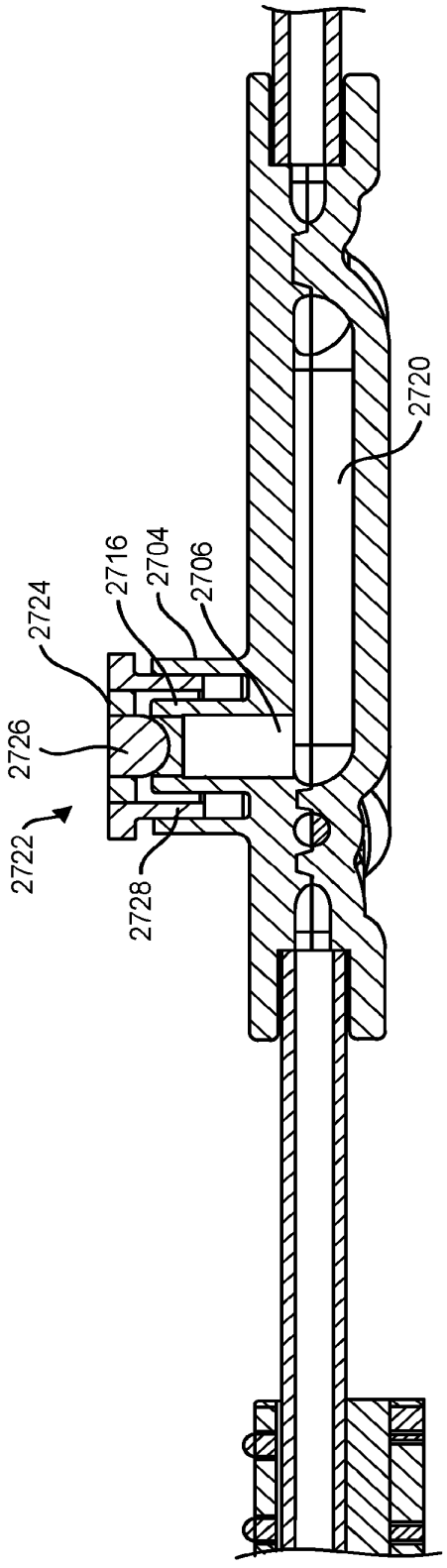


FIG. 27C

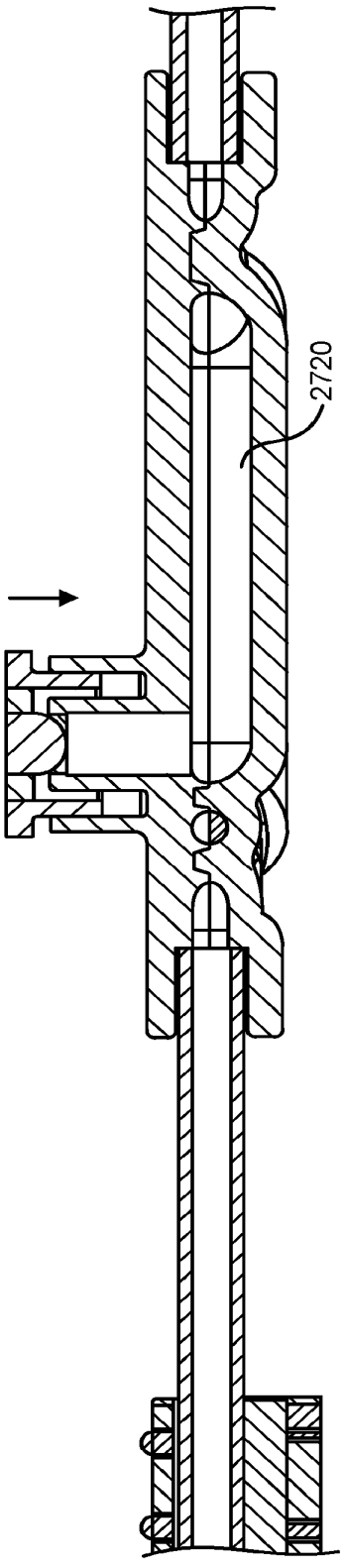


FIG. 27D

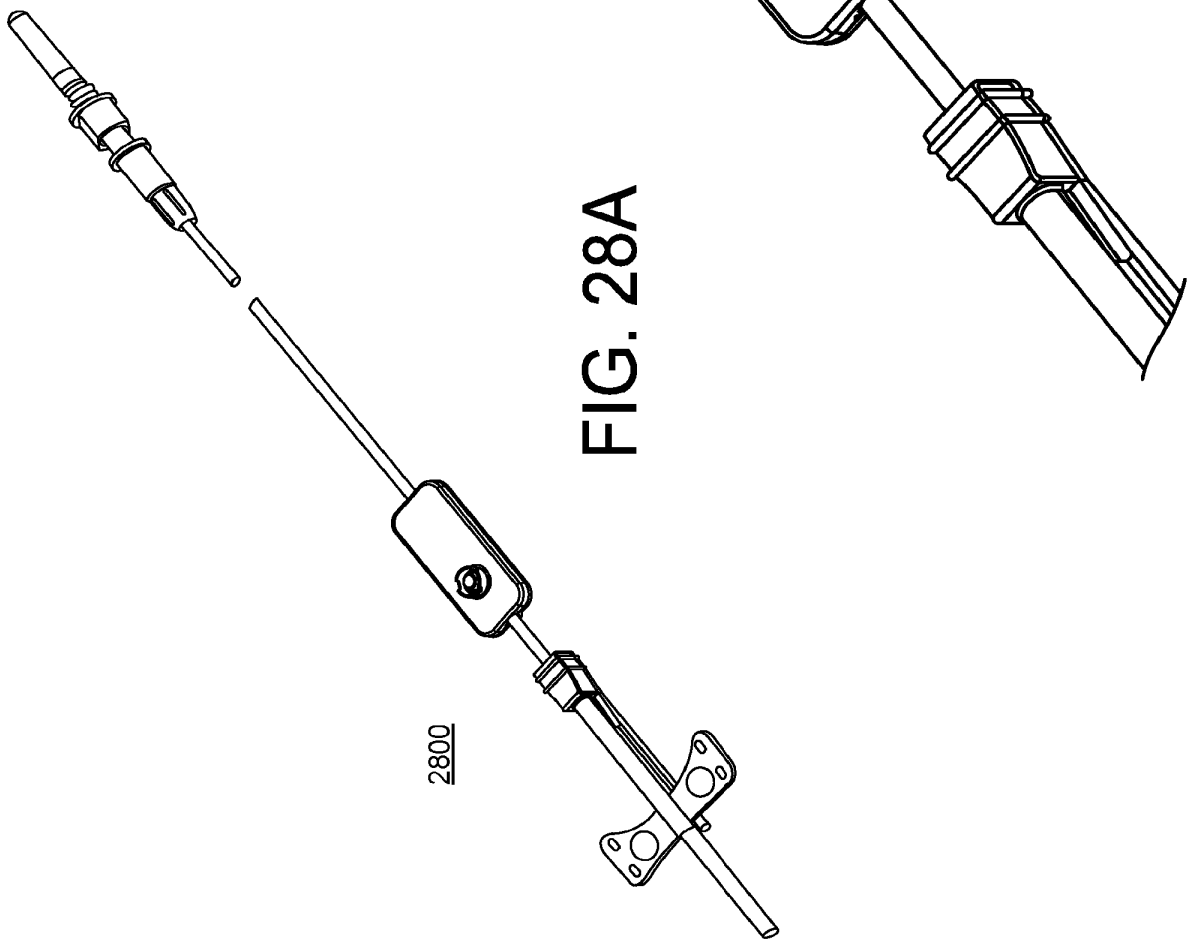


FIG. 28A

FIG. 28B

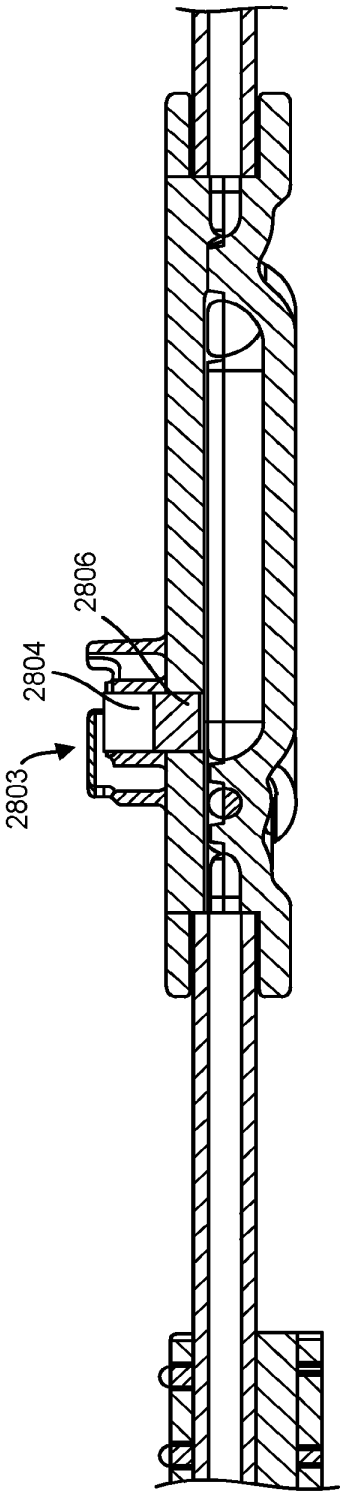


FIG. 28C

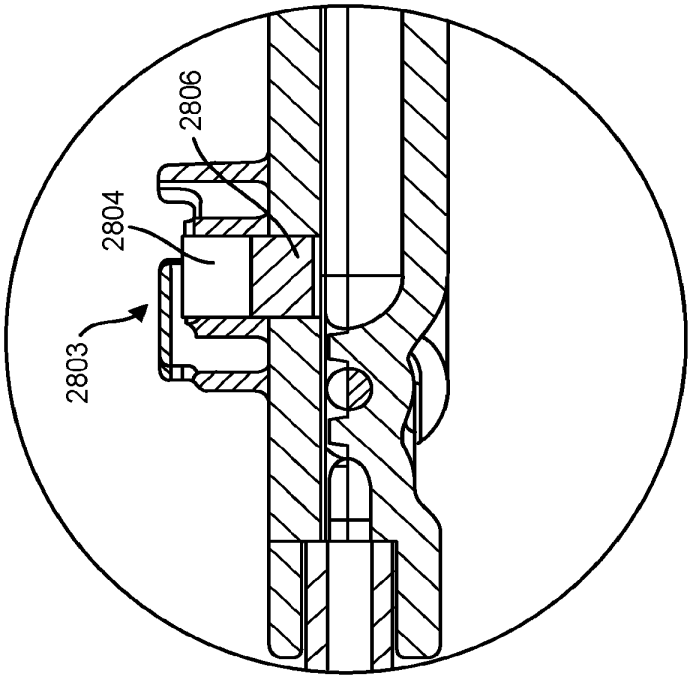


FIG. 28D

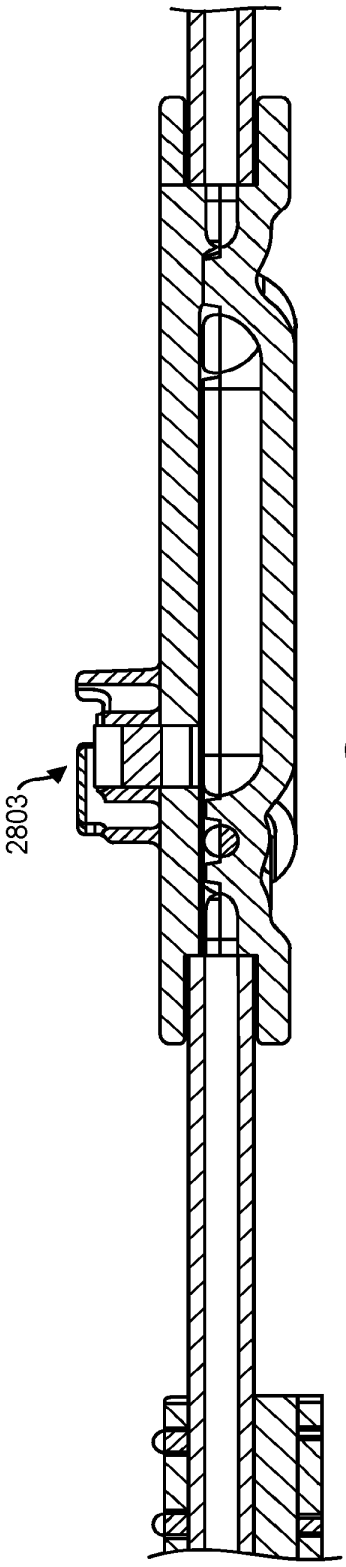


FIG. 28E

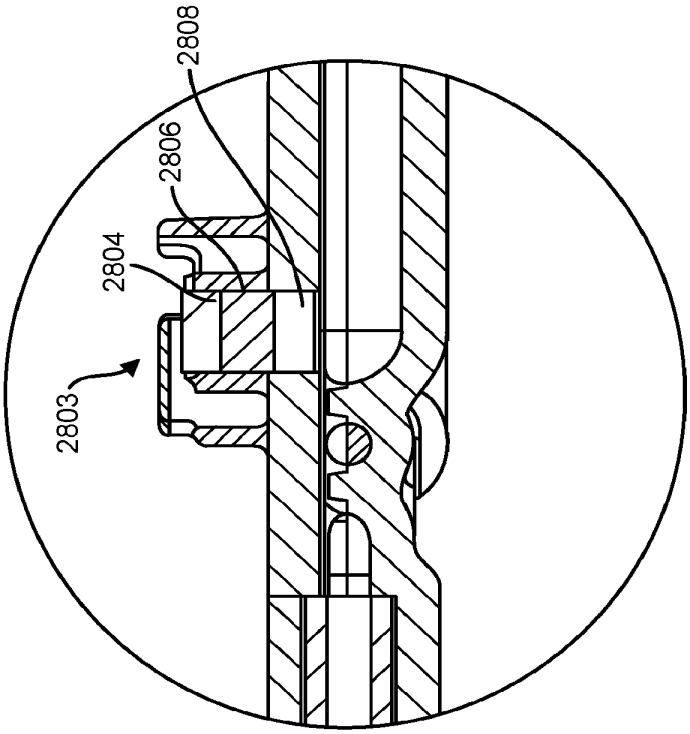


FIG. 28F

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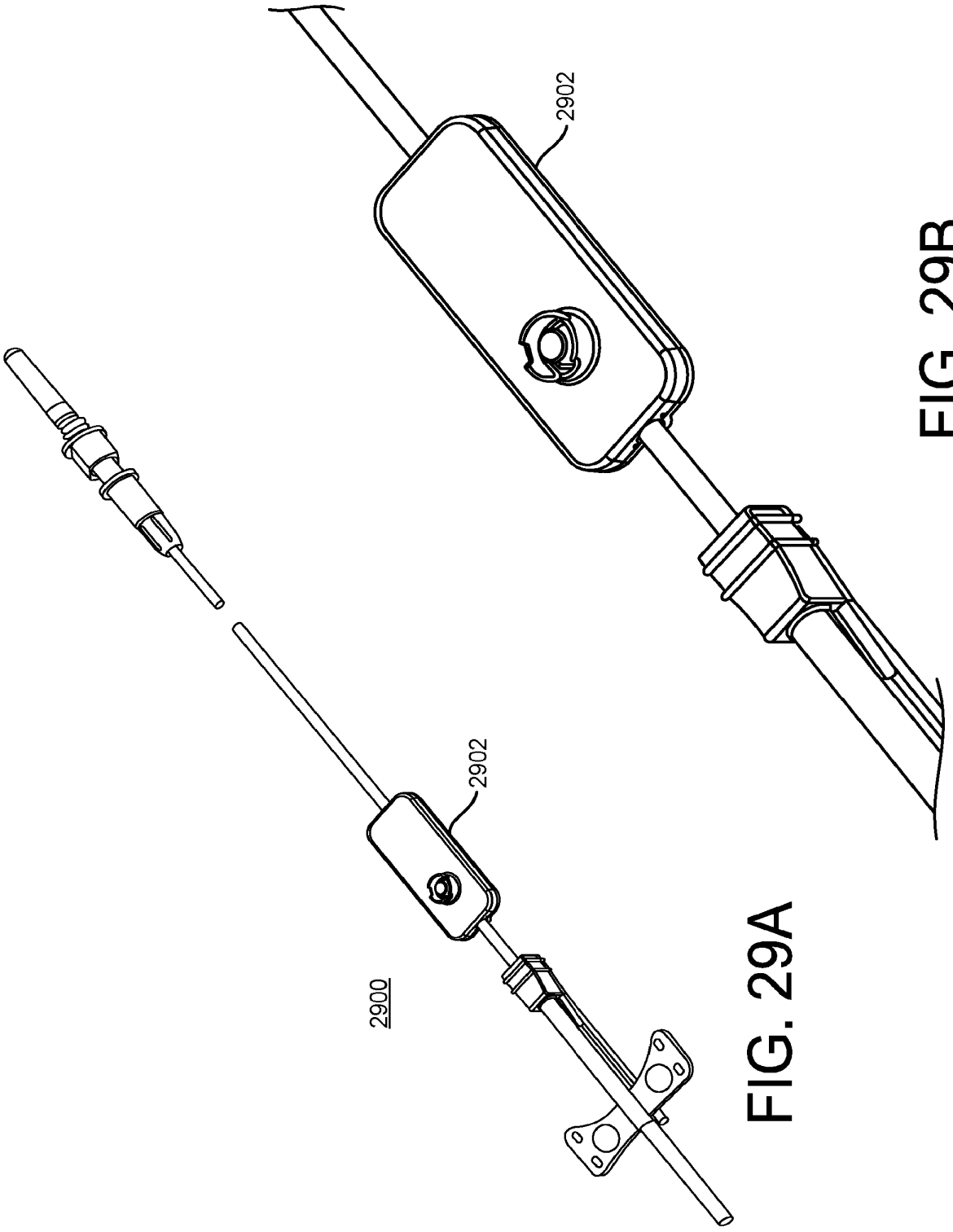


FIG. 29B

FIG. 29A

Replacement Sheet
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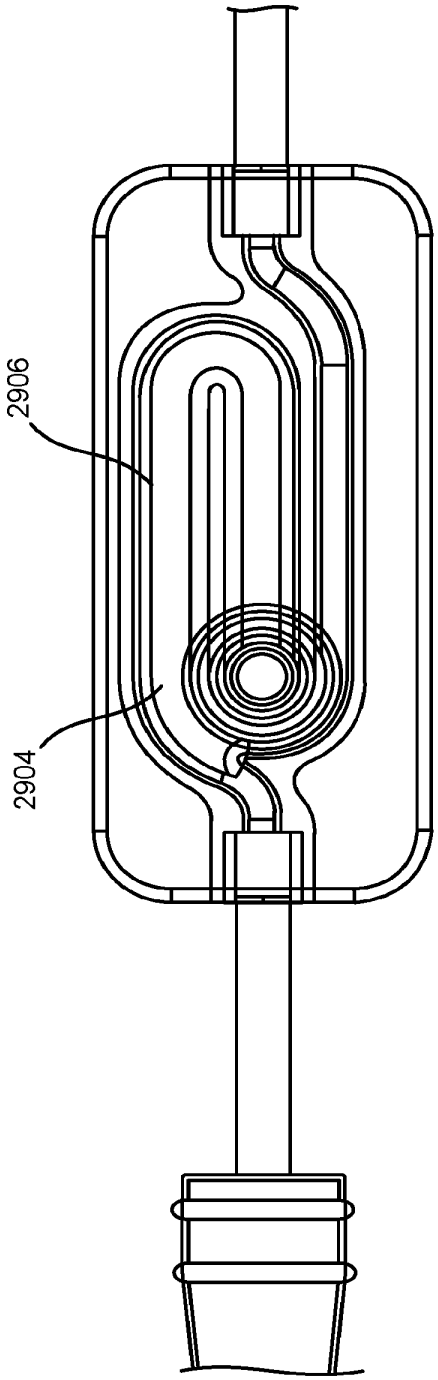


FIG. 29C

Replacement Sheet
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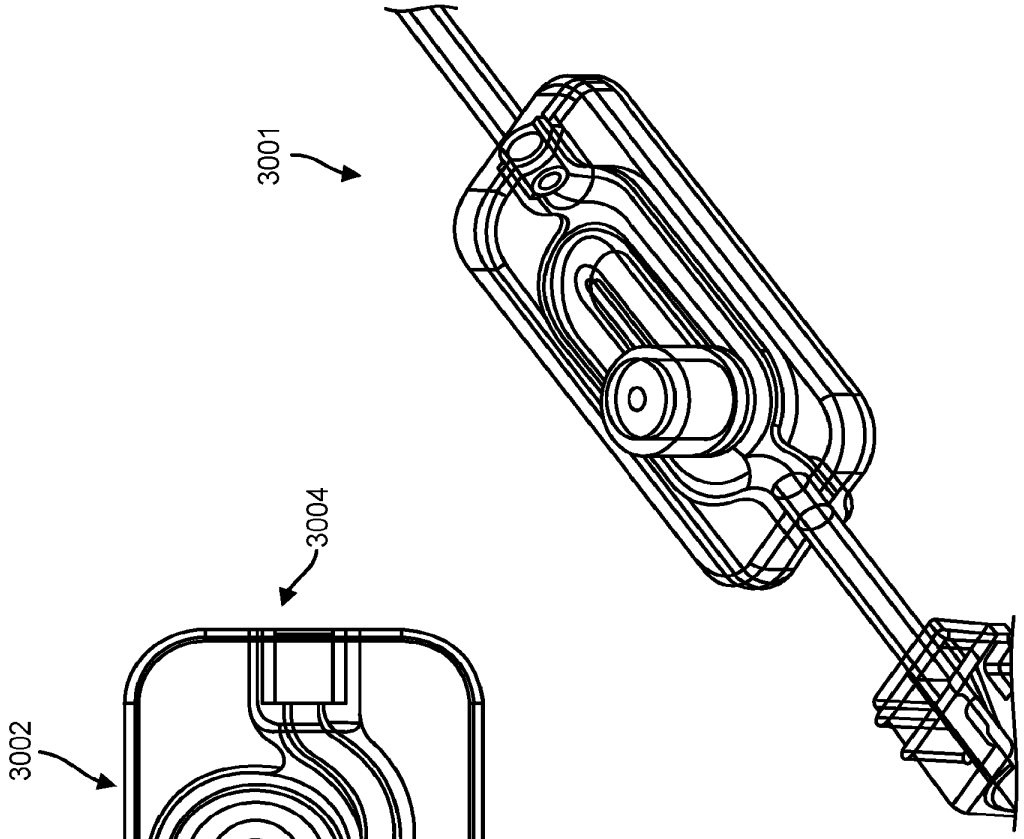


FIG. 30B

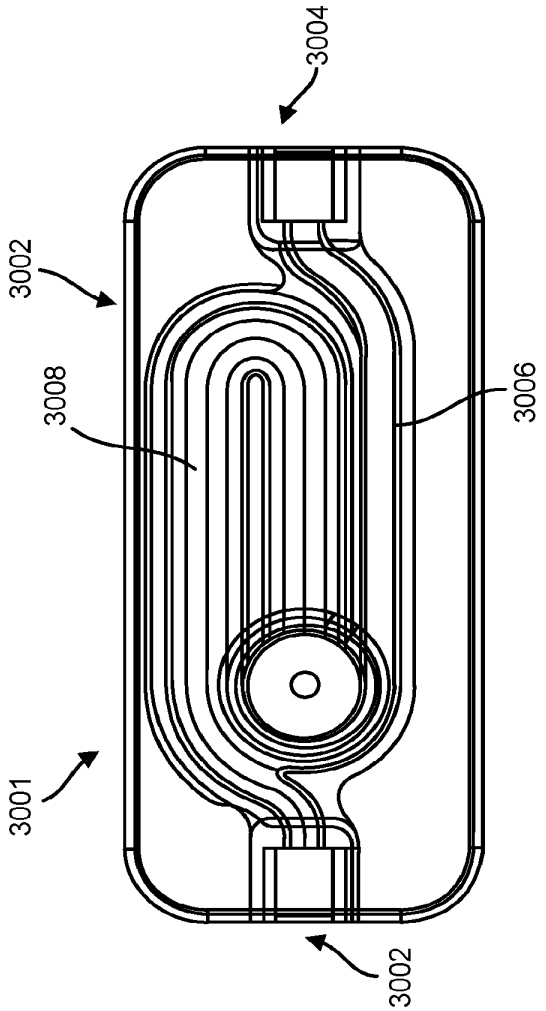


FIG. 30A

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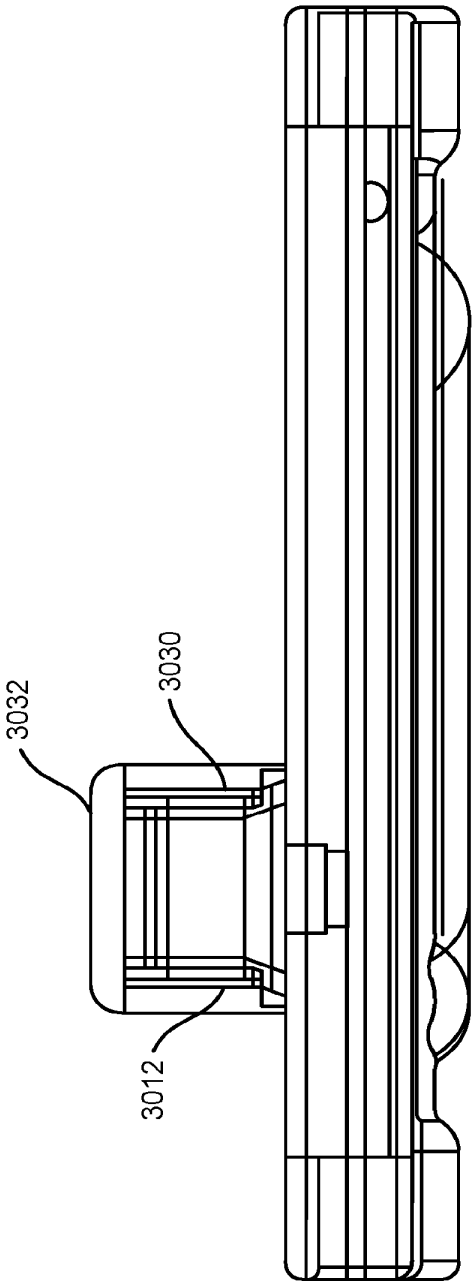


FIG. 30C

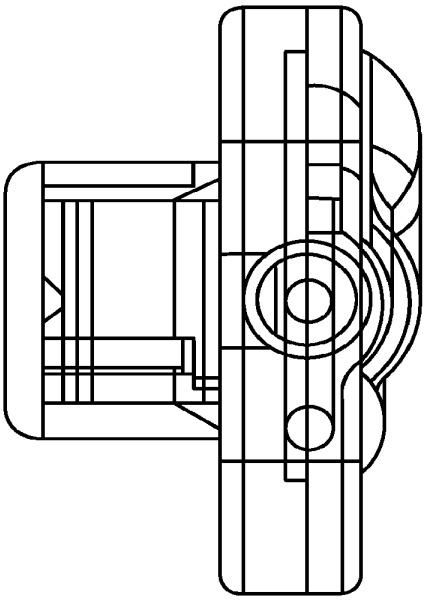


FIG. 30D

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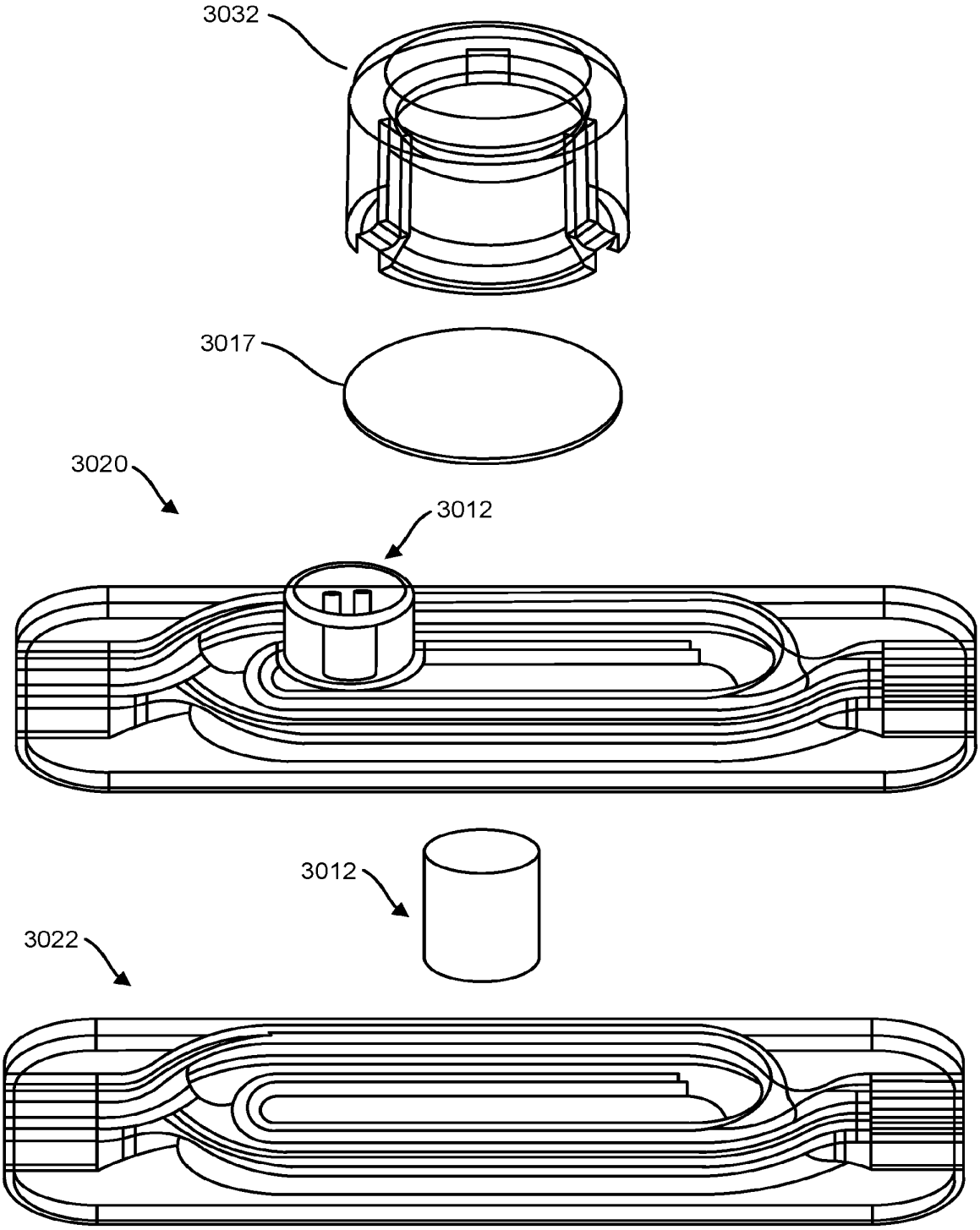


FIG. 30E

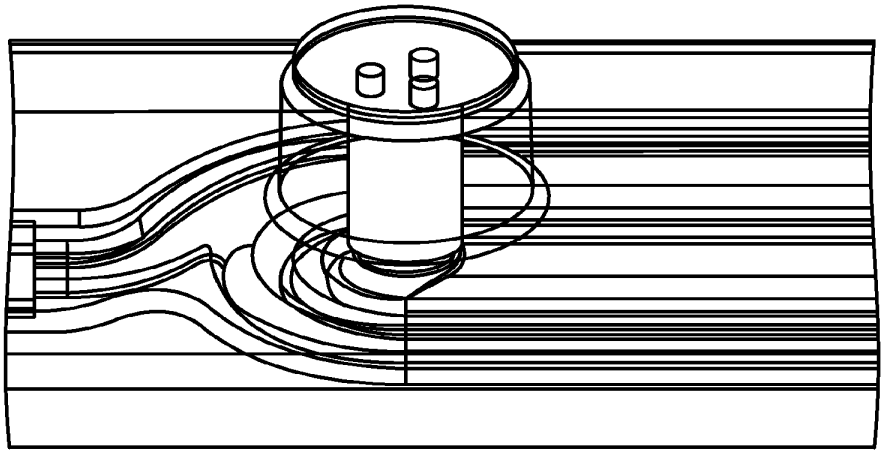


FIG. 30F

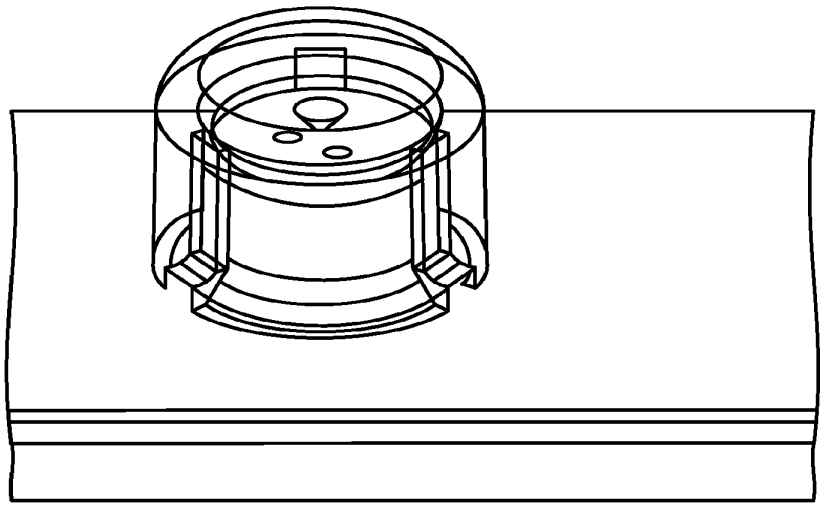


FIG. 30G

FEATURES

Better Blood Transfusion

There has been renewed interest in the safety and effectiveness of transfusion practice in recent years because of:-

- data from the Serious Hazards of Transfusion (SHOT) scheme showing that the safety of transfusion practice in hospitals should be improved,
- increases in the cost of blood associated with the introduction by Blood Services of safety measures such as universal leucocyte-depletion of blood components and nucleic acid testing,
- concerns about the transmission of variant Creutzfeldt-Jakob disease (vCJD) by blood transfusion and the potential effect that measures to minimise this risk might have on the blood supply.

Research is being carried out both on new approaches for the safety of the transfusion process, and to determine the appropriate indications for transfusion. The use of blood components only when there is a real clinical need is arguably the best way of avoiding the risks of transfusion. These issues apply to critical care as much if not more than to other clinical areas where transfusions are regularly used.

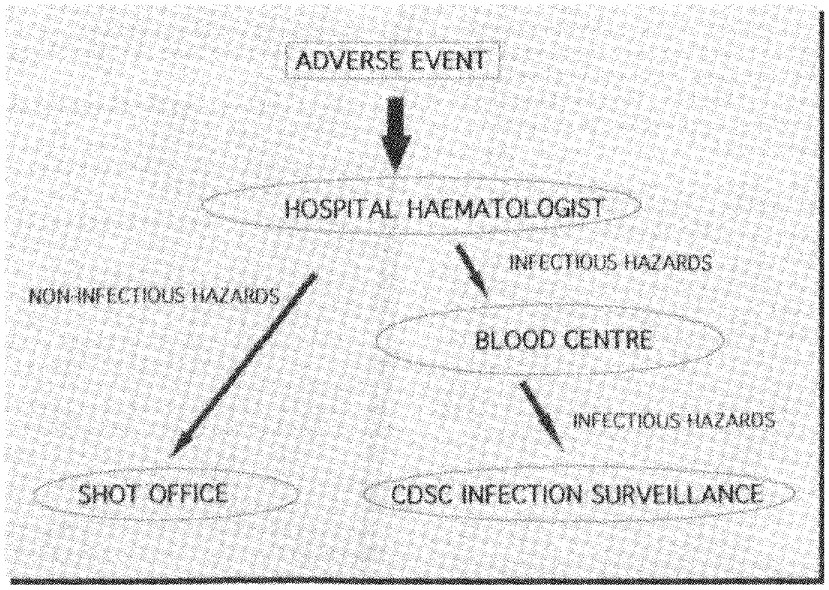
Risks of transfusion and new approaches to reducing the risks

The Serious Hazards of Transfusion (SHOT) scheme was established in 1996 to collect reports of major adverse events associated with the transfusion of blood components in the UK (1). Figure 1 shows the mechanism for reporting. 92% of eligible hospitals participated in 2001/02.

It is striking that the most frequent event is incorrect blood transfused (IBCT). Immune complications of transfusion are all represented to varying degree, but episodes of transfusion-transmitted infection are infrequent. Recent figures from the National Blood Service indicate that the risk of HIV transmission has been reduced to less than 1 in 8 million (less than the risk of being struck by lightning), the risk of hepatitis B transmission is 1 in 900,000, and the risk of HCV has decreased to less than 1 in 30 million since the introduction of nucleic acid testing.

The increase in reports over the 5 years of the SHOT scheme is due to an increase in incidents of IBCT. This may be due to better reporting or a real increase in the number of incidents; the latter is thought to be less likely, but cannot be excluded. IBCT is defined as an episode where a patient was transfused with blood which did not meet the appropriate requirements or was intended for another patient. Out of the 699 incidents reported between 1996/97 and 2000/01, there were 161 ABO incompatible transfusions (resulting in 9 deaths and 37 cases of major morbidity), 73 RhD incompatible transfusions, and 37 cases involving other red cell incompatibilities. 195 wrong transfusions were by chance ABO and RhD compatible. Analysis of the distribution of errors causing IBCT shows that they occur throughout the transfusion process. The most frequent site of error is at the time of collection and/or

Figure 1. Mechanism of SHOT reporting. (CDSC- Communicable Disease Surveillance Centre)



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administration of blood (55%), followed by errors in the laboratory (28%), and errors at the time of request, sampling or prescription of blood (13%). The SHOT data have clearly demonstrated that multiple errors often contribute to IBCT; in 2001/02, 54% of IBCT cases involved multiple errors. IBCT was found to occur in all sites where blood is used, with both elective and emergency transfusion, and to involve many types and grades of staff.

In over 70% of cases, there was minor or no morbidity. However, 14% of incidents were associated with major morbidity e.g. admission to an intensive care unit, renal dysfunction, or confirmed infection. The death of the patient was definitely attributed to transfusion in 37 cases (3%), and was possibly associated with transfusion in a further 32 cases (2%). The most frequent cause of death was transfusion-associated graft-versus-host disease (TA-GvHD) (13 cases). The most frequent cause of death or major morbidity was IBCT (71 cases) followed by transfusion-related acute lung injury (TRALI) (67 cases).

TRALI is a complication of transfusion particularly relevant to critical care. It is severe acute reaction characterized by respiratory distress, hypoxia and pulmonary infiltrates soon after transfusion with no other apparent cause. In many cases, preformed leucocyte antibodies have been found in the plasma of the donors, and these are thought to cause pulmonary leucostasis and leucocyte activation resulting in capillary leak and pulmonary damage. TRALI has been reported to occur after the transfusion of all types of blood components, but is particularly likely to occur with those with a large volume of plasma such as fresh frozen plasma (FFP). TRALI is clinically indistinguishable from acute respiratory distress syndrome (ARDS), and the occurrence of ARDS with a possible association with transfusion provides grounds to consider TRALI as the cause. Unlike ARDS, TRALI is self-limiting, and there is usually clinical improvement within 48–96 hours provided prompt respiratory support is provided. The production of FFP from only male donors, and reducing the volume of plasma in platelet concentrates are under consideration as measures to reduce the risk of TRALI.

The SHOT scheme has no mechanism for implementing its recommendations, and is reliant on other organisations to do so. Some parallel initiatives have supported the work of the SHOT scheme, including the development of national guidelines for transfusion practice by the British Committee for Standards in Haematology (BCSH), for example on the administration of blood (2). The SHOT scheme has recommended that further research should be carried out into information technology solutions for safer transfusion. An example is the use of barcode technology for patient identification and for the confirmation that the right blood will be transfused. A barcode patient identification system was recently found to simplify the clinical transfusion process and improve practice (3). Further work is required on the development of such systems for transfusion, and also for other hospital procedures requiring patient identification such as drug administration. These systems are particularly relevant for clinical areas such as critical care where the patient cannot verbally confirm their identification.

SHOT has also recommended the introduction of new strategies for reducing the risk of bacterial contamination. New methods are being introduced for cleaning the arms of blood donors and for diverting the initial 20ml of donor blood into a pouch for laboratory testing, and bacterial testing of platelet concentrates is being considered.

Measures to encourage the appropriate use of blood components and blood products

Concerns about blood safety have probably been the main driver for changes in transfusion practice in recent years. The threat of transfusion-transmitted infection has outweighed other risks of transfusion, and maybe it is time to 'realign transfusion safety with risks' using data from schemes such as SHOT about the observed risks of transfusion (4). At a clinical level, evidence does influence practice, but the level of evidence is critical. Guidelines and recommendations from experts appear to have limited impact, but level 1 evidence from systematic reviews or randomised controlled trials can have a major impact. For example, in the field of critical care, the publication of a systematic review on the absence of benefit of the use of albumin and possible increased mortality rapidly reduced its use (5), and a randomised controlled trial on transfusion triggers for red cell transfusion resulted in a change in practice in many centres (6). Greater efforts are needed to develop a sound evidence-base for the use of blood components and blood products in critical care as well as other clinical areas.

Better Blood Transfusion is an initiative led by the UK Chief Medical Officers to improve the safety and effectiveness of transfusion practice. Its output has been two Health Service Circulars (HSCs) setting out a number of recommended actions to hospital Chief Executives (7 8). An audit of the implementation of the HSC 1998/224 Better Blood Transfusion showed that most hospitals had established Hospital Transfusion Committees (HTCs), were participating in the SHOT scheme, and had protocols for the administration of blood (9). However, there was evidence of poor provision of training for clinical staff and patient information, few protocols for the appropriate use of blood, few

FEATURES

audits of transfusion practice, and limited use of autologous transfusion. The HSC 2002/009 Better Blood Transfusion – Appropriate Use of Blood was published in July 2002, and it included an action plan and an ongoing programme for Better Blood Transfusion to be taken forward in each Trust. It recommended the establishment of a Hospital Transfusion Team (HTT) in each Trust. The HTT is tasked with implementing the agreed actions recommended by the HTC; it should be led by a senior doctor interested in transfusion medicine (not necessarily a haematologist) and include one or more Transfusion Nurses (depending on the size of the Trust), senior blood bank laboratory staff and specialists who work in clinical areas with large or high risk blood usage. It should be provided with managerial, information technology, and administrative support. The main work of the HTT and HTC is directed to:-

- the development and implementation of local policies for safe and appropriate transfusion based on national guidelines, and the use of alternatives to blood where appropriate,
- the provision of training for the many staff involved in transfusion,
- the provision of better information for patients.

The Chief Medical Officer's National Blood Transfusion Committee (NBTC) was established in England in 2001 (for details, see www.doh.gov.uk/blood/nbtcommittee.htm). It provides a potentially powerful framework through its Regional Transfusion Committees for improving transfusion practice and supporting the work of the HTCs. It oversees the national Better Blood Transfusion initiative, and acts as the Steering Group for an initiative for national comparative audit of clinical transfusion practice based on an earlier pilot scheme (10). The NBTC reviews the findings of the SHOT scheme, and supports its recommendations. One of its main roles is to provide educational material for hospitals and patients, for example it has recently developed a national patient information leaflet, recommendations on the resources to implement Better Blood Transfusion, and an audit tool for the use of blood (available on www.doh.gov.uk/bbf2). Recommendations on strategies for the avoidance of transfusion are in preparation. Specific measures which could be considered in critical care practice include better compliance with evidence-based triggers for transfusion, greater use of near patient testing to determine the need for transfusion, and minimising blood loss due to sampling. ■

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REVIEW

Detecting Bacterial Contamination in Platelet Products

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SUMMARY

Bacterial contamination of platelets is an important cause of transfusion-associated morbidity and mortality. It is currently the most frequent infectious complication of transfusion therapy, with between 1 in 1,000 and 1 in 3,000 platelet units being bacterially contaminated at time of transfusion. Several factors have contributed to the persistence of this problem including lack of sensitive detection methods, lack of recognition of the frequency of the problem, inadequate recognition of septic reactions by clinicians treating patients receiving platelet transfusions, differences in transfusion reactions between bacterial species and bacterial inocula transfused, and differing methodologies and time of testing for detection of bacteria in platelet units. There are also important correlations between the receipt of bacterially contaminated platelet units and the development of transfusion reactions and bacteremia. In the last few years the recognition of the importance of platelet bacterial contamination prompted the College of American Pathologists (CAP) and the American Association of Blood Banks (AABB) to set new standards requiring the screening of platelets for bacterial contamination. In the wake of these standards, an increasing number of approaches have been and are being developed to deal with this problem. The clinical sensitivity, specificity and predictive value of these detection methods vary considerably and need to be defined for routine laboratory practice. In this review, we focus on the practical aspects and feasibility of implementing FDA-cleared detection methods for identifying bacterially contaminated platelet units. We also present details of a number of methods under development for at-issue use. (Clin. Lab. 2006;52:443-456)

BACKGROUND

Platelets are currently administered as single donor plasmapheresis (SDP) and whole-blood derived, random donor platelet (RDP) units, with the latter typically being administered in pools of 4-6 units. Bacterial contamination of these platelet products is an ongoing problem associated with significant transfusion-associated morbidity and mortality.[1-10] Currently, platelet-transfusion-associated sepsis is the most frequent infectious complication of transfusion therapy, with between 1 in 1,000 and 1 in 3,000 platelet units being bacterially contaminated at time of transfusion.[1, 8, 11] Transfusion of contaminated units is estimated to cause life-threatening sepsis in between 10% and 40% of recipients receiving a bacterially contaminated platelet unit. Based on passive-reporting studies from the United States, the United Kingdom and France, the risk of death from a platelet transfusion due to bacterial contamination is between 1 in 7,500 and 1 in 100,000 transfusions.[8] These risks are up to two orders of magnitude higher than the incidence of transfusion-associated viral transmission.[1, 6, 7] Platelet units are more susceptible to contamination than other blood products because of the requirement to store platelets at room temperature to preserve platelet function.[12] At 22-24 °C, a small bacterial inoculum can grow into very high numbers within a short time period and therefore, older ("at-risk") units are most likely to be contaminated with a large number of organisms and to cause a septic reaction in the recipient.[11, 13, 14] In recognition that older platelets are at risk for significant bacterial contamination, the storage period of platelets was shortened by the United States Food and Drug Administration (US-FDA) from seven to five days in 1986 in response to an increased number of reports of transfusion-related sepsis in older platelet units.[9, 15] Only in

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Table 1: Bacteria associated with 60 cases of fatalities resulting from transfusion of platelet products as reported to the US-FDA, 1995-2004.[17]

Bacterial species	No. of cases
Gram-positive organisms (n = 22)	
Staphylococcus epidermidis	11
Staphylococcus aureus	4
Streptococcus group G	2
Clostridium perfringens (anaerobe)	1
Enterococcus spp	1
Streptococcus group B	1
Streptococcus group F/Eikenella	1
Gram + rods (unidentified)	1
Gram-negative organisms (n = 38)	
Klebsiella pneumoniae	10
Escherichia coli	9
Serratia marcescens	5
Enterobacter aerogenes	2
Enterobacter cloacae	2
Pseudomonas aeruginosa	2
Salmonella spp	2
Bacillus spp	1
Enterobacter agglomerans	1
Klebsiella oxytoca	1
Morganella/Providencia	1
Pasteurella multocida	1
Gram-negative rods (unidentified)	1

2005, with the advent of licensed storage containers for single donor apheresis platelets combined with aerobic and anaerobic culture testing under an US-FDA-approved post-market surveillance protocol, did it become permissible once again to store platelets (SDP only) for up to seven days following collection.[16]

The predominant organisms implicated in platelet bacterial contamination are the skin flora, including staphylococci (*Staphylococcus aureus* and coagulase-negative staphylococci), *Corynebacterium* species, and *Propionibacterium* species. Other contaminants include streptococci, Gram-negative bacilli and *Bacillus* species. Although Gram-positive organisms cause the majority of septic reactions, Gram-negative organisms are implicated in the majority of fatalities.[1, 3, 6] Among the Gram-negative organisms reported to contaminate platelet units are *Pseudomonas aeruginosa*, *Escherichia coli*, *Klebsiella pneumoniae*, *Salmonella* species, *Enterobacter* species, *Morganella morganii*, and *Serratia* species.[9, 17] Indeed, *Klebsiella pneumoniae* was responsible for the majority of platelet transfusion-associated deaths related to Gram-negative organisms reported to the US-FDA from 1995 to 2004 (Table 1).[17] Although some of these organisms have a preference for anaerobic conditions, all are able to grow in aerobic conditions, with the exception of *Propionibacterium* spp., which grows only under anaerobic conditions. A single case of contamination of a platelet unit with *Clostridium perfringens*, also a strict anaerobe, has been reported.[17]

PREVALENCE OF BACTERIAL CONTAMINATION OF PLATELETS

The reported prevalence of bacterial contamination of platelets is highly variable and, in many cases, is difficult to assess due to differences in surveillance and testing methodologies and in case definitions. However, it is generally accepted that approximately 1 in 1,000 to 1 in 3,000 platelet units are contaminated with bacteria.[1, 8] Based on 1999 data, over 4 million platelet units are transfused per year in the USA, in the form of 1 million SDP units and 3 million RDP units, the latter administered in 0.5 to 0.75 million pools of 4-6 units.[10, 18] On this basis, it is likely that 1,300 to 4,000 platelet units and 500 to 1,500 platelet transfusions per year are bacterially contaminated. Projected fatalities from these transfusions, based on extrapolation from surveillance and other studies, vary from 15 to over 200 per year. Our nearly 15-year experience with bacterial contami-

nation surveillance in a university hospital using passive (transfusion-reaction triggered) and active (culture at issue) surveillance demonstrated that, while active surveillance detected 38 instances of bacterial contamination (1:2,090 RDP units and 1:2,213 SDP units), only one instance of contamination was detected by passive surveillance (0:48,067 SDP units and 1:168,216 RDP units).[11] The failure of passive surveillance to detect instances of bacterial contamination is attributed to the widespread lack of recognition of septic versus nonseptic reactions, and failure to associate signs of bacterial sepsis with the transfusion of a platelet unit. Additionally, transfusion of platelet units contaminated with bacterial species of low virulence such as coagulase-negative staphylococci frequently does not elicit signs and symptoms of a transfusion reaction.

Thus, there remain important outstanding questions relating to the clinical significance of detecting, defining and quantitating bacterial contamination in platelet units. Although the search for the perfect method is elusive, in the last few years a variety of different methodologies have been developed and evaluated for detection of bacteria in platelet units. Currently, three commercial methods have been cleared by the US-FDA for screening of platelets for bacterial contamination, BacT/ALERT (bioMerieux, Inc, Durham, NC), Pall eBDS (Medsep Corporation, Covina, CA), and Scansystem (Hemosystem, Marseilles, France). Based on the published information from centers that have used one or more of these systems for screening single donor platelet products,[19-23] these methods are sensitive and specific, but the culture-based systems have not detected all contaminated units in the clinical setting.[10, 24] Therefore, patients are still at risk for being transfused with bacterially contaminated platelet units due to false negative results. In addition to these US-FDA-cleared methods, there are several additional methods in various stages of development. It is our goal to present the feasibility and logistics of the application of various methods – both cleared and under development – for bacterial detection testing in platelet units and to describe their advantages and disadvantages.

CORRELATION OF TRANSFUSION OF BACTERIALLY CONTAMINATED PLATELET UNITS, BACTERIAL LOAD AND TRANSFUSION REACTIONS

The critical factor for the clinical use of any detection method is defining the number of bacteria, expressed as colony-forming units per mL (CFU/mL) that will result in a clinically significant transfusion reaction. Transfusion reactions may occur with as few as 10^2 to 10^3 CFU/mL, even with organisms of low virulence such as *S. epidermidis*.[1, 11, 25]

Transfusion of a contaminated platelet unit is often not recognized or directly associated with subsequent sepsis. Over a 3-year period, 1998 through 2000, from suspected cases reported to the CDC during the BaCon study, a voluntary reporting study with very restricted criteria for case definition, the rate of transfusion-transmitted bacteremia (in events/million) was estimated to be 9.98 for SDP and 10.64 for pooled RDP units. The rates of fatal reactions were 1.94 and 2.22 respectively.[6] Overall, the BaCon study estimated a fatality rate of 1 in 500,000 units for both SDP and RDP units.[6]

In France, over a 2-year period, of 16 cases of bacterial contamination associated with platelet transfusion 9 (56%) resulted in severe sepsis or shock. Estimates of the incidence of life-threatening reactions were 9.4 per million (1:106,000) units for RDP units and 17.7 per million (1:56,500) for SDP units.[26] A more recent report from the French Haemovigilance System identified seven confirmed cases of transfusion-transmitted bacterial contamination. Of these two were related to SDP and two to RDP pools, while the other cases were related to transfusion of red blood cells.[27] In the United Kingdom during six years of voluntary participation of blood services, the SHOT (Serious Hazards of Transfusion) study identified 26 episodes of bacterial contamination out of 40 transfusion-transmitted infection incidents reported. Twenty-two of these episodes were related to the transfusion of platelets, accounting for 5 of 6 deaths.[28]

A major problem in determining the magnitude of the problem of platelet bacterial contamination is the lack of recognition and reporting of cases, due in large measure to the failure to associate chills, rigors and fever – signs and symptoms common in patients receiving platelet transfusion therapy – with the possibility of transfusion of a bacterially contaminated platelet unit.[11, 25] Based on the reported prevalence of transfusion reactions and the detection rate of contaminated platelet units, however, it is estimated that a severe episode of transfusion-associated bacterial sepsis occurs in connection with about 17% of contaminated units transfused.[1] More serious clinical events, such as shock and death occurring in immunocompromised platelet transfusion recipients, are likewise often not linked to transfusion of a bacterially contaminated platelet unit.[11]

The data obtained by our group during more than 14 years of surveillance for bacterial contamination of platelets showed, for the first time, the correlation between the organism load in bacterially contaminated units, transfusion reactions and positive blood cultures.[11] From this study, it was clear that bacteremia did not correlate with transfusion reactions, with bacteremia not being documented in the three patients with fatal outcomes, while two patients showing no signs of a transfusion reaction were bacteremic. Absence of bacteremia was likely related to patients receiving antimicrobial agents and delays in obtaining blood cultures following transfusion. Correlation of organism load with occurrence of transfusion reactions showed that a system with a sensitivity of 10^5 CFU/ml would detect 10/11 (91%) serious reactions and 15/19 (79%) of all reactions, while one with a sensitivity of 10^4 CFU/ml would detect all 11

serious reactions and 16/19 (84%) of all reactions.[11, 29] Additionally, our study showed that rates of bacterial contamination, transfusion of contaminated units, transfusion reactions and bacteremia for RDP pool transfusions were significantly higher than those for SDP unit transfusions. These differences, however, were associated with the use of pools of 5 RDP units per transfusion as these rates were not statistically different based on the number of individual platelet units transfused. Our study also demonstrated the superiority of active surveillance over passive surveillance in detecting platelet bacterial contamination, with 38 of the 39 instances of platelet bacterial contamination being detected only by active surveillance. While our experience also highlights the finding that the vast majority of transfusion reactions with signs and symptoms consistent with sepsis are not due to transfusion of bacterially contaminated platelet units, paradoxically it demonstrates that the majority of patients who received bacterially contaminated platelet units and developed signs and symptoms of sepsis were not recognized or reported to the Blood Bank or Transfusion Service for further evaluation.

In 2004, the Infectious Diseases Society of America conducted a survey to assess clinician experience with transfusion-associated bacterial infections among infectious diseases specialists who are members of the Emerging Infections Network in the United States.[10] Among the 399 members that responded, 48 (12%) recalled consulting on 85 reactions to blood transfusions potentially caused by bacterial contamination, with 10 of these cases being fatal. A total of 143 (36%) respondents were aware that bacterial contamination of platelets is now the most common infectious risk of transfusion therapy while only 78 (20%) were aware of the new AABB standard for testing platelets for bacterial contamination. It is clear from this survey that efforts should be made to communicate with clinicians not only the new requirements from AABB and CAP, but also to recognize and request the appropriate testing to confirm the diagnosis of sepsis related to transfusion of potentially bacterially contaminated platelet units.[10]

STRATEGIES TO REDUCE OR PREVENT CONTAMINATION OF BLOOD PRODUCTS

In March of 2004, the AABB, an accrediting organization for Advancing Transfusion and Cellular Therapies Worldwide, added a new standard that requires members of this organization to implement measures to detect and limit bacterial contamination in all platelet components.[30] In an effort to assist blood banks and transfusion services, the AABB, in a supplemental guideline, suggested various strategies for reducing transfusion of bacterially contaminated platelet units and described several methods for detecting bacterial contamination,[31] which will be described in more detail below. In addition to the AABB, in 2002 the CAP added a requirement for laboratories to have a system in place to detect the presence of bacteria in platelet components.[32, 33] Thus, in order to be in compliance with the CAP Laboratory Accreditation Program, blood banks and transfusion medicine services need to have a system to detect the presence of bacteria in platelet components.

While bacterial detection methods garner most of the attention, additional strategies have been developed to reduce the risk of transfusion of bacterially contaminated platelets. These strategies include bacterial contamination avoidance methods, and bacterial growth inhibition or inactivation methods.[15] In order to accomplish the goal of eliminating bacterial contamination of platelets, these strategies likely will need to be used in combination with a detection method. Ideally, the responsibility for limiting bacterial contamination is shared between the collection center, which needs to insure suitable donor selection, proper aseptic collection technique and absence of measurable bacteria by using a sensitive detection method shortly after product collection, and by the transfusion service, which should ideally use a rapid test for detecting bacterial contamination at the time the platelet unit is issued for transfusion.

Bacterial Contamination Avoidance Methods

Platelet units are most commonly contaminated at the time of collection when bacteria from the skin or from bacteremia in the donor gain entry into the collection set during the phlebotomy process. Exhaustive donor screening and deferral if a history or symptoms of possible bacteremia is elicited has reduced contamination of blood products. Additional measures to minimize the entrance of bacteria into the blood collection system include improved disinfection of the skin, and diversion or removal of the first 20-30 mL of blood collected.[34, 35] Overall, rates of bacterial contamination of SDP and RDP units have been similar, but the rate of transfusion of contaminated products is proportionately higher in RDP pools than in SDP units.[11, 25, 36]

Bacterial Growth Inhibition and Inactivation Methods

While bacteria may gain entry into a platelet unit during collection, the number of bacteria entering the collection system is usually very small and it is only during room temperature platelet storage that the organisms may grow into large numbers. This problem can potentially be prevented by using a substance that inactivates bacteria or that inhibits bacterial growth during storage. The use of substances that inhibit or inactivate organisms present within a platelet bag should be implemented by the collection center. In order for this strategy to be feasible and practical, these substances should not cause substantial damage to platelet function, and the process should be automated and linked to the collection instrument. These

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inhibitory substances need to be added in a particular concentration, and the instrument should be able to calculate and dispense the pathogen inhibitory reagent in a closed system and according to the volume collected. Although the cost is substantial, and safety concerns about the additive solutions remain, the potential application of inactivation methods seems to be a promising approach to avoiding bacterial contamination of blood products.[37] Two inhibitory substances are being evaluated for use in platelets: amotosalen S59, which is being developed as the Intercept PLT System (Cerus, Concord, CA), and riboflavin, which is being developed by Navigant (Lakewood, CO). When activated by light, amotosalen S59 binds to the nucleic acid of pathogens and prevents replication.[38, 39] A pilot study assessing the use of 7-day-old buffy-coat platelets treated photochemically with amotosalen S59 to transfuse patients with thrombocytopenia showed that treated platelets produced acceptable efficacy and safety compared to 7-day-old untreated platelets.[40] The Intercept PLT System obtained regulatory approval in 2002 in Europe to treat platelets for transfusion, and regulatory approval is being pursued in the United States. The other pathogen inhibitory system under development for platelets is a photochemical decontamination process utilizing riboflavin, and preliminary reports are encouraging.[41, 42]

Bacterial Detection Methods

At present, the focus in identifying and preventing bacterial contamination of platelet components by the collection centers as well as the transfusion services is on detection methods. The ideal detection method should be sensitive and specific, have a rapid turn-around time, require a small sample volume for testing and be inexpensive.

For SDP platelets, the CAP and AABB recommend the use of one of the commercial systems that have been cleared by the US-FDA for in-process quality control testing of platelet units. For RDP units, where application of testing with an US-FDA-cleared method may be impractical unless applied to pooled units, a variety of less sensitive testing methods are permissible. These include detection of decreased pH, detection of decreased glucose concentration, microscopic examination of dried smears stained with acridine orange or Gram stain, plate culture, and broth culture. These methods should be validated by the user.

As discussed above, the methods that have been cleared for bacterial contamination testing of platelet products by the US-FDA are two culture-based instruments, the BacT/ALERT and PALL eBDS. More recently, the US-FDA has also cleared the Scansystem, a scanning cytometry method that uses an automated microscopic analysis of particles stained with a fluorescent stain. Both culture-based methods (BactT/ALERT and eBDS) may potentially delay the use of platelets and shift the inventory to the use of older platelets because they require a 24-h holding period prior to sampling and a generally 24-h incubation period after sampling.

Description of US-FDA Cleared Bacterial Detection Methods for Quality Control Testing of SDP units

BacT/ALERT

A sample of platelet rich plasma from a leukocyte-reduced SDP unit is inoculated into aerobic (BPA) and anaerobic (BPN) culture bottles containing broth media and then placed into an instrument that automatically monitors the production of CO_2 as a result of growth of bacteria. This and similar systems have been used for many years for the routine culture of blood for clinical purposes. The manufacturer strongly recommends using one aerobic and one anaerobic bottle, each inoculated with 4 ml of the platelet product. For optimal bacterial detection, the manufacturer recommends that the platelet specimen should be taken at least 24 hours after collection to allow for natural proliferation in the platelet product. During this time bacteria, if present at the time of collection, would have an opportunity, in most instances, to reach a level adequate for sampling and subsequent growth in the culture system. Although procurement of the aliquot from the platelet unit is achieved with the use of a sterile docking device, the subsequent inoculation of the sample into the culture bottle involves an open system using a needle and syringe. Therefore, strict adherence to the manufacturer's instructions for antisepsis of the septum of the blood culture bottle and inoculation instructions are critical factors to prevent the occurrence of false positive results due to contamination during inoculation of the platelet unit itself. Distinguishing false positive culture results from true contamination is often confounded by the fact that the same bacterial species are commonly detected in both circumstances. According to the manufacturer's directions, the inoculated culture bottles are held for the shelf-life of the platelet unit unless a signal indicating bacterial growth is generated before this time period has elapsed.

Once the system identifies a bottle as being "positive", indicating that the CO_2 content is above the baseline, an aliquot is removed for Gram stain and subculture to agar media. Most collection centers send positive bottles and a sample from the original unit to a microbiology laboratory for further testing. Absolute proof that a true positive result is correct requires that the same organism be isolated from original platelet unit and positive culture bottle. If the culture from the original platelet unit is negative, it is likely that the positive culture bottle is a false positive.

In the USA, the BacT/ALERT culture bottles are accompanied by product inserts indicating that BacT/ALERT System (3D and 240) and culture bottles may be used for quality control testing of platelets and that the laboratory should follow its own quality control pro-

cedures for this use.[43] The product inserts also state that the BacT/ALERT System, including the culture bottles, should not be used in determining suitability for release of platelets for transfusion and that users considering such release testing should first consult the Center for Biologics Evaluation and Research (CBER) of the Food and Drug Administration (FDA) for the appropriate clinical studies. A report of "negative" should not be interpreted as meaning that the original product is sterile. The negative status could be due to underinoculation of the bottle, no organisms present in the inoculum, the number of organisms were too small for detection, or a culture bottle/medium that does not support the growth of the organism.[43]

eBDS

This method is a novel culture-based system, which assesses the reduction of the O_2 content in the head space of a sample pouch containing an enriched medium, compared to ambient O_2, as a marker for bacterial growth.[23] This method involves docking an eBDS sample pouch onto the tubing of a platelet bag, transfer of an aliquot of 2-3 mL of the platelet product into the sample pouch, which is then separated from the platelet unit using a heat sealer. The eBDS pouch is then incubated at 35 °C for 24 hrs. Pouches are then removed from the incubator, kept at room temperature for at least 2 minutes and the probe of the oxygen analyzer inserted into the sample port of the pouch. The oxygen analyzer automatically reads the oxygen concentration in the sample pouch. The instrument then gives a reading with a positive or negative interpretation for bacterial contamination.

Scansystem

This method detects bacteria using a laser-based, solid-phase scanning cytometry detection method. This method is a highly sensitive bacterial screening system, and can detect very low levels of bacteria after concentration from a larger volume by filtration.[60] The Scansystem solid-phase cytometry analyzer includes four modules: (i) a scan module, in which the black membrane is placed; (ii) an argon laser module (488 nm excitation light), which is connected directly to the scan module to scan the black membrane; (iii) an epifluorescence microscope with a suitable light source and filters, which has an automated motor-driven stage, for visual discrimination by the operator of fluorescent particles detected by the laser scan as bacteria or nonbacterial particles; and (iv) a computer with proprietary software to monitor the other modules.

The Scansystem is used by drawing a 3 ml sample of platelets into the syringe of a Scansystem Platelet kit through the sample injection port. The kit is then agitated in a platelet incubator at 22 °C for forty minutes in order to achieve platelet aggregation. The contents of the syringe are then expressed through a filter, which retains the aggregated platelets and allows passage of bacteria into the second portion of the kit. The kit is then incubated at room temperature for twenty minutes to allow labeling of any bacteria present with the fluorescent stain. A black membrane in a holder attached to a vacuum pump is then attached to the bottom port, and the contents of the pouch are then filtered through the black membrane. Any bacteria present will be deposited on the surface of this membrane. The membrane is then removed from the holder and placed into the Scansystem scan module for detection of fluorescent particles by laser scanning. The final step is visual determination, using the epifluorescence microscope, of the identity of fluorescent particles as bacteria or as other particles.

Other Detection methods

Although traditional culture and culture-based methods are far more sensitive than staining and measurement of pH or glucose, the latter methods have the advantage of having a rapid turn-around time and therefore the testing can be done at or near the time of releasing the platelet unit, while final culture results may not be available until after transfusion. For this reason, and because these non-culture based methods are among the suggested methods in the current AABB and CAP guidelines for testing of RDP units, many transfusions services and blood banks have adopted them for routine testing; and, as is discussed below, despite poor sensitivity for detection of bacterially contaminated platelet units, their use may reduce the fatalities associated with transfusion of bacterially contaminated platelet units.

Staining Methods

Among the staining methods recommended by AABB and CAP are the Gram stain and the acridine orange stain.

Gram stain procedure: A smear is prepared using a sterile pipette or syringe to transfer 1 or 2 drops from a platelet unit to a clean glass slide. The drop is spread into an even film and allowed to either air dry or heat dry on a slide warmer. Smears can also be prepared using a cytospin slide centrifuge to concentrate the sample. Cytospin preparations deposit the concentrated sample within a limited area for viewing.[44] The Gram stain procedure includes sequential staining steps with crystal violet, alcohol decolorization, and counterstaining with safranin or neutral red. Bacteria stain either Gram-positive (deep violet) or Gram-negative (red) on the basis of differences in their cell wall composition. Gram-positive bacteria have a thick peptidoglycan layer and they are unaffected by the decolorization step and retain the initial stain, appearing deep violet. Gram-negative bacteria have a thin peptidoglycan layer attached to an outer membrane containing lipids. This membrane is damaged by the decolorizer, allowing the initial stain to leak out and be replaced by the red counterstain. The smear is examined microscopically using a light microscope with a 100X oil objective. The sensitivity of the

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Gram stain is 10^5 CFU/mL, or 10^4 CFU/mL if the specimen has been prepared with a cytocentrifuge.[44] Use of the Gram stain has been successful in interdicting platelet units heavily contaminated with bacteria prior to transfusion.[5]

Acridine orange stain procedure: Acridine orange is a fluorochromatic dye that binds to nucleic acids of bacteria and other cells. Under UV light, bacteria stain bright orange, whereas human cells and background debris stain pale green to yellow, although nuclei of activated leukocytes may also stain orange or red. The smear is prepared as for a Gram stain and stained with acridine orange (0.1 g/L in 0.5M acetate buffer) for 2 min. The smear is read on a suitable fluorescent microscope with a 40X dry or 100X oil objective. The sensitivity of the acridine orange stain is approximately 10^4 CFU/mL.[45]

Interpretation of Gram and acridine orange stains involve consideration of staining characteristics and cell size, shape, and arrangement. Sample preparation, reagents, and staining procedures may influence these characteristics. Therefore, use of quality control slides and competency training of the personnel reading the stains is essential. It is advisable that these staining methods be done in a clinical microbiology laboratory. In institutions where a microbiology laboratory is not available, the Gram stain can be performed by blood bank or transfusion service personnel that have been adequately trained to perform and interpret Gram stains. In addition, these laboratories should be participating in a Gram stain proficiency testing program.

pH and glucose analysis: Testing can be done separately using a handheld device or pH paper, or in combination on a multi-reagent dipstick. Although, handheld pH meters provide a more accurate result than do dipsticks, both methods are easy and rapid to perform and, for that reason, they have been adopted for many blood banks and transfusion services for testing RDP units.[46-49]

The sensitivity of pH and glucose testing, using one or both methods, is approximately10^6 to 10^7 CFU/mL. Because of this limited sensitivity, the AABB recommends that facilities use these methods on individual units rather than pooled units. A recent study showed that as platelets age, the rate of pH failures increases, and only 4 of 405 random platelet units that failed pH were culture positive.[49] A lower rate of pH failure has been demonstrated in random units that have undergone prestorage leukoreduction compared to non-leukoreduced, random platelets.[50]

IMPLEMENTATION OF DETECTION METHODOLOGY

A summary of the AABB fall 2004 survey of members on practices related to the new guidelines on detection and prevention of bacterial contamination in platelet units was presented at the US-FDA Blood Products Advisory Committee Meeting in January of 2005.[51] The survey results showed that the majority (88%) of blood centers were using a culture method – usually BacT/ALERT- to screen for bacterial contamination of SDP units. Most centers (85%) using BacT/ALERT did only aerobic cultures and held the cultures for 5 to 7days. Four out of the 34 blood centers surveyed used glucose or pH by dipstick or meters. A few transfusion services cultured platelets by plate culture or performed Gram stains. Among hospital blood banks, most cultured platelets if their supplier did not, or if the platelets were collected in-house. Half of the blood banks performing cultures used anaerobic and aerobic cultures, while the remainder used only aerobic culture.[51]

It is clear from the results of the survey that many transfusion services are using less sensitive techniques – glucose, pH or Gram stain as compared to methods cleared by the US-FDA - for quality control of platelets, particularly RDP units. The advantage of using these methods is that they are easy to implement in any hospital blood bank or transfusion service and they can be performed at or near the time of issue. However, there have been reports of false negatives with fatal consequences with these methods,[10] and investigators have strongly advised against the use of surrogate markers of bacterial metabolism, such as pH and glucose concentration, for detecting bacterial contamination of platelets due to the analytic insensitivity of these methods.[52]

Some of the practical aspects relating to implementation of the US-FDA-cleared detection methods are discussed below. In addition, the BacT/ALERT and the eBDS systems have also been evaluated for screening of individual and of pooled RDP units, and have been found to be reliable for monitoring bacterial contamination in these products.[53, 54] Table 2 summarizes the published contamination rates found by routine testing in a clinical setting using different detection methods. The rates of bacterial contamination varied considerably between and within methods, with methods such as plate culture, eBDS and BacT/ALERT generally reflecting realistic true positivity rates (0.02-0.05% for SDP and RDP units, and 0.1-0.25% for RDP pools), while Gram stain, pH determination and glucose determination resulted in low true positive rates while in the case of pH and glucose determination, very high false positive rates were also found. In many instances especially when the BacT/ALERT method was positive, the platelet product had already been transfused and was no longer available for retesting, and these cases are regarded as unconfirmed positives.

Table 2: Results of various methods used for routine testing of platelet products to detect bacterial contamination. Realistic true positive rates based on 1:1,000 to 1:3,000 units being contaminated are 0.03-0.1% for SDP and RDP units, and 0.17-0.5 for RDP pools of 5 units. Data was obtained or derived from the references indicated.

Method	Platelet product (total tested)	Overall positive rate (%)	True positive rate (%)	False positive rate (%)	Unconfirmed positive rate* (%)	False negative rate (%)	Reference #
Gram stain at issue	RDP pools of 5 units (N=7716) SDP (N=8761)	0.12 0	0.078 0	0.039 0	0 0	0.16 0.046	11
pH at issue	Individual RDP (N=37067)	1.09	0.01	1.08	0	NR	49
	Individual RDP (N=6590) SDP (N=671)	1.97 1.93	0 0	1.97 1.93	0 0	0.03 0.30	11
pH + glucose at issue	Individual RDP (N=3093)	0.96	0.06	0.9	0	0 (N=203)	47
BacT/ALERT at 12-24 h	SDP (N=350658)	0.06	0.02	0.03	0.01	0.0008	55
	RDP pools and SDP (N=4000)	1.2	0.13	0.9	0.02	NR	57
	Individual RDP units (N=10141) RDP pools of 5 units (N=2063)	1.4 3.4	0.02 1.9	0.75 1.5	0.64 0	NR NR	54
	RDP pools (N=28104)	0.72	0.65	0.06	0	NR	24
	RDP pools of 4 units and SDP (N=36896)	0.24	0.03	0.04	0.12	0.18 (N=1061)	20
eBDS at 24 h	Individual RDP units (N=12062) RDP pools of 5-6 units(N=2201)	0.04 3.6	0.02 0.04	0.008 3.5	0.008 0	NR NR	53
Plate culture at issue	RDP pools of 5 units (N=12,961) SDP (N=15,493)	0.26 0.077	0.24 0.045	0.023 0.032	0 0	0.0077 0	11

SDP: Single donor platelets; RDP: Random donor platelets; NR: Not reported
* Unconfirmed positives are those where the platelet product had been used at the time the bacterial detection system became positive

Implementation of BacT/ALERT: Laboratory and clinical studies have demonstrated the efficacy of this system in identifying many instances of bacterial contamination of platelets.[19-22] The American Red Cross implemented routine quality control testing for bacterial contamination in SDP products with BacT/Alert in all 36 regional blood centers in March 2004.[55] Platelet samples (4 ml) were obtained at least 24 h after collection and cultured in BacT/ALERT aerobic bottle only until the end of the product shelf life or until a positive reaction occurred.[55] Products were released for use if negative after incubation for at least 12 h, and, if not used, removed from supply when culture became positive. Reports and investigations of potential septic reactions to SDP platelets were also reviewed. In the first 10 months of bacterial testing, 226 of 350,658 collections tested initially positive. Sixty-eight (30%) were confirmed as true positives. Of the 354 apheresis platelet products derived from all 226 initial test-positive cases, 38 (10.7%) had been transfused by the time of the initial positive result, although none of these were confirmed positive. During this period, three septic episodes probably related to transfusion of bacterially contaminated platelets, which had negative screening, were documented, with *S. lugdunensis* implicated in one and other coagulase-negative staphylococci in the other two instances. In Norway, from May 1999 to May 2004, RDP pools were monitored for bacterial growth using BacT/ALERT during an average period of 6.5 days. The investigators found that from 88 platelet pools that were initially positive, only 12 (13.6%) were confirmed as true positives.[20] The main limitations related to culturing, either using traditional culture or using an automated system, is the time required to obtain results. In order to increase the sensitivity of culture, sample for testing should be taken 24 hours after collection, inoculated into culture media and incubated for at least five days before reporting it as negative. Although most of the bacterial organisms implicated in bacterial contamination of platelets are detected after 24 hours of incuba-

tion (48 hours after collection), slow growing organisms cannot be detected for several days. As documented in the survey described above, in most instances, because of the logistics of sample handling, BacT/ALERT testing is performed at the collection center rather than the transfusion service. Documentation of training of the personnel performing the testing is required by accrediting organizations. While inter-laboratory proficiency testing is currently not required due to lack of available defined methodologies, it is anticipated that this will soon be required.[56]

The survey did not evaluate whether the blood centers were performing Gram stains or confirmation cultures from positive BacT/ALERT bottles on site or whether the bottles were sent to an external microbiology laboratory. Because it is known that false positive bacterial contamination results may occur with this system,[57] if the bottles are sent out for confirmation results could be delayed, which may lead to an increase in wastage of products and unnecessary treatment of patients who received these units.

Another limitation of culturing using an automated system is the specimen volume required for testing, usually 4 ml per bottle, which for a SDP unit represents only 1.5% of the unit volume if using aerobic bottles only, or 3% if using both aerobic and anaerobic bottles, but if testing is done on a single RDP unit, the volume required for testing could represent 10% to 40% of the unit volume. This limitation makes routine culturing of individual random units impractical.

Implementation of Pall eBDS: The features of this culture-based US-FDA cleared test are similar to those of the BacT/ALERT. This system also requires that a large sample (3 ml) be obtained at least 24 hours after collection and requires an incubation period of 24 hours. Published laboratory studies have shown that the Pall eBDS system is able to detect 1 to 15 CFU/ml of aerobic bacteria in a contaminated unit.[58] The initial version of this system (BDS) gave some invalid or negative readings with organisms that rapidly consume O_2 during their metabolism, particularly *Klebsiella pneumoniae*, but the newer enhanced version (eBDS) has overcome this problem.[15, 58, 59]

There are several potential advantages of the eBDS system compared to automated blood culture systems: (1) it is easier to utilize in a laboratory environment not generally familiar with bacterial testing instrumentation; (2) the sampling and inoculation occurs in a closed system, reducing the opportunity for false positive culture results; and, (3) unlike the BacT/ALERT system in which continuous monitoring of the culture bottles is performed throughout the shelf-life of the platelet unit, the eBDS system is read at a single, discreet time point, eliminating the possibility that a positive result will be generated after the platelet unit has been transfused. It is believed that many of the positive results generated after the platelet unit has been transfused are either false positives or are not clinically significant, while adding a significant burden of work. A potential disadvantage of the eBDS compared to the BacT/ALERT is that only aerobic organisms are detected. And with a smaller sample volume than the BacT/ALERT, it is possibly slightly less sensitive. With both systems, since sampling is done relatively early in the storage period when the bacteria have had limited time for growth, it is possible that bacterial contamination will be missed entirely. While the number of such "breakthrough" cases is uncertain they have occurred, and some have been clinically significant.[29]

Implementation of the Scansystem: Our group and other investigators have evaluated this system and found that this method is able to detect most typical bacterial platelet contaminants in leukocyte-reduced SDP units 30 h after contamination, with a sensitivity equal to that of BactT/ALERT.[60, 61] The Scansystem can detect both live and dead bacteria, so that the presence of bacterial species such as *Pseudomonas aeruginosa* and *Staphylococcus epidermidis*, which are frequently inhibited or killed in the presence of human plasma,[62, 63] may still be detected, provided some bacterial growth occurred.

Advantages of the Scansystem method are that platelets, from 30 to 72 h after collection, can rapidly be tested for the presence of bacteria, with a total test time of approximately ninety minutes.[60, 64] Thus the Scansystem allows testing of platelets closer to time of use, and allows platelet units to be used as early as 32 h after collection, compared to typically 48 h for the BactT/ALERT and eBDS methods. Moreover, the Scansystem method is able to detect both live and dead bacteria, which may prevent transfusion of endotoxin-containing products. Disadvantages of the Scansystem are the labor-intensive nature of the system, the need to verify visually the presence or absence of bacteria for each positive test, and the need to test platelet units within 72 hours of collection as platelet aggregation – a requisite of the testing methodology as noted above – is less efficient after 3 days of storage.

Implementation of non US-FDA cleared culture methods: Traditional culture using plated or broth media as well as commercially available automated blood culture systems other than BacT/ALERT can be used for platelet bacterial contamination testing but requires strict validation to ensure that the performance of the technique is as expected.[11, 65, 66] The validation plan should be developed by each institution or laboratory before routine testing can be in place. AABB Association Bulletins, published to supplement the required AABB Standard, provide guidance on acceptable validation methods.[31, 67] Published studies have documented these systems to reliably detect bacterial contamination of platelets.[65, 66] In many cases, the burden of the internal validation pro-

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cess is placed on the microbiology laboratory[68] and the cost of testing is passed on to the hospital. The legal risks of using a non-US-FDA-cleared detection system for quality control of platelets for which US-FDA cleared tests are available also need to be considered.

It is important to note that in emergency situations, as promulgated by the FDA any standard procedure may be bypassed if the clinical need is paramount. (see 21 Code of Federal Regulations 606.121(h) and www.fda.gov/ora/inspect_ref/igs/blood.html)

CHANGES IN REGULATIONS FOR PLATELET STORAGE

As discussed above, in 1984 the US-FDA extended the platelet storage from five to seven days based on the functional quality of the platelets. However, in response to an increasing number of reports of bacterial contamination episodes, the US-FDA reduced the storage time back to five days in 1986. Nevertheless, to comply with the new AABB and CAP recommendation for screening platelet products for bacterial contamination, the average time between collection and issuing the product has been increased and most SDP products are released three days after collection, making a difficult task for blood centers to satisfy the need for platelet products. In 2005, the US-FDA approved platelet bags made by Gambro BCT and Baxter for 7-day storage of SDP platelets provided that a US-FDA-cleared detection method is used,[15] and the US-FDA-approved protocol, the PASSPORT Study (www.passportstudy.com) is followed. The extended storage time would improve detection and confirmation of positive results before units have been used, and could limit the wastage of units.

SDP VERSUS RDP UNITS

Although several reports have demonstrated a reduced incidence of transfusion-associated platelet bacterial contamination with the use of SDP platelets compared with pooled RDP units,[11, 25, 36] the difficulty of maintaining a SDP platelet inventory has forced transfusion services to continue using pooled RDP units. However, if RPD units are screened for bacterial contamination with a sensitive method at the time of issue, the risk of transfusing a bacterially contaminated unit should be similar to that of SDP units. The obstacle in reaching that goal is that the US-FDA-approved methods for detection of bacterial contamination have been approved for quality control of SDP and, in some cases, RDP units, but not until recently (see below) for RDP pools, making approved systems prohibitively expensive to use on each RDP unit used to prepare a pool. Most hospital blood banks are therefore using methods such as pH or glucose determination, which have low sensitivity, but are rapid and easy to perform at the time of issue. The main reason that transfusion services and blood banks need to do the testing of RDP units is because the pooling of the units is done just before releasing the product for transfusion. This problem could be overcome by the allowance of early pooling along with screening for bacterial contamination with one of the methods already cleared by the US-FDA for SDP units.

Investigators have assessed the effectiveness of storing RDP platelets as a pool compared to SDP platelets and found that there is no detrimental effect of pooling RDP platelets as relates to platelet quality for products stored for up to 7 days.[69, 70] In February 2006, the US-FDA approved a platelet storage bag, the Pall Acrodose PL system, for the pooling of 4 to 6 ABO identical, leukocyte-reduced, RDP units shortly after collection and subsequent storage for up to 5 days after blood collection when coupled with a device cleared by US-FDA for detection of bacterial contamination in pooled, leukoreduced RDP units.[71]

Although some investigators have stated that the sensitivity of culture testing of pools may be insufficient to detect all contaminated products, and that manipulation of pools can also increase false positive results,[54] others have found pool testing to be reliable.[72-74] In addition, the use of both aerobic and anaerobic BacT/ALERT bottles may enhance the detection of contaminated units. This finding seems to be related to the volume of sample cultured rather than the isolation of strict anaerobic organisms.[74]

DETECTION METHODS UNDER DEVELOPMENT

Several detection methods suitable for use at the time of issue of platelet products are currently being developed, and include the following:

Detection of bacterial 16S ribosomal RNA with oligonucleotide probes. A chemiluminescence-linked universal bacterial rRNA probe for the detection of bacterial contamination in 0.4 mL aliquots of platelet concentrates detected the majority of samples containing 10^4 CFU/mL of *Bacillus cereus, P. aeruginosa, S. aureus* and *S. epidermidis*, and all samples with 2.1×10^5 CFU/mL or greater of these species.[75] Further development of this method is currently not being pursued.

Detection of conserved regions of bacterial 23S rRNA and a heat shock protein by real-time, reverse transcriptase PCR assay. Two real-time reverse transcriptase PCR (RT-PCR) assays performed in a LightCycler instrument were developed and compared regarding specificity and sensitivity by the use of different templates to detect the majority of the clinically important bacterial species in platelets.[76] Primers and probes specific for the conserved regions of the eubacterial 23S rRNA

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gene or the *groEL* gene (encoding the 60-kDa heat shock protein Hsp60) were designed. With r*Tth* DNA polymerase in a one-enzyme system, 500 CFU/mL of *Escherichia coli* or *Staphylococcus epidermidis* were detected. With a two-enzyme system consisting of Moloney murine leukemia virus RT and *Taq* DNA polymerase, 16 CFU/mL were detected. With *groEL* mRNA as the target of RT-PCR under optimized conditions, 125 CFU/mL of *E. coli* were detected. False-positive results caused by reagent contamination or a cross-reaction with human nucleic acids were found with the 23S rRNA, but not with the *groEL* gene detection systems.

BacSTAT Antibody-based lateral flow device for detection of bacteria. This system, being developed by GenPrime Inc., Spokane, WA, (www.genprime.com) is a broad-spectrum, antibody-based lateral flow device for detection of bacteria in SDP or RDP units, and uses a unique lateral-flow scanning system and a reader with pass/fail software.[77] The antibody targets used in this system are unique surface antigens. Specimen processing is simple, and total test time is less than 20 minutes. The expected sensitivity of this method is 10^3 to 10^4 CFU/mL.

Rapid Bioluminescent Bacterial Detection System using Luciferase. This method, which detects bacterial ATP by generation of light in the presence of bioluminescent luciferase firefly extract, is being developed by SUBC Inc., Rochester, Minnesota.[78] The method consists of removing platelets and cellular debris from 2-3 mL platelet concentrate samples, isolation and immobilization of any bacteria present in an isolation chamber, rinsing the isolation chamber with buffer, adding a lysing solution in combination with localized heat to rapidly lyse bacterial membranes and release bacterial ATP, adding bioluminescent firefly extract, and detecting generated light with a photon counter. The burst of light is then converted into a bacterial inoculum in CFU/mL. The sensitivity of this method is claimed to be 10^2 to 10^3 CFU/mL. A fully automated, microprocessor-driven instrument with an internal reagent cartridge, GloBac, has been developed for this application, and processing time is 4 min per specimen.

Bacterial lipotechoic acid and lipopolysaccharide detection by lateral flow immunoprecipitation. This test is being developed as the Verax Biomedical Platelet PGD Test by Verax Biomedical Inc., Worcester, MA (www.veraxbiomedical.com).[79] This system consists of test kits with a double-sided, lateral flow test cartridge and a central specimen well. Testing is performed by adding 8 drops of a platelet lysis reagent to 0.5 mL of a platelet sample, and centrifuging for 5 min to sediment any bacteria present. The supernatant is decanted off and 8 drops of a resuspension agent and 4 drops of a bacterial lysis reagent are then added, and the fluid is then added to the central well of the lateral flow test cartridge. The test cartridge contains antibodies to bacterial lipotechoic acid on one side and lipopolysaccharide on the other side to detect Gram-positive and –negative bacteria, respectively. A positive test is shown by the development of a pink precipitation line on one side. The system is designed for use with leukoreduced or non-leukoreduced RDPs, pooled RDPs and SDPs, with testing taking 30 min, with 2 to 3 minutes attended labor per test. The sensitivity of this method is claimed to be 10^3 to 10^4 CFU/mL.

Bacteriological Biosensor using engineered spores as fluorogenic nanodetectors. This system, being developed by BCR Diagnostics, Jamestown, Rhode Island (www.bcrbiotech.com), is able to detect and count low bacterial levels quantitatively in less than 20 minutes with a linear detection response over a range of one to 10,000 bacteria per sample.[80] The instrumentation cost is low and the system is suitable for automated high-throughput operations. A 0.5 mL platelet sample is processed to separate bacteria, and the resulting suspension is mixed with engineered bacterial spores. The mixture is then combined with a germinogenic substrate and then filtered through a filter mounted on a biochip – the filter contains 80,000 micro-colanders, which are 20 μm in diameter and contain engineered biosensor bacterial spores. The presence of a bacterial aminopeptidase, present in all bacteria, in the platelet specimen triggers the biosensors on the spores, resulting in production of fluorescent light, which is detected by a camera. The expected sensitivity of this method is 10^3 CFU/mL.

Bacterial peptidoglycan chromogenic immunoassay. This method is being developed as BacTx by Immunetics, Inc., Boston, MA (www.immunetics.com) and consists of a test kit containing all needed reagents and a chromogenic reader.[81] The system has a turnaround time of less than one hour, a 1 mL sample volume, and premeasured vial reagent dispensers. The system detects bacterial peptidoglycan in Gram-positive and Gram-negative bacteria when a peptidoglycan binding protein triggers enzymatic conversion of a chromogenic substrate to a visible product with measurable absorbance. A 1 mL platelet sample is centrifuged for 10 min, the sediment incubated for 30 min with reagents, and absorbance is read on a reader. Assay sensitivity is claimed to be 10^3 to 10^4 CFU/mL.

CONCLUSIONS

Bacterial contamination of platelet units is the most prevalent infectious risk of blood products in the United States. In the last 3 years, a unified effort from professional and regulatory agencies has been committed to limiting bacterial contamination of platelet products. Strategies beginning with donor selection, collection guidelines, use of detection methods after collection and at time of issue have been developed in order to deal with this problem. Because of the multi-factorial etio-

logy of bacterial contamination and the heterogeneous growth and metabolic characteristics of the organisms involved, different strategies should be used in combination. Now that FDA-cleared methods and guidelines are available to meet the requirement that all platelet units be tested for bacterial contamination, it is hoped that data will continue to be collected and new strategies will be developed to reduce the occurrence and the fatalities associated with bacterial contamination of platelets. Several promising methods for at-issue testing are being developed and will hopefully obtain regulatory approval soon.

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ORIGINAL PAPER

Diversion of first blood volume results in a reduction of bacterial contamination for whole-blood collections

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Vox Sanguinis

Background and Objectives In a previous study we established a reliable setpoint for the prevalence of bacteria in whole blood. In the present study we investigated the possible preventive effect, of diversion of the first 10 ml of a blood donation, on the bacterial contamination rate.

Materials and Methods To divert the first 10 ml of a whole-blood donation, we used a special five-bag system equipped with a Composampler® device. After venepuncture, the first 10 ml of a donation was sampled into a vacutainer tube. This was followed by the collection of the whole-blood unit. The extra bag allowed direct sampling of the final donation in a closed system for BacT/Alert. Whole-blood samples were taken after storage (2–14 h at 20 °C) and subsequent mixing. BacT/Alert culture bottles were incubated until positive, or for 7 days if negative. Confirmation and identification of positive cultures was performed according to internationally recognized standard reference methods.

Results The prevalence of bacteria in whole blood, as determined by using standard collection techniques, was 0·35% (95% confidence interval 0·27–0·44%, n = 18 257). After diversion of the first 10 ml this value was significantly lower: 0·21% ($P < 0·05$, 95% confidence interval 0·12–0·35%, n = 7087). Most strikingly, a reduction in the frequency of staphylococcal species was observed ($P < 0·02$, reduction from 0·14 to 0·03%).

Conclusions Diversion of the first 10 ml of blood was shown to contribute significantly to a reduction in the prevalence of superficial skin bacteria in whole-blood units. In our opinion, blood collection systems should be adapted to use the first 10–30 ml of a whole-blood donation for testing purposes.

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Key words: bacteria, collection, diversion, reduction, whole blood.

Introduction

Since the implementation of programmes for reducing the contamination of the blood supply by blood-borne viruses, transfusion-transmitted bacterial infections (TTBI) have become one of the major hazards of blood transfusion. Sazama [1] estimated that 10% of blood transfusion-associated deaths are caused by bacterial contamination of the transfused product.

In the last decade, increased attention has been given to the prevention of possible systematic contamination during the collection (i.e. by disinfection) and preparation stages (i.e. closed systems, by the use of sterile-docking devices, etc.) of blood components. Reliable data on the frequency of bacterial contamination of donated whole blood, used for component preparation, is needed in order to validate the occurrence of systemic contamination, or to evaluate measures taken to decrease contamination. Recently, we showed that 0·34% of whole blood units were contaminated with bacteria [2]. That

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study compromised a number of units tested, resulting in a narrow 95% confidence interval (CI) of 0·27–0·44%.

Because the majority of bacteria involved in TTBI are skin organisms, it is probable that contamination is introduced during venepuncture. Investigators have speculated that a skin-plug is punched out by the needle during phlebotomy [3,4]. Therefore, one of the suggested measures to reduce the bacterial contamination of whole-blood collections is diversion of the first volume of whole blood collected [4]. Olthuis *et al.* [5] were the first to show that for apheresis collections, the first 10 ml had a higher rate of bacterial contamination than the next two aliquots of 10 ml. Recently, Wagner *et al.* [6] showed the effectiveness of the diversion approach in an *in vitro* model system. Bruneau *et al.* [7] showed that the first aliquot (15-ml) of whole blood collected has a higher contamination rate than the second aliquot, without testing the final whole-blood unit collected.

We investigated, under routine blood bank conditions, whether diversion of the first 8–10 ml of whole blood from the primary collection container reduced the degree of bacterial contamination in the final whole-blood collection.

Materials and methods

Blood collection

Whole blood (500 ± 50 ml) was collected under standardized blood bank conditions in four-bag Compoflex CPD/SAGM systems (Fresenius Hemocare, NPBI International, Emmer-Compascuum, the Netherlands), with an additional fifth bag. These blood-collection systems were designed and validated [2] for use in this particular study (see Fig. 1). They allow both diversion of the whole blood (by Composampler) and sampling in a closed system, with the only aseptic handling being the transfer (in a laminar airflow cabinet) of a sample from the final donation to anaerobic and aerobic culture bottles (BacT/Alert; Organon Teknika, Boxtel, the Netherlands).

At all different collection sites of the De Meierij and CLB Sanquin Blood Banks, standardized methods for disinfection (double-swab method with isopropyl alcohol swabs), blood collection and storage were used. After venepuncture, an EDTA-vacutainer tube (nominal volume 10 ml; Becton-Dickinson, Franklin Lakes, NJ) was filled via the Composampler device (the mean collected volume was 9·8 ml with ≈ 1 ml of anticoagulant derived from the tube between the needle and the Composampler), followed by filling of the primary collection bag utilizing a clamp on the line before the Composampler. The only difference between the Blood Banks was the storage time on butane-diol cooling plates [8] (Fresenius Hemocare/NPBI International) between collection and sampling for BacT/Alert (2–3 h in Group A; De Meierij Blood Bank, and overnight in Group B; CLB Blood Bank). Butane-diol cooling plates were used to rapidly cool down the blood to 20 °C (within 2 h) and to hold the blood at this temperature during subsequent storage [8].

Automated microbe-detection system

Sampling was performed as described previously [2]. Both aerobic and anaerobic culture bottles were inoculated with a 10-ml sample of whole blood under aseptic conditions in a laminar airflow cabinet, using the integrated sampling

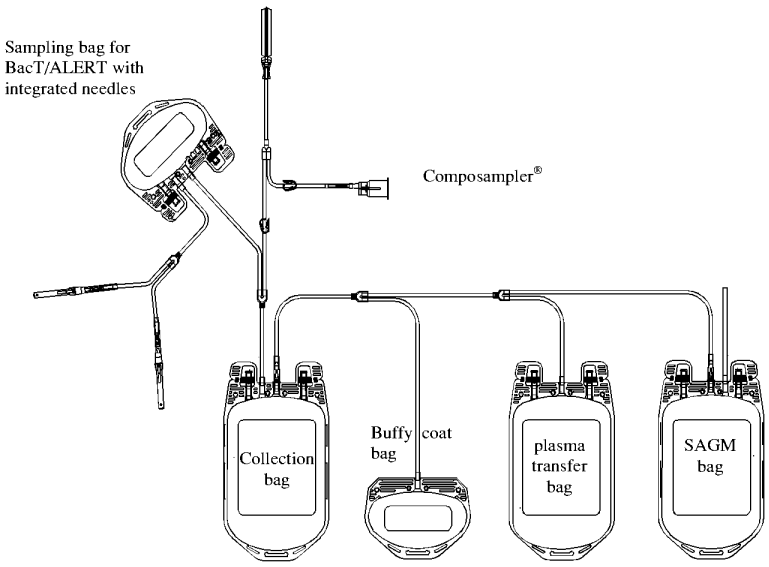


Fig. 1 Special five-bag Compoflex® blood-collection system, consisting of a conventional four-bag system with an additional BacT/ALERT sampling bag (the fifth bag) containing integrated transfer needles and equipped with a Composampler® to allow vacutainer sampling.

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needle of the extra sampling bag. Culture bottles were incubated at 35 °C in the BacT/Alert® system (an automated microbial detection system, based on the colorimetric detection of CO_2 [9]) until flagged positive, or for 7 days if negative. Subculture and identification of positive flagged bottles was performed as described previously [2].

Statistical analysis

Statistical analysis was performed using the computer program INSTAT 2·03 (GraphPad Software, San Diego, CA). The difference in proportions between the two groups was analysed using a one-sided χ^2-test (one-sided because of the hypothesis that diversion would lower the contamination rate). *P*-values of < 0·05 were considered significant. Confidence intervals (CI) were calculated according to Fleiss [10].

Results

Degree of bacterial contamination

In group A (sampling within 3 h after collection of whole blood), a total of 3405 units was collected and tested by using the BacT/ALERT® system. Out of these 3405 units, seven were culture positive, i.e. 0·21% (95% CI: 0·09–0·44%). In group B (sampling after overnight storage) in total 3682 units were collected and tested. In this group eight units were culture positive, i.e. 0·22% (95% CI: 0·10–0·45%). No significant difference was found between the two test groups (χ^2-test, $P = 0·48$). Combining these results, in total 7087 units of whole blood were tested (Table 1), with a bacterial contamination rate of 0·21% (95% CI: 0·12–0·35%). Using our standard collection method without diversion of the first 10 ml of sample, the prevalence was 0·35% (18 257 units tested [2]), which is significantly different (χ^2-test, one-sided because of the hypothesis that diversion would reduce the contamination rate; $P = 0·044$). Except for the diversion step, the collection procedures were similar for both studies. Furthermore, the distribution over the year of the collections for both studies was similar (to avoid seasonal effects).

Table 1 Summarized results of both studies

	Diversion of the first 10 ml	Standard, whole-blood collections [2]
Donations tested	*n* = 7087	*n* = 18 257
Positive cultures	*n* = 15	*n* = 63
Contamination rate[a]	0·21%	0·35%
95% CI of rate[b]	0·12–0·35%	0·27–0·44%

[a]Significant difference, $P < 0·05$ (χ^2-test; one-sided).
[b]Difference between the rates, (95% CI): 0·133 (–0·02 to 0·29).

Table 2 Differentiation of positive samples

	Diversion of the first 10 ml	Standard, whole-blood collections [2]
Resident skin flora		
Staphylococcus[a,b]	2 (0·03)	25 (0·14)
Propionibacterium[c]	10 (0·14)	27 (0·15)
Micrococcus	0	1 (0·01)
Diphteroids, *Corynebacterium* spp	0	5 (0·03)
Transient skin flora		
Bacillus	0	3 (0·02)
Gemella morbillorum	1 (0·01)	0
Klebsiella pneumoniae	1 (0·01)	0
(Upper) Gastrointestinal flora		
Streptococcus bovis	1 (0·01)	0
Peptostreptococcus	0	1 (0·01)
Not identified[d]	0	1 (0·01)

Values are expressed as absolute numbers per series (% prevalence).
[a]Coagulase-negative isolates, i.e. no occurrence of *Staphylococcus aureus*. Isolates were mainly *Staphylococcus epidermidis*.
[b]Significant difference, $P = 0·015$.
[c]Mainly *Propionibacterium acnes*.
[d]Growth curve in the BacT/ALERT was suggestive for *Propionibacterium*.
Resident skin flora: bacteria normally living on the skin. Transient skin flora: bacteria normally present in the air, but transient on skin. Gastrointestinal flora: bacteria normally present in the (upper) gastrointestinal system.

Identification of positive samples

Table 2 shows the bacterial species isolated from the subcultures derived from the BacT/ALERT® bottles that were flagged as positive. When the first 10 ml of blood was diverted, the majority of bacteria cultured were *Propionibacterium* spp, i.e. common skin flora. One isolate of *Streptococcus bovis* was found; this bacterial species is not normally part of the resident skin flora and therefore may have been transient skin flora that was not removed during the pre-bleed hygiene procedures. An examination of the donor from whom an isolate of *Klebsiella pneumoniae* was recovered revealed that the donor had no clinical signs of infection, and no blood products from this donation were used for transfusion. Culture results from both the red cell concentrate and the plasma from this donation were negative. Six months later a whole-blood sample from this donor was found to be culture negative.

The rate of contamination with *Staphylococcus* spp was significantly lower in the series tested after diversion of the first 10 ml of the blood donation ($P = 0·015$), whereas the contamination rate for *Propionibacterium* spp was similar (Table 2). Contamination rates for diphteroids and *Bacillus* spp were lower after diversion of the first 10 ml of the blood donation, but not significantly so.

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Discussion

In this study, under routine blood bank conditions diversion of the first 10 ml of whole blood was shown to significantly reduce the rates of bacterial contamination of final whole-blood units. Although previous studies by Wagner *et al.* [6] (using an *in vitro* model system) and Bruneau *et al.* [7] (with culture of diverted samples), strongly suggested that diversion of an initial blood sample would be effective in reducing skin contaminants in the collected unit, our study is the first to prove this for whole-blood collections.

A rather unexpected finding was the specific reduction of contamination with *Staphylococcus* spp upon diversion of the first 10 ml of sample, whereas contamination with *Propionibacterium* spp was similar, regardless of whether or not the first 10 ml of sample was diverted. A possible explanation for this might be that venepuncture, rather than coring skin plugs (which are transferred into the diverted volume, and include both superficial and intrinsic bacteria), results in skin flaps that do not become transferred into the diverted volume. Superficial skin bacteria such as *Staphylococcus* spp might be rinsed from the skin flaps by the initial diverted volume, whereas bacteria such as *Propionibacterium* spp (which colonize the deeper skin layer, the sebaceous glands and hair roots) are eluted from the flap during prolonged flow and thus are still able to enter the collected unit.

Compared to *Staphylococcus* spp, *Propionibacterium* spp are slow growing, yielding a positive signal in the BacT/Alert between 5 and 6 days after culture. Because culture in the BacT/Alert is carried out under optimal conditions with respect to medium composition and temperature, it is probable that *Propionibacterium* will rarely reach critical levels in platelet concentrates during the standard storage time of 5 days. Based on the findings of the present study, the effect of diversion on the actual frequency of (stored) erythrocyte and platelet concentrates containing sufficient bacteria to cause health problems might be greater than expected.

It is unknown whether the origin of the *Strep. bovis* and *K. pneumoniae* contaminants was the upper gastrointestinal tract of the donor, as these bacteria can easily be part of transient skin flora not removed from either the donor or phlebotomist during the pre-bleed hygiene procedures.

To prevent waste of collected whole blood, the initial diverted volume could be used for test purposes and, based on the results of Wagner *et al.* [6] and Bruneau *et al.* [7], a volume larger than 10 ml (current tests need ≈ 25 ml) could only be beneficial in terms of the final contamination rate. However, our diversion system cannot easily be used to fill several tubes without affecting the integrity of the closed system, because the Composampler membrane is no longer intact after its first use. Therefore, as long as clotting of the test sample is prevented, the collection system used by Bruneau *et al.* [7] might be an alternative.

Using whole blood as a source material for platelet components, the theoretical prevalence of bacteria in pooled platelet concentrates, composed of five single-donor units, would still be considerable (≈ 1%), despite the reduced contamination rate of whole blood. Therefore, in addition to diversion of the first volume during blood collection, all platelet concentrates should be tested for bacterial contamination in order to increase the safety of the blood supply.

In conclusion, the rate of bacterial contaminants in whole-blood units could be reduced by diversion of the first 8–10 ml of collected volume, especially with respect to contamination with *Staphylococcus* spp, commonly considered to be superficial skin flora.

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Bacterial Contamination of Blood Components

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INTRODUCTION

Allogeneic blood for transfusion is a potential source of infection by a variety of known and unknown transmissible agents. Since the 1980s, with the recognition of human immunodeficiency virus contamination of the blood supply, only a blood supply with a zero risk to recipients has been politically acceptable (67). This approach has led to the concept of "creeping precautionism" in the blood supply (46). The precautionary principle has grown out of the environmental movement. Briefly, it states ". . .where there are threats of serious or irreversible damage to the environment, lack of full scientific certainty should not be used as a reason for postponing cost-effective measures to prevent environmental degradation. . ." (46). To this end, astounding reductions in the viral risk of allogeneic blood has been accomplished (27). However, a number of transfusion safety measures have been implemented to achieve this level of safety, despite relatively poor cost-effectiveness, in order to assuage the public's fears (32).

Given the reduction of viral transmission via allogeneic blood, the low but known risk of bacterial contamination has emerged as the greatest residual threat of transfusion-transmitted disease (Fig. 1).

TRANSFUSION-TRANSMITTED BACTERIAL INFECTION OF RED CELLS

Each year, approximately 13,898,000 units of red cells or whole blood are transfused in the United States alone (1). This equates to one unit being transfused every 2.3 s. Despite this large number, sepsis associated with the transfusion of bacterially contaminated red cell blood components is generally regarded as a very rare event. From 1976 through September 1998, 26 fatalities thought to be secondary to contaminated whole blood or red cells were reported to the U.S. Food and Drug Administration (FDA) (36). Thus, approximately one red cell-related death per year has been reported. The majority of deaths reported to the FDA involved *Yersinia enterocolitica*. The highest reported incidence of *Y. enterocolitica* contamination was reported in New Zealand, with an incidence rate of 1 in

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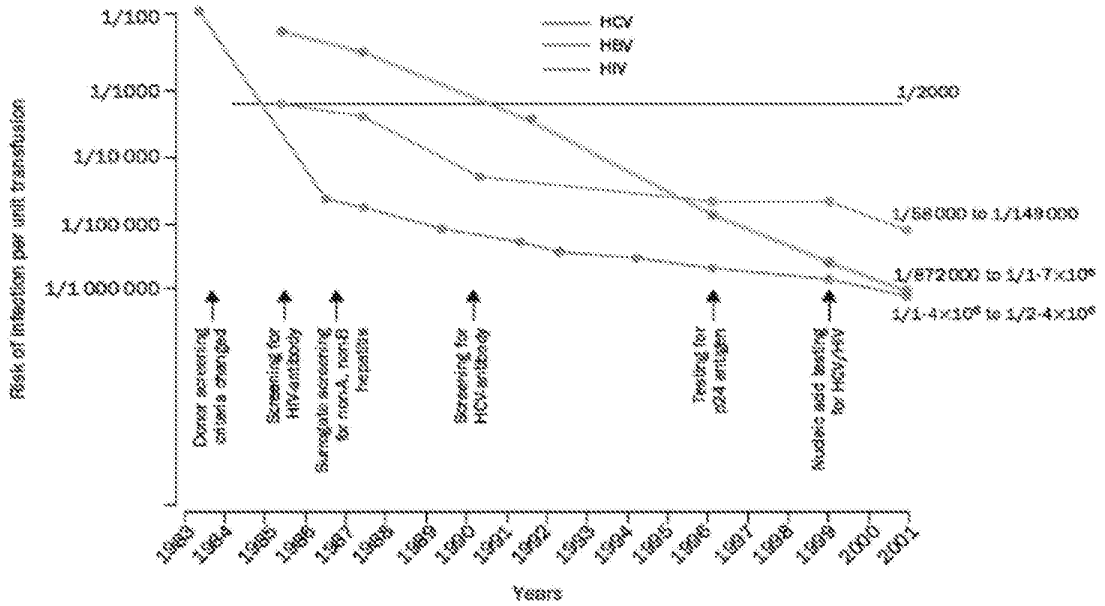


FIG. 1. Risk of infectious disease transmission per unit transfused by year, 1983 to 2001. Reprinted from reference 27 with permission of the publisher.

65,000 and a fatality rate of 1 in 104,000 red cell units transfused (59). Unrecognized cases, underreporting, and regional variation may account for observed differences in this incidence.

Interestingly, more recent passive reporting studies of bacterially contaminated red cells from the United States, France, and the United Kingdom that caused symptoms of infection show a relative paucity of *Yersinia* cases (Table 1) (35, 51, 57). Of the reported deaths, one was due to a coagulase-negative

TABLE 1. Organisms isolated from red cells implicated in transfusion-associated infections[a]

Organism	No. of contaminated units in:			Total no.
	United States	United Kingdom	France (29 isolates, 25 implicated units)	
Gram positive				
Coagulase-negative staphylococci	2 (1)	2	3	7 (1)
Streptococcus spp.			4[d]	4
Staphylococcus aureus			2[b]	2
Enterococcus faecalis			1[c]	1
Bacillus cereus			2	2
Propionibacterium acnes			1	1
Subtotal	2 (1 or 50%)	2 (0 or 0%)	13 (0 or 0%)	17 (1 or 6%)
Gram negative				
Serratia liquifaciens	2 (2)	1	2 (1)	5 (3)
Serratia marcescens	1			1
Yersinia enterocolitica		1 (1)	1	2 (1)
Enterobacter spp.			1 (1)	1 (1)
Acinetobacter spp.			5 (1)[b]	5 (1)
Pseudomonas spp.			2 (1)	2 (1)
Escherichia coli			3[c]	3
Klebsiella pneumoniae			1	1
Proteus mirabilis			1	1
Subtotal	3 (2 or 67%)	2 (1 or 50%)	16 (4 or 25%)	21 (7 or 33%)
Total	5 (3 or 60%)	4 (1 or 25%)	29 (4 or 14%)	38 (8 or 21%)

[a] Summary of organisms identified in the BACON, SHOT, and BACTHEM studies (35, 51, 57). Numbers and percentages of fatalities are given in parentheses.
[b] In one case, *S. aureus* and *A. baumannii* were both isolated from the implicated bag.
[c] In one case, *E. faecalis* and *E. coli* were both isolated from the implicated bag.
[d] In two cases, two isolates of *Streptococcus* were isolated from the implicated bag. Of the eight reported fatalities, seven (87.5%) were due to gram-negative organisms.

TABLE 2. Organisms implicated in infections associated with platelet transfusions[a]

Organism	No. of contaminated units in:			Total no.
	United States	United Kingdom	France	
Gram positive				
Bacillus cereus	1	4 (1)	2	7 (1)
Coagulase-negative staphylococci	9	6 (1)	5	20 (1)
Streptococcus spp.	3 (1)	2		5 (1)
Staphylococcus aureus	4	2 (1)		6 (1)
Propionibacterium acnes			3	3
Subtotal	17 (1 or 6%)	14 (3 or 21%)	10 (0 or 0%)	41 (4 or 10%)
Gram negative				
Klebsiella spp.			2 (1)	2 (1)
Serratia spp.	2 (2)		1 (1)	3 (3)
Escherichia coli	5 (1)	2 (1)	1	8 (2)
Acinetobacter spp.			1	1
Enterobacter spp.	2 (1)	1 (1)	1	4 (2)
Providencia rettgeri	1 (1)			1 (1)
Yersinia enterocolitica	1			1
Subtotal	11 (5 or 45%)	3 (2 or 67%)	6 (2 or 33%)	20 (9 or 45%)
Total	28 (6 or 21%)	17 (5 or 29%)	16 (2 or 13%)	58 (11 or 19%)

[a] Summary of organisms identified in the BACON, SHOT, and BACTHEM studies (35, 51, 57). Numbers and percentages of fatalities are given in parentheses.

Staphylococcus strain and seven were due to a variety of gram-negative organisms (including *Serratia liquefaciens* in three cases). These organisms are all capable of growth at 1 to 6°C. Sepsis associated with the transfusion of red cells contaminated with gram-negative bacteria is typically severe and rapid in onset. Patients frequently develop high fever (temperatures as high as 109°F have been observed) and chills during or immediately following transfusion. From 1987 to February 1996, 20 recipients of *Yersinia*-infected red cells were reported to the Centers for Disease Control (S. T. Cookson, M. J. Arduino, S. M. Aguero, W. R. Jarvis, and the *Yersinia* Study Group, Program Abstr. 36th Intersci. Conf. Antimicrob. Agents Chemother., abstr. 237, 1996). Twelve of the 20 recipients died, and the median time to death was only 25 h. Of the seven who developed disseminated intravascular coagulopathy, six died.

Prospective bacterial cultures of whole blood or red cells, however, have shown a much higher incidence of bacterial contamination (2 to 4 per 1,000 units); however, the organisms commonly cultured are *Staphylococcus* or *Propionibacterium* spp., which generally proliferate poorly during storage at 1 to 6°C (4).

TRANSFUSION-TRANSMITTED BACTERIAL INFECTION OF PLATELETS

Each year, within the United States approximately 4 million platelet units are transfused (1×10^6 single-donor apheresis platelets and 3 million whole-blood-derived platelet concentrates) (1). This equates to one platelet unit being transfused every 8 s. Unlike red cell or whole-blood components, which are stored at 1 to 6°C, platelets are stored at 20 to 24°C to preserve function and survival. Such storage makes them an excellent growth medium for a broad spectrum of bacteria. Multiple aerobic-culture surveillance studies have demonstrated that 1 in 1,000 to 2,000 platelet units are bacterially contaminated (4). Thus, 2,000 to 4,000 bacterially contaminated units would be expected to be transfused per year. Estimates of the fraction of cases that result in patient symptoms have been as low as 1 in 10 cases. However, in the only study that has prospectively cultured platelets that were transfused, eight culture-positive but Gram stain-negative platelet pools that were bacterially contaminated resulted in symptoms in three patients (37.5%) [A. Dykstra, G. Hoeltge, M. Jacobs, J. Miller, R. Domen, and R. Yomtovian, Transfusion 38(Suppl.): 104S, 1998]. Notably, six Gram stain-positive pools (which would be expected to have had the highest bacterial load) were interdicted and never transfused.

Thus, clinical sepsis would be expected in at least 1 in 10 to 2 in 5 contaminated transfusions (200 to 1,600 cases). National passive-reporting studies from the United States, the United Kingdom, and France (Table 2) suggest that one-fifth to one-third would result in death (40 to 533 deaths per year) (35, 51, 57). This translates to a risk of death from a transfusion of a bacterially contaminated platelet unit of between 1 in 7,500 and 1 in 100,000. Clinical observations from university hospitals actively pursuing suspected cases of platelet-related sepsis confirm these estimates. Ness et al. from Johns Hopkins University, reported a fatality rate of 1 in 17,000 with pooled whole-blood-derived platelets and 1:61,000 with single-donor-apheresis-derived platelets (48). Similarly, University Hospitals of Cleveland observed a fatality rate of 1 in 48,000 per random platelet unit (21). The French BACTHEM study documented a fatality rate due to bacterially contaminated platelets of 7 per 10^6 (1 in 140,000) (51).

From 1976 through September 1998, 51 fatalities thought to be secondary to contaminated platelets were reported to the U.S. FDA (36). Gram-negative organisms accounted for the majority of deaths (59.7%). Similarly, passive surveillance studies from the United Kingdom, the United States, and France show that gram-positive organisms were implicated in 41 (71%) of 58 of cases but gram-negative organisms (mostly members of the *Enterobacteriaceae*) account for the majority (9 [82%] of 11) of the fatalities (Table 1) (35, 51, 57).

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Clinical Presentation

Clinical sequelae of the infusion of bacterially contaminated platelets are variable and may be acute or delayed (contributing to missed diagnoses). Ironically, the majority (85%) of platelets are transfused to patients in the medical oncology, hematology, pediatric hematology/oncology, and bone marrow transplantation settings, all typically immunosuppressed patients (61). A study of platelet transfusions in autologous bone marrow transplant patients found that 1 in 2,000 units of platelet concentrates associated with a febrile episode (within 24 h of transfusion) were linked to bacterially contaminated platelets (16). Of the 10 patients known to have received a bacterially contaminated unit, 4 experienced septic shock.

Because of the severity of the patient's underlying disease and the variability in presentation and timing, sepsis resulting from bacterially contaminated platelets may go unrecognized. For example, an outbreak of *Salmonella enterica* serovar Choleraesuis sepsis in seven patients was traced to one repeat platelet donor, subsequently found to have occult chronic osteomyelitis (52). One patient died, and two had long-term recurrences of *Salmonella* sepsis. The time to the onset of illness ranged from 5 to 12 days (mean, 8.6 days). In many cases, the platelet-related bacterial sepsis is discovered only in retrospect. Investigations of two *Serratia liquefaciens*-contaminated red cell units led to platelet products from the whole-blood donations and to the recognition of an associated septic death in one recipient and bacteremia in the other recipient (53).

TRANSFUSION-TRANSMITTED BACTERIAL INFECTION OF PLASMA AND CRYOPRECIPITATE

Cell-free products such as plasma and cryoprecipitate are stored frozen and thus are rarely associated with contamination. However, in some cases *Pseudomonas cepacia* and *P. aeruginosa* have been cultured from cryoprecipitate and plasma thawed in contaminated water baths.

SOURCES OF CONTAMINATION

Gram-positive skin commensals such as *Staphylococcus epidermidis* and *Bacillus cereus* are the organisms most often recovered from donated blood (and implicated in bacterial contamination of platelets). Such contamination is thought to occur principally during phlebotomy, as a result of incomplete disinfection and/or skin core removal (including skin appendages where the skin disinfectants may not penetrate) by the collection needle (25). These organisms typically do not grow at 1 to 6°C but survive and multiply readily at the platelet storage temperature of 20 to 24°C.

In the case of gram-negative bacterial contamination, asymptomatic donors with transient bacteremia are presumed to be responsible for most cases of contamination. For example, in the case of *Y. enterocolitica* contamination of red cells, implicated donors typically are found to have elevated antibody titers (immunoglobulin M or G) to *Y. enterocolitica*, implying a recent infection (38, 39, 60).

An outbreak of *Serratia marcescens* contamination of red cells in Denmark and Sweden (29, 30) was thought to involve the manufacturing process since the sterile bag sets were autoclaved and put in a clean but not sterile outer plastic package. It was thought that *S. marcescens* present in the dust in the factory contaminated the outside of the containers and that in the presence of moisture and a nutrient (the plasticizer diethylhexyl phthalate) the bacteria proliferated and gained entry into the bag (58).

In rare cases, unusual circumstances have been identified as the source of bacterial contamination. For example, a donor with a pet boa constrictor, who reported fever and bloody diarrhea treated with antibiotics 13 days prior to his donation, was linked to *Salmonella enterica* platelet sepsis in two patients (33). Scarring or dimpling of the venipuncture site (due to prior donations) can result in recessed pits that are difficult to adequately sterilize (3). A repeat single donor with a "dimpled" venipuncture site resulted in four cases of gram-positive bacterial platelet sepsis in recipients (3). Another unusual association was made between one donor in a platelet pool and the death of a leukemic recipient from septic shock. The contaminating organism was identified as *C. perfringens* and was thought to originate from a donor who had two young children and frequently changed their diapers (42). As stated above, an outbreak of *S. enterica* serovar Choleraesuis platelet sepsis in seven patients at the National Institutes of Health Clinical Center was traced to a repeat platelet donor with an occult osteomyelitis (52). However, in most cases the source of the bacterial contamination remains unidentified.

METHODS TO REDUCE THE RISK OF POST-TRANSFUSION SEPSIS

There are multiple strategies to reduce transfusion-related bacterial infection. The various approaches can be grouped into four major categories: avoidance, bacterial detection, bacterial elimination, and growth inhibition.

Avoidance

Donor screening. Screening of donors to detect a possible risk of infection or transient bacteremia (e.g., from recent dental procedures) is routinely performed. However, questioning about symptoms suggestive of infection are often problematic; for example, gastrointestinal symptoms have not been a specific predictor (13% of donors have had gastrointestinal symptoms in the previous 30 days) (28). Such questioning also lacked sensitivity, since only 13 of 20 donors associated with *Y. enterocolitica*-contaminated red blood cells recalled a history of gastrointestinal symptoms (38, 39, 60; Cookson et al., Prog. Abstr. 36th ICAAC, 1996).

Skin preparation. Skin disinfection reduces the skin bacterial load (65), but a sterile venipuncture cannot be guaranteed due to inaccessibility of organisms present in sebaceous glands and hair follicles; organisms present in skin fragments may be drawn into the component bag (25). Multiple studies have evaluated skin disinfection in the context of blood donation (25, 26, 43). A summary of the effectiveness of some of the more commonly used skin disinfection methods is given in Table 3 (43). In general, either iodine or povidone iodine are used. In donors with allergies to iodine, chlorhexidine or double isopropyl alcohol skin disinfection is employed. The differ-

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TABLE 3. Percentage and mean count of donors with bacteria after skin disinfection[a]

No. of CFU/plate	% of contaminated donors after disinfection with:			
	Povidone iodine × 2	IPA[b] and iodine	IPA × 2 (sponge)	IPA × 2 (swab)
0	39	79	0	29
≤10	57	93	69	50
≤100	75	100	86	68
≤1,000	96	100	97	89
Mean count	175	3	161	237

[a] Data are from reference 43.
[b] IPA, isopropyl alcohol.

ence noted in Table 3 for two different isopropyl alcohol scrubs was attributed to the abrasive nature of the sponge used in one of the preparations.

Diversion of the initial blood draw. Several studies have demonstrated the partial effectiveness of diverting the first 10 to 30 ml of blood from the initial collection. A study performed with 22,000 samples of donated blood by the Red Cross in The Netherlands, in which the first 10 ml of donor blood was diverted from the primary bag, showed that 16 of the first 5-ml aliquots were bacterially contaminated while only 2 of the second 5-ml aliquots were positive after culture (19). A second study in France showed that removal of the first 10 ml of donor blood was associated with a significant decrease in bacterial contamination (18,263 collections with 0.39% contamination compared with 7,115 collections with 0.21% contamination; $P < 0.05$) (12).

Such methods are most effective with respect to skin contaminants (12, 19). However, it has been said that "one should not be diverted by diversion," since most fatal cases of bacterial contamination involve gram-negative organisms and thus would not minimized by diversion. Interestingly, the addition of a diversion bag to whole-blood collections in the United States has been initially complicated by hemolysis with certain sample tubes (from Pall, East Hills, N.Y.) and dilution of the sample with anticoagulant (from Baxter, Round Lakes, Ill), requiring redesign of both diversion systems (data presented at the HHS Advisory Committee on Blood Safety and Availability, Washington, D.C.; http://www.hhs.gov/bloodsafety/pastmeetings.html#n).

Apheresis versus whole-blood-derived platelet concentrates. Therapeutic doses of platelets can be obtained from two sources. Platelets can be collected from a donor by the use of an automated cell separator (apheresis); such collections can yield one to three therapeutic doses. Alternatively, platelets can be obtained from whole-blood donations (whole blood platelet concentrates [WBPCs]); however, a therapeutic dose requires the pooling of four to six WBPCs. Current estimates suggest that 69% of all therapeutic doses of platelets transfused in the United States are apheresis derived (1). Usage varies considerably by country.

Since bacterial contamination may result from a contaminated venipuncture or an asymptomatic bacteremic donor, it would be expected that pooled platelet products would be associated with a higher risk of contamination than a single donor product. From 1986 to 1998, the incidence of septic events related to platelets at Johns Hopkins University Hospital decreased from 1 in 4,818 to 1 in 15,098 as the hospital went from transfusing 51.7% to 99.4% single-donor apheresis units (48). The overall clinical sepsis rate was approximately 1 in 2,500 for WBPC pools and 1 in 13,400 for single-donor apheresis transfusion. The related mortality rate was approximately 1 in 17,000 for WBPC pools and 1 in 61,000 for single-donor apheresis platelets. It was concluded that the use of single-donor apheresis platelets is a simple means of reducing septic platelet transfusion reactions. Similarly, the University Hospitals of Cleveland have monitored the contamination rates of both single-donor and whole-blood-derived concentrates [A. Dykstra, M. Jacobs, and R. Yomtovian, Transfusion **38**(Suppl.):104S, 1998]. The rate of bacterial contamination of apheresis-derived platelets was 1 in 2,184. While the rate for random-donor platelets was similar at 1 in 1,861, random-donor platelet concentrates in a pool of six units would be expected to result in a contamination rate of 1 in 310.

Bacterial Detection

Timing of detection. Culture studies performed both on red cell units and platelets have shown that culture on the day of collection invariably misses bacterially contaminated units that would possibly achieve dangerous levels of overgrowth during storage of the blood components [5a, 10; M. A. Blajchman, A. Ali, P. Lyn, L. Bardossy, and H. Richardson, Transfusion 7(Suppl.):7S, 1997]. This is in contrast to viral contamination of blood components, in which the virus or the immune response to the virus (antibodies) is detected from a sample obtained at the time of donation. Bacterial contamination of blood components generally requires time for the organisms to proliferate before being detectable in a small representative sample of the product. Therefore, knowledge of the growth characteristics of bacteria in blood components is essential before one considers implementation of a detection strategy (Fig. 2 and 3).

Growth characteristics of 165 platelet units inoculated (to 1 to 50 or 1,000 CFU/ml) within 1 day of collection with one of the following: *B. cereus*, *P. aeruginosa*, *K. pneumoniae*, *S. marcescens*, *S. aureus*, and *S. epidermidis* showed that after 1 day of storage all samples of *B. cereus*, *P. aeruginosa*, and *K. pneumoniae* had concentrations of ≥10 CFU/ml (the level of detection), while only 71.4 and 84.2% of the *S. marcescens* and *S. aureus* samples were at concentrations of ≥10 CFU/mL (10). By day 3 of storage, all units inoculated with *B. cereus*, *P. aeruginosa*, *K. pneumoniae*, *S. marcescens*, and *S. aureus* contained $\geq 10^5$ CFU/ml. Units contaminated with *S. epidermidis* showed slower and more varied growth.

Bacterial culture. Although there are a variety of automated and semi-automated systems, only two are FDA cleared for quality control of bacterial culture in platelets in the United States. The first is an automated liquid culture system (BacT/ALERT; bioMérieux, Durham, N.C.) that uses broth bottles with a colorimetric sensor which changes color as a consequence of increasing CO_2 produced by bacterial proliferation. The machine monitors both the rate of change of the colorimetric sensor and the absolute color change of the sensor. Generally, one aerobic (and in some cases one aerobic and one anaerobic) bottle is inoculated with 4 ml of the platelet product. This system is not completely closed, since a needle is used

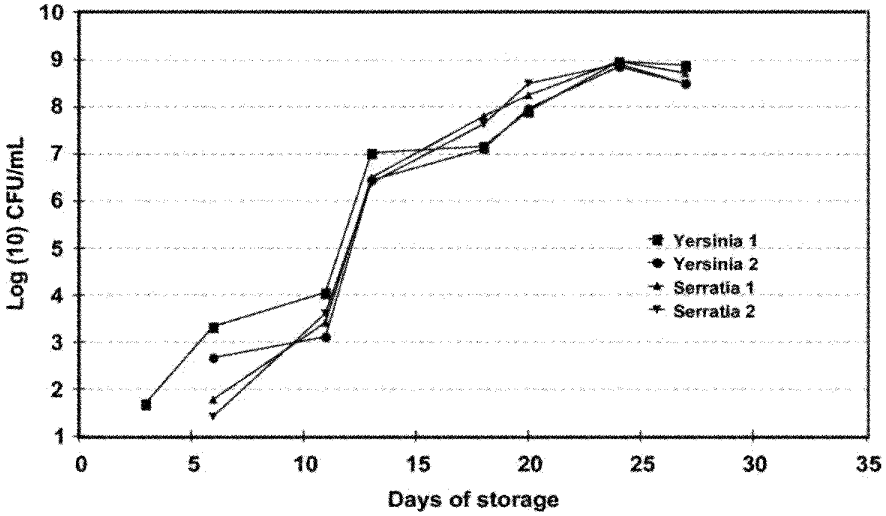


FIG. 2. Growth curves of four units of AS-3 red blood cells inoculated with *S. liqueifaciens* (two units inoculated to 4.2 CFU/ml) and *Y. enterocolitica* (two units inoculated to 11.6 CFU/ml) (5a). Bacteria were not detectable by culture until days 3 to 6. Isolates were from strains actually implicated in post-red-blood-cell-transfusion sepsis (the isolates were kindly provided by M. Arduino, Centers for Disease Control and Prevention, Atlanta, Ga.).

to inoculate the bottles. It has been extensively validated by tests with a wide range of potentially contaminating organisms (7, 8, 11, 44). The method reliably detects contamination of platelets inoculated to 10 CFU/ml and in many cases to ≤5 CFU/ml (e.g., *B. cereus*, *S. marcescens*, *C. perfringens*, *S. epidermidis*, *S. pyogenes*, *E. coli*, *K. pneumoniae*, *S. aureus*, and viridans streptococci) in 12 to 26 h. *Propionibacterium acnes* (which is of questionable clinical significance in this setting) required longer incubations. Recently, our laboratory completed an 11-month pilot program in which we cultured 2,397 apheresis-derived platelets on day 2 of storage (collection day = day 0) and again at the time of issue (or following outdate: days 6 to 8) (6). This study involved the inoculation of 9,588 bottles; one "machine" false-positive bottle (negative subculture, Gram stain, and repeat culture), and one inadvertent contamination false-positive bottle (*Propionibacterium* sp.) were detected. Thus, the overall false-positive rate was 2 in 4,794 samplings (0.04%, or 1 in 2,397 samplings) or 2 in 9,588 bottles (0.02% or 1 in 4,794 bottles). During this period, we successfully interdicted three apheresis-derived units (one collection) contaminated with *S. epidermidis* but were unable to prevent the transfusion of four apheresis units contaminated

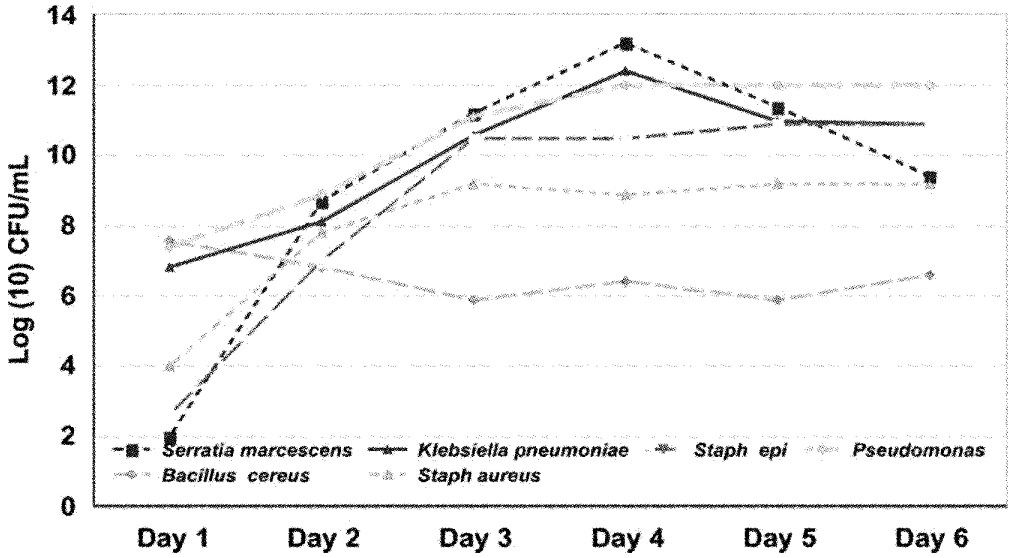


FIG. 3. Growth curves of six bacteria species (*S. marcescens*, $n = 7$; *K. pneumoniae*, $n = 21$; *S. epidermidis*, $n = 21$; *Pseudomonas* sp., $n = 15$; *B. cereus*, $n = 9$; *S. aureus*, $n = 22$) in 95 platelet units. All bacteria were inoculated on day zero at 10–50 CFU/ml (10).

TABLE 4. Summary of recent experiences with culturing of apheresis-derived platelets at three large blood centers[a]

Center	No. (rate) of results[b]		
	True positive	False positive	No. tested
New York Blood Center	5 (1/4,101)	5 (1/4,101)	20,506
Florida Blood Services	6 (1/1,790)	5 (1/2,147)	10,737
Puget Sound Blood Center	5 (1/1,800)	15 (1/600)	8,999
Total	16 (1/2,515)	25 (1/1,610)	40,242

[a] http://www.hhs.gov/bloodsafety/pastmeetings.html#n.
[b] True positive = positive bottles in which an organism was identified and a repeat sample from the bag or a retention sample also contained the same organism. False positive = positive bottles that contained no organism (machine false positive) or from which the organism could not be reisolated from the original bag or a retained sample.

with *Propionibacterium* sp., for which the culture bottles were reactive after 6 days of incubation. Thus, the overall true-positive rate was 7 of 2,397 apheresis units (0.29%), with a true-positive rate for aerobic organisms of 3 of 2,397 (0.13% or 1 of 799 units) and an anaerobic true-positive rate of 4 of 2,397 (0.17% or 1 of 599 units). Within our facility, transition from a research setting to a clinical microbiology laboratory has resulted in a higher false-positive (laboratory contamination) rate of 0.6% per unit (with one aerobic and one anaerobic bottle) (unpublished data). More recent experience from three large blood centers is included in Table 4.

The second culture system is the Pall Bacterial Detection System (BDS) (49). Sampling is obtained so as to maintain an effectively closed system. Approximately 5 to 6 ml of leukocyte-reduced platelet-rich plasma is removed from the bag and passed through a filter that removes residual white cells and platelets but allows approximately 50% of the bacteria (variable by organism) and plasma to pass into an incubation bag. The incubation bag holds 2 to 3 ml and contains sodium polyanethol sulfonate, which facilitates the growth of gram-negative organisms by inhibiting both complement and plasma lysosomal enzymes and by antagonizing the action of growth-retarding lipoproteins normally present in plasma. The incubation bag is then incubated at 35°C for at least 24 h before the oxygen concentration of the bag's headspace is measured with an oxygen analyzer. A decrease in the oxygen concentration to 19.5% or lower is an indication of bacterial growth. Thus, this system does not detect obligate anaerobic organisms. Leukocyte-reduced platelets challenged with 10 known platelet contaminants at doses of 100 to 500 CFU/ml were detected at a rate of 96.5% at 24 h and 100% at 30 h (49). External validation studies have shown lower than expected sensitivity for *S. epidermidis* and *S. agalactiae* [K.-A. T. Nguyen, T. Yamamoto, and N. Hirschler, Transfusion **43**(Suppl.):S63-030K, 2003; H. C. Pleasant, G. A. Geele, and M. P. Holub, Transfusion **43**(Suppl.):S62-030K, 2003 (abstract)]. Most recently, an enhanced version of this system has been cleared by the FDA, it includes modifications to the configuration (with removal of the filter, which removed some bacteria), and the incubation bag now contains a platelet-aggregating agent and tryptic soy medium to enhance the sensitivity and decrease the incubation time (http://www.pall.com/BDS.asp??noleftnav).

Less sensitive methods of detection such as Gram or Wright stains or the use of glucose and pH determination (in some case with multireagent strips) are used for rapid detection of bacteria in platelet components prior to transfusion. However, the overall sensitivity is only 10^6 to 10^7 CFU/ml (13, 62, 63, 66). Werch et al., from the M. D. Anderson Cancer Center, reported on the screening of 3,093 platelet concentrates, in which they found that multireagent strips for 30 bags had glucose levels or pH outside of the reference range (63). Two of these platelet units were culture positive for *B. cereus*. This screening method resulted in 1 unit per 110 being wasted but prevented two patients from receiving contaminated platelets.

Molecular biology techniques. Because of the high sensitivity and specificity and the rapidity of obtaining results, molecular biological approaches are theoretically appealing for the detection of contaminating organisms in blood components. One such approach is the use of a nonamplified chemiluminescence-linked universal bacterial rRNA probe (5, 9). This technique was shown to detect four bacterial species in the range of 10^4 to 10^5 CFU/ml. In some cases, *S. aureus* was detected at levels as low as 10^2 to 10^3 CFU/ml. Other investigators have pursued the use of PCR-based amplification for a limited number of organisms (56).

However, bacterial DNA contamination of nucleotide amplification reagents (particularly the bacterially derived enzymes) and laboratory materials and the presence of bacterial DNA sequences commonly found in human blood complicate the usefulness of universal bacterial amplification techniques (22, 45, 47). It also remains to be seen if complex molecular biology techniques could be successfully deployed to a wide range of transfusion services.

Detection systems recently approved in Europe. Recently, two bacterial detection systems were approved in Europe. The Scansystem (Hemosystem, Marseilles, France) involves a 70-min solid-phase laser cytometry. In a few studies, the Scansystem detected 11 organisms in the range of 10 to 10^3 CFU/ml [P. Morel, M. Deschaseaux, X. Bertrand, C. Naegelen, and D. Talon, Transfusion **43**(Suppl.):SP13, 2003]. Positive samples require a technologist to perform a microscopic confirmation.

A second "rapid" method recently approved detects bacteria by using dielectrophoresis (Cell Analysis, Slough, United Kingdom). Platelet concentrates inoculated with six organisms at concentrations of 10^3 to 10^5 CFU/ml were detected after 30 min of dielectrophoresis by image analysis as they were released from the electrodes when the electric field was discontinued [C. P. McDonald, R. Smith, J. Colvin, S. Robbins, J. Barbara, W. Betts, R. Anthony, K. Chan, A. Brown, and K. Gregory, Transfusion **41**(Suppl.):S119-040H, 2001].

Detection systems under development. Currently, there are at least three other rapid-detection systems under development. Genpoint (Oslo, Norway) has developed a unique system that uses paramagnetic particles to concentrate bacteria (BUGS'n BEADS) coupled with a PCR for highly conserved DNA. The target sensitivity of this assay is 1,000 CFU/ml, and the total time is 2.5 h. Immunetics, Inc. (Cambridge, Mass.) is developing a 96-well 1-h enzyme immunoassay which employs proteins and derived peptides that bind to the peptidoglycan component of the bacterial cell wall. Preliminary results suggest a sensitivity of 10^3 to 10^4 CFU/ml (or lower) for a variety of organisms [L. A. Beausang and A. Levin, Transfusion

43(Suppl.):20A, 2003; D. Kagan, and A. E. Levin, Transfusion 41(Suppl.):S118-040H, 2001]. Verax Biomedical (Worcester, Mass.) is developing an immunoassay embodied in a lateral-flow format. Preliminary results suggest a sensitivity of 10^3 to 10^4 CFU/ml for a variety of organisms [F. Kenny, C. Woodbury, M. Pelak, J. Weinberg, and J. A. Hall, Transfusion 43(Suppl.):10A, 2003].

Implementation of detection systems: problems and considerations. (i) Platelet concentrates and prestorage pooling. Bacterial detection of whole-blood-derived platelet concentrates presents logistical problems for systems that do not allow the prestorage pooling of platelet concentrates (e.g., United States, Canada, and Hong Kong). In Europe, whole-blood-derived buffy coat platelets are prepooled prior to storage; this allows for the culturing of platelets by the methods described above. If prepooling is not allowed, culturing of each individual platelet sample is generally not thought to be practical due to the loss of volume from each bag required per culture and the high cost of culture for each individual bag. In the absence of prepooling, many centers have chosen or are contemplating the use of less sensitive bacterial detection strategies such as Gram stains or glucose or pH measurement (or the use of multireagent strips) (2).

(ii) Anaerobic organisms. Anaerobic organisms such as *Propionibacterium* sp. can be identified in platelets; however, it is not known whether anaerobic organisms such as propionibacteria are clinically significant since growth in the aerobic environment of platelet storage is slow and not favorable. Although a few cases of *Propionibacterium*-contaminated units have been infused into patients, no long-term sequelae have been reported (6, 40, 55). Debate continues as to the value of an anaerobic culture in this context. It is worth noting that some aerobic organisms or isolates (e.g., viridans streptococci) can be more rapidly detected in an anaerobic culture system (7, 8, 11).

(iii) Potential for reduced shelf-life. Some centers have chosen to incubate platelet cultures for 12 to 24 h prior to release. This has in many cases led to a decrease in the available shelf-life of the platelets. Given that the current platelet products have a shelf-life of only 5 days (and that, for 1 to 2 days, such products are not available, pending completion of viral testing), any further reduction in available shelf-life can impact inventory control and hospital supply.

(iv) Use of noncleared detection systems. Use of non-FDA-cleared detection systems (e.g., alternative automated culture systems) would at a minimum require internal validation. Examples of validation of detection systems are available in the literature (7, 8, 11, 44, 49). Patent issues currently preclude certain companies from actively pursing this market. Use of a non-FDA-cleared device for bacterial quality control of platelets, when cleared devices are available, may place an institution at higher legal risk should a patient die after receiving bacterially contaminated platelets.

Bacterial Elimination

Pathogen reduction technologies. Continued efforts to create a "zero-risk" blood supply have led to various pathogen reduction technologies. A variety of photoactive sensitizers have been investigated for use in the reduction of viruses, bacteria, and parasites.

The best studied of these methods is the use of amotosalen HCL (S-59), a synthetic psoralen combined with a photochemical treatment process that causes permanent cross-links in DNA and RNA (INTERCEPT Platelet System; Baxter Healthcare Corp., Round Lake, Ill.) (41, 64). However, organisms capable of spore formation may be resistant to photochemical inactivation (34). The SPRINT trial, a multi-center phase III trial, has evaluated the hemostatic effectiveness of S-59 pathogen-inactivated platelets. Treated platelets were found to be as effective as conventional platelets for the prevention and treatment of bleeding; however, the treated platelets resulted in a lower post-transfusion platelet response, resulting in the need for 35% more platelets to support transfusion-dependent patients (18, 41). Concerns also remain regarding mutagenicity and teratogenicity associated with such technologies.

Growth Inhibition

The addition of antibiotics to blood components has been considered but has not been adopted due to the added risk of drug reactions (trading one infrequent reaction for another) and the potential for the development of antibiotic resistance if small amounts of antibiotics were infused with every transfusion (31).

THE PROSPECT OF SEVEN-DAY STORAGE WITH DETECTION

Currently, within the United States platelet storage is limited to 5 days due to the fear of bacterial overgrowth during storage at 20 to 24°C. In 1983, platelet storage in the United States was extended to 7 days; however, in 1986 the FDA shortened the outdate to 5 days following reports of bacterial sepsis with older units (65). With the prospect of bacterial detection, the possibility of an extended shelf-life is being reconsidered. European reports have described the use of bacterial culturing of platelets on days 1 to 3 of storage in order to extend the shelf-life of platelets to 7 days, thereby reducing the number of outdates [M. Ollgaard, I. Albjerg, and J. Georgen, Vox Sang. 74(Suppl. 1):1126, 1998; D. Vuetic, J. Taseki, B. Balint, and V. Mirovic, Vox Sang. 80(Suppl. 1):P371, 2000]. Within the United States, premarket multicenter studies (or possibly postmarket studies) are currently under discussion to provide data that may allow the extension of storage to 7 days. It would be expected that the cost of culturing would be mitigated by the savings obtained by the extension of platelet storage time (20). For example, in Denmark, when bacterial culture was implemented in 1997, it was anticipated to be cost neutral if the outdating could be reduced from 18 to 8% by extending the storage time to 7 days (24). The actual outdating rate decreased to 3 to 6%.

CONCLUSIONS

Regulatory oversight in the United States and Canada has generally concentrated on new emerging threats such as West Nile virus (leading to nationally mandated efforts to screen the

blood supply with West Nile virus nucleic acid testing). However, there is no similar mandate in these countries for bacterial screening. To place these risks into some perspective, in 2002 23 transfusion-transmitted cases of West Nile virus were identified in the United States (50). Of these 23 recipients, 7 died, but only 5 of these deaths were associated with West Nile virus meningoencephalitis. During the same period, 17 deaths from bacterial contamination of blood components were reported to the FDA (14). Contaminated apheresis-derived platelets and pooled platelets were the products most often implicated. Gram-negative bacteria were the causative agents in the majority of these fatalities. It is perplexing that similar (or greater) government emphasis has not been placed on the detection of bacteria.

In blood banking and transfusion medicine, our paramount concern is to improve transfusion safety for patients, in our attempt to achieve a zero-risk blood supply. Unlike other recent threats (existing or theoretical) to blood safety, the movement for reducing bacterial contamination has come from the blood-banking and the transfusion medicine community. In this case, voluntary accrediting agencies such as the American Association of Blood Banks and the College of American Pathologists have taken the lead by developing standards to reduce the risk of bacterial contamination of blood components (17, 23). Our patients deserve no less.

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The Clinical Significance of Positive Blood Cultures in the 1990s: A Prospective Comprehensive Evaluation of the Microbiology, Epidemiology, and Outcome of Bacteremia and Fungemia in Adults

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To assess changes since the mid-1970s, we reviewed 843 episodes of positive blood cultures in 707 patients with septicemia. The five most common pathogens were *Staphylococcus aureus, Escherichia coli,* coagulase-negative staphylococci (CNS), *Klebsiella pneumoniae,* and *Enterococcus* species. Although CNS were isolated most often, only 12.4% were clinically significant. Half of all episodes were nosocomial, and a quarter had no recognized source. Leading identifiable sources included intravenous catheters, the respiratory and genitourinary tracts, and intraabdominal foci. Septicemia-associated mortality was 17.5%. Patients who received appropriate antimicrobial therapy throughout the course of infection had the lowest mortality (13.3%). Multivariate analysis showed that age (relative risk [RR], 1.80), microorganism (RR, 2.27), source of infection (RR, 2.86), predisposing factors (RR, 1.98), blood pressure (RR, 2.29), body temperature (RR, 2.04), and therapy (RR, 2.72) independently influenced outcome. Bloodstream infections in the 1990s are notable for the increased importance of CNS as both contaminants and pathogens, the proportionate increase in fungi and decrease in anaerobes as pathogens, the emergence of *Mycobacterium avium* complex as an important cause of bacteremia in patients with advanced human immunodeficiency virus infection, and the reduction in mortality associated with infection.

The presence of living microorganisms in blood has substantial clinical importance. From the diagnostic standpoint, a positive blood culture yielding a clinically important microorganism represents either failure of host defenses to contain an infection at its primary focus or failure of the physician to effectively eradicate, drain, excise, or otherwise remove that focus of infection. The presence of bacteremia or fungemia also is an indicator of disseminated infection and, as such, generally indicates a poorer prognosis than that associated with localized disease. A positive blood culture, however, is not always clinically significant, since contamination may occur or the positive result might represent the transient and self-limited presence of microorganisms in the blood [1].

Our current understanding of the clinical significance of positive blood cultures has been enhanced by studies reported over several decades [2–21]. In recent years there have been many changes in medical practice, influenced in part by technologic advances and in part by the increased incidence of diseases not recognized previously. Just a few examples include the more frequent use of invasive or prosthetic devices; the increase in solid-organ and bone marrow transplantation as well as improvements in posttransplantation medical management; the introduction of HIV infection and AIDS as a scourge on late 20th century society; and therapeutic advances in the form of improved imaging techniques, less invasive methods of draining pus from closed spaces, and availability of broader spectrum antiinfective therapy.

We therefore undertook a comprehensive analysis of positive blood cultures in the 1990s. As a template for this project, we used an earlier review of bacteremia and fungemia [10, 11] authored by two of the current investigators (M.P.W. and L.B.R.). Although the earlier work has been widely recognized, the aforementioned changes in medicine and its practice argued for the need to reevaluate the clinical and prognostic importance of positive blood cultures. The primary goal of this study, therefore, was to determine the current microbiology, epidemiology, and prognostic importance of positive blood cultures, with special reference to similarities with and differences from the earlier reports from our group [10, 11, 22, 23].

Materials and Methods

For a 12-month period, February 1992 through January 1993, all inpatients ≥18 years of age with culture-positive blood

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were evaluated at Duke University Medical Center (DUMC), in Durham, NC; Robert Wood Johnson University Hospital (RWJUH), in New Brunswick, NJ; and the Salt Lake City Veterans Administration Medical Center (SLCVAMC), in Salt Lake City. Each patient was observed prospectively from the time the blood culture became positive, unless the patient had been discharged or had died before review of the hospital records by one of the investigators, in which case the review of the medical record was retrospective. Charts were evaluated according to the method of Feinstein et al. [24, 25], such that if the presence or absence of a particular finding was not clearly indicated, that case was excluded from analysis for that finding.

During the study period, 20 mL or more of blood was obtained for each culture and inoculated into media for processing on the BACTEC NR660 (Becton Dickinson Diagnostic Instrument Systems, Sparks, MD) or BacT/Alert (Organon Teknika, Durham, NC) blood culture system or both systems at all three centers. Blood was obtained at the bedside by house officers, medical students, or other trained health care personnel (nurses, phlebotomists, etc.) using 70% isopropyl alcohol and then 10% povidone-iodine. Although most of the blood culture specimens were obtained by peripheral venipuncture, it was not possible to determine specifically which ones were obtained in this manner and which were obtained through access devices.

Bottles were transported to the laboratory and incubated until flagged as positive or for 7 days in either BACTEC nonradiometric instruments (NR6 and NR7 bottles) or BacT/Alert continuous-monitoring instruments (BacT/Alert aerobic and anaerobic bottles). Broth from positive bottles was gram-stained and subcultured with use of standard techniques [26]. Susceptibility testing of isolates was done according to guidelines established by the National Committee on Clinical Laboratory Standards [27, 28].

All information obtained from patients' records was recorded on data worksheets and then transferred to a database software program for analysis.

Definitions

Definitions for this study for the most part were identical to those of Weinstein et al. [10, 11]. Only a few will be detailed here. New or modified definitions also will be detailed.

True septicemia vs. contamination. Each positive blood culture was assessed critically by one of the investigators, each an infectious disease physician. All isolates were categorized as true-positives, contaminants, or of unknown clinical significance. The categorical decision was made after the following factors were taken into account: the patient's clinical history, physical findings, body temperature at the time of the blood culture, leukocyte count and differential cell counts, number of positive blood cultures out of the total number performed, results of cultures of specimens from other sites, imaging results, histopathologic findings, and clinical course and response to therapy. If the clinical significance of the positive culture was not clear on the basis of the available information, the isolate was categorized as being of unknown significance.

Episode. An episode of bacteremia, fungemia, or mycobacteremia was defined by the first positive blood culture in a series or by any new positive blood culture result that occurred >48 hours after the previous positive result, unless it was clear to the investigator that the new positive culture was part of the same episode. For example, a positive blood culture for *Staphylococcus aureus* on the fifth day of antibiotic therapy for *S. aureus* endocarditis was considered part of the original bacteremic episode.

Community- vs. hospital-acquired septicemia. Each episode was classified as either community- or hospital-acquired septicemia, according to guidelines of the Centers for Disease Control and Prevention [29]. Septicemia in nursing home patients with positive blood cultures was always classified as hospital-acquired, whereas that in patients transferred from other outside facilities was classified according to their total period of hospitalization at both institutions.

Antimicrobial Therapy

Data on antimicrobial therapy were obtained at four chronologic points for each episode. These points were as follows: (1) at the time the first positive blood culture specimen was obtained, (2) after the blood culture was performed but before positive culture results were reported (i.e., empirical therapy), (3) after the blood culture was reported to be positive and gram-stained smear results were made known to the primary physician(s) but before organism identification and susceptibility test results were available, and (4) after organism identification and susceptibility test results were reported to the physicians.

Therapy was assessed critically at each time point on the basis of the clinical information available (time points 1–3) or the identification of the isolate and susceptibility test results (time point 4).

Treatment was judged to be the first choice if it was in accordance with the recommendations of a standard reference for antimicrobial therapy [30] and an alternative choice if the etiologic microorganism(s) was (were) susceptible to the agent administered but that agent was not considered the first choice. For purposes of judging the adequacy of therapy, both first-choice and alternative-choice agents were considered appropriate. Therapy was designated as the wrong choice if the causative microorganism was resistant to the antibiotic given. Superfluous therapy was defined as either the administration of unnecessary antibiotics in addition to a first- or alternative-choice agent or the administration of antibiotics for contaminant isolates. Ineffective or superfluous agents given for infections elsewhere in the body were recorded separately.

If a patient died before susceptibility results became available, that fact was recorded. When no therapy was given after the report of a positive blood culture to the physician, one of

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three assessments was made: (1) appropriate, if the isolate was a contaminant; (2) appropriate, if the episode was judged to represent true but transient bacteremia or fungemia that resolved spontaneously without adversely affecting the patient; or (3) inappropriate, if the culture represented true sepsis and the patient's status deteriorated because of the infection.

Outcome

The outcome of each episode was categorized as follows. The patient was (1) discharged alive, (2) alive but still hospitalized 30 days or longer after the onset of bacteremia or fungemia, (3) dead from causes attributable to the septicemic episode, or (4) dead from causes unrelated to septicemia. For the purposes of this study, mortality is termed associated or nonassociated in the subsequent text and tables.

Statistical Methods

For univariate analyses, statistical significance was calculated with the χ^2 test as described by O'Brien and Shampo [31]. The multivariate analysis and the resulting significance calculations were based on the logistic regression model [32], as implemented by the function "glm" in the statistical package S+ [33].

Results

During the study period, 1,585 blood culture–positive episodes occurred in 1,267 patients and yielded 1,844 microorganisms. Nine hundred forty-four microorganisms were isolated from 707 patients who had 843 episodes of true bacteremia or fungemia. There were 658 contaminant episodes and 84 episodes of unknown clinical significance.

Microbiological Features

The microorganisms isolated from positive blood cultures and the frequency with which they caused true bacteremia or fungemia are shown in table 1. The most common isolates from blood were coagulase-negative staphylococci. *S. aureus* was the microorganism most frequently causing true bacteremia; 87.2% of isolates were judged clinically significant. In contrast, only 12.4% of the coagulase-negative staphylococci were clinically significant, but they ranked as the third most frequent cause of bacteremia by virtue of their high prevalence.

Given the frequency with which coagulase-negative staphylococci were isolated from blood and the difficulty in determining their clinical significance, we analyzed *Staphylococcus epidermidis* isolates on the basis of the number of culture sets positive vs. the number of sets performed for each episode. The results are shown in table 2. When only a single culture set yielded *S. epidermidis,* the culture result almost always was judged to be of indeterminate significance or to represent contamination. When all of two or three culture sets yielded *S. epidermidis,* the isolates usually were judged clinically significant, but a substantial minority were of unknown (i.e., indeterminate) significance.

Whereas pneumococci always represented real infection, enterococcal isolates did so only 70% of the time, and viridans streptococci more often were contaminants (49%) than clinically significant isolates (38%) (table 1). Among the gram-negative aerobic and facultative bacteria, *Escherichia coli* was the most common isolate, and this microorganism was second only to *S. aureus* as a cause of septicemia. Overall, the Enterobacteriaceae and *Pseudomonas aeruginosa* represented true bacteremia >95% of the time when isolated.

Anaerobic bacteria were not common blood pathogens, accounting for only 3.9% of clinically important isolates. The isolation of a member of the *Bacteroides fragilis* group, however, almost always indicated true bacteremia (89%). *Clostridium perfringens* usually represented contamination when isolated from the blood, whereas the isolation of other *Clostridium* species usually represented true bacteremia.

Yeasts were relatively common isolates from blood cultures and almost always represented true fungemia when detected (91.7%). These organisms were present as clinically important pathogens almost twice as often as anaerobic bacteria, and *Candida albicans* ranked among the top 10 microorganisms causing septicemia. All mycobacteria and all but one *Cryptococcus neoformans* isolate were isolated from HIV-infected patients.

Of the 843 episodes of bacteremia and fungemia, 764 (90.6%) were unimicrobial and 79 (9.4%) were polymicrobial. Two microorganisms were isolated in 57 (72.2%) of the polymicrobial episodes, and ⩾3 microorganisms were isolated in 22 episodes (27.8%).

Epidemiological Features

Age and sex. Patients ranged in age from 17 to 103 years (mean, 56.2 years). Patients with HIV infection were younger (mean age, 36.9 years). Four hundred ninety of the episodes (58.1%) occurred in men. Ninety-nine percent of the episodes at the SLCVAMC, vs. 54% at both DUMC and RWJUH, were in men.

Community- vs. hospital-acquired infection. Of the 843 episodes, 404 (47.9%) were of community-acquired infection and 439 (52.1%) were of nosocomial infection. The microorganisms isolated in these episodes, categorized according to place of acquisition, are shown in table 3. Microorganisms more often associated with nosocomial acquisition were coagulase-negative staphylococci, enterococci, Enterobacteriaceae other than *E. coli, P. aeruginosa, Clostridium* species, *Bacteroides* species, and yeasts other than *C. neoformans.* A somewhat surprising finding was that nearly 40% of *P. aeruginosa* bacteremias were community-acquired.

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Table 1. Microorganisms isolated from blood of patients at Duke University Medical Center, Robert Wood Johnson University Hospital, and the Salt Lake City VA Medical Center, February 1992 through January 1993.

Microorganism (no. of isolates)	No. (%) of isolates per indicated category		
	True pathogen	Contaminant	Unknown
Aerobic and facultative bacteria			
Gram-positive			
Staphylococcus aureus (204)	178 (87.2)	13 (6.4)	13 (6.4)
Coagulase-negative staphylococci (703)	87 (12.4)	575 (81.9)	41 (5.8)
Enterococcus species (93)	65 (69.9)	15 (16.1)	13 (14.0)
Viridans streptococci (71)	27 (38.0)	35 (49.3)	9 (12.7)
Streptococcus pneumoniae (34)	34 (100)	0	0
Group A streptococci (3)	3 (100)	0	0
Group B streptococci (15)	10 (66.7)	3 (20.0)	2 (13.3)
Other streptococci (13)	8 (61.5)	3 (23.1)	2 (15.4)
Bacillus species (12)	1 (8.3)	11 (91.7)	0
Corynebacterium species (53)	1 (1.9)	51 (96.2)	1 (1.9)
Listeria monocytogenes (2)	1 (50.0)	0	1 (50.0)
Lactobacillus species (15)	6 (54.5)	2 (18.2)	3 (27.3)
Other gram-positive bacteria (15)	2 (13.3)	12 (80)	1 (6.7)
Gram-negative			
Escherichia coli (143)	142 (99.3)	0	1 (0.7)
Klebsiella pneumoniae (65)	65 (100)	0	0
Enterobacter cloacae (25)	25 (100)	0	0
Serratia marcescens (22)	22 (100)	0	0
Proteus mirabilis (16)	16 (100)	0	0
Other Enterobacteriaceae (45)	41 (91)	1 (2.2)	3 (6.7)
Pseudomonas aeruginosa (55)	53 (96.4)	1 (1.8)	1 (1.8)
Pseudomonas species (8)	6 (75)	0	2 (25)
Stenotrophomonas maltophilia (7)	5 (71.4)	0	2 (28.6)
Acinetobacter baumanii (16)	13 (81.2)	1 (6.2)	2 (12.5)
Haemophilus influenzae (3)	3 (100)	0	0
Other gram-negative bacteria (16)	10 (62.5)	3 (18.8)	3 (18.8)
Anaerobic bacteria			
Clostridium perfringens (13)	3 (23.1)	10 (76.9)	0
Clostridium species (15)	12 (80)	3 (20)	0
Propionibacterium species (48)	0	48 (100)	0
Other gram-positive anaerobic bacteria (7)	4 (57.1)	2 (28.6)	1 (14.3)
Bacteroides fragilis group (18)	16 (88.9)	0	2 (11.1)
Other gram-negative anaerobic bacteria (5)	2 (40)	2 (40)	1 (20)
Yeasts and fungi			
Candida albicans (30)	27 (90)	0	3 (10)
Other *Candida* species (15)	15 (100)	0	0
Cryptococcus neoformans (8)	8 (100)	0	0
Torulopsis glabrata (15)	14 (93.3)	0	1 (6.7)
Other yeasts and fungi (4)	2 (50)	1 (25)	1 (25)
Mycobacteria			
Mycobacterium avium complex (16)	16 (100)	0	0
M. tuberculosis (1)	1 (100)	0	0
All microorganisms (1,844)	944 (51.2)	791 (42.9)	109 (5.9)

Hospital service. Six hundred twenty of the 843 bacteremic and fungemic episodes (73.5%) occurred in patients hospitalized on the medical services of our institutions. Patients hospitalized on the nontransplantation surgical services accounted for 21.3% of total episodes, with the remaining 5.2% of episodes distributed among the transplantation surgery, obstetric and gynecologic services, and emergency and outpatient departments. Pneumococcal bacteremia, not surprisingly, was seen almost exclusively in patients on the medical service.

Proportionately, enterococcal and pseudomonas bacteremias were twofold more common on the general and transplantation surgical services than on the medical service. Indeed, *P. aeruginosa* accounted for only 4.4% of septicemias on the medical service. Fungemia was proportionately most common on the

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Table 2. Clinical significance of *Staphylococcus epidermidis* isolates (unimicrobial episodes only).

No. of culture sets		Clinical significance: no. (%) of isolates		
Positive	Performed	Significant	Contaminant	Indeterminate
1	1	0	33 (97.1)	1 (2.9)
1	2	3 (2.2)	129 (94.8)	4 (3.0)
2	2	18 (60.0)	1 (3.3)	11 (36.7)
1	3	0	2 (100)	0
2	3	3 (75.0)	0	1 (25)
3	3	4 (100)	0	0

transplantation surgical service, accounting for nearly 25% of septicemic episodes. Anaerobic bacteremia, which was uncommon in general, was seen most frequently in patients on the general surgery service (6.6% of episodes) and obstetric and gynecologic service (11.1% of episodes).

Sources of infection. The sources of bacteremia and fungemia were identifiable in 627 (74.4%) of episodes and are listed in table 4. Intravenous catheters were the most common primary foci for septicemia. Despite the availability of increasingly sophisticated imaging techniques, the sources for nearly one-fourth of episodes could not be determined.

The relationship between microorganism and sources of unimicrobial bacteremia and fungemia are presented in table 5, which also delineates those episodes confirmed by cultures of specimens other than blood or by clinical evidence. The majority of *S. aureus* and coagulase-negative staphylococcal bacteremias were associated with intravascular devices. Not surprisingly, pneumococcal bacteremia was most often associated with pneumonia, but in 7 of 34 episodes (20.6%) a primary source could not be determined. Among the Enterobacteriaceae, primary foci of infection below the diaphragm predominated (table 5), as would be expected given the normal habitat of these bacteria. In contrast, the most common focus for bacteremia due to *P. aeruginosa* was the respiratory tract, which was the focus more than twice as frequently as the next most common focus, the genitourinary tract.

Several microorganisms or microorganism groups were associated at a particularly high frequency with bacteremia or fungemia in which a primary focus for infection could not be determined. These included the viridans streptococci (44.4%), *Enterobacter cloacae* (58.3%), *Klebsiella pneumoniae* (33.3%), *Candida* species (37.5%), *Torulopsis glabrata* (41.7%), and *Mycobacterium avium* complex (100%). All of the *E. cloacae* bacteremias and many of the fungemias and *K. pneumoniae* bacteremias with unknown sources occurred in patients with underlying malignancies.

Table 3. Community-acquired and hospital-acquired microorganisms and major microorganism groups involved in episodes of bacteremia and fungemia.

	No. (%) of isolates per place of acquisition of infection	
Microorganisms	Community	Hospital
Staphylococcus aureus	90 (50.6)	88 (49.4)
Coagulase-negative staphylococci	27 (31.0)	60 (69.0)
Streptococcus pneumoniae	31 (91.2)	3 (8.8)
Other streptococci	32 (68.1)	15 (31.9)
Enterococcus species	15 (23.1)	50 (76.9)
Escherichia coli	87 (61.3)	55 (38.7)
Other Enterobacteriaceae	61 (36.1)	108 (63.9)
Pseudomonas aeruginosa	21 (39.6)	32 (60.4)
Other nonfermentative gram-negative rods	16 (51.6)	15 (49.4)
Clostridium species	5 (33.3)	10 (66.7)
Bacteroides species	7 (38.9)	11 (61.1)
Candida species	7 (16.7)	35 (83.8)
Cryptococcus neoformans	8 (100)	0
Torulopsis glabrata	2 (14.3)	12 (85.7)
Mycobacterium avium complex	16 (100)	0

Clinical Observations

In order to determine whether certain indicators might assist in assessing the clinical significance of positive blood cultures, we examined the relationship between positive cultures and the peripheral leukocyte count, absolute neutrophil count, blood pressure, and body temperature at the time the first positive blood culture specimen was obtained for a given episode. We also examined the relationship between each of these variables and the microorganisms isolated from true positive cultures. In addition, we critically assessed the antimicrobial therapy as described in the Materials and Methods section.

Leukocyte count and absolute neutrophil count. Patients with culture-positive blood and a peripheral leukocyte count of $<4{,}000/\mu L$ or $\geq 20{,}000/\mu L$ were significantly more likely

Table 4. Sources of bacteremia and fungemia.

	No. of episodes confirmed by		
Source	Culture	Clinical evidence	Total no. (%) of episodes
Intravascular catheter	29	97	161 (19.1)
Genitourinary tract	115	28	147 (17.4)
Respiratory tract	56	46	104 (12.3)
Bowel and peritoneum	22	21	45 (5.3)
Biliary tract	9	21	33 (3.9)
Intraabdominal abscess	9	15	24 (2.8)
Skin	11	29	42 (5.0)
Bone and joint	11	5	16 (2.0)
Surgical wound	7	2	11 (1.3)
Other	25	18	44 (5.2)
Unknown	0	0	216 (25.6)

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Table 5. Sources and confirmatory evidence for episodes of unimicrobial bacteremia and fungemia, according to microorganism.

Microorganism(s) (no. of episodes)	No. of sources confirmed by		Common source(s) (no. of episodes)*
	Culture	Clinical evidence	
Staphylococcus aureus (159)	56	74	IV (56), skin (19), respiratory (18), bone/joint (10)
Coagulase-negative staphylococci (73)	16	45	IV (59), skin (5)
Streptococcus pneumoniae (34)	5	22	Respiratory (26)
Group B streptococci (8)	4	3	Skin (3), GU (3)
Viridans group streptococci (24)	3	10	Respiratory (3), skin (2)
Enterococcus species (38)	13	9	GU (15), IV (3)
Escherichia coli (116)	70	30	GU (67), biliary (11), peritoneal (10)
Klebsiella pneumoniae (48)	15	15	Biliary (10), GU (8), peritoneal (5)
Enterobacter cloacae (12)	3	2	Biliary (2), respiratory (2)
Serratia marcescens (20)	11	6	GU (4), respiratory (4), IV (3)
Proteus mirabilis (13)	10	2	GU (9)
Pseudomonas aeruginosa (48)	25	12	Respiratory (19), GU (9)
Acinetobacter baumanii (12)	4	0	Respiratory (3)
Bacteroides fragilis group (9)	3	4	Abscess (6)
Candida albicans (21)	7	2	IV (5), peritoneal (2)
Candida tropicalis (7)	1	4	IV (1), GU (1), peritoneal (1)
Torulopsis glabrata (12)	1	4	GU (4)
Mycobacterium avium (15)	0	0	No sources identified

NOTE. The list of microorganisms includes all those isolated ≥5 times as causes of unimicrobial bacteremia or fungemia.

* Abscess = intraabdominal abscess; GU = genitourinary tract; IV = intravascular device; respiratory = respiratory tract.

($P < .001$) to have true bacteremia or fungemia episodes (62.5% and 60.3%, respectively) than contaminant episodes when compared with patients who had peripheral leukocyte counts between 4,000 and 19,999/μL (proportion of true bacteremias, 49.2%). Similarly, patients with absolute neutropenia were significantly more likely ($P < .001$) than nonneutropenic patients to have a positive blood culture represent true bacteremia or fungemia (70.2% vs. 51.4% of positive cultures, respectively).

The distribution of microorganisms causing septicemia in neutropenic and nonneutropenic patients is shown in table 6. Neutropenic patients were significantly less likely to have bacteremia due to *S. aureus* ($P < .0001$; RR, 0.33) but were significantly more likely to have fungemia ($P < .01$; RR, 1.81) and polymicrobial bacteremia ($P < .0001$; RR, 2.63) than were nonneutropenic individuals.

Blood pressure. Approximately 14% of patients were hypotensive at the time the first positive blood culture specimen was obtained. The positive blood cultures of these patients were more likely to represent true bacteremia than were positive blood cultures of patients with normal blood pressure at the time cultures were performed (72.7% vs. 51.1% of positive cultures, respectively; $P < .0001$). The distribution of microorganisms causing bacteremia and fungemia in these patients is shown in table 7. There were no statistically significant differences in microorganisms or microorganism groups in hypotensive vs. normotensive patients. However, polymicrobial episodes occurred significantly more often in hypotensive patients than in patients whose blood pressure was normal at the time of blood culture ($P < .05$; RR, 1.58).

Temperature. Cultures of patients who were hypothermic (temperature, <36°C) or who had marked fever (temperature, ≥40°C) were more likely to be true-positives (67.7% and 69.6% of positive cultures, respectively) than were those of patients whose temperatures were normal (39.2% of positive cultures) or moderately elevated (55.9% of positive cultures) at the time the positive blood culture specimen was obtained.

Endocarditis. Of 31 episodes (in 31 patients) of endocarditis, 11 were due to *S. aureus,* 10 to viridans streptococci, and 3 to enterococci. All episodes were unimicrobial; 30 of the 31 were due to gram-positive bacteria, and one was caused by *K. pneumoniae.* Twenty-one patients presented following <1 week of symptoms, 8 following 1–3 weeks of symptoms, and 2 following >3 weeks of symptoms. Seven of 11 patients with endocarditis due to *S. aureus* and 7 of 10 patients with endocarditis caused by viridans streptococci presented following <1 week of symptoms.

Antibiotic therapy. Of the 1,585 episodes of positive blood cultures, 454 (28.6%) involved patients receiving antimicrobial agents at the time the first positive blood culture specimen was obtained. The proportion of patients who were receiving antibiotics was the same regardless of whether growth repre-

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Table 6. Microorganisms recovered from and types of episodes in patients with bacteremia and fungemia, according to absolute neutrophil count.

Variable	No. (%) of isolates from patients with indicated neutrophil count	
	<1,000/μL	≥1,000/μL
Microorganisms		
Staphylococcus aureus	9 (6.0)*	169 (21.1)*
Coagulase-negative staphylococci	12 (8.1)	75 (9.4)
Streptococci	9 (6.0)	78 (9.7)
Enterococcus species	13 (8.7)	52 (6.5)
Enterobacteriaceae	58 (38.9)	253 (31.6)
Pseudomonas aeruginosa	11 (7.4)	42 (5.2)
Other nonfermentative gram-negative rods	2 (1.3)	29 (3.6)
Anaerobic bacteria	9 (6.1)	29 (3.6)
Yeasts and fungi	17 (12.1)†	48 (6.0)†
Type of episode: total no. (%)		
Unimicrobial	96 (69.6)	668 (87.4)
Polymicrobial	24 (30.4)*	55 (12.6)*

* $P < .0001$.
† $P < .01$.

sented true bacteremia or contamination. Of the 843 episodes of true bacteremia or fungemia, 71 (8.4%) occurred in patients who were receiving therapy that was effective against the microorganism(s) that grew in the blood culture. This proportion was the same at all three hospitals (range, 8.0%–9.1%).

Appropriate antimicrobial therapy was administered to a substantial majority of patients at all of the time points assessed. Excluding the 48 patients who died prior to the availability of susceptibility test results, 620 of 795 patients (78%) received appropriate therapy at all time points. In addition, 111 patients (14%) were given appropriate therapy after susceptibility test results were available, regardless of whether they had received inappropriate empirical therapy at an earlier time point.

Patients with unimicrobial septicemia were more likely than those with polymicrobial septicemia to be treated with appropriate therapy, especially after susceptibility test results were available (92.7% vs. 83.6%, respectively). At all time points assessed, medical patients were somewhat more likely than surgical patients to receive appropriate therapy. Among medical patients, the proportion who received appropriate therapy at the different time points ranged from 89.4% to 91.0%, versus a range of 83.0% to 87.1% among surgical patients.

After susceptibility test results were available, approximately one-quarter of all patients were receiving antimicrobial agents judged to be superfluous for the infecting microorganism(s) and clinical setting. Twenty-six patients (3.3%) were receiving agents to which their infecting organisms were resistant in vitro, and nine patients (1.1%) received no antimicrobials despite a clinical setting that should have mandated therapeutic intervention.

Outcome and Factors Influencing Prognosis

One hundred forty-eight patients (17.5%) died of causes directly or indirectly attributable to an episode of septicemia (associated mortality). Five hundred thirty-five patients (63.5%) were discharged alive, 118 (14.0%) were alive but remained hospitalized 30 days after onset of the septicemic episode, and 42 (5.0%) died from causes that were judged by the investigators not to be associated with the bacteremia or fungemia. There were no significant differences in mortality at the three collaborating hospitals.

Univariate Analyses

Age and sex. The effect of age on outcome of bacteremia and fungemia was assessed according to the decade of life of the infected patients. As shown in figure 1, septicemia-associated mortality gradually increased with age and was especially notable after the age of 70 years. The infection-associated mortality for septicemic patients over 70 years of age was 24.2% compared with 15.2% for patients 70 years of age or less. In comparison with other patients, the relative risks of death from bacteremia and fungemia for patients between 71 and 80 years of age and >80 years of age were 2.58 and 3.4, respectively. There were no significant differences in infection-associated mortality between septicemic men and women.

Hospital service. The septicemia-associated mortality rates ranged from zero among obstetric and gynecologic patients to 19% and 23% among medical and cardiovascular surgery patients, respectively. However, none of the differences in mortality, when sorted according to hospital service, were statistically significant.

Table 7. Microorganisms recovered from and types of episodes in hypotensive and normotensive patients with bacteremia and fungemia.

Variable	No. (%) of isolates from patients with indicated blood pressure status	
	Hypotensive	Normotensive
Microorganism		
Staphylococcus aureus	21 (16.0)	157 (19.3)
Coagulase-negative staphylococci	6 (4.6)	81 (10.0)
Streptococcus pneumoniae	8 (6.1)	26 (3.2)
Other streptococci	6 (4.6)	41 (5.0)
Enterococcus species	13 (10.0)	52 (6.4)
Enterobacteriaceae	46 (35.1)	265 (32.6)
Pseudomonas aeruginosa	7 (5.3)	46 (5.7)
Other nonfermentative gram-negative rods	1 (0.8)	30 (3.7)
Anaerobic bacteria	5 (3.8)	33 (4.1)
Yeasts and fungi	12 (9.2)	54 (6.6)
Type of episode: total no. (%)		
Unimicrobial	96 (85.7)	668 (91.4)
Polymicrobial	16 (14.3)*	63 (8.6)*

* $P < .05$.

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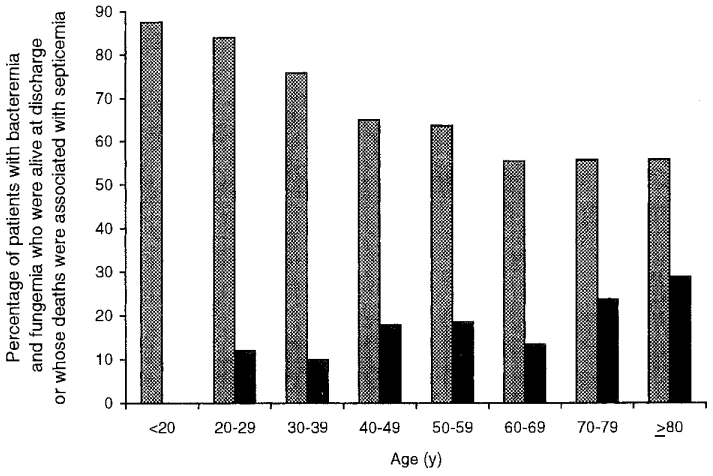


Figure 1. Outcome of bacteremia or fungemia, according to age group of patients (▩ = alive at discharge; ■ = death, associated with septicemia).

Place of acquisition of bacteremia and fungemia. Patients who developed bacteremia or fungemia during the course of hospitalization had an infection-associated mortality rate of 20.3%, vs. 14.6% for patients with community-acquired disease. The relative risk of death associated with nosocomial septicemia was 1.39 ($P < .05$).

Table 8. Associated mortality in episodes of bacteremia and fungemia and relative risk of death, as related to etiologic microorganisms in unimicrobial episodes and to the type of episode.

Variable	Associated mortality: no. (%) of deaths per no. of episodes	Relative risk of death
Microorganisms		
Staphylococcus aureus	19/159 (11.9)	2.18
Coagulase-negative staphylococci	4/73 (5.5)*	1.0
Streptococcus pneumoniae	6/34 (17.6)	3.22
Other streptococci	5/38 (13.1)	2.40
Enterococcus species	5/38 (13.1)	2.40
Other gram-positive aerobic bacteria	1/9 (11.1)	2.03
Escherichia coli	14/116 (12.1)	2.20
Other Enterobacteriaceae	31/125 (24.8)†	4.53
Pseudomonas aeruginosa	8/48 (16.7)	3.04
Other nonfermentative gram-negative rods	3/25 (12.0)	2.19
Other gram-negative aerobic bacteria	0/6	0.04
Gram-negative anaerobic bacteria	2/14 (14.3)	2.61
Gram-positive anaerobic bacteria	2/8 (25.0)	3.65
Yeasts and fungi	19/53 (35.8)‡	6.54
Mycobacteria	2/16 (12.5)	2.28
Type of episode		
Unimicrobial	120/764 (15.7)	1.0
Polymicrobial	27/79 (34.2)‡	2.16

* $P < .05$.
† $P < .01$.
‡ $P < .001$.

Microorganism. The microorganism isolated and type of bacteremia or fungemia (i.e., unimicrobial or polymicrobial) influenced outcome (table 8). Among the common etiologic agents of bacteremia and fungemia, the lowest associated mortality occurred with coagulase-negative staphylococci (5.5%) and the highest with yeasts and fungi (35.8%). Infection-associated mortality was lower with gram-positive unimicrobial bacteremia (11.1%) than with gram-negative bacteremia (17.6%), anaerobic bacteremia (18.2%), or fungemia (35.8%).

The mortality associated with pneumococcal bacteremia was greater than that associated with enterococcal or *S. aureus* bacteremia (table 8). Also noteworthy was the mortality rate with *P. aeruginosa* bacteremia, which was less than that with bacteremia due to enteric gram-negative rods other than *E. coli* (table 8). The mortality associated with polymicrobial bacteremia was more than twice that associated with unimicrobial episodes.

Table 9. Associated mortality in episodes of bacteremia and fungemia, according to source of infection.

Source of infection	Associated mortality: no. (%) of deaths per no. of episodes	Relative risk of death
Intravascular catheter	12/161 (7.4)*	1.0
Genitourinary tract	16/147 (10.8)†	1.46
Respiratory tract	26/104 (25.0)†	3.35
Bowel and peritoneum	23/45 (51.1)‡	6.86
Biliary tract	4/33 (12.1)	1.63
Intraabdominal abscess	3/24 (12.5)	1.68
Skin	6/42 (14.3)	1.92
Bone and joint	1/16 (6.25)	0.84
Surgical wound	0/11	0.01
Other	3/44 (6.8)	0.91
Unknown	54/216 (25.0)*	3.35

* $P < .01$.
† $P < .05$.
‡ $P < .001$.

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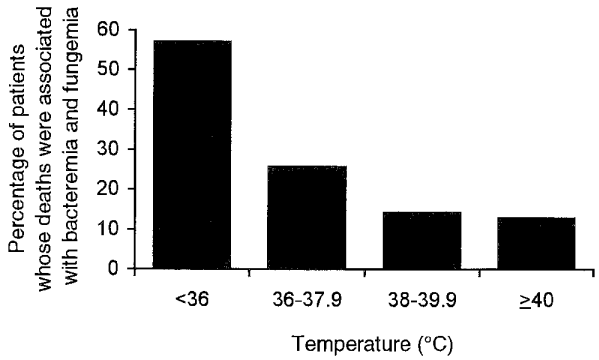


Figure 2. Septicemia-associated mortality as related to temperature of patients at the time the first positive blood culture specimen was obtained.

Source of infection. The outcome of bacteremia and fungemia was affected by the primary source of infection (table 9). For risk factor analysis, we assigned a risk of 1.0 to septicemia associated with iv catheters in order to maintain consistency with our earlier work [11]. Significantly increased septicemia-associated mortality and relative risk of death occurred with respiratory tract sources ($P < .05$), with bowel and peritoneal sources ($P < .01$), and when a primary focus of infection could not be found ($P < .05$).

Body temperature. The mortality associated with bacteremia and fungemia was inversely related to the body temperature of patients at the time the first positive blood culture specimen was obtained (figure 2). Risk factor analysis showed significantly increased mortality ($P < .05$) among the patients who were hypothermic at the onset of septicemia.

Blood pressure. Septic shock, as evidenced by the presence of hypotension at the time the first positive blood culture specimen was obtained, was associated with increased mortality. Table 10 reveals that this relationship was a virtually uniform finding, regardless of the etiologic microorganism or the type of septic episode.

Leukocyte count and absolute neutrophil count. The relationship between septicemia-associated mortality and total leukocyte count or absolute neutrophil count is shown in table 11. Patients who had leukocyte counts of $<4{,}000/\mu L$ or $\geq 20{,}000/\mu L$ had a twofold increase in relative risk of death from septicemia. Patients with absolute neutropenia had a significantly increased relative risk of death in comparison with that for nonneutropenic patients.

Predisposing factors. The influence of predisposing factors on the outcome of septicemia was analyzed both when individual factors were present alone and when multiple factors were present (table 12). Nearly one-quarter of the patients had no predisposing factors, and these patients had the lowest septicemia-associated mortality (8.2%; RR, 1.0). The greatest mortality was associated with moderate renal failure (61.5%; RR, 7.54).

Table 10. Associated mortality in episodes of bacteremia and fungemia, as related to etiologic microorganism in unimicrobial episodes, type of episode, and blood pressure status at the time of onset of septicemia.

Variable	Associated mortality: no. (%) of deaths per no. of episodes in indicated group	
	Hypotensive	Normotensive
Microorganisms		
Staphylococcus aureus	5/18 (27.8)*	14/141 (9.9)*
Coagulase-negative staphylococci	1/4 (25)	3/69 (4.3)
Streptococcus pneumoniae	1/8 (12.5)	5/26 (19.2)
Other streptococci	1/3 (33.3)	3/35 (8.6)
Enterococcus species	1/5 (20)	4/33 (12.1)
Escherichia coli	4/13 (30.8)*	10/103 (9.7)*
Other Enterobacteriaceae	12/23 (52.2)†	19/104 (18.3)*
Pseudomonas aeruginosa	3/6 (50)*	5/42 (11.9)*
Other nonfermentative gram-negative rods	0/1	3/28 (10.7)
Anaerobic bacteria	1/2 (50)	3/24 (12.5)
Yeasts and fungi	5/7 (71.4)*	14/46 (30.4)*
Type of episode		
Unimicrobial	35/96 (36.4)‡	85/668 (12.7)
Polymicrobial	10/16 (62.5)†	17/63 (27.0)

* $P < .05$.
† $P < .01$.
‡ $P < .001$.

Although the relative risk of death was high in the presence of severe renal failure and biopsy-proven cirrhosis, statistical significance was not achieved because of the relative infrequency of each of these predisposing factors as the sole underlying problem. Not surprisingly, there was a direct relationship between septicemia-associated mortality and the number of predisposing factors present. Thus, mortality was greater among the patients with multiple predisposing factors than among patients with only a single factor.

Table 11. Associated mortality in episodes of bacteremia and fungemia, as related to leukocyte count and absolute neutrophil count.

Variable	Associated mortality: no. (%) of deaths per no. of episodes	Relative risk of death
Total leukocyte count (per μL)		
$<4{,}000$	42/177 (23.7)	2.11*
4,000–10,999	28/249 (11.2)	1.0
11,000–19,999	48/293 (16.4)	1.46
20,000–49,999	27/115 (23.5)	2.09*
$\geq 50{,}000$	2/8 (25)	2.22
Absolute neutrophil count (per μL)		
$<1{,}000$	31/120 (25.8)	1.58*
$\geq 1{,}000$	115/702 (16.4)	1.0

* $P < .05$.

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Table 12. Influence of predisposing factors on associated mortality in episodes of bacteremia and fungemia.

Factor(s)	Associated mortality: no. (%) of deaths* per no. of episodes	Relative risk of death
None	16/196 (8.2)	1.0
Hematologic malignancy	14/70 (20.0)	2.45†
Other neoplasm	27/150 (18.0)	2.20†
Corticosteroids	3/28 (10.7)	1.31
AIDS	11/51 (21.6)	2.64†
Trauma	1/11 (9.1)	1.11
Recent surgery	7/49 (14.3)	1.75
Diabetes mellitus	6/59 (10.2)	1.25
Creatinine level, 2–5 mg/dL	16/26 (61.5)	7.54‡
Creatinine level, >5 mg/dL	4/16 (25)	3.06
Cirrhosis	2/6 (33.3)	4.08
One factor	91/477 (19.1)	2.34†
Two or more factors	41/168 (24.4)	2.99†

* No. of deaths among patients in whom listed predisposing factor was the only one present.
† $P < .05$.
‡ $P < .01$.

Antibiotic and other therapy. The mortality associated with bacteremia and fungemia clearly was affected by the type of antimicrobial therapy administered (table 13). The great majority (78%) of patients received appropriate therapy at all three time points at which assessments were made, and this group of patients had the lowest septicemia-associated mortality. Patients who received inappropriate empirical therapy but whose physicians administered appropriate therapy once the blood culture was reported to be positive also had low mortality. By contrast, among the small group of patients who received inappropriate therapy at all three time points, three of nine (33%) died of causes attributable to sepsis.

Indeed, the data shown in table 13 clearly indicate that septicemia-associated mortality increased in proportion to the duration of inappropriate antimicrobial therapy. Since our definition of appropriate empirical therapy allowed for the possibility that the organism(s) grown in blood culture might not be susceptible to the agents given, we also assessed outcome in terms of whether the infecting organisms were susceptible to therapy being administered at each time point. The results of this analysis were very similar; that is, associated mortality was lowest (9.8%) when the organism was susceptible at all three time points and also was low (12.6%) when patients received effective antimicrobial therapy after blood cultures were reported to be positive.

When mortality following the availability of susceptibility test results was analyzed alone, the mortality rates when first-choice or alternative-choice agents were given were identical (8.3%), but the rate was 24% when superfluous therapy was given. Since superfluous therapy included at least one agent with in vitro activity against the infecting microorganism, other factors that may have influenced outcome were assessed. Patients receiving superfluous therapy were twofold to threefold more likely to have absolute granulocytopenia, fungemia, or polymicrobial episodes than were patients who received first-choice or alternative-choice agents.

The removal, excision, or drainage of a primary focus of infection, if feasible, often has a salutary effect on the outcome of septicemia. Therefore, we assessed outcome when such therapeutic maneuvers were undertaken. The results confirmed the beneficial effect of these interventions. Among patients who survived until susceptibility test results were available, associated mortality was 6.2% (14 of 224) when an infected focus was excised, drained, or removed, vs. 15.6% (87 of 557) when no additional interventions were (or could be) undertaken ($P < .001$). Among patients with catheter-associated bacteremia or fungemia, removal of the catheter was associated with death due to septicemia in only 3.9%.

Table 13. Associated mortality in episodes of bacteremia and fungemia, as related to appropriateness of antimicrobial therapy at different time points during septicemia.

Assessment of therapy at indicated time point*				
Initial empirical therapy	After culture reported positive	After susceptibility results available	Associated mortality: no. (%) of deaths per no. of patients	RR
A	A	A	65/620 (10.5)	1.0
I	A	A	6/45 (13.3)	1.27
A	I	A	7/35 (20.0)	1.91
A	A	I	7/35 (20.0)	1.91
I	I	A	8/31 (25.8)	2.46
A	I	I	4/14 (28.6)	2.73
I	A	I	0/2	0.05
I	I	I	3/9 (33.3)	3.18

* A = appropriate; I = inappropriate. Therapy was considered appropriate after susceptibility test results became available if the microorganism(s) were susceptible (on the basis of in vitro testing) to at least one agent administered, whereas therapy was considered appropriate at the earlier time points it if was appropriate for the clinical situation.

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Multivariate Analysis

Based on the results of univariate analysis, high- and low-risk categories were established for each variable assessed. When there was more than one high-risk component for a variable (e.g., microorganism, source, or predisposing factor), these components were grouped and assigned a univariate relative risk for the purpose of multivariate analysis. Then, with use of logistic regression, the relative risk of death was determined for each variable in the presence of all others.

The results of this analysis are shown in table 14. Those variables associated with a significantly increased risk of death in multivariate analysis were advanced age (>70 years); isolation of fungi or Enterobacteriaceae other than *E. coli;* a primary source of infection in the respiratory tract, bowel, or peritoneum or that was unknown; underlying malignancy, AIDS, or renal failure; shock, as manifested by hypotension; inability to mount a febrile response to sepsis; and inappropriate antibiotic therapy at two or more of the time points assessed.

Discussion

It was our hypothesis that the many changes in medicine since the mid-1970s, when two of us and other investigators [10, 11] comprehensively reviewed a large series of patients with bacteremia and fungemia, would lead to substantive changes in the microbiology, epidemiology, and clinical and prognostic significance of positive blood cultures in the 1990s. Indeed, the more aggressive and widespread use of prosthetic materials and intravascular devices, the occurrence of syndromes such as AIDS not known 2 decades ago, and therapeutic advances in imaging, interventional radiology, and antimicrobial therapy virtually ensured the presence of important differences and underscored the need for this update.

In order to best compare the differences and similarities of bacteremia and fungemia in the 1990s versus the mid-1970s, we used definitions, including clinical and diagnostic criteria, that were similar to those in our earlier work [10, 11]. However, we performed this study prospectively, gathering data concurrently on patients with culture-positive blood, to better assess the ways in which physicians used laboratory results for therapeutic decisions.

Laboratory Observations

True septicemia vs. contamination. The observations from this study suggest that contaminants in blood cultures are more frequent in the 1990s than they were 2 decades ago. Of 1,582 positive blood culture episodes in the current study, 655 (41.5%) were judged to represent contamination and another 84 (5.3%) were of indeterminate significance. Thus, only about half of all positive blood cultures represented true bloodstream infection. These findings contrast markedly with the observations in our earlier study, in which approximately one-third of all positive blood cultures represented contamination [10].

There are several possible explanations for these findings. One is the increasing use of central, long-term intravascular catheters (e.g., Hickman and Broviac) and the utilization of these access devices for the purpose of obtaining blood for culture. Access ports from intravascular devices may be more difficult to sterilize than skin at venipuncture sites, thereby resulting in increased contamination rates; at least one study has documented increased contamination rates when blood culture specimens are obtained from central lines [34].

Although physicians may believe they are benefiting their patients by obtaining blood culture specimens from catheters (i.e., saving patients from needlesticks), they actually may be doing a disservice, since culture contaminants (false-positives

Table 14. Comparison of univariate and multivariate analysis of factors affecting risk of death in patients with bacteremia and fungemia.

Variable	Univariate high risk	Univariate RR	Multivariate RR
Age	>70 y	1.88	1.80*
Place of acquisition	Hospital	1.39	1.12
Microorganisms	Fungi and Enterobacteriaceae other than *E. coli*	5.13	2.27†
Type of episode	Polymicrobial	2.16	1.55
Source of infection	Respiratory tract, bowel, peritoneum, or unknown	2.56	2.86†
Predisposing factor	Malignancy, AIDS, or renal failure	1.92	1.98†
Blood pressure	Hypotension	2.85	2.29†
Leukocyte count	<4,000/μL or >20,000/μL	1.67	1.24
Absolute neutrophil count	<1,000/μL	1.58	0.65
Body temperature	Absence of fever (<37.9°C)	2.06	2.04†
Antibiotic therapy	Inappropriate at ≥2 time points	2.32	2.72†

* $P < .05$.
† $P < .01$.

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cultures) have been shown to result in longer hospitalizations and increased costs to patients and institutions [35].

A second possible reason for the increased incidence of contaminants is blood culture technique. Although several recent studies have indicated that the current single-needle technique for obtaining blood and inoculating cultures is not associated with increased rates of contamination [14, 36, 37], Spitalnic et al. [38], in a meta-analysis, have suggested otherwise. Alternatively, it may be that in institutions such as ours, in which house officers and medical students obtain the majority of blood culture specimens, failure to apply antiseptic solutions (usually iodophors and alcohol) properly and to let them exert their antimicrobial effect over 1–2 minutes as recommended results in increased contamination.

Possible remedies include use of blood culture teams from the laboratory's phlebotomy service, which seems unlikely in the managed care era, or the development and use of potentially more effective antiseptic skin preparation materials (e.g., 2% iodine tincture) before blood sampling. A final possible explanation for increased rates of contamination of blood cultures could be that newer blood culture systems and media are more sensitive and capable of detecting the few viable skin bacteria that might remain after appropriate antiseptic preparation.

Of the 843 septicemias, a source was confirmed by culture in 294 (34.9%) and by clinical evidence in 282 (33.4%). Of the remaining 267 episodes, at least two blood cultures were positive for the same microorganism in 181 (67.8%; 21.5% of total septicemias). Thus, there was objective evidence of true infection in 757 of the 843 episodes (89.8%), an observation that is remarkably similar to that in our earlier study [10]. This finding is important clinically, since it suggests that, despite increased rates of contamination of blood cultures, in the great majority of instances physicians should be able to determine with some confidence whether a positive blood culture represents significant infection.

Nevertheless, positive blood cultures yielding coagulase-negative staphylococci may present great interpretative difficulties, even when more than one culture set is positive. For example, Zaidi et al. [39] have found that coagulase-negative staphylococci with identical species designations, serotypes, and antibiograms recovered from the blood of infants sometimes represented different strains when the isolates were analyzed by molecular typing techniques. Similarly, even when both of two blood cultures yielded *S. epidermidis* of the same biotype in the current study, we were frequently not certain of the isolates' clinical significance (table 2).

Patterns of positive blood cultures. In our earlier study [10], we noted different patterns of blood culture positivity in patients with endocarditis, those with true septicemia that was not due to endocarditis, and those with contaminant isolates. Similar observations were made in this study. Thus, in patients with endocarditis, a disease characterized by continuous seeding of blood from the infected heart valve, all blood cultures obtained in a series were positive.

By contrast, for patients with septicemia not due to endocarditis, most but not all blood cultures obtained in a series were positive, a finding consistent with the understanding that bloodstream infection in such patients may be short-lived or intermittent (abscesses). For patients whose blood cultures were contaminated, an initial positive culture in a series virtually always was followed by negative cultures. When a subsequent culture was positive, it usually was positive with a different microorganism (e.g., *S. epidermidis* followed by a diphtheroid).

The proportion of patients with polymicrobial septicemia in this study (79 of 843; 9.4%) is consistent with findings in earlier studies, in which frequencies of polymicrobial bacteremia ranged from 6% to 18% [10, 17, 40–43].

Epidemiological Observations

Place of acquisition of septicemia. At our institutions the proportions of episodes that were of community-acquired septicemia and hospital-acquired septicemia were nearly equal (48% vs. 52%). This observation contrasts with the results of our earlier study at the University of Colorado hospitals, in which nearly two-thirds of episodes were nosocomial [10]. The difference may relate not only to patient-population variability [44, 45] but also to changes in health care, particularly shorter lengths of stay in the 1990s than those of 2 decades ago, as well as outpatient surgery and chemotherapy.

In contrast to the relative equivalence of community- and hospital-acquired septicemic episodes overall, there were important differences with regard to individual microorganisms. For example, 91% of pneumococcal bacteremias and all mycobacteremias and cryptococcemias were community-acquired. These observations are consistent with prior reports (on pneumococci) and with our understanding of the epidemiology of infections due to these microorganisms [10, 44, 46]. However, nosocomial pneumococcal bacteremia can occur and may be relatively common in institutions with longer patient stays [47, 48].

Fungemia, enterococcal bacteremia, and coagulase-negative staphylococcal bacteremia disproportionately were nosocomial in origin (table 3). The observations for fungi and enterococci were virtually identical to those in our earlier studies of bacteremia [10] and probably relate to the fact that infection with these microorganisms tend to occur in more debilitated patients. The predominance of hospital-acquired coagulase-negative staphylococcal bacteremia is explained by the current use of long-term indwelling central and peripheral catheters as well as other prosthetic devices, the ubiquity of these bacteria as normal skin flora, and the ability of these relatively avirulent microorganisms to adhere to the surfaces of biomaterials.

P. aeruginosa bacteremia usually occurs as a nosocomial infection. In the current study, *P. aeruginosa* bacteremia was community-acquired in 39.6% of episodes, compared with 17% in our earlier study. The explanation for this difference in the epidemiology of *P. aeruginosa* bacteremia may be related in

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part to the prevalence of HIV infection. In bacteremic patients known to be infected with HIV, *P. aeruginosa* was the third most frequently isolated pathogen, and in seven of 11 episodes in these patients, bacteremia was community-acquired. Several recent reports have documented similar findings in patients with HIV infections [49–51].

Hospital service. The overwhelming majority of bloodstream infections in this series occurred in patients hospitalized on either the medical services (73.6%) or nontransplantation surgical services (21.3%), an observation similar to that in our previous report [10] in which 54.6% of episodes occurred in medical patients and 27.2% of episodes occurred in surgical patients.

The current study also confirmed the rarity of *P. aeruginosa* bacteremia in medical patients (4.4% of episodes), the absence of enterococcal bacteremias in obstetrical and gynecologic patients, the high proportion of fungemias in transplantation patients (23.1% of episodes), and the proportionately increased frequency of anaerobic bacteremia in patients hospitalized on the surgical and gynecologic services (6.6% and 11.1% of episodes, respectively).

Sources of septicemia. Onc of the striking findings in the currcnt scries in comparison with our earlier work [10] was the ascendancy of intravascular catheters as an important source of bloodstream infections. Whereas only 3% of episodes were catheter-related in the previous study, iv catheters were the source of 19% of the episodes in the current series. The increasing importance of intravascular catheters also was noted by Mylotte et al. [47], who examined nosocomial bacteremia between 1979 and 1987; in that study, the proportion of episodes associated with intravascular devices increased from 6% (1979) to 19% (1987). During a similar time period, the proportion of bloodstream infections due to intravascular devices at a university hospital in Berlin was consistently ~16% [19].

The inability to determine the focus of bacteremia and fungemia remains a vexing problem. Despite substantial advances in diagnostic imaging over the past 2 decades, 26% of the septicemic episodes in this series, compared with 31% in our earlier study [10], had no discernible focus. Leibovici and colleagues [20] noted similar results; 23% of episodes during 1988 and 1989 at their university hospital in Israel were of unknown origin.

Since episodes with unknown foci are associated with increased mortality ([11, 20] and present study), improved methods for determining the primary site of infection in septicemic patients clearly are needed. Microorganisms from unknown foci commonly are assumed to have a gut mucosal source. The organisms associated highly with an unknown source in this study (e.g., *E. cloacae, K. pneumoniae, Candida* species, *T. glabrata,* viridans streptococci, and *M. avium* complex) support this hypothesis.

When we examined the sources of septicemia according to each microorganism or microorganism group (table 5), there were several noteworthy observations. For example, in the years since our previous study, the proportion of *S. aureus* bacteremias associated with intravascular catheters has nearly doubled, from 20% to 35%. Respiratory and skin sources remained important primary foci for staphylococcal bacteremia. The recent report by Roberts and colleagues [18] confirmed the importance of intravascular and pulmonary foci for staphylococcal bacteremia. In addition, in the current study and in the report by Roberts et al. [18], respiratory foci for klebsiella bacteremia were considerably less prominent than we observed previously [10]; intraabdominal and genitourinary sources now predominate. In contrast to the findings of Roberts et al., who found enterococcal bacteremia most commonly to have wound sources [18], our patients most often had genitourinary tract foci.

Epidemiology of septicemia in neutropenic patients. The differences in the microbiology of bacteremia and fungemia in neutropenic patients compared with nonneutropenic patients (table 6) stand in contrast with the observations in our earlier report [10]. In the present series bacteremia due to *S. aureus* was significantly less common and fungemia significantly more common in neutropenic than nonneutropenic patients, whereas there were no such differences noted in the previous study. However, in both series, polymicrobial episodes were more frequent in granulocytopenic patients.

A study of bacteremia and fungemia in granulocytopenic patients during 1985 and 1986 at the University of Colorado Health Sciences Center [52], which was the site of our earlier study, showed both similarities to and differences from the distributions of microorganisms in the 1975–1977 review [10] and the current one. For example, in the study by Ehni et al. [52], fungemias were proportionately less common (2%, vs. 11% [10] and 12% [current study]) and *P. aeruginosa* bacteremias were more common (27%, vs. 9% [10] and 7% [current study]). However, the proportionate frequency of bacteremias due to Enterobacteriaceae was similar in all three studies.

In the study by Ehni and colleagues [52] and the present report, bacteremia due to *S. aureus* accounted for ~5% of episodes in neutropenic patients, whereas in the 1975–1977 review [10], 13% of episodes in neutropenic patients were caused by *S. aureus.* Finally, the increasing importance of bacteremia due to coagulase-negative staphylococci in neutropenic patients was evident in the study of Ehni et al. [52] and in the current one (14% and 8% of episodes in neutropenic patients, respectively). In our earlier review, coagulase-negative staphylococcal bacteremia was sufficiently uncommon in granulocytopenic patients that it did not merit mention [10].

A possible explanation for the higher rates of fungemia currently includes the extensive use of more effective antipseudomonal β-lactam drugs such as piperacillin, ceftazidime, and imipenem. Although their early and empirical use may decrease mortality owing to *P. aeruginosa* infection, their prolonged pressure on normal gut flora is associated with overgrowth of yeasts and increased risk of subsequent fungemia [53]. The relative importance of coagulase-negative staphylococci presently probably relates to the common and prolonged use of

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central iv catheters and the resistance of this group of organisms to commonly used antimicrobial agents.

Epidemiology of septicemia in hypotensive patients. Septic shock most frequently has been associated with gram-negative bacteremia. Indeed, in our earlier review [10], aerobic or facultative gram-negative rods accounted for 53% of the isolates from hypotensive patients. In the current series, however, whereas we observed that aerobic or facultative gram-negative rods continued to be common etiologic agents of septic shock, they were isolated less frequently than in the past (43% of isolates). *S. aureus* was detected twice as frequently in hypotensive patients in the current series (16%, vs. 7% in the earlier series), and anaerobic bacteria were detected substantially less often in hypotensive patients (4%, vs. 11% in the earlier series). In both series, hypotensive patients were twice as likely as normotensive patients to have polymicrobial bacteremia ([10] and table 7).

Clinical and Prognostic Observations

Our observations suggest that the mortality associated with bacteremia and fungemia appears to have decreased during the past 2 decades. However, this conclusion may not be applicable widely and should be interpreted with caution. Indeed, the differences in patient population as well as the prospective nature of the current study vs. our retrospective earlier review [11] limited the ability to make direct comparisons with the previous work. Nonetheless, mortality attributable to septicemia in this study was markedly less than in the 1975–1977 study (17.5% vs. 31%, respectively). Moreover, Geerdes et al. [19] recently reported that between 1979 and 1989, mortality from septicemia at a university hospital in Berlin decreased from 34% to 21%.

Crude mortality has varied substantially in recent reports of bacteremic patients, ranging from 16% at a Swedish university hospital from 1973 to 1980 [54] to >40% among patients with nosocomial bacteremia from 1981 to 1983 at a university hospital in the United States [55] and with gram-negative bacteremia at a Turkish university hospital from 1983–1989 [21]. By comparison, crude mortality among septicemic patients at the University of Colorado during 1975–1977 was 42% [11], vs. 22.5% in this study (patients were followed for a maximum of 30 days after detection of bacteremia). Most comparable to our data are the observations of Roberts and colleagues, who recently reported a 30-day mortality of 27% among bacteremic patients studied during 1984–1987 in western Canada [18].

Age and sex. Numerous reports have emphasized the importance of advanced age as an unfavorable prognostic factor in septicemic patients [11, 15, 18, 21, 54, 55]. In contrast to our earlier data, which showed a statistically significant increase in mortality due to septicemia after age 40 years [11], in this series significantly increased mortality occurred after age 70 years. No differences in mortality according to sex were evident in this study or in a recent report from a Swedish university hospital [54].

Place of acquisition of bacteremia and fungemia. Nosocomial septicemias historically have been associated with substantially higher mortality than community-acquired septicemias [9, 11, 44]. In the current series and in another recent report [21], however, the evidence suggests that the increase in mortality associated with hospital-acquired bacteremia and fungemia may be less dramatic than reported in the past. Uzun et al. [21] noted crude mortality of 46% in episodes of nosocomial bacteremia vs. 37% in those of community-acquired bacteremia. In this series, associated mortality due to nosocomial septicemia was 20.3%, vs. 14.6% due to community-acquired septicemia.

Microorganisms. Many studies have looked at the mortality rates with bloodstream infections due to individual microorganisms; some have focused only on certain patient populations. Unfortunately, definitions of mortality in the various reports have not been uniform: some have evaluated total (or crude) mortality, others have evaluated only septic deaths (those judged to be directly related to septicemia), and still others have addressed mortality judged directly or indirectly attributable to septicemia. Furthermore, not all studies have indicated clearly whether mortality rates have been calculated on the basis of unimicrobial episodes, thereby excluding the confounding variable of concomitant bacteremia with other microorganisms. These differences make direct comparisons of mortality in other reports problematic, and the comments that follow should be interpreted accordingly.

The lower mortality overall from bacteremia in this series compared with that noted in our earlier work [11] was reflected in the mortality rates associated with individual microorganisms or groups thereof (table 8). Several comparisons and contrasts with regard to etiologic microorganisms deserve emphasis.

Fungemia, which was associated with more than a sixfold increased risk of death in the earlier series [11], also carried a sixfold increased relative risk of death in the present study (table 8). Overall mortality associated with fungemia, however, was lower in the current series than in our earlier report [11], and the associated mortality in this series was somewhat less (36%) than that due to candida and torulopsis fungemias (44%) in Detroit in the mid-1980s [56].

Among episodes of polymicrobial septicemia, for which the directly related mortality was 35% in the earlier series [11], the associated mortality in this series was 34% and the risk of death was significantly increased compared with that in unimicrobial episodes. The mortality associated with polymicrobial bacteremia in the recent report by Cooper et al. [17] was remarkably similar to the observations in our earlier and current series.

In our earlier review, the mortality directly related to pneumococcal bacteremia was 15% (crude mortality, 22%), vs. 17.6% associated mortality in this series. Data from other recent reports are consistent with these findings [57, 58]. These data

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provide impressive evidence that there has been little change in the outcome of *Streptococcus pneumoniae* bacteremia since the classic studies of Austrian and Gold >3 decades ago [59].

By contrast, the dramatically increased risk of death from bacteremia due to *P. aeruginosa* in our earlier report (RR, 6.84) was moderated in this study (RR, 3.04). The mortality associated with pseudomonas bacteremia was 16.7%, compared with 36% for deaths directly due to bacteremia in the earlier review [11]. Two studies examining pseudomonas bacteremia during the early 1980s revealed case fatality rates attributable to sepsis of 41% and 48% [60, 61]. Thus, our data suggest the possibility that the outcome of bacteremia due to *P. aeruginosa* may have improved over the past decade.

Mortality from bacteremia due to gram-positive organisms also was lower in the current study than in the prior review [11]. In the case of *S. aureus,* septicemia-associated mortality in the current series was 11.9%, compared with crude mortality of 33% and directly related mortality of 9% in the earlier series. By comparison, in the recent report from Lautenschlager et al. [62] encompassing the years 1980–1986 in Basel, Switzerland, total mortality was 34% and directly related mortality was 20%.

Coagulase-negative staphylococcal bacteremia had the lowest attributable mortality of all microorganism groups in the current study (5.5%); case-fatality rates were somewhat higher during the mid-1980s: 13.6% at the University of Iowa Hospital [63] and 18% at a large hospital in Spain [64]. The mortality associated with enterococcal bacteremia was 13% in this series, considerably lower than the crude or directly related mortality (45% and 27%, respectively) in our earlier series [11], despite the presence of vancomycin-resistant enterococci at both RWJUH and DUMC during the current study period. By comparison, reports based on data from the 1980s have described case fatality rates associated with enterococcal bacteremia varying from 12% to 51% [65–67].

Several studies have recently provided data on the outcome of bacteremia due to members of the family Enterobacteriaceae. Mortality due to *E. coli* bacteremia appears to be lower now than 2 decades ago. In our earlier report [11], 41% of patients died of causes directly related to bacteremia, compared with an associated mortality of 10.3% in this study.

Grandsen et al. [68] prospectively evaluated *E. coli* bacteremia in London from 1969 through 1987 and noted a case-fatality rate of 20.7%; approximately half the deaths were judged to be directly related to sepsis. Similarly, the recent review by Roberts and colleagues [18] noted that the 30-day mortality due to *E. coli* bacteremia was 21.5%. Mortality associated with *K. pneumoniae* bacteremia has ranged from 14.6% in the current study to 37% (crude mortality) in another recent report [69]. Korvick et al. [70] reported 19% mortality at 14 days in a recent multicenter study of 230 patients with klebsiella bacteremia.

Mortality associated with serratia bacteremia was 30% among our patients; by contrast, Saito and colleagues [71] reported a mortality rate of 23% in cancer patients between 1982 and 1987. In the present series, associated mortality among 12 patients with *E. cloacae* bacteremia was 8.3%, compared with crude mortality of 24% in a recent multicenter study of 129 patients with enterobacter (all species) bacteremia [72]. The attributable mortality between 1980 and 1992 among patients with *Proteus mirabilis* bacteremia was 25.6% in a recent report [73], remarkably similar to the bacteremia-associated mortality of 23.1% in this series.

Source of infection. As in our earlier study [11], the mortality associated with bacteremia was increased when the primary focus of infection was either unknown or at a site that was difficult to treat, such as the respiratory tract or the bowel and peritoneum. Similarly, when the primary focus of infection could be removed or drained easily (e.g., the genitourinary tract), the mortality was reduced (table 9). The higher mortality in septicemia with an unknown primary focus of infection also has been noted by others [19–21].

Body temperature. The current study confirmed the observations made in our earlier report [11], namely, that the inability of a patient to mount a febrile response to septicemia is a poor prognostic sign (figure 2). This relationship has been noted by others [9, 74, 75] but could not be confirmed in a study designed to examine independent predictors of mortality associated with bloodstream infections [55]. Kluger [76] and Roberts [77] have each recently presented information to support the premise that the presence of physiologically elevated body temperature is beneficial.

Blood pressure. The well-known association between hypotension as a marker for septic shock and poor outcome was again confirmed during this study. This association was noted not only in prior studies [9, 11, 74] but also in more recent reports [18–21]. Compared with data in our earlier review [11], the incremental risk of death when hypotension was present was greater in the current series than was noted previously (RR, 2.8 vs. 2.0).

Total leukocyte count and absolute neutrophil count. Infection-associated mortality and relative risk of death from bacteremia were increased among patients with leukopenia and absolute granulocytopenia, as in our earlier study [11]. In addition, in this study mortality was increased also among patients with total leukocyte counts $\geq 20{,}000/\mu L$. Recent studies in varied patient groups have provided similar observations [17, 60].

Predisposing factors. For consistency and to enable accurate comparisons of risk associated with various underlying conditions that may affect mortality among patients with bacteremia and fungemia, we used the same criteria and definitions as in our earlier review [11] and included HIV infection and AIDS, neither of which were known at the time the earlier study was undertaken. Moreover, the risk associated with each factor was judged when that condition was the only one present (table 12).

As in the earlier study [11], increased risk of death in bacteremia was associated with the presence of malignancies and

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biopsy-proven hepatic cirrhosis. In contrast with our earlier observations, the presence of moderate renal failure (serum creatinine level, 2.0–5.0 mg/dL) but not severe renal failure (serum creatinine level, >5 mg/dL) was associated with increased mortality among bacteremic patients.

Although this observation may seem paradoxical, we interpret the results to suggest that patients with chronic renal failure probably were undergoing dialysis and therefore had stable albeit poor renal function, whereas those with moderate renal failure were more likely to have acute deterioration of function and greater metabolic instability which, in turn, was associated with a greater likelihood of a poor outcome. Finally, the presence of AIDS was associated with an increased risk of death associated with bacteremia or fungemia.

Antibiotic and other therapy. Intuitively, one would expect that administration of antimicrobial agents active in vitro against the infecting microorganism(s) would be associated with improved prognosis. Our prior study and others [11, 78, 79] have supported this assumption, and the current study again confirmed the principle (table 13). By assessing therapy at several different time points, we hoped to determine that degree to which appropriate treatment affected outcome at each stage.

One might have expected, for example, that appropriate therapy given early (empirical therapy time point) would be associated with lower attributable mortality than would appropriate therapy delayed until after susceptibility test results were available to the physician. Indeed, this was the case. As is evident in table 13, the lowest attributable mortality occurred among those patients who received appropriate therapy throughout the course of their septicemic episodes (10.4%). Prompt initiation of appropriate therapy by physicians after notification of a positive blood culture also was associated with low mortality (13.3%). If appropriate therapy was not initiated until after susceptibility test results were available, mortality was 25.8%.

Why 60 (7.6%) of 791 septicemic patients received inappropriate therapy even after the identification and antibiotic susceptibilities of infecting microorganisms were reported is uncertain (table 13). Antibiotic misuse has been studied by others. In one report [80], the most common form of misuse in bacteremic patients was the administration of superfluous agents, a finding that corroborates our observations. In another study [81], multivariate analysis showed that four clinical variables (i.e., nosocomial bacteremia, recent prior antibiotic therapy, nursing home residence, and central iv catheters) and four microorganisms (i.e., *Candida, Acinetobacter, Enterococcus,* and *Pseudomonas* species) were independently associated with inappropriate antimicrobial therapy. Our data also showed that the use of inappropriate therapy was more likely to occur on the surgical services.

A fundamental principle in the management of bloodstream infections has always been that eradication of the primary source of infection is a necessary component of the therapeutic regimen. Thus, removal, drainage, or excision of an infected focus, when possible, should result in an improved prognosis. Both the current study and our prior report [11] provide support for this principle. Indeed, in the current study, infection-associated mortality among patients who had a primary focus that was excised, drained, or removed was less than one-third that among patients who did not have these interventions (6.2% vs. 22.0%, respectively).

Multivariate Analysis of Factors Influencing Prognosis

As in the earlier review by our group [11], we subjected each of the variables that were associated with an increased risk of death in univariate analyses to multivariate analysis (table 14). In the earlier report, seven variables were independently associated with an increased risk of death; all but one were confirmed in the current study. These included advanced age, microorganism, source of infection, predisposing factors, hypotension, and absence of fever. Nosocomial acquisition of bacteremia was not an independent predictor of death in the current study, in contrast to the observations in the earlier report.

In our earlier report we were unable to include antimicrobial therapy in the multivariate analysis. Inclusion of therapy was possible in this study and confirmed the importance of administering appropriate antimicrobial agents.

Although advanced age again was an independent predictor of poor prognosis, the increased risk statistically was greatest after age 70 years in the current study, compared with age >40 years in the earlier series. Septicemia caused by a high-risk microorganism also was again an independent risk factor in multivariate analysis, but there were some changes in the individual microorganisms associated with a high risk of death. In the earlier report there was increased risk with gram-negative rods generally, whereas in the current study increased risk was observed only with Enterobacteriaceae other than *E. coli.*

The reasons for this difference are not readily apparent. Speculation might focus on greater resistance to antimicrobial agents among these strains than among *E. coli.* In contrast to the results of the earlier series, enterococcal bacteremia was not associated with increased risk in the current study. However, fungemia was confirmed to be associated with poor prognosis, in concordance with our earlier observations.

Primary foci of infection in the respiratory tract, bowel, or peritoneum and septicemia from an unknown source again were shown to be independent predictors of poor prognosis. However, primary foci in abscesses, skin, and surgical wounds, each of which was associated with an increased risk of death in the earlier series, were not associated independently with increased risk in the present study.

As in the earlier study, the presence of underlying diseases associated with high risk in univariate analysis was an independent predictor of increased mortality in the multivariate analysis. The underlying diseases associated with high risk were somewhat different from those in the earlier report and included AIDS, a syndrome that was unknown at the time of the earlier

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review; renal failure, which was not a high-risk factor in the prior study; and malignancies, which were high-risk factors in the earlier study.

Comparative Features of Bacteremia and Fungemia in the 1970s and 1990s

During the past 20 years, numerous changes have occurred in medicine and health care. Nevertheless, several fundamental aspects of bloodstream infections have remained constant. Major examples include the continued frequency with which *S. aureus* and *E. coli* are causative agents of bacteremia; the importance of the respiratory tract, genitourinary tract, and bowel as primary foci; the association between gram-negative or polymicrobial bacteremia and septic shock; and the importance of advanced age, difficult-to-eradicate or unknown sources, malignancies and renal failure, hypotension, and absence of fever as independent predictors of a poor outcome (table 15).

The differences noted in the 1990s provide cause for concern but perhaps also for optimism (table 15). The increased proportion of blood isolates representing contamination is of concern, especially in an environment that mandates cost-effective care. The frequency of coagulase-negative staphylococcal isolation particularly is problematic, since it often is difficult for clinicians to determine the clinical significance of these bacteria. The decrease in anaerobic bacteremia and proportionate increase in fungemia have prompted some authorities to recommend changes in routine blood culture techniques [82].

Table 15. Major similarities and differences in positive blood cultures, 1975–1977 [10, 11] and 1992–1993.

Similarities	• *Staphylococcus aureus* and *Escherichia coli* most frequent etiologic agents
	• Importance of respiratory tract, genitourinary tract, and bowel as primary foci
	• Association of gram-negative and polymicrobial bacteremia with septic shock
	• Importance of age, source of infection, predisposing factors, hypotension, and absence of fever as independent predictors of poor outcome
Differences	• Increased importance of iv catheters as source of septicemia
	• Increased proportion of isolates representing contamination
	• Increased isolation of coagulase-negative staphylococci, both as contaminants and as pathogens
	• Increased frequency of *Pseudomonas aeruginosa* as a community-acquired pathogen
	• Emergence of *M. avium* complex as cause of bloodstream infection in HIV-infected patients
	• Proportionate increase in fungemia and decrease in anaerobic bacteremia
	• Decreased mortality

The most frequent source of bloodstream infections has become the intravenous catheter, and it may be expected that prosthetic materials and devices will continue to be important sources of infection. HIV infection and AIDS have allowed *M. avium* complex to become a bloodstream pathogen, and the increased frequency of community-acquired *P. aeruginosa* bacteremia also seems to be associated with HIV-infected patients [49–51].

The most optimistic finding with regard to bacteremia and fungemia in the 1990s is that mortality associated with these serious infections has decreased. The reasons for this improved outcome are not fully explained but could be related to earlier detection with use of modern blood culture systems; more sophisticated imaging methods that better elucidate primary foci of infection; the frequency of infections emanating from easily removed (iv catheters) or drained (genitourinary tract) foci; and improved antimicrobial agents and use thereof by clinicians.

Although we have shown that mortality is lower than it was 2 decades ago, bacteremia and fungemia remain serious syndromes with substantial risk. Moreover, the combination of an aging population, improved survival among immunocompromised patients and those with organ transplants, and the emergence of β-lactam-drug-resistant gram-positive and gram-negative bacteria as well as vancomycin-resistant enterococci (and possibly staphylococci in the future) [83], will continue to challenge all who care for patients with bloodstream infections.

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Interventions Implemented to Reduce the Risk of Transmission of Bacteria by Transfusion in the English National Blood Service

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Abstract

Summary

Background

Bacterial contamination remains a significant problem in transfusion medicine. A National Health Service Blood and Transplant (NHSBT) study and surveillance data indicated skin commensals derived from the skin of the donor are the major contaminants of blood components. NHSBT therefore explored two interventions: improved donor arm disinfection and diversion.

Methods

Improved donor arm disinfection: Commercial and in-house methods of disinfection were evaluated. Swabs of the venepuncture site were taken before and after disinfection and the reduction in bioburden determined. Diversion: Special collection bags were manufactured to allow the initial volume of blood to flow into a pouch, representing the diversion pouch and then the next flow of blood into another pouch representing the collection bag. Pouches were screened for the presence of bacteria. The reduction in bacterial contamination was then determined.

Results

A two-step commercial procedure (Donor Prep Kit; DPK) consisting of 70% isopropyl alcohol followed by tincture of iodine was shown to be a best practice procedure (2-min procedure). A 99.79% reduction was obtained, and this method was 10 times more effective than current practice at that time. The DPK was shown in a field trial to increase donor waiting time. A second study was initiated to find a more rapid procedure. ChloraPrep®, consisting of 2% chlorhexidine gluconate and 70% isopropyl alcohol, was shown to have equivalent disinfection efficiency as the DPK, but only took 1 min to perform. In 2006, ChloraPrep was introduced as the national method of donor arm disinfection. Diversion was shown to give a 47% reduction in contamination and was introduced nationally in 2002.

Conclusion

Improved donor arm disinfection and diversion are effective, low-cost interventions, but do not eliminate all bacterial transmissions. In 2011, bacterial screening of platelet components was introduced by NHSBT to further increase the safety of the blood supply.

KeyWords: Bacterial contamination, Blood donation, Blood safety, Haemovigilance, Platelet concentrates, Transfusion reaction, Transfusion risks, Transfusion-associated infectious Bacteria, Diversion, Disinfection

Introduction

Since the 1970s, the risk of viral transmission by transfusion has been markedly reduced [1]. Transmission of bacteria by transfusion is not a new problem, having been reported nearly 70 years ago [2, 3]. In the mid 1990s, the attention of the blood community was drawn to bacterial transmissions due to case reports in the literature and the establishment of haemovigilance systems. In 1995 the U.K. Serious Hazards of Transfusion (SHOT) voluntary surveillance system was established, reporting that between 1995 and 2001 bacterial transmissions accounted for 64% (21/33) of microbial transmissions [4]. In this period in the UK, 85% (6/7) of microbial fatalities reported to SHOT were due to transmission of bacteria by transfusion. Platelet concentrates accounted for 81% (17/21) of these transmissions.

From 1994 to 1999, the French haemovigilance surveillance system (a mandatory requirement under French law), attributed 18 deaths (four occurring in 1997) to blood components contaminated with bacteria [5, 6]. Between 1994 and 1999, bacterial transmissions comprised 22% of total transfusion-associated fatalities [7]. Transmission of bacteria by transfusion was reported to the haemovigilance surveillance system as the most frequently identified cause of death [5].

In the USA, from 1985 to 1989 bacterial contamination was second only to haemolytic reactions as the most frequent reported cause of mortality, accounting for over 10% (77/694) of transfusion fatalities [8]. From 2001 to 2003, the transmission of bacteria by transfusion accounted for 37 deaths, amounting to 14.1% of all transfusion fatalities [9].

A National Health Service Blood and Transplant (NHSBT) retrospective monitoring study was established in 1995 to determine the bacterial contamination rate in blood components using an automated microbial detection system [10, 11]. The study was also used to determine the effectiveness of any interventions implemented to reduce bacterial contamination.

Data from this study and SHOT surveillance data indicated that the vast majority of organisms that contaminate blood components are skin commensals derived from the skin of the donor at venepuncture. NHSBT therefore explored two interventions:

– improved donor arm disinfection,
– diversion.

Material and Methods

Improved Donor Arm Disinfection

A study was undertaken to determine the effectiveness of in-house and commercial disinfection protocols [12]. Swabbing of the venepuncture site was performed before and after disinfection. Swabs were inoculated onto agar plates, and the reduction in bioburden pre and post disinfection was determined. A second study was undertaken to derive a disinfection procedure that would only take 1 min to perform [13].

Diversion

In 1995, Olthuis et al. [14] proposed that diversion of the initial volume of blood donation from the collection bag had the potential to dramatically reduce bacterial contamination. The rationale behind this is that (as previously mentioned) the major source of bacterial contamination of blood components occurs at the collection stage, due to inadequate donor arm disinfection and/or a small core of skin entering the collection bag from coring by the phlebotomy needle. Re-direction of the initial flow of blood from the collection bag into a pouch or side arm would thus reduce the risk of bacterial contamination of the donation contents.

Special collection bags were manufactured for a study to determine the effectiveness of diversion [15]. These bags consisted of two sampling pouches attached to the standard collection bag configuration. At donation, blood was made to flow initially into pouch P1, which represented a diversion pouch. Pouch P1 was then closed causing the blood to flow into pouch P2, which acted as a representative sample of the collection bag post diversion. P2 was then closed, and blood was

diverted into the collection bag as in a routine donation. The pouches were sampled and inoculated into culture bottles and incubated on an automated microbial detection system for 7 days. Any bacteria that grew were sub-cultured and identified.

Results

Improved Donor Arm Disinfection

The Donor Prep Kit (DPK) (Ecolab (formerly Medi-Flex), Leadwood, KS, USA) was shown to be a best-practice technique, consisting of an initial application of isopropyl alcohol and tincture of iodine. The procedure took 2 min, with an application time of 30 s and drying time of 30 s for each disinfectant. A percentage reduction of 99.79% ($\log_{10}$ reduction 2.67%) was obtained compared with 78.2% ($\log_{10}$ reduction 1.31%) for the then current method, 0.5% chlorhexidine isopropyl alcohol wipe (Guardpack, Chelmsford, Essex, UK) [12].

The DPK was implemented for apheresis platelet donations in July 2001, and the reduction in the bacterial contamination rate of time-expired platelet donations was shown to be 57% [16]. Previously an experimental study predicted a 57% reduction in contamination [15]. A 67% reduction in clinically apparent cases of bacterial transmission following transfusion of NHSBT blood donations reported to SHOT was observed [17]. In the period 1997 to 2000 prior to implementation, 6 clinical cases (including 2 deaths) were reported. After the introduction of the DPK at apheresis clinics in the 4-year period from July 2001 to 2005, only 2 clinically apparent reactions from transfusion of platelet concentrates manufactured by NHSBT have been reported.

An extensive field evaluation of the use of the DPK procedure has been undertaken at mobile blood donor sessions. It was however, deemed inappropriate for routine use by NHSBT because it would increase donor waiting times. This was due to the additional 3 min that was required with the DPK compared with the routine method in use at that time. The NHSBT National Bacteriology Laboratory (NBL) was therefore tasked with identifying a disinfection procedure that was of comparable disinfection efficacy as the DPK, but was only 1 min in duration.

The ChloraPrep® disinfection method (CareFusion Ltd, Reigate, UK), consisting of a 30-second application of 70% isopropyl alcohol and 2% chlorhexidine gluconate with a 30-second drying time was shown to give equivalent disinfection efficiency as the DPK [13]. In 2006, ChloraPrep was implemented throughout NHSBT for both routine and apheresis donations.

Diversion

A 47% reduction in bacterially contaminated blood donations was observed in our study on the effectiveness of diversion [15]. On the basis of this study, diversion was implemented nationally in 2002. Monitoring data derived from testing outdated platelet concentrates showed a 66% reduction in contamination [16]. Prior to the implementation of diversion in the 3-year period 1999 to 2001, there were 11 clinically apparent cases from NHSBT-produced pooled platelet concentrates (n = 9) and red cell units (n = 2). After the implementation of diversion in the 3-year period 2003 to 2005, there were only 2 reports of clinically apparent transmission of bacteria by transfusion, a reduction of 82% [17].

The NHSBT diversion study also indicated that diversion, together with improved donor arm disinfection, would reduce bacterial contamination by approximately 77% [15].

Discussion

Donor arm disinfection is the first physical intervention applied to prevent microbial contamination of a blood donation. Many blood services have now validated and implemented best-practice procedures [18, 19]. In Canada the DPK system was shown to be a best-practice procedure, a finding confirmed by our studies [20]. Studies in the USA and Canada with the ChloraPrep disinfection device have confirmed the findings of NHSBT [21, 22]. This device has been adopted for use in these countries. Since the work of NHSBT, the evidence-based practice in Infection Control Guidelines Version 2 (epic 2) for National Health Service hospitals in England recommend "a single patient use application of alcoholic chlorhexidine gluconate solution, preferably 2% chlorhexidine in 70% isopropyl alcohol" for central venous access device decontamination [23].

The NHSBT diversion study indicated that a 47% reduction in bacterial contamination would be obtained, although a greater reduction of 66% was observed in the outdated platelet study, and clinically apparent transmissions were reduced by as much as 82%. Studies in the Netherlands by de Korte et al. [24] and by Ohbins et al. [16] showed a 40% and 82% reduction respectively. Brunead et al. [25] in France reported a 72% and Benjamin et al. in the USA a 54% reduction in bacterial contamination [26]. Diversion has now been widely adopted by blood services.

Improved donor arm disinfection and diversion have been shown to be highly effective, relatively low-cost interventions for reducing the transmission of bacteria by transfusion. An NHSBT study indicated that improved donor arm disinfection in conjunction with diversion would reduce bacterial contamination by approximately 77% [27]. Residual contamination levels of blood units after the introduction of diversion may be in the order of 30–40% [23, 27].

Since 2006, improved donor arm disinfection and diversion have been used for all NHSBT donations. In the period of SHOT haemovigilance 2006–2009, bacterial transmission was reported from 10 NHSBT donations which resulted in 4 deaths [27]. In November 2005 in the UK, it became mandatory to report adverse transfusion reactions, which resulted in an increase in bacterial investigations, revealing more cases of transmission. In 2011, in view of this data, NHSBT implemented bacterial screening of platelet concentrates to further increase the safety of the blood supply.

Disclosure Statement

The author declared no conflicts of interest.

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US) 72) [Inventor] [Name] Edward El Nazyant (72) [Inventor] [Name] Josef Kaufman (74)

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(57) [Abstract] Since this gazette is application data before electronic filing, abstract data is n ot recorded.

The scope of the claims open —

Claims:

(1) a housing having a forward end and a rearward end; a sample collection chamber within s aid housing; and a first open passageway at said forward end and in fluid communication with said sample collection chamber. a first puncture needle extending outwardly from said first op en passageway for insertion into a collection source; and a second puncture needle at said rea rward end in fluid communication with said sample collection chamber. a sample collection de vice for collecting one or more liquid samples from a collection source and discharging into a n egative pressure vessel for collection, comprising: an open passageway in said second open p assageway; a second piercing needle extending into the sample collection chamber to a point spaced from the first open passageway, the second piercing needles mutually extending into t he sample collection chamber; having spaced apart first and second openings, the first and se cond openings providing fluid communication between the sample collection chamber and the lumen of the second puncture needle; from a first position that closes the opening of and ope ns the second opening to a second position that opens the first opening along the second pun cture needle so as to be able to reciprocate the sample collection a gas permeable, liquid imp ermeable, annular porous plug positioned within the chamber, wherein liquid is introduced int o the sample collection chamber when the first puncture needle is engaged with the collection source; all of the gas is pushed out and flows into the second puncture needle through the firs t and second openings, and when the second puncture needle receives the negative pressure

container, the annular porous plug is closed on both sides thereof. The action of the differentia l pressure moves toward the second opening passage to open the first opening and into the s ample collection chamber to the second opening located on the negative pressure side of the annular porous plug. A sample collection device, wherein residual gas is expelled so that the li quid in the sample collection chamber can be collected into the negative pressure container th rough the second puncture needle.

(2) The sample collection device according to claim 1, wherein the annular porous plug is mad e of sintered polyethylene, open-cell foamed polyethylene, or porous polyethylene.A sample c ollection device which is a member made from any of the group consisting of ethylene, porous polyfluorocarbon, and mixtures thereof.

(3) In the sample collection device according to claim 1, a third opening provided in a portion of the second puncture needle extending outward from the housing and the second puncture needle a resilient sleeve extending over the distal end of the sample collection chamber oppos ite the sample collection chamber, wherein the sleeve extends into the third opening when the negative pressure container is penetrated by the second puncture needle; A sample collection device, characterized in that it closes the

(4) The sample collection device of claim 1, having a resilient sleeve slidably engaging said se cond puncture needle at an end opposite said sample collection chamber. and said needle-eng aging surface on the inside of said sleeve has a plurality of longitudinally extending grooves, s aid needle-engaging grooves being gas permeable and liquid impermeable. A sample collectio n device characterized by:

(5) A sample collection device as claimed in claim 1, wherein said housing includes means for connecting a support for a vacuum vessel.

(6) A sample-collecting device according to claim 5, wherein a support for a negative pressure vessel is connected to said housing.

(7) The sample collection device of claim 3, wherein said housing includes means for connecti ng a support for a vacuum vessel.

(8) The sample collection device of claim 1, wherein said housing includes a device for observi ng the contents of said sample collection chamber.

(9) A sample collection device according to claim 8, wherein the device for observing the cont ents is a transparent housing wall adjacent to the sample collection chamber.

(10) The collection device of claim 1, comprising a resilient sleeve slidingly engaging the punc ture needle at the end of the puncture needle opposite the sample collection chamber, The ne edle-engaging surface on the inside of the sleeve forms a stepped inner surface, and a portion of the longitudinal region of the surface sealingly engages the outer surface of the associated second needle. forming an internal bore of small diameter for mating, and another portion of t he lengthwise region of the stepped inner surface forms an air passageway with the mating o uter surface of the second puncture needle. A sample collection device characterized by formi ng a large diameter internal aperture.

detailed description open —

DETAILED DESCRIPTION OF THE INVENTION

The present invention relates to a device for collecting a liquid sample such as blood from a p atient. More particularly, the invention relates to needle assemblies for collecting one or more liquid samples from such patients. The device of the present invention employs an introductio n chamber with transparent or translucent walls to allow observation of whether the needle in question is in close proximity to the proper position. The introduction chamber has therein a r eciprocating plug formed of a material which provides an obstruction wall for the liquid receive d and an exhaust passageway for the gas pushed out by the liquid sample received in the intr oduction chamber. incorporated.

When the stopper initially receives the sample liquid, it reciprocates to prevent the liquid sam ple from being expelled while at the same time causing gas to be expelled by the liquid sampl e. Then, as the liquid sample is discharged into one or more of the vacuum collection vessels, the plug is assembled to continuously discharge the collected sample through the one or more vacuum collection vessels. It reciprocates in cooperation with vent holes in the discharge are a. In the case where multiple samples are continuously collected and discharged into multiple vacuum vessels, the assembly may be used with the discharge opening of the device during t he exchange period of the vacuum collection vessel in preparation for the next sample dischar ge. It includes a cooperating flexible sleeve.

As noted above, it is desirable to provide a mechanism for informing the user of such a needle assembly that the venous needle has penetrated the patient's vein from which a blood sample is to be collected. Venous placement is often difficult when collecting blood from a patient and there may be inadequate blood flow to the collection container for other reasons. thisIn such c ases, it is beneficial to be able to quickly perceive the entry of the needle into the vein and th e flow of blood into the needle assembly. Upon such sensing of needle entry, a negative press ure collection container is inserted into the collection assembly in accordance with well-known blood sampling techniques during a single sample collection procedure.

One of the problems encountered during the venipuncture step is air pockets found in various needle assemblies for one or more blood samplings. When a venipuncture is performed and a negative pressure collection container is not yet attached to the opposite end of the needle as sembly, under normal atmospheric conditions blood will always flow through the needle due to the pool of air remaining inside the needle assembly. It does not necessarily flow into the asse mbly. Thus, once the venipuncture is accomplished, blood flow is not initiated simply by the o bstruction of an air pocket within the needle assembly.

In accordance with the present invention, by contrast, the use of a porous plug within the coll ection chamber forces air out of the collection chamber so that the collection chamber receive s the collected blood sample. In addition, the plug initially evacuates expelled air during the a cceptance period of the procedure for receiving the sample, and the needle assembly to disch arge the sample to the vacuum collection container when the vacuum container is attached to the needle assembly. is positioned within the collection chamber to cooperate with an outlet in the negative pressure puncture needle. For example, in one embodiment for a single sample c ollection procedure of the present invention, the assembly of the present invention vents expe lled air as the sample is introduced, and a negative pressure vessel is attached to the assembl y for evacuation of the negative pressure puncture. A porous plug that moves to open a passa geway in the assembly in response to the differential pressure to expel the introduced sample into the vacuum collection vessel when the needle penetrates into the vacuum collection vess el. have.

Another embodiment of the invention has a flexible sleeve that covers the discharge opening of the negative pressure needle. The flexible sleeve is arranged to expel air from the third eva cuation outlet in the evacuation needle during sample introduction. The flexible sleeve then fle xes and moves to cover the third discharge outlet when the negative pressure blood collection container is inserted into the assembly as it is penetrated by the negative pressure puncture n eedle. Once one sample is obtained in the negative pressure blood collection device and the n egative pressure container is removed from the assembly, the flexible sleeve is then held neg ative until the negative pressure container is attached for a second sample collection. It cover s the exit opening of the pressure puncture needle. As is well known to those skilled in the ar t, this procedure is repeated to collect the required number of samples into separate negative pressure blood collection containers.

Considering the use of porous plugs in blood collection devices of the type described herein, p rior U.S. Ser. William N. Eldvidge, inventor (assigned to the same person) in "Blood Sampling Assembly Having Vein Entry Indicator" states that an air pool can be perceived by the user thr ough a venous needle. He knew he was preventing the desired flow of blood to the point. The Eldridge invention includes a porous plug that mates with a one-way valve that allows air insid e the needle assembly to pass out of this vent during the initial stages of the blood collection procedure. The vent prevents passage of blood until the user adheres the blood collection devi ce to the needle assembly. Upon contact with the negative pressure of the negative pressure blood collection container, a separate one-way valve opens to carry blood from the patient's v ein through the needle assembly and into the collection container.

Although the Eldridge invention recognized the use of a porous material to vent the displaced air while receiving blood, there remains room for improvement of such devices, particularly th e present invention. Related. That is, the plug of the present invention does not reciprocate a nd act merely as a vent, but acts as a valve mechanism itself without a separate and complex structure to provide valve action. That is, the plug of the present invention cooperates with an

d reciprocally engages the blood introduction chamber to vent air from the introduction cham ber, but not to expel the blood sample, but not the blood introduced when the assembly is ad hered to the negative pressure blood collection container. move to expel the

Next, description will be made with reference to the drawings. In the drawings, the same part s are denoted by the same reference numerals. Fig. 1 shows the housing12 shows the basic e xternal components of the needle assembly 10 including a first needle 14 for insertion into a p atient and a second needle 15 subjected to negative pressure at the opposite end of the housi ng 12; ing. A second puncture needle 15 is adapted to be inserted into a negative pressure co ntainer 16 for collecting a blood sample. Housing 12 includes a threaded portion 25 having thr eads 18 adjacent a second puncture needle 15 into which a container support 19 is threaded by an inner combination thread 20 provided at its forward end. The vacuum container 16 is in serted into the container support 19 so that the second puncture needle 15 penetrates the sto pper 21 at the front end of the vacuum container 16 . Such general aspects of sample collecti on vessels are well known to those skilled in the art.

Description will be made with reference to FIG. Housing 12 preferably has a forward end 24 a nd a rearward end 25 which are separable for insertion of a porous plug 27 therein. Forward e nd 24 is preferably cylindrical and has a large mouth opening 28 for reciprocatingly receiving a porous plug 27 therein. The opposite end of this portion is provided with a small port 29 for receiving the first puncture needle 14 therein. In this embodiment the small port 29 extends t o a smaller small diameter conduit 30 which communicates the ports 29 and 28 with each oth er. A stepped portion 33 for receiving the first puncture needle 14 in a contacting state is form ed at the junction of the mouth hole 29 and the conduit 30 . The first puncture needle 14 may be secured within the aperture 29 by a suitable adhesive. Those skilled in the art will recogniz e that the conduit 30 is not an essential element for this construction, but merely a preferred form. Further, the diameter of conduit 30 can be varied to regulate the flow rate of fluid passi ng therethrough.

The forward end 24 of the housing also includes a number of longitudinal ribs 31 surrounding the outwardly extending first needle. A sheath (not shown) having internal ribs that mate with ribs 31 substantially covers the outwardly extending first puncture needle. Interlocking ribs be tween the puncture needle armor and the needle assembly facilitate insertion and removal of the armor from the needle assembly by the user. Forward end 24 also includes an annular flan ge 32 which serves as a mating surface when the two portions of the housing are joined into an assembly. Again, an adhesive or similar suitable fastening material can be used to secure t he two parts of the housing and assembly.

Rear end 25 includes a slightly protruding cylindrical portion 40 sized to fit inside port 28 of th e forward end. Opposite this rearward end, external threads 18 are provided at 26 on rearwar d end 25, as previously described in connection with the tube support. An aperture 70 similar to aperture 29 at the forward end of the housing extends through the rearward end of the hou sing. The aperture 70 is sized to match the diameter of the second puncture needle 15 and ag

ain the second puncture needle is secured to the aperture 70 by a suitable material such as a n adhesive. An annular flange 46 is provided corresponding to the annular flange 32 to join th e two ends 24 and 25 of the housing together. It will be appreciated that the flanges 32 and 4 6 may be secured by a suitable securing material such as adhesive when the two portions of t he housing are assembled with the plug 27 positioned therein. A mouth opening 28 in forward end 24 defines a tubular chamber 50 for receiving the liquid sample to be collected.

Annular wall 88 at the forward end of tubular chamber 50 is made of a translucent or transpar ent material to allow viewing of the contents of tubular chamber 50 and to inform the user of the device that the puncture needle has reached the vein. is preferably formed of Those skille d in the art will appreciate that from a manufacturing standpoint, the entire forward end of th e needle assembly is preferably made of a transparent material such as a hard thermoplastic r esin. However, a sealed window, port or other device for observing the contents of tubular cha mber 50 by the user of the device is within the scope of the invention.

The porous plug 27 is reciprocally mounted in the orifice 28 and has an inner orifice 72 for rec iprocating engagement with the forward end of the puncture needle 15 which is subjected to negative pressure. As is well known, the porous plug 27 is an opening.The bore 28 is cylindric al in shape, the diameter of which engages the wall of the tubular chamber 50 in a fluid-tight manner, and the action of the differential pressure on the opposite surface thereof causes the plug 27 to reciprocate within the bore 28. It is defined so that it can be done.

The porous plug 27 is made of a so-called gas-permeable, liquid-impermeable material which allows the passage of gas, eg air, but not the passage of liquid, eg blood. Examples of materia ls that may be used to form the porous plug 27 include sintered polyethylene, open cell foame d polyethylene, and other similar moldable polymeric materials such as porous polypropylene and porous polyfluorocarbon.

As shown in FIG. 2, negative pressure needle 15 includes a notch 74 adjacent end 84 thereof. In this regard, depending on the positioning of the porous plug 27, the notch 74 communicate s between the tubular chamber 50 and the lumen of the second piercing needle 15 so that the end 84 of the porous plug 27 is not blocked by the plug. or deformed or otherwise closed. An additional notch or opening 76 is provided to provide communication between the rearward en d 51 of tubular chamber 50 and second puncture needle 15 . Further, as shown in FIG. 2, a thi rd notch or opening 78 is provided which provides communication between the atmosphere, t he peripheral region of the assembly of the present invention, and the lumen of the second pu ncture needle 15 .

Next, description will be made with reference to FIG. A needle assembly connected to support 19 is shown. A first puncture needle 14 is shown being inserted into a patient P during venipu ncture. When first puncture needle 14 enters patient P's vein, blood flows from the vein throu gh first puncture needle 14 and small bore conduit 30 into tubular chamber 50 . When blood e nters tubular chamber 50 , the air in tubular chamber 50 is forced out of tubular chamber 50 t hrough porous plug 27 , but blood does not pass through porous plug 27 due to the characteri

stics of porous plug 27 . Air passing through plug 27 passes from tubular chamber 50 through notches 74 and 76 and further through the lumen of second puncture needle 15 and external notch 78 to the flexible tube covering the outer end of negative pressure puncture needle 15 . 2, into the area 82 (FIG. 2) between the flange 92 of the armor 80 and the end face 106 of th e end 25 of the housing. The plug 27 now remains in the position shown in FIG. 2 over the ori fice or notch 74. FIG. Further here a blood sample taken from patient P is located in tubular c hamber 50 .

Referring now to FIG. 3, the assembly is shown having support 19 attached to hub portion 26 of rear housing 25. As shown in FIG. Negative pressure blood collection container 16 is shown fitted into support 19 with a resilient plug pierced by the end or point 100 of negative pressur e puncture needle 15 . Penetration of puncture needle 15 into plug 21 creates a vacuum, whic h vacuum or negative pressure draws any air remaining in tubular chamber 50 away from the inner region of negative pressure vessel 16 and notch 74 and Withdraw through porous plug 2 7 by communicating 76 through the lumen of puncture needle 15 . As the plug 27 becomes oc cluded by blood, a differential pressure is created between the upper tubular chamber 50 and the lower tubular chamber 51 causing the plug 27 to move downward toward the plane of the extension 40 as shown in FIG.

This movement causes plug 27 to uncover opening or notch 74 . Any residual air trapped in th e lower tubular chamber 51 during this movement passes through the notch 76 and aids the movement of the plug 27 . When the notch 74 is uncovered, communication is provided betwe en the tubular chamber 50 and the negative pressure container 16 through the lumen of the n egative pressure puncture needle 15 . On the other hand, the insertion of the vacuum vessel 16 into the support 19 and the penetration of the puncture needle 15 through the plug 21 by t he point 100 causes the armor 80 to be pulled upwards, as shown in FIG. 26 to a position wh ere it engages the bottom surface 106 . Thus, the blood sample that has been drawn from the patient P's vein and contained in the tubular chamber 50 moves into the negative pressure col lection container 16 . Once the sample has been withdrawn into container 16 , container 16 is removed from support 19 thereby returning armor 80 to a position covering notch 78 and ove r end 100 of negative pressure puncture needle 15 . In this manner, the first puncture needle 14 remains in the vein without leaking blood, allowing a plurality of needles to be inserted int o the vein.Allows for continuous mounting of container 16 into support 19 for receiving a bloo d sample.

Referring now to FIG. 4, there is shown another embodiment in which notch 78 is not used in negative pressure puncture needle 15a. Identical parts in this device are designated by the sa me reference numerals with the suffix a. In this embodiment, puncture needle 15a has flange 108 instead of air passage or opening 78 which is always positioned adjacent surface 106a of extension 26a and in gas-tight closed engagement. A sleeve 90 is formed. As shown in FIG. 6, the sleeve 90 is positioned in sliding engagement over the puncture needle 15a. However, sle eve 90 has a plurality of internal grooves 94 where points 95 inside the grooves actually enga

ge the outer surface of puncture needle 15a. The groove thus provides gas communication be tween the puncture needle end 100a and the upper end of the sleeve 90 where air leaks betw een the adjacent surface of the flange 108 of the sleeve 90 and the surface 106a of the exten sion 26a. The grooves 94 are sized to allow passage of gas but not liquid. It will be appreciate d that the upper surface of flange 108 may similarly include grooves to provide ventilation bet ween end 100a and the atmosphere.

Yet another example of the invention which provides a single blood sample collection assembl y is shown in FIG. As shown in this assembly, no special sleeve 80 is used and puncture needl e 15b does not have a third notch or opening such as notch 78 in the embodiment shown in F IG. . Thus, when puncture needle 14 is inserted into a patient's vein, fluid communication is p rovided between the vein and tubular chamber 50 and a sample is collected in tubular chamb er 50 . The device does not allow the blood sample to flow through the porous plug 27 as in t he embodiment shown in FIG. However, the air forced out by the blood sample entering tubul ar chamber 50 passes through air permeable plug 27, notches 74, 76, the lumen of puncture needle 15, and exits end 100b of negative pressure puncture needle 15b. be done. When a su pport is mounted on extension 26b and point 100b of puncture needle 15b is inserted through the plug into negative pressure blood collection container 16, tubular chamber 50 above and t ubular chamber 51 below plug 27 are closed. A differential pressure is created between them which causes the plug 27 to move downward and open the notch 74 . This provides fluid com munication between the tubular chamber 50 and the vacuum vessel 16 for single sample colle ction into the vacuum vessel 16 . Since no further samples are collected by this assembly in t his embodiment, the puncture needle 14 is removed from the patient P's vein and the assemb ly is discarded as the required single sample has been collected into the vacuum container.

Another multiple sampling embodiment similar to that shown in FIG. 4 is shown in FIGS. 8a a nd 8b, in which air is communicated between point 100c of negative pressure puncture needle 15c and the atmosphere. In this embodiment, the inner diameter of sleeve 110 is stepped, an d the surface of sleeve 110 and puncture needle 15 combined with the small inner diameter 1 14 of sleeve 110 in close contact with the outer surface of puncture needle 15c. provides a lar ge inner diameter 116 that forms a vent passageway 118 for the . Thus, in the position shown in Figure 8a, ventilation occurs between the end 100c of the puncture needle 15c and the atm osphere through the passageway 118, and in the position shown in Figure 8b, the passagewa y 118 is closed preventing all ventilation.

As will be appreciated from the foregoing, in accordance with the present invention, a blood c ollection needle assembly is provided for collecting single or multiple samples incorporating a device that indicates venous penetration to its user. be. In addition, the device of the present i nvention with a porous plug having a simple form which is permeable to gas but impermeable to liquid and has the function of a valve is very simple and inexpensive to manufacture. It is p articularly suitable for mass production as will be appreciated by those skilled in the art.

Brief description of the drawing

open

BRIEF DESCRIPTION OF THE DRAWINGS FIG.
1 is a perspective view of a sample collection needle assembly, a support for a negative press ure container and a negative pressure blood collection container used to obtain a blood sampl e from a patient.
2 is an enlarged cross-sectional view taken along line 2--2 of FIG. 1 showing one embodiment of the present invention; FIG.
3 is an enlarged cross-sectional view along line 3--3 of FIG. 1; FIG.
FIG. 4 is a partial sectional view similar to FIG. 2 showing the present invention.Fig. 3 shows another embodiment of the light;
FIG. 5 is a perspective view of a needle assembly inserted into a patient and connected to a s upport to allow the user to visualize venous entry;
6 is a cross-sectional view along line 6--6 of FIG. 4; FIG.
FIG. 7 is a view similar to FIG. 2 but an enlarged cross-sectional view of a single sampling ne edle assembly illustrating another embodiment of the present invention;
Figure 8a is an enlarged partial cross-sectional view of a single sampling needle assembly sho wing another embodiment of the present invention;
Figure 8b is the embodiment of Figure 8a in the closed, non-vented position.
DESCRIPTION OF SYMBOLS 10... Needle assembly 12... Housing
14... First puncture needle 15... Second puncture needle 16...
Negative pressure container 19... Support tool 24
... Front end 25... Rear end
27... Annular shape Porous plug 29 First opening
50 Sample collection chamber 70 Second opening
74 First opening 76 Second opening
78 Third opening 80 Flexible sleeve
94 Groove 114 Small inner diameter
116 Large inner diameter

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SAMPLE COLLECTING APPARATUS

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A single or multiple liquid sample needle assembly is provided which incorporates means for determining whether access to the sample in question has been achieved. The assembly includes a housing (12) with a receiving chamber (50) having translucent or transparent walls (88) for such determination. The invention utilizes a porous plug (27) in the chamber (50) which provides, simultaneously, a liquid barrier for the sample received, and gas displacement venting means for gas displaced by the liquid sample received. The assembly may be modified to receive only a single sample for subsequent discharge to a vacuum collection device, or multiple samples for sequential discharge to a plurality of vacuum collection devices. For multiple collection, the assembly incorporates a flexible sleeve (80) and a separate gas discharge opening (78) in combination with the sample discharge opening of the assembly.

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⑤4試料採集装置

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明　　細　　書

1.〔発明の名称〕

試料採集装置

2.〔特許請求の範囲〕

(1)　前方端および後方端を有するハウジングと；該ハウジングの中にある試料採集室と；前記前方端にあり前記試料採集室と液体的に連通する第1の開口通路と；採集源の中に挿入するために前記第1の開口通路から外方へ向つて伸長する第1の穿刺針と；前記後方端にあり前記試料採集室と流体的に連通する第2の開口通路と；から構成され採集源から1つ又はそれ以上の液体試料を採集し負圧容器の中へ排出して採集するための試料採集装置において、前記第2の開口通路の中にあり前記試料採集室の中へ前記第1の開口通路から間隔を置いた点まで伸長する第2の穿刺針を有し、該第2の穿刺針は前記試料採集室の中へ伸長する部分に互に離間する第1および第2の開口部を有し、該第1および第2の開口部は前記試料採集室と前記第2の穿刺針の管腔の間を流体的に連通し、前記第1の開口部を閉鎖し前記第2の開口部を開口する第1の位置から前記第1の開口部を開口する第2の位置まで前記第2の穿刺針に沿つて往復動可能に前記試料採集室の中に置かれた気体透過性で液体不透可性の環状多孔質栓を有し、前記第1の穿刺針が前記採集源と係合すると液体が前記試料採集室の中へその中の気体を全て押し出して流入し前記第1および第2の開口部を通じて前記第2の穿刺針へ出てまた前記第2の穿刺針が負圧容器を受け入れると前記環状多孔質栓はその両側の差圧の作用によつて前記第2の開口通路に向つて移動して前記第1の開口部を閉口し、前記環状多孔質栓の負圧側に位置する前記第2の開口部へ前記試料採集室に残留する気体を押し出して前記試料採集室の中の液体を前記第2の穿刺針を通じて前記負圧容器の中へ採集できるようになつていることを特徴とする試料採集装置。

(2)　特許請求の範囲第1項に記載の試料採集装置において、前記環状多孔質栓が、焼結ポリエチレン、開放セル型発泡ポリエチレン、多孔性ポリ

エチレン、多孔性ポリフルオロカーボン、及びこれらの混合物、より成る群のいづれかにより作られた部材である試料採集装置。

(3) 特許請求の範囲第1項に記載の試料採集装置において、前記第2の穿刺針の前記ハウジングから外方へ伸長する部分に設けられた第3の開口部と前記第2の穿刺針の前記試料採集室とは反対側の端末部の上に伸長する弾力のあるスリーブとを有し、負圧容器が前記第2の穿刺針によつて貫入されると前記スリーブが前記第3の開口部を閉鎖することを特徴とする試料採集装置。

(4) 特許請求の範囲第1項に記載の試料採集装置において、前記試料採集室とは反対側の端末部において前記第2の穿刺針と滑動的に係合する弾力のあるスリーブを有し、該スリーブの内側の前記穿刺針に係合する面は複数個の縦方向に伸長する溝部を有し、前記穿刺針と係合した前記溝部が気体透過性で液体不透過性であることを特徴とする試料採集装置。

(5) 特許請求の範囲第1項に記載の試料採集装

置において、前記ハウジングが負圧容器用支持具を接続するための装置を有することを特徴とする試料採集装置。

(6) 特許請求の範囲第5項に記載の試料採集装置において、負圧容器用支持具が前記ハウジングに接続されることを特徴とする試料採集装置。

(7) 特許請求の範囲第3項に記載の試料採集装置において、前記ハウジングが負圧容器用支持具を接続するための装置を含むことを特徴とする試料採集装置。

(8) 特許請求の範囲第1項に記載の試料採集装置において、前記ハウジングが前記試料採集室の内容物を観察するための装置を有することを特徴とする試料採集装置。

(9) 特許請求の範囲第8項に記載の試料採集装置において前記内容物を観察するための装置が前記試料採集室に隣接した透明なハウジング壁であることを特徴とする試料採集装置。

(10) 特許請求の範囲第1項に記載の採集装置において前記穿刺針の前記試料採集室とは反対側の

端部で前記穿刺針と滑動的に係合する弾力のあるスリーブを有し、該スリーブの内側の前記穿刺針に係合する面は段付きの内側表面を形成し、該面の長さ方向領域の一部は組み合わされる前記第2の穿刺針の外側表面と密閉的に係合するために小さな径の内部口孔を形成しており、前記段付きの内側表面の長さ方向領域の他の一部は組み合わされる前記第2の穿刺針の外側表面と共に空気通路を形成する大口径の内部口孔を形成することを特徴とする試料採集装置。

3.〔発明の詳細な説明〕

本発明は患者から血液の如き液体試料を採集するための装置に関する。特に本発明はそのような患者から1つあるいは複数の液体試料を採集するための針組み立て体に関する。本発明の装置は問題となる針が適正な位置に近接したか否かを観察できるような透明あるいは半透明の壁を有する導入室を用いている。再に導入室は、受け入れた液体に対しては障害壁となりその導入室に受け入れられた液体試料によつて押し出される気体に対し

ては排気通路となる材料で形成される往復動する栓をその中に組み込んでいる。

その栓は試料液体を最初に受け入れるとその液体試料が排出されるのを防ぎながら同時にその液体試料によつて気体が排気するように往復動する。次いで液体試料が1つあるいは複数の負圧採集容器に排出される時にその栓は採集された試料を1つあるいはそれ以上の負圧採集容器へ連続的に排出して通過させるように組み立て体の排出領域にある通気孔との協働作用で往復動する。複数の試料を採集し続けて複数個の負圧容器へ排出する場合において、その組立体は次の試料の排出に備えての負圧採集容器の交換期間の間にその装置の排出開口部と協働する可撓性スリーブを包含する。

上述の如くそのような針組立体の使用者に静脈針が血液試料を採集する患者の静脈に貫入した事を知らせる機構を備えることが望ましい。患者から血液を採集する際に往々にして静脈に定置することは困難でありまた他の理由によつて採集容器への血液の流れが適正でないことがある。このよ

うな場合に静脈の中へ針が入り血液が針組み立て体の中へ流入することを迅速に知覚できることは有益である。針が入つたことをこのように知覚すると単一試料採集の手順中の周知の血液試料採集手法に従つて負圧採集容器が採集組み立て体の中へ挿入される。

静脈穿刺段階で起こる問題の1つは1つあるいは複数の血液試料採取のための種々の針組み立て体において見い出される空気の溜りである。静脈穿刺がなされ負圧採集容器がまだ針組み立て体の反対側端部に取り付けられていない時には、通常の大気圧条件下では針組み立て体の内側に残留する空気の溜りのために血液は常に針組み立て体の中へ流入するとは限らない。したがつて静脈穿刺が完遂されても、単に針組み立て体の中の空気溜りの妨害によつて血液の流れは開始されない。

本発明によれば、対照的に採集室内の多孔質栓の使用によつてその栓が採集された血液試料を採集室が受け入れるように採集室から空気を押し出す。更にこの栓は試料を受け入れるための手順の

受け入れ期間において最初は押し出された空気を排気し、負圧容器が針組み立て体に取り付けられるとその試料を負圧採集容器へ排出するように針組み立て体の負圧穿刺針における出口と協働するように採集室の中に配置されている。例えば本発明の単一試料採集手順用の1つの実施態様において本発明の組み立て体は試料が導入されると押し出された空気を通気し、負圧容器が組み立て体に取り付けられ排出用負圧穿刺針が負圧採集容器の中へ貫入するとその導入された試料を負圧採集容器の中へ排出するために差圧に応答して組み立て体の通路を開口するために移動する多孔質の栓を有する。

本発明の他の実施態様は負圧穿刺針の排出開口部を覆う可撓性スリーブを有する。可撓性スリーブは試料導入中に排出穿刺針における第3の排出出口から空気を排出するように配置される。続いてこの可撓性袖部は負圧血液採集容器が負圧穿刺針によつて貫入されるように組み立て体の中へ挿入されるとたわみかつ移動しこの第3の排出出口

を塞う。一旦1つの試料を負圧血液採集装置の中に得て組み立て体から負圧容器が取り外されると、可撓性スリーブは次に第2の試料採集のために負圧容器が取り付けられるまでは負圧穿刺針の排出開口部を被つている。当業者には周知であるがこの手順は必要とされる数の試料を別々の負圧血液採集容器の中へ採集するために繰り返される。

ここに記載する種類の血液採集装置における多孔質栓の使用について考えてみると、先願である1978年6月15日に出願された米国出願番号915,670の「静脈穿刺表示付血液採集組み立て体」(Blood Sampling Assembly Having Vein Entry Indicator)において発明者(譲受人は本願と同一人)ウイリアム・エヌ・エルドリッジ(William N. Eldvidge)は空気の溜りが静脈針を通つて使用者が知覚し得る点まで流れる望ましい血液の流れを防げていることを認識していた。エルドリッジの発明においては1方向性弁と結合する多孔質栓を備えておりその1方向性弁は針組み立て体の内側の空気を血液採集手順の

最初の段階でこの通気装置の外へ通過させる。この通気装置は使用者が血液採集装置を針組み立て体に接着させるまで血液の通過を防止する。負圧血液採集容器の負圧と接すると分離された1方向性弁が開き患者の静脈から血液を運び針組み立て体を通して採集容器へ血液を入れる。

エルドリッジの発明は血液を受け入れている間に押しのけられた空気を通気させる多孔質材料の使用を認識していたがそのような装置の改良する余地は残されており、特にその余地は本発明に関連する。すなわち本発明の栓は往復動し単に通気口として作用するのではなく弁作用を提供するような分離されたまた複雑な構造を持たずにそれ自身が弁機構として作用する。すなわち本発明の栓は血液導入室と協働して往復動的に係合し導入室から空気は通気するが血液試料は排出せず組み立て体が負圧血液採集容器と接着した時に導入した血液を排出するように移動する。

次に図面を参照し説明する。なお図面において同一部分は同一符号で示す。第1図はハウジング

１２、患者の中へ挿入するための第１の穿刺針１４およびハウジング１２の反対端にある負圧を受ける第２の穿刺針１５を包含する針組み立て体１０の基本的な外部構成要素を示している。第２の穿刺針１５は血液試料を採集するための負圧容器１６の中へ挿入されるようになつている。ハウジング１２は容器支持具１９がその前方端に設けられている内側の組み合わせねじ２０によつてねじ込まれる第２の穿刺針１５に隣接するねじ１８を有するねじ部２５を包含する。負圧容器１６は第２の穿刺針１５が負圧容器１６の前方端にあるストツパ２１を貫通するように容器支持具１９の中へ挿入される。試料採集容器のこのような一般的な態様は当業者には周知である。

第２図を参照し説明する。ハウジング１２は前方端２４および後方端２５を有しこれら両端は多孔質の栓２７を挿入するために分離できることが好ましい。前方端２４は円筒状であるのが好ましくその中に多孔質の栓２７を往復運動可能に受け入れるように大きな口孔２８を有する。この部分

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入あるいは針状組み立て体からの脱着を容易にする。前方端２４はまたハウジングの２つの部分を接合して組立体にするとき接合面としての役割を果す環状のフランジ３２を包含する。ここでもハウジングおよび組み立て体の２つの部分を固定するために接着剤あるいは類似の適当な固定材料を用いることができる。

後方端２５は前方端の口孔２８の内側に適合するように寸法を定められた少し突き出た円筒部４０を包含している。この後方端の反対側には管支持体の連結機構で前述したように外ねじ１８が後方端２５の符号２６の部分に設けられている。ハウジングの前方端における口孔２９と同様の口孔７０がハウジングの後方端を通つて伸長している。口孔７０は第２の穿刺針１５の直径と適合するように寸法を定められておりここにおいても例えば接着剤の如き適当な材料によつて第２の穿刺針が口孔７０に固定される。ハウジングの２つの端部２４および２５を組合わせるにあたり環状フランジ３２に対応し環状フランジ４６が設けられ

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の反対端にはその中に第１の穿刺針１４を受け入れるための小さな口孔２９が設けられている。本実施例においては小さな口孔２９は口孔２９と口孔２８を互いに連通させるさらに小さな小口径導管３０まで伸長している。口孔２９と導管３０の接合点には第１の穿刺針１４を接する状態で受け入れるための段付部３３が形成されている。第１の穿刺針１４は適宜な接着剤によつて口孔２９の中に固定されても良い。この構造に対しては導管３０は必須の要素ではなく単に好ましい形態に過ぎないことは当業者には周知であろう。更に導管３０の直径はその中を通過する流体の流量を調節するために変えることができる。

ハウジングの前方端２４はまた外側に向つて伸長する第１の穿刺針を包囲する多数の縦方向のリブ３１を包含している。リブ３１と組み合わされるリブを内部に有する鎧装（図示せず）が外側に向つて伸長する第１の穿刺針をほぼ被つている。穿刺針の鎧装と針状組み立て体の間の組み合わされるリブは使用者の鎧装の針状組み立て体への挿

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ている。ハウジングの２つの部分をその中に位置定めされた栓２７とともに組み立てる際にフランジ３２および４６が例えば接着剤の如き適当な固定材料によつて固定できることは理解されるであろう。前方端２４の口孔２８は採集する液体試料を受け入れるための管状室５０を形成する。

管状室５０の内容物を観察するためにまた本装置の使用者に穿刺針が静脈に到達したことを知らせるために、管状室５０を形成する前方端の環状壁８８は半透明あるいは透明な材料で形成されるのが好ましい。製造面から考えれば針状組み立て体の前方端全体が熱可塑性硬質樹脂の如き透明な材料で作られるのが好ましいことは当業者に理解されるであろう。しかしながら本装置の使用者が管状室５０の内容物を観察するための密閉された窓、口孔あるいは他の装置も本発明の範囲にある。

多孔質栓２７は口孔２８の中に往復運動可能に取り付けられまた負圧を受ける穿刺針１５の前方端と往復運動可能に嵌入させるための内側の口孔７２を有している。多孔質栓２７は周知の如く口

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孔２８に従つて円筒形の形状をしておりその径は管状室５０の壁と液体密封的に係合するがまたその反対面との差圧の作用によつて口孔２８の中で栓２７が往復動することができるように定められている。

多孔質栓２７は例えば空気の如き気体の通過は許すが例えば血液の如き液体の通過は許さないいわゆる気体透過性・液体不透過性材料でできている。多孔質栓２７を形成するために用いられる材料の例として焼結ポリエチレンや開放セル型の発泡ポリエチレンや他の同様な型成形可能な重合体物質例えば多孔のポリプロピレンや多孔のポリフルオロカーボン等がある。

第２図に示すように負圧穿刺針１５はその端部８４に隣接した切り欠き７４を包含する。この点において多孔質栓２７の位置定めに依存するが切り欠き７４が管状室５０と第２の穿刺針１５の管腔の間を連通するので多孔質栓２７の端部８４は栓で塞がれるかあるいは変形させるか又は他の方法により閉じられる。付加的な切り欠きすなわち

開口７６が管状室５０の後方端５１と第２の穿刺針１５の間を連通するために設けられている。更に第２図に示されるように大気すなわち本発明の組み立て体の外周領域と第２の穿刺針１５の管腔の間を連通させる第３の切り欠きすなわち開口７８が設けられている。

つぎに第５図を参照し説明する。支持具１９に連結されている針状組み立て体が図示されている。静脈穿刺中の患者Ｐの中に挿入されている第１の穿刺針１４が示されている。第１の穿刺針１４が患者Ｐの静脈に入ると血液は静脈から第１の穿刺針１４および小口径導管３０を経て管状室５０の中へ流入する。血液が管状室５０に流入すると管状室５０の中の空気は多孔質栓２７を通じて管状室５０から押し出されるが血液は多孔質栓２７の特性によつて多孔質栓２７を通過しない。栓２７を通過した空気は管状室５０から切り欠き７４および７６を経てさらに第２の穿刺針１５の管腔および外部切り欠き７８を通つて負圧穿刺針１５の外側端部を被つている柔軟な鎧装８０のフランジ

９２とハウジングの端部２５の端面１０６の間の領域８２（第２図）の中へ押し出される。ここにおいて栓２７はオリフイスすなわち切り欠き７４を覆つて第２図に示す位置に留つている。更にここにおいて患者Ｐから採集された血液試料は管状室５０の中に位置している。

次に第３図を参照すると、組み立て体が後方ハウジング２５のハブ部２６に取り付けられた支持具１９を有するのが示されている。負圧穿刺針１５の端部すなわち点１００によつて貫通された弾力性の栓を有し支持具１９の中に嵌入されている負圧の血液採集容器１６が示されている。穿刺針１５が栓２１に貫入することによつて真空状態が作り出されるがこの真空すなわち負圧は管状室５０の中に残留しているすべての空気を、負圧容器１６の内部領域と切り欠き７４および７６を穿刺針１５の管腔を通じて連通することによつて、多孔質栓２７を通して引き抜く。栓２７が血液によつて閉塞されるため上部管状室５０と下部管状室５１の間に差圧が生じ栓２７は第３図に示すよ

うに延長部４０の面に向つて下方へ移動する。

この移動によつて栓２７は開口すなわち切り欠き７４の覆いを取り除く。この移動の間に下部管状室５１の中に閉じ込められていた残留空気は全て切り欠き７６を通りプラグ２７の運動を助長する。切り欠き７４の被覆が取り除かれると負圧穿刺針１５の管腔を通じて管状室５０と負圧容器１６の間の流通がもたらされる。一方、負圧容器１６の支持具１９の中への挿入および穿刺針１５の点１００による栓２１への貫通によつて第３図に示すように鎧装８０は鎧装８０の上側フランジ９２が軸頭２６の底面１０６と係合する位置まで上方へ移動する。このように患者Ｐの静脈から抜かれ管状室５０に収納されていた血液試料は負圧採集容器１６の中へ移動する。試料が容器１６の中へ引き抜かれたならば容器１６は支持具１９から取り外されこれによつて鎧装８０は切り欠き７８を塞ぎかつ負圧穿刺針１５の端部１００を覆う位置まで戻る。このように第１の穿刺針１４は血液を漏洩することなく静脈の中に留つて複数の

血液試料を受け入れるために容器１６を支持具１９の中へ連続して取り付けることを可能にする。

次に第４図を参照すると、負圧穿刺針１５ａに切り欠き７８が用いられていない別の実施態様が示されている。この装置では同一の部分は添字ａを付した同一符号で示してある。本実施態様においては、穿刺針１５ａには空気通路すなわち開口７８に代つてそのフランジ１０８が常に延長部２６ａの表面１０６ａと隣接して気体は密閉しないように閉じて係合して位置するようなスリーブ９０が形成されている。第６図に示されるようにスリーブ９０は穿刺針１５ａの上に摺動式に係合するように配置されている。しかしながらスリーブ９０は溝の内側の点９５が穿刺針１５ａの外側面と実際に係合する複数の内部溝９４を有する。したがつて溝は穿刺針端部１００ａとスリーブ９０の上側端部の間の気体連通を提供しそこにおいて空気はスリーブ９０のフランジ１０８の隣接面と延長部２６ａの表面１０６ａの間を漏洩する。溝９４は気体は通過させ液体は通過させないよう

な寸法に定められる。フランジ１０８の上方面も同様に端部１００ａと大気の間の通気作用を提供する溝を包含可能なことは理解されるであろう。

単一血液試料採集組み立て体を提供する本発明の更に他の例を第７図に示す。この組み立て体に示されるように特殊なスリーブ８０は使用されておらずかつ穿刺針１５ｂは第２図に示される実施態様における切り欠き７８のような第３の切り欠きすなわち開口を有していない。したがつて穿刺針１４が患者の静脈に挿入されると静脈と管状室５０の間に液体的連通がもたらされ管状室５０の中に試料が採集される。本装置は第２図に示される実施態様のように血液試料は多孔質栓２７を通つて流れない。しかしながら血液試料が管状室５０に入ることによつて押し出された空気は空気透過性栓２７を通り更に切り欠き７４，７６、穿刺針１５の管腔を通つて負圧穿刺針１５ｂの端部１００ｂから排出される。支持具が延長部２６ｂの上に取り付けられ穿刺針１５ｂの点１００ｂが栓を通つて負圧血液採集容器１６の中へ挿入され

ると栓２７の上方の管状室５０と下方の管状室５１の間に差圧が生じそれによつて栓２７は下方へ移動して切り欠き部７４を開口する。これによつて負圧容器１６の中への単一試料採集のための管状室５０と負圧容器１６の間の液体の連通が提供される。この実施態様においてはこの組み立て体によつて更に試料を採集しないので穿刺針１４は患者Ｐの静脈から取り外され組み立て体は必要とする１個の試料が負圧容器の中に採集されたので捨てられる。

負圧穿刺針１５ｃの点１００ｃと大気の間で空気を流通させる第４図に示す態様と類似の他の複数試料採集の実施態様を第８ａおよび８ｂ図に示す。本実施態様においては袖部１１０の内径は段付きになつており、穿刺針１５ｃの外側表面と密着する袖部１１０の小さな内側の径１１４と組み合わされる袖部１１０の表面と穿刺針１５の間の通気通路１１８を形成する大きな内側の径１１６を提供する。したがつて第８ａ図に示す位置においては穿刺針１５ｃの端部１００ｃと大気の間で

通路１１８を通じて通気が起こり、第８ｂ図に示す位置においては通路１１８は閉じられてすべての通気を妨げる。

上述のことから理解されるように本発明においては血液採集針組み立て体はその使用者に静脈への針入を示す装置を組み込んだ単一あるいは複数の試料を採集するために提供されるものである。更に気体を通過させ液体を通過させず弁の機能を有する単純な形態を有する多孔質栓をした本発明の装置は非常に簡素化され製造するに廉価である。当業者に理解されるように特に大量生産に適している。

4.〔図面の簡単な説明〕

第１図は試料採集針組み立て体、負圧容器用支持体および患者からの血液試料を得るために用いる負圧血液採集容器の斜視図。

第２図は本発明の１つの実施態様を示す第１図の線２－２に沿つた拡大断面図。

第３図は第１図の線３－３に沿つた拡大断面図。

第４図は第２図に類似の部分断面図にして本発

明の他の実施態様を示す。

第5図は患者に挿入され使用者が静脈への針入を視覚できるように支持体に連結された針組み立て体の斜視図。

第6図は第4図の線6－6に沿つた断面図。

第7図は第2図に類似の図面であるが本発明の他の実施態様を示す単一試料採集針組み立て体の拡大断面図。

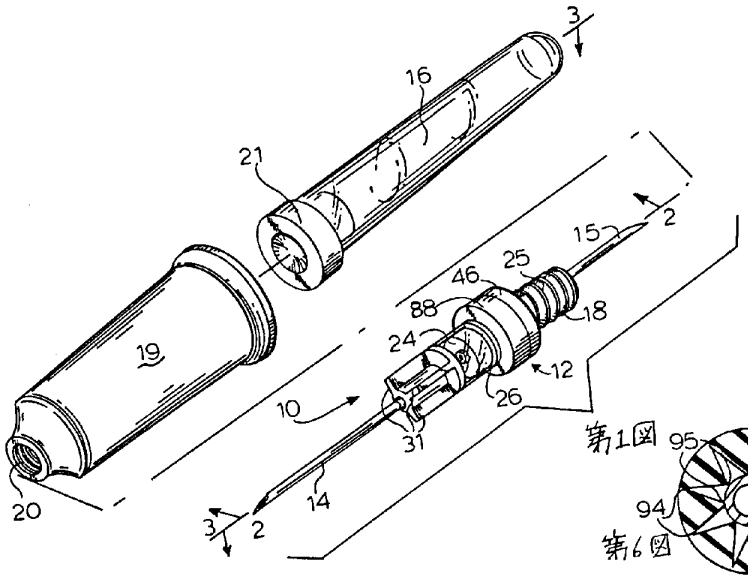
第8a図は本発明の他の実施態様を示す単一試料採集針組み立て体の部分拡大断面図。

第8b図は閉鎖されて非通気位置にある第8a図の実施態様。

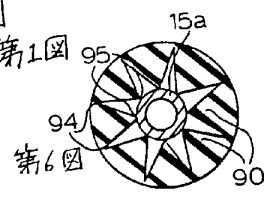
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14……第1の穿刺針、15……第2の穿刺針、
16……負圧容器、　19……支持具、
24……前方端、　25……後方端、
27……環状多孔質栓、29……第1の口孔、
50……試料採集室、　70……第2の口孔、
74……第1の開口部、76……第2の開口部、
78……第3の開口部、80……可撓性スリーブ、
94……溝、　114……小さな内側口径、
116……大きな内側口径

特許出願人　ベクトン・デイッキンソン・アンド・カンパニー

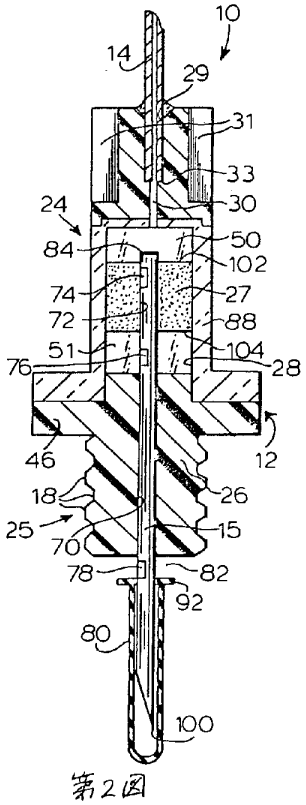
代理人　弁理士　湯浅恭三（外4名）



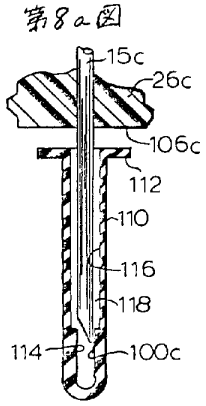
第1図



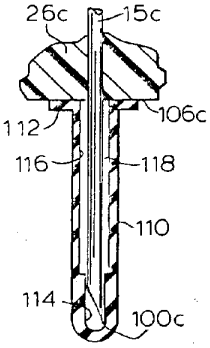
第6図



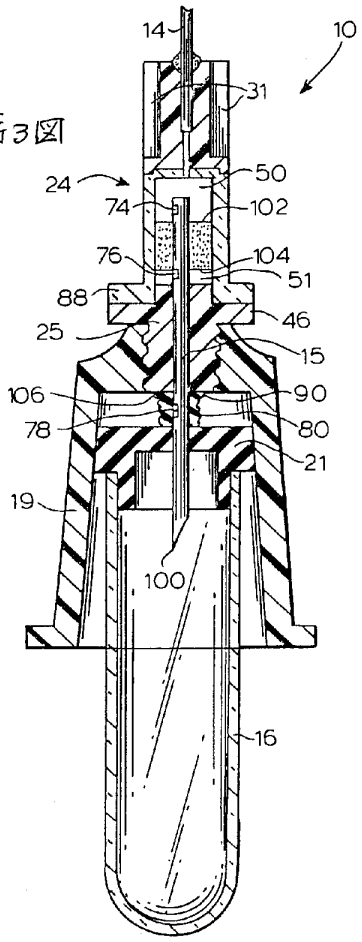
第2図



第8a図

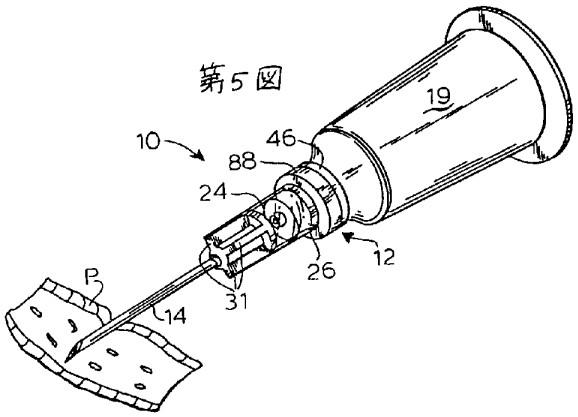


第8b図

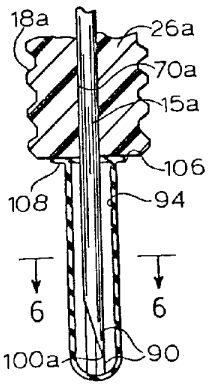


第3図

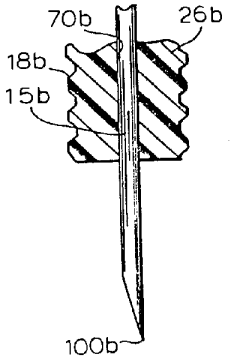
第5図


19
10
46
88
24
26
12
P
14
31

第4図


18a
26a
70a
15a
106
108
94
6
6
100a
90

第7図


70b
26b
18b
15b
100b

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APPLICATION #	RECEIPT DATE / TIME	ATTORNEY DOCKET #
18/113,710	**05/10/2023 06:56:23 PM ET**	**069366-0574153_KUR2C04US**

Title of Invention

BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE AND METHOD

Application Information

APPLICATION TYPE	Utility - Nonprovisional Application under 35 USC 111(a)	PATENT #	-
CONFIRMATION #	2715	FILED BY	Trent Tercenio
PATENT CENTER #	62047483	FILING DATE	02/24/2023
CUSTOMER #	27500	FIRST NAMED INVENTOR	Bobby E. ROGERS
CORRESPONDENCE ADDRESS	-	AUTHORIZED BY	Benjamin Hudson

Documents

TOTAL DOCUMENTS: 100

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069366-0574153_KUR2C04US_Transmittal-Letter.pdf	1	Transmittal Letter	497 KB
069366-0574153_KUR2C04US_PTO_IDS-Form-A.pdf	27	Information Disclosure Statement (IDS) Form (SB08)	1041 KB

Digest

DOCUMENT	MESSAGE DIGEST(SHA-512)
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(57) [Summary]
An apparatus includes a pre-sample reservoir, a flow dividing mechanism and a flow meterin g mechanism. The flow diverting mechanism includes an inlet port couplable to the lumen-defi ning device to receive bodily fluid from the patient, a first outlet port fluidly couplable to the p re-sample reservoir, and a second outlet port fluidly couplable to the sample reservoir. and an exit port. The flow diverter mechanism defines a first fluid flow path and a second fluid flow p ath configured to place the first outlet port and the second outlet port in fluid communication with the inlet port, respectively. The flow metering mechanism meters a flow of a predetermin ed volume of bodily fluid through the first fluid flow path into the pre-sample reservoir, meters a flow of a second volume of bodily fluid through the second fluid flow path into the sample re servoir, and meters a predetermined volume of bodily fluid through the second fluid flow path into the sample reservoir. It is configured to display a volume indicator associated with the vol ume and the second volume.
[Selection drawing] Fig. 2

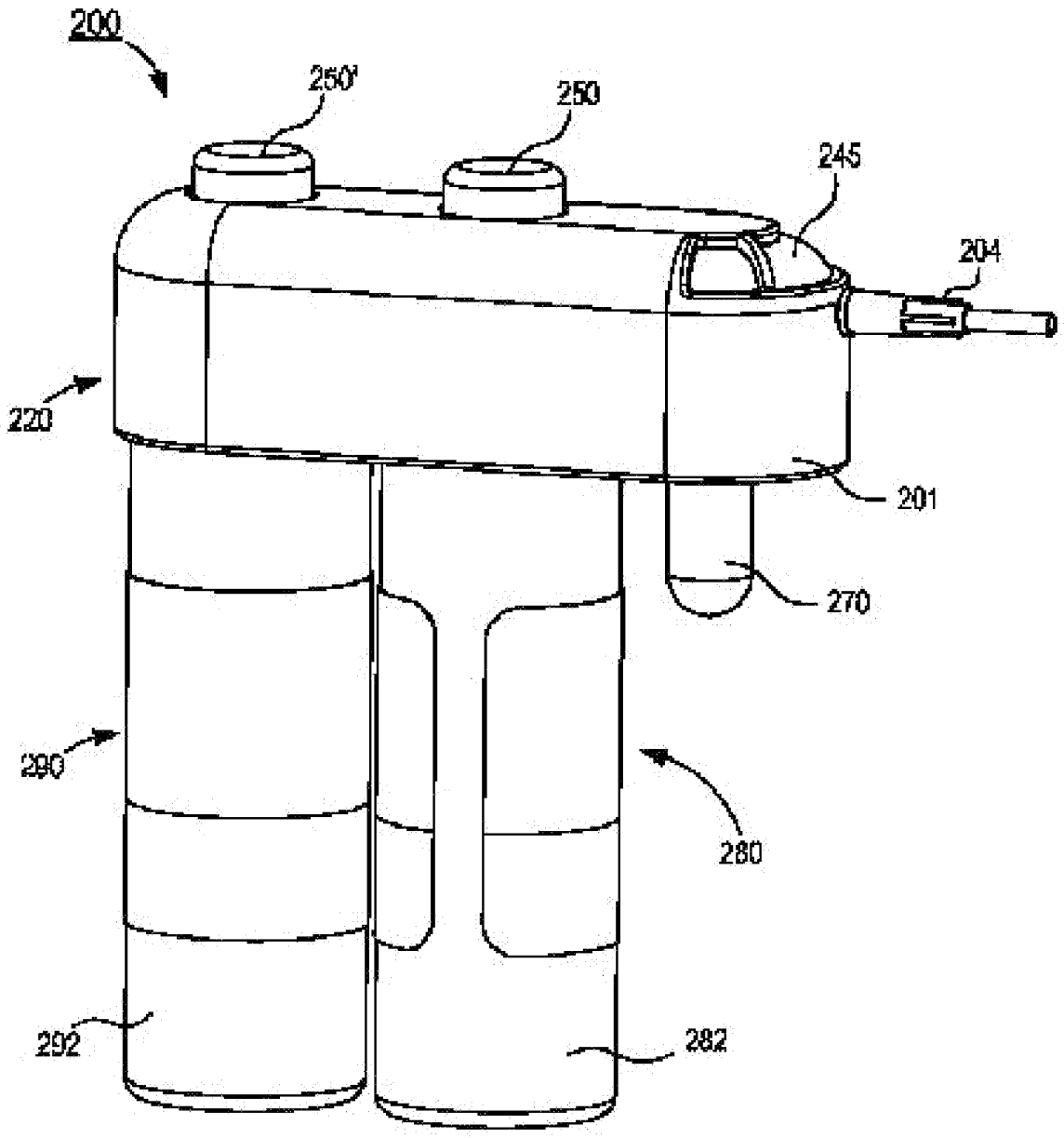


FIG. 2

The scope of the claims open

1. An apparatus for
obtaining a bodily fluid sample from a patient, comprising a
pre-sample reservoir configured to receive a first volume of bodily fluid withdrawn from the

patient; an

inlet port; A flow diverting mechanism including an outlet port and a second outlet port, whe rein the inlet port is configured to be coupled to a lumen defining device to receive bodily fluid from a patient, and the first outlet port is connected to the flow diverting mechanism. and the second outlet port is configured to fluidly couple the sample reservoir to the flow diverting me chanism, the flow diverting mechanism configured to fluidly couple the pre-sample reservoir t o the first outlet port. a first fluid flow path configured to place a in fluid communication with t he inlet port; and a second fluid flow path configured to place the second outlet port in fluid c ommunication with the inlet port. and a flow metering mechanism in fluid communication with

said first fluid flow path and said second fluid flow path, wherein a first volume of bodily fluid passes through said first fluid flow path. configured to meter flow into a pre-sample reservoir and meter flow of a second volume of bodily fluid through said second fluid flow path into said sample reservoir; and a flow metering mechanism configured to display an associated volume indicator.

2. A

first volume of said bodily fluid flows in said first fluid flow path during a first period of time, and a second volume of said bodily fluid flows in said second volume of fluid during a second period of time after said first period of time. 2. The device of claim 1, which flows in a two-flui d flow path.

3. The apparatus of claim

1, wherein the first volume of bodily fluid comprises contaminants present on the skin and t he second volume of bodily fluid is substantially free of contaminants present on the skin. .

4.

The apparatus of claim 1, wherein said pre-sample reservoir is at least partially defined by a portion of said flow divider mechanism.

5.

The apparatus of claim 1, wherein said volume indicator is a visual indicator.

6.

The flow diverting mechanism includes a moveable member configured to move through the second outlet port to place the sample reservoir in fluid communication with the second fluid f low path. Item 1. The device according to item 1.

7.

The apparatus of claim 6, wherein said flow metering mechanism is at least partially dispose d within a portion of said movable member.

8. The

flow diverting mechanism fluidly isolates the pre-sample reservoir and at least a portion of t he first fluid flow path when the first volume of blood is disposed within the pre-sample reserv oir. 2. The device of claim 1, wherein the device comprises:

9.

The flow diverting mechanism includes a third outlet port configured to fluidly couple a secon d sample reservoir to the flow diverting mechanism, the third outlet port being in fluid commu nication with the inlet port. 2. The device of claim 1, defining a third fluid flow path configured to be positioned in the .

10.

A flow controller defining a first lumen and a second lumen, wherein said first lumen places s aid first fluid flow path in fluid communication with said inlet port in a first configuration. and a second configuration in which the second lumen places the second fluid flow path in fluid co mmunication with the inlet port, further comprising a flow controller configured to move betw een Apparatus as described.

11. The method of claim 10,

wherein the flow controller is configured to move from the first configuration to the second c onfiguration after the first volume of bodily fluid is placed in the pre-sample reservoir. Apparat us as described.

12.

An apparatus for obtaining a bodily fluid sample from a patient, comprising a

pre-sample reservoir configured to receive a first volume of bodily fluid withdrawn from the patient, an

inlet port, a first outlet port and a second outlet. A flow diverting mechanism comprising a p ort, wherein the inlet port is configured to be coupled to a lumen defining device to receive bo dily fluid from a patient, and the first outlet port directs the pre-sample reservoir to the flow d iverting mechanism. a flow diverting mechanism configured for fluid coupling, wherein the sec ond outlet port is configured to fluidly couple a sample reservoir to the flow diverting mechani sm; and a flow diverting mechanism disposed at least partially within the flow diverting mech anism

. a flow controller, wherein the flow controller defines at least a portion of a fluid flow path b etween the inlet port and the first outlet port in a first configuration; a flow controller configur ed to move between a second configuration defining at least a portion of a fluid flow path bet ween the port;

a first configuration of a movable member movably coupled to the flow diverting mechanism, wherein the sample reservoir is fluidly isolated from a fluid flow path between the inlet port a nd the second outlet port; a reservoir configured to move through the second outlet port betw een a second configuration in fluid communication with the fluid flow path between the inlet p ort and the second outlet port, the sample reservoir a movable member configured to receive a second volume of bodily fluid withdrawn from the patient when the flow controller is in its se cond configuration and the movable member is in its second configuration.

13. The apparatus of claim 12,

wherein the first volume of bodily fluid comprises contaminants present on the skin and the second volume of bodily fluid is substantially free of contaminants present on the skin. .

14.

The apparatus of claim 12, wherein the flow controller rotates between its first configuration and its second configuration relative to the flow diverter mechanism.

15.

The apparatus of claim 12, wherein said flow controller moves in linear motion relative to sai d flow diverter mechanism.

16. The apparatus of claim 12,

wherein the flow controller is configured to fluidly isolate the pre-sample reservoir when in it s second configuration.

17.

The apparatus of claim 12, wherein said movable member includes a piercing member config ured to pierce a portion of said sample reservoir when in its second configuration.

18. The apparatus of claim 12,

wherein said movable member is coupled to a biasing member configured to at least tempor arily maintain said movable member in its first configuration.

19.

The device of claim 12, wherein said flow diverter mechanism includes a third outlet port con figured to fluidly couple a second sample reservoir to said flow diverter mechanism.

20. The

movable member is a first movable member, the device

is a second movable member, and the second sample reservoir is defined between the inlet p ort and the third outlet port. a first configuration that is fluidly isolated from the fluid flow pat h; and the second sample.

a reservoir configured to move through the third outlet port between a second configuration in fluid communication with the fluid flow path defined between the inlet port and the third outle t port; A second movable member configured to receive a third volume of bodily fluid withdra wn from the patient when the flow controller is in its second configuration and the second mo vable member is in its second configuration. 20. The device of Claim 19, further comprising a member.

21.

An apparatus for obtaining a bodily fluid sample from a patient, the

flow diverting mechanism comprising a pre-sample reservoir configured to receive a first vol ume of bodily fluid withdrawn from the patient, a

housing and a distribution member. said housing defining a first opening and a second openi ng, said first opening being in fluid communication with said pre-sample reservoir, said distrib ution member being disposed at least partially within said housing; and defining a fluid flow p ath in fluid communication with the second opening, wherein the distribution member is confi gured to be in fluid communication with the flow path and physically and fluidly coupled to a s ample reservoir. and an

inlet port configured to be coupled to a lumen-defining device to receive bodily fluid from the patient, the flow controller being rotatably coupled to the flow diversion mechanism, and a flo w controller configured to move between a first configuration in which the inlet port is in fluid communication with the first opening and a second configuration in which the inlet port is in fl uid communication with the second opening; Equipment to equip.

22. The apparatus of claim 21,

wherein the first volume of bodily fluid comprises contaminants present on the skin and the second volume of bodily fluid is substantially free of contaminants present on the skin. .

[Claim 23]

22. The apparatus of claim 21, wherein said pre-sample reservoir is at least partially defined by a portion of said distribution member.

24. The method of claim 21,

wherein the coupling portion includes a piercing member configured to pierce a portion of th e sample reservoir to place the sample reservoir in fluid communication with the fluid flow pat h. Apparatus as described.

25. Said

piercing of said portion of said sample reservoir by said piercing member causes bodily fluids from said patient to enter said sample reservoir through said inlet port and said flow path whe n said flow controller is in its second configuration. 25. The device of claim 24, which initiates inward flow.

26.

The first volume of bodily fluid is a first predetermined volume of bodily fluid, the fluid flow p ath is configured to receive a second predetermined volume of bodily fluid, and the second pr edetermined volume of bodily fluid is a sample volume. 22. Apparatus according to claim 21, r elated to volume.

27.

The apparatus of claim 26, wherein said sample volume is between about 10 milliliters and a bout 50 milliliters.

28.

The apparatus of claim 26, wherein said sample volume is approximately 30 milliliters.

[Claim 29]

said flow diverter mechanism including a seal member, said seal member forming a substant ially fluid tight seal with a surface of said flow controller and a surface of said housing when s aid flow controller is coupled to said flow diverter mechanism; Disposed between the housing and the flow controller, the seal member defines a first opening and a second opening, the firs t opening of the seal member substantially flush with the first opening of the housing. and wh erein said second opening of said seal member is substantially coaxial with said second openi ng of said housing.

The apparatus described in .

30.

A method of obtaining a predetermined sample volume of bodily fluid from a patient using a flow metering transfer device, wherein the flow metering transfer device is selectively placed i n fluid communication with a pre-sample reservoir and a sample reservoir. and a flow meterin g mechanism configured to meter the flow of bodily fluid from the patient to the pre-sample r eservoir and to the sample reservoir; A method comprising: establishing fluid communication between the patient

and the port of the flow metering transfer device; establishing fluid communication between the

port and the pre-sample reservoir;

metering a flow of bodily fluid transferred to a pre-sample reservoir; and

via said flow metering mechanism of said flow metering transfer device, a pre-sample volum e of bodily fluid disposed within said pre-sample reservoir to a predetermined pre-sample of b odily fluid.

fluidly isolating the pre-sample reservoir from the port to confine a pre-sample volume of th e bodily fluid within the pre-sample reservoir

; metering

a flow of bodily fluid transferred from the patient to the sample reservoir; and

via the flow metering mechanism of the flow metering transfer device disposed within the sa mple reservoir. and C. verifying that the obtained sample volume of bodily fluid is a predeterm ined sample volume of bodily fluid.

[Claim 31]

The flow metering transfer device has a first configuration in which fluid communication is es tablished between the patient and the pre-sample reservoir, and a second configuration in whi ch fluid communication is established between the patient and the sample reservoir. 31. The method of claim 30, including a flow controller configured to move between.

32.

The method of claim 30, wherein said bodily fluid is blood.

33. The method of claim 32

, wherein the sample reservoir comprises at least one of an aerobe medium or an anaerobe medium.

34.

The method of claim 30, wherein said predetermined pre-sample volume is between about 1 milliliter and about 10 milliliters.

35.

The method of claim 30, wherein said predetermined sample volume is between about 20 mi lliliters and about 60 milliliters.

36.

The method of claim 30, wherein said predetermined sample volume is approximately 60 m

liliters.

37. verified that

said sample reservoir is a first sample reservoir, said sample volume is a first sample volum e, and said first sample volume within said first sample reservoir is said predetermined sampl e volume;

subsequently establishing fluid communication between the port and a second sample reservo ir;

metering the flow of bodily fluid transferred from the patient to the second sample reservoir ; verifying, via a metering mechanism, that a second sample volume of bodily fluid disposed within the second sample reservoir is the predetermined sample volume of bodily fluid;

31. The method of claim 30, further comprising:

38. The method of claim 37, wherein

said first sample volume and said second sample volume collectively equal between about 2 0 milliliters and about 60 milliliters.

39.

After verifying that said second sample volume in said second sample reservoir is said prede termined sample volume, establishing fluid communication between said port and a third sam ple reservoir

; metering a flow of bodily fluid transferred from a patient to said third sample reservoir; an d a third sample volume of bodily fluid

disposed within said third sample reservoir via said flow metering mechanism of said flow m etering transfer device. 38. The method of claim 37, further comprising verifying that is the pr edetermined sample volume of bodily fluid.

40.

The method of claim 39, wherein said first sample volume, said second sample volume and s aid third sample volume collectively equal between about 30 milliliters and about 60 milliliter s.

41.

The method of claim 39, wherein said first sample volume, said second sample volume and s aid third sample volume collectively equal approximately 60 milliliters.

detailed description open —

Description: CROSS-REFERENCE TO RELATED APPLICATIONS

[

1001] This application is entitled "Sterile Bodily-Fluid Collection Device and Method", filed D

c. 4, 2012. and Methods),” the disclosure of which is hereby incorporated by reference in its e ntirety. [1002] Embodiments described herein relate generally to the parenteral procurement of bodily fluid samples, and more particularly to microbial or other external sources of bodily f luids, such as those present on the skin. Devices and methods for obtaining bodily fluid sampl es parenterally with reduced contamination from contaminants. BACKGROUND ART [0003]

[1003] Health care practitioners routinely perform various types of microbiological tests on pa tients using parenterally obtained bodily fluids. In some cases, a patient sample (eg, bodily flu id) is tested for the presence of one or more potentially unwanted microorganisms, such as ba cteria, fungi or yeast (eg, Candida). Microbial testing may involve culturing patient samples in one or more sterile containers containing media that promote microbial growth, real-time diag nostics and/or molecular PCR-based techniques. Generally, when such microorganisms are pre sent in a patient sample, they will multiply in the culture medium over time. After a variable a mount of time (eg, hours to days), automated continuous monitoring can detect organism gro wth. Such automated monitoring can detect carbon dioxide produced by the growth of organis ms. The medium can then be tested for the presence of microorganisms. The presence of mic roorganisms in the medium indicates the presence of the same microorganisms in the patient sample, which in turn indicates the presence of the same microorganisms in the patient's bodi ly fluid from which the sample was obtained. Therefore, if it is determined that microorganism s are present in the culture medium, the patient is administered one or more antibiotics or ot her treatments specifically designed to treat or otherwise eliminate the undesirable microorga nisms from the patient. may be prescribed.

[0004]

[1004] However, patient samples can be contaminated during acquisition and/or otherwise pr one to false positive results. One process by which contamination of patient samples can occu r is microbes from the body surface (e.g., microbes present on the skin) that are removed dur ing needle insertion into the patient's body and subsequently transferred to the culture mediu m with the patient sample.) by transfer. Surface microbes and/or other unwanted external mi crobes may be removed either directly or through removed tissue debris, hair follicles, sweat glands and other skin appendage structures. Another possible source of contamination comes from the person who draws the patient sample. For example, doctors, phlebotomists, nurses, etc. may transfer contaminants from their bodies (eg, fingers, arms, etc.) to patient samples and/or to equipment containing patient samples. To further elaborate, the instruments and/or devices used during the patient sample acquisition process (e.g., patient to needle, needle/t

be to sample container, etc.) can each introduce potential points of contamination. It often co ntains multiple fluid interfaces. Use of such instruments and/or devices typically involves man ual intervention to connect and/or fluidly couple various interfaces. Because these interfaces a re pre-assembled and non-sterilized as a single, fluidly coupled system, the user (e.g., physici an, phlebotomist, etc.) and/or other sources of contamination (e.g., ambient air, hospital roo m contaminants on table and counter surfaces, microorganisms transferred from linens or clot hing, etc.) may be introduced into the patient sample. In some cases, these contaminants can grow in the culture medium and ultimately result in a positive microbial test result, thereby fal sely indicating the presence of such organisms in the body.

[0005]

[1005] In some cases, false positive and/or false negative results may result from a given vol ume of patient sample. For example, by overfilling volume-sensitive blood culture bottles, as noted in the instructions for use and/or warning labels from the manufacturers of such culture bottles and associated automated continuous monitoring microbial detection systems, Can lea d to false positive results. On the other hand, as another example, insufficient patient sample volume in culture medium can lead to false negative results. As an example, in a study condu cted by the Mayo Clinic entitled "Optimized Pathogen Detection with 30- Compared to 20-Millil iter Blood Culture Draws", published in the December 2011 issue of the Journal of Clinical Micr obiology, 20 milliliters (mL) of A patient sample volume allows detection of the presence of ap proximately 80% of bacteremia present in a patient sample, a patient sample volume of 40 m L allows detection of approximately 88% of bacteremia, and a patient sample volume of 60 m L allows detection of approximately 88% of bacteremia. Approximately 99% of bacteremia ca n be detected by sample volume.

[0006]

[1006] Such inaccurate results as a result of contamination, insufficient patient sample volum e, etc. are a problem when trying to diagnose or treat a suspected disease or condition. For e xample, a false negative result from a microbiological test can lead to misdiagnosis and/or del ay in treatment of a patient's illness, which in some cases can lead to death of the patient. Co nversely, a false-positive result from a microbiological test can lead to the patient receiving on e or more antimicrobial therapies unnecessarily, thereby causing serious side effects in the pa tient, including death, for example. Together, this can result in unnecessary burden and expen se to the health care system due to prolonged hospitalization of the patient and/or other com plications associated with the wrong treatment. In addition, the use of diagnostic imaging equ ipment due to these false positive results also increases the cost and unnecessary exposure of high doses of radiation associated with various imaging procedures (e.g., CT scans) to long-te rm patient health. It is also problematic from a patient safety perspective, as it has many kno wn adverse effects.

[1007

] Thus, for example, reducing microbial contamination in bodily fluid test samples by minimi

ng exposure to non-sterile conditions and/or other external sources of contamination around patient samples and/or fluid interfaces. There is a need for a sterile "one-piece" bodily fluid co llection device and method. Further, such fluid collection devices provide visual, calculated, or must include means for accurately weighing, measuring, and/or otherwise assessing body flui ds transferred from the patient to the sample reservoir or culture medium, which can be other wise communicated. It is

SUMMARY OF THE INVENTION

[1008

] The present invention provides a non-toxic method for treating a body fluid sample by reduc ing contamination from microorganisms external to the body fluid source, such as microorgani sms present on the skin and/or other undesirable external contaminants. An orally acquired d evice is described. In some embodiments, a device for obtaining a bodily fluid sample from a patient includes a pre-sample reservoir, a flow diversion mechanism and a flow metering mec hanism. The pre-sample reservoir is configured to receive a first volume of bodily fluid withdra wn from the patient. The flow diverting mechanism includes an inlet port, a first outlet port an d a second outlet port and defines a first fluid flow path and a second fluid flow path. An inlet port can be coupled to the lumen-defining device to receive bodily fluid from the patient. A fir st outlet port and a second outlet port are configured to fluidly couple the pre-sample reservoi r and the sample reservoir, respectively, to the flow diverting mechanism. The first fluid flow p ath is configured to place the first outlet port in fluid communication with the inlet port and th e second fluid flow path is configured to place the second outlet port in fluid communication w ith the inlet port. is configured to A flow metering mechanism is in fluid communication with t he first fluid flow path and the second fluid flow path. A flow metering mechanism meters a fl ow of a first volume of bodily fluid through the first fluid flow path into the pre-sample reservo ir and a second volume of bodily fluid through the second fluid flow path into the sample reser voir. is configured to The flow metering mechanism is configured to display volume indicators associated with the first volume and the second volume.

BRIEF DESCRIPTION OF THE DRAWINGS

[0009]

FIG. 1 is a schematic diagram of a bodily fluid collection device according to an embodiment; 2 is a perspective view of a bodily fluid collection device according to an embodiment; FIG. 3 is an exploded perspective view of the bodily fluid collection device of FIG. 2; FIG. 4 is a side cross-sectional view taken along line X 1 -X 1 of FIG. 3 of a housing included in the bodily fluid c ollection device of FIG. 2;

5 is a cross-sectional view taken along line X 2 -X 2 of FIG. 3 of a movable member included i n the bodily fluid collection device of FIG. 2 ;

6 is a cross-sectional view taken along line X 3 -X 3 of FIG. 3 of the flow controller included in the bodily flui d collection device of FIG. 2;

7 is a cross-sectional view taken along line X 4 -X 4 of FIG. 3 of the flow controller included in the bodily fl

d collection device of FIG. 2;

8 is a top view of the bodily fluid collection device of FIG. 2 in a first configuration; FIG.

9 is a cross-sectional view taken along line X 5 -X 5 of FIG. 8 of the body fluid collection device of FIG. 2 in t he first configuration;

10 is a top view of the bodily fluid collection device of FIG. 2 in a second configuration; FIG.

11 is line X 6 -X 6 of FIG. 10 of the body fluid collection device of FIG. 2 in a second configuration; 1 is a cross-sec tional view taken along .

12 is a cross-sectional view taken along line X 6 -X 6 of FIG. 10 of the bodily fluid collection device of FIG. 2 in a third configuration;

13 is a cross-sectional view taken along line X 6 -X 6 of FIG. 10 of the bodily fluid collection device of FIG. 2 in a fourth configuration;

14 is a perspective view of a bodily fluid collection device according to an embodiment; FIG.

15 is a side cross-sectional view taken along line X 7 -X 7 of the bodily fluid collection device of FIG. 14; FI G.

16 is a perspective view of a bodily fluid collection device according to an embodiment; FIG.

17 is an exploded perspective view of a flow diverting mechanism included in the body fluid co llection device of FIG. 16; FIG.

18 along line X 8 -X 8 of FIG. 16 of a distribution member included in the bodily fluid collection device of FIG. 16; is a side cross-sectional view taken out.

19 is a top view of the bodily fluid collection device of FIG. 16 in a first configuration; FIG.

20 is a cross-sectional view taken along line X 9 -X 9 of FIG. 19 of the partial bodily fluid collection device of FIG. 16 in the first configuration;

21 is a top view of the bodily fluid collection device of FIG. 16 in a second configuration; FIG.

22 is a cross-sectional view taken along line X 10 -X 10 of FIG. 21 of the bodily fluid collection device of FI G. 16 in a second configuration;

FIG. 23 is a perspective view of a bodily fluid collection device according to an embodiment; F igure 24 is a cross-sectional view taken along line X11 - X11

of a portion of the bodily fluid collection device of Figure 23 in a first configuration ; 25 is a cr oss-sectional view taken along line X 11 -X 11 of the bodily fluid collection device of FIG. 23, in a second config uration; FIG. FIG. 26 is a perspective view of a bodily fluid collection device according to an emb odiment; 27 is an exploded perspective view of a flow diverting mechanism included in the bo dily fluid collection device of FIG. 26; FIG. 28 is a cross-sectional view taken along line X 13 - X 13 of FIG. 27 of a distribution member included in the bodily fluid collection device of FIG. 27;

29 is a cross-sectional view taken along line X 14 -X 14 of FIG. 27 of a coupling member included in the bod ily fluid collection device of FIG. 26;

30 is a cross-sectional view taken along line X 15 -X 15 of FIG. 27 of the dial included in the bodily fluid collection device of FIG. 26;

31 is a cross-sectional view taken along line X 16 -X 16 of FIG. 27 of the valve included in the bodily fluid collection device of FIG. 26;

32 is a cross-sectional view taken along line X 12 -X 12 of the bodily fluid collection device of FIG. 26 in the first configuration; FIG.

33 is a cross-sectional view taken along line X 12 -X 12 of the bodily fluid collection device of FIG. 26 in a second configuration; FIG.

34 is a perspective view of a bodily fluid collection device according to an embodiment; FIG.

35 is an exploded perspective view of a flow diverting mechanism included in the bodily fluid collection device of FIG. 34; FIG.

36 is a cross-sectional view taken along line X 17 -X 17 of a distribution member included in the flow diverting mechanism of FIG. 35; FIG.

37 is a top view of a portion of the bodily fluid collection device of FIG. 34 in a first configuration; FIG.

38 is a cross-sectional view taken along line X 18 -X 18 of the partial bodily fluid collection device of FIG. 37 in the first configuration; FIG.

39 is a top view of the bodily fluid collection device of FIG. 33 in a second configuration; FIG.

Figure 40 is a cross-sectional view taken along line X19 - X19

of Figure 39 of the body fluid collection device of Figure 33 in a second configuration ; 41 is a perspective view of a bodily fluid collection device in a first configuration according to embodiments; FIG. 42 is an exploded perspective view of a portion of the bodily fluid collection device of FIG. 41; FIG. 43 is a cross-sectional view taken along line X 20 -X 20 of the bodily fluid collection device of FIG. 41 in the first configuration; FIG. Figure 44 is a cross-sectional view taken along line X20 - X20 of the bodily fluid collection device of Figure 41 in a second configuration ; Figure 45 is a cross-sectional view taken along line X20 - X20 of the body fluid collection device of Figure 41 in a third configuration ; Figure 46 is a perspective view of a bodily fluid collection device in a first configuration according to an embodiment; 47 is an exploded perspective view of a portion of the bodily fluid collection device of FIG. 45; FIG. 48 shows the distribution member included in the bodily fluid collection device of FIG. 46, line X of FIG. 47. FIG.

Figure 21 is a side sectional view taken along 21 - X21 ;

49 is a side sectional view taken along line X 22 -X 22 of FIG. 47 of a movable member included in the bod

y fluid collection device of FIG. 46;

50 is a top view of the bodily fluid collection device of FIG. 46 in a first configuration; FIG. Fig ure 51 is a cross-sectional view taken along line X23 - X23

of Figure 50 of the partial bodily fluid collection device of Figure 46 in the first configuration ; 52 is a top view of the bodily fluid collection device of FIG. 46 in a second configuration; FIG. Figure 53 is a cross-sectional view taken along line X24 - X24 of Figure 52 of the body fluid coll ection device of Figure 46 in a second configuration ; FIG. 54 is a perspective view of a bodily fluid collection device according to an embodiment; 55 is a top view of the bodily fluid collecti on device of FIG. 54; FIG. FIG. 56 is a flowchart illustrating a method of obtaining bodily fluid samples with reduced contamination using a collection device according to embodiments; DET AILED DESCRIPTION OF THE INVENTION [0010]

[1063] Described herein are devices for obtaining bodily fluid samples parenterally with reduc ed contamination from microorganisms external to the bodily fluid source, such as microorgan isms present on the skin and/or other undesirable external contaminants. It is In some embod iments, a device for obtaining a bodily fluid sample from a patient includes a pre-sample reser voir, a flow diversion mechanism and a flow metering mechanism. The pre-sample reservoir is configured to receive a first volume of bodily fluid withdrawn from the patient. The flow diverti ng mechanism includes an inlet port, a first outlet port and a second outlet port and defines a first fluid flow path and a second fluid flow path. An inlet port can be coupled to the lumen-def ining device to receive bodily fluid from the patient. A first outlet port and a second outlet por t are configured to fluidly couple the pre-sample reservoir and the sample reservoir, respectiv ely, to the flow diverting mechanism. The first fluid flow path is configured to place the first ou tlet port in fluid communication with the inlet port and the second fluid flow path is configured to place the second outlet port in fluid communication with the inlet port. is configured to A flo w metering mechanism is in fluid communication with the first fluid flow path and the second f luid flow path. A flow metering mechanism meters a flow of a first volume of bodily fluid throu gh the first fluid flow path into the pre-sample reservoir and a second volume of bodily fluid th rough the second fluid flow path into the sample reservoir. is configured to The flow metering mechanism is configured to display volume indicators associated with the first volume and the second volume.

[0011]

[1064] In some embodiments, an apparatus for obtaining a bodily fluid sample from a patien

includes a pre-sample reservoir, a flow diversion mechanism, a flow controller, and a movable member. The pre-sample reservoir is configured to receive a first volume of bodily fluid withdrawn from the patient. The flow diverting mechanism includes an inlet port, a first outlet port and a second outlet port. The inlet port is couplable to the lumen-defining device to receive bodily fluid from the patient. A first outlet port fluidly couples the pre-sample reservoir to the flow diverter mechanism and a second outlet port fluidly couples the sample reservoir to the flow diverter mechanism. A flow controller is disposed at least partially within the flow diverting mechanism and comprises a first configuration in which the flow controller defines at least a portion of a fluid flow path between the inlet port and the first outlet port; is movable between a second configuration that defines at least a portion of the fluid flow path between the inlet port and the second outlet port. The movable member is movably coupled to the flow diverting mechanism in a first configuration in which the sample reservoir is fluidly isolated from the fluid flow path between the inlet port and the second outlet port; It is movable through the second outlet port to and from a second configuration in fluid communication with the fluid flow path between the outlet port. The sample reservoir is configured to receive a second volume of bodily fluid withdrawn from the patient when the flow controller is in its second configuration and the movable member is in its second configuration.

[1065

] In some embodiments, a device for obtaining a bodily fluid sample from a patient includes a pre-sample reservoir, a flow diversion mechanism and a flow controller. The pre-sample reservoir is configured to receive a first volume of bodily fluid withdrawn from the patient. The flow diverting mechanism includes a housing and a distribution member. The housing has a first opening in fluid communication with the pre-sample reservoir.

defines a portion and a second opening. A distribution member defines a fluid passageway disposed at least partially within the housing and in fluid communication with the second opening. The distribution member includes a coupling portion configured to be in fluid communication with the flow path and physically and fluidly coupled to the sample reservoir. The flow controller includes an inlet port configured to be coupled to the lumen defining device to receive bodily fluid from the patient. A flow controller is rotatably coupled to the flow diverter mechanism and is movable between a first configuration in which the inlet port is in fluid communication with the first opening and a second configuration in which the inlet port is in fluid communication with the second opening. is.

[0013]

[1066] In some embodiments, a flow diverting mechanism including an inlet port configured to be selectively placed in fluid communication with the pre-sample reservoir and the sample reservoir, and bodily fluid from the patient to the pre-sample reservoir. and a flow metering mechanism configured to meter flow into a sample reservoir comprising the steps of: establishing fluid communication between a patient and an inlet port of the flow metering transfer device; including. Fluid communication is then established between the port and the pre-sample r

servoir. A flow of bodily fluid transferred from the patient to the pre-sample reservoir is meter ed. The method includes verifying, via a flow metering mechanism of the flow metering transf er device, that a pre-sample volume of bodily fluid disposed within a pre-sample reservoir is a first pre-sample volume of bodily fluid. With the pre-sample volume disposed within the pre-s ample reservoir, the pre-sample reservoir is fluidly isolated from the port to seal the pre-samp le volume of bodily fluid within the pre-sample reservoir. With the pre-sample reservoir fluidly isolated, the method includes establishing fluid communication between the port and the sam ple reservoir. A flow of bodily fluid transferred from the patient to the sample reservoir is met ered. The method includes verifying, via the flow metering mechanism of the flow metering tr ansfer device, that the sample volume of bodily fluid disposed within the sample reservoir is a first sample volume of bodily fluid.

[0014]

[1067] In some embodiments, an apparatus includes a flow diversion mechanism and a flow c ontroller. The flow diverting mechanism can define an inlet port, a first outlet port, a second o utlet port and a third outlet port. a first outlet port fluidly coupled to the pre-sample reservoir, a second outlet port fluidly coupled to the first sample reservoir, a third outlet port fluidly cou pled to the second sample reservoir; etc. All of the fluid reservoirs can be fluidly isolated from each other. The flow controller includes various fluid channels, which can allow fluid movemen t in specified directions and can be configured to be operatively coupled to the flow diverting mechanism. In use, the flow controller can allow bodily fluid flow into the pre-sample reservoi r when the flow diverter mechanism is in the first configuration. The flow diverter mechanism can be moved to a second configuration, in which the flow controller can allow bodily fluid flo w to enter the first sample reservoir. In addition, the flow diverter mechanism can then be mo ved to the third configuration so that the flow controller can allow bodily fluid flow to enter the second sample reservoir.

[0015]

[1068] In some embodiments, the bodily fluid collection device allows a second volume of bod ily fluid to flow into the first sample reservoir and/or a third volume of bodily fluid to flow into the second sample reservoir. previously, it can be configured to selectively divert a first predet ermined volume of bodily fluid to a pre-sample reservoir. In this way, the second and/or third volume of bodily fluid can be used for diagnosis or other testing, while the presence of microo rganisms from the body surface or other microbial sources external to the patient from whom the sample is obtained. A first volume of bodily fluid that may contain is isolated. In some em bodiments, the bodily fluid collection device can include additional sample reservoirs (eg, 3, 4, 5, 6 or more) depending on the analysis and/or testing protocols to be performed.

[1069

] In some embodiments, the bodily fluid collection device is configured such that an appropria te volume of bodily fluid is collected from the patient and/or transferred to a predetermined pr e-sample reservoir and/or sample reservoir.

Flow metering can be included to ensure that the A bodily fluid collection device can be config ured to automatically divert and/or control fluid flow after a metered volume of bodily fluid ha s been collected. For example, once a first metric pre-sample volume has been collected, the f low diverter mechanism can be configured to divert body fluid flow to a first sample reservoir, and then divert the flow after the first metric sample volume has been collected. The mechani sm can be configured to divert body fluid flow to a second sample reservoir, and so on. In so me embodiments, the bodily fluid collection device includes a metered volume display, such a s a liquid crystal display (LCD), to provide a visual indication of how much bodily fluid has bee n collected in each predetermined individual sample reservoir. can be provided to the user. In some embodiments, multiple displays can be provided to allow for customized pre-sample an d/or sample volume collection.

[1070

] As used in this specification and the appended claims, the singular forms "a, an" and "the" r efer to the plural unless the context clearly dictates otherwise. including referents of Thus, for example, the term "(a) member" is intended to mean a single member or combination of me mbers, and "(a) material" is intended to mean one or more materials or combinations thereof. intended to mean

[1071

] As used herein, "bodily fluid" includes, but is not limited to, blood, cerebrospinal fluid, urine, bile, lymph, saliva, synovial fluid, serous fluid, pleural fluid, amniotic fluid, etc., or any combin ation thereof. , can include any fluid obtained from the patient's body.

[0019]

[1072] As used herein, the terms "first predetermined amount," "first amount," and "first volu me" are configured to be received or contained by a first reservoir or a pre-sample reservoir. State the volume of body fluids. The terms "first amount" and "first volume" do not explicitly s tate a predetermined amount, but unless explicitly stated otherwise, the first amount may be a first predetermined amount. should be understood.

[1073

] As used herein, the terms "second volume" and "second volume" describe the amount of bo dily fluid configured to be received or contained by a second reservoir or sample reservoir. . T he second amount can be any suitable amount of bodily fluid and it need not be a predetermi ned amount. Conversely, when so explicitly stated, the second volume received and contained by the second reservoir or sample reservoir may be the second predetermined volume.

[1074

] As used herein, the term "set" can refer to a single feature comprising multiple features or multiple parts. For example, when referring to a set of walls, the set of walls can be considere d a single wall with separate portions, or the set of walls can be considered multiple walls. Si milarly, an integrally constructed article can include a set of walls. Such a set of walls can incl ude, for example, multiple portions that are discontinuous from each other. A set of walls ca

also be made from multiple articles that are manufactured separately and later joined togethe r (eg, via welding, adhesives, or any suitable method).

[0022]

[1075] As used herein, the terms "proximal" and "distal" refer to directions toward and away f rom, respectively, a user placing the device in contact with a patient. Thus, for example, the e nd of the device that first contacts the patient's body would be the distal end, and the opposit e end of the device (eg, the end of the device being operated by the user) would be the proxi mal end of the device. becomes.

[1076

] As used herein, the terms "about," "approximately," and "substantially," when used in conne ction with numerical values, are nominally indicative of the value so defined. is intended to m ean that the value In other words, the terms about, approximately and substantially when use d in connection with numerical values generally include the indicated value plus or minus a giv en tolerance.

nothing. For example, in some cases a suitable tolerance may be ±10% of the indicated valu e, thus about 0.5 includes 0.45 and 0.55; 11, and about 1000 includes 900-1100. In other ca ses, a suitable tolerance may be plus or minus an acceptable percentage of the last significant digits of the indicated value. For example, a suitable tolerance might be ±10% of the last sign ificant digit, so approximately 10.1 includes 10.09 and 10.11, and approximately 25 includes 24.5 and 25.5. including. Such variations may result from manufacturing tolerances or other p ractical considerations (eg, tolerances associated with measurement equipment, acceptable h uman error, etc.).

[0024]

[1077] When describing the relationship between a given volume of bodily fluid and a collecte d volume of bodily fluid, it should be understood that these values include suitable tolerances such as those set forth above. For example, when stating that a collected volume of bodily flui d is substantially equal to a predetermined volume of bodily fluid, the collected volume and th e predetermined volume are nominally equal within suitable tolerances. In some cases, tolera nce can be determined by the intended use of the collected volume of bodily fluid. For exampl e, in some cases, blood culture assays are performed when the collected volume of blood is wi thin 1.0% to 5.0% of the manufacturer's (or evidence-based best practice) recommended vol ume. It can be about 99% accurate. As an example, the manufacturer's recommended volum e for the body fluid assay is 10 milliliters (mL) (ie total volume is 40 ml to 60 ml) ± 5%. Thu s, a collection volume of 10.5 mL provides results with greater than about 99% confidence, an d a collection volume of 11 mL provides results with less than about 99% confidence. In other cases suitable tolerances are 0.1%, 0.5%, 1.0%, 2.0%, 3.0%, 4.0%, 5.0%, 6.0% , 7.0%, 8. 0%, 9.0%, 10.0% or any fractional value therebetween. In still other cases, the tolerance can exceed 10.0%. Accordingly, any of the embodiments described herein may be any suitable flo w rate configured to meter the flow rate of body fluid and/or otherwise measure the volume

f body fluid within suitable tolerances. It can include and/or be used with measurement mech anisms and/or devices. Additionally, flow metering mechanisms and/or devices can be arrange d to minimize or eliminate tolerance build-up that can result from a combination of inaccurate measurements, human error, and the like.

[0025]

[1078] FIG. 1 is a schematic illustration of a portion of a bodily fluid collection device 100, acc ording to an embodiment. In general, the bodily fluid collection device 100 (also referred to h erein as a "fluid collection device" or "collection device") allows for the withdrawal of bodily flu id from a patient, wherein a first portion or a first portion of the withdrawn bodily fluid is so th at a quantity separates from a second portion or volume and/or a third portion or volume of t he withdrawn bodily fluid used as a biological sample, such as to be tested for medical diagno stic and/or therapeutic purposes configured to be shunted. In other words, as described in mo re detail herein, the collection device 100 can transfer a first predetermined volume of bodily f luid to a pre-sample collection reservoir, second and third volumes of bodily fluid (or, in some i mplementations, 4th, 5th, etc.) to one or more sample collection reservoirs (eg, sample reser voirs) fluidly isolated from the pre-sample reservoir.

[1079

] The collection device 100 includes a flow diverter mechanism 120 , a flow controller 140 , a pre-sample reservoir 170 , a first sample reservoir 180 , and a second sample reservoir 190 t hat is different from the first sample reservoir 180 . The flow diverting mechanism 120 include s an inlet port 121 and at least two outlet ports, such as a first outlet port 125 and a second o utlet port 126, as shown in FIG. In some embodiments, flow diverter 120 can include a set of exit ports equal to the total number of pre-sample and sample reservoirs. For example, if coll ection device 100 has one pre-sample and four sample reservoirs, flow diverter 120 may inclu de five outlet ports. In some embodiments, a flow divider

Mechanism 120 can be operably coupled to an actuator (not shown in FIG. 1) that can facilitat e movement of flow diverter mechanism 120 between configurations. Inlet port 121 is configu red to be fluidly coupled to a medical device that defines a pathway X for withdrawing and/or transporting bodily fluid from a patient to collection device 100 . For example, entry port 121 can be fluidly coupled to a needle or other lumen defining device (eg, flexible sterile tubing). As such, the flow diverting mechanism 120 can receive bodily fluid from the patient via a nee dle or any other lumen defining device.

[1080

] The first outlet port 125 of the flow diverter mechanism 120 may be fluidly coupled to the pr e - sample reservoir 170 . In some embodiments, pre-sample reservoir 170 is integrally forme d with first outlet port 125 and/or part of flow diverter mechanism 120 . In other embodiment s, the pre-sample reservoir 170 is attached via adhesives, resistance fits, mechanical fastener s, any number of mating recesses, threaded connections and/or any other suitable connection or combination thereof. , can be mechanically and/or fluidly coupled to the flow diverting me

hanism 120 . Similarly, pre-sample reservoir 170 can be physically (e.g., mechanically) couple d to flow diverting mechanism 120 such that the volume defined by pre-sample reservoir 170 is the flow diverting mechanism. 120 in fluid communication with a first outlet port 125 . In st ill other embodiments, the pre-sample reservoir 170 is operably coupled to the first outlet por t 125 of the flow diverting mechanism 120 via an intervening structure (not shown in FIG. 1) such as flexible sterile tubing. can be done. More particularly, the intervening structure can de fine a lumen configured to place the pre-sample reservoir 170 in fluid communication with the first outlet port 125 .

[1081

] The pre-sample reservoir 170 is configured to receive and contain a first predetermined volu me of bodily fluid. In some embodiments, the pre-sample reservoir 170 stores a first volume of bodily fluid (which may be the same as or different from the first volume of bodily fluid), a second volume of bodily fluid that is subsequently withdrawn from the patient, and a second v olume of bodily fluid. /or configured to receive in a fluidly isolated manner from the third volu me. Pre-sample reservoir 170 is described in "Systems and Methods for Parenterally Procuring Bodily-Fluid Samples with Reduced Contamination", which is incorporated herein by reference in its entirety. It can be any suitable reservoir for containing bodily fluids, such as the pre-sa mple reservoir described in detail in US Pat. No. 8,197,420.

[0029]

[1082] In some embodiments, the second outlet port 126 of the flow diverting mechanism 12 0 is fluidly coupled to a lumen defining device that can be coupled to the first sample reservoi r 180 and the second sample reservoir 190. is configured to Optionally, in other embodiments, the second outlet port 126 of the flow diverter 120 can be coupled to the first sample reservoi r 180, and the flow diverter 120 was coupled to the second sample reservoir 190 (Fig. (not sh own) can have a third exit port. In some embodiments, the first sample reservoir 180 can be i ntegrally formed with the second outlet port 126 and/or part of the flow diverting mechanism 120 . In other embodiments, the first sample reservoir 180 is mechanically coupled or operabl y coupled to the second outlet port 126 via intervening structures such as those described ab ove with respect to the pre-sample reservoir 170. can be combined. First sample reservoir 18 0 is configured to receive and contain a second volume of bodily fluid. For example, the secon d volume of bodily fluid can be the amount withdrawn from the patient following the withdraw al of the first pre-sample volume. In some embodiments, first sample reservoir 180 is configu red to contain a second volume of bodily fluid such that the second volume is fluidly isolated f rom the first volume of pre-sample bodily fluid.

[1083

] First sample reservoir 180 and second sample reservoir 190 may be, for example,

It can be any suitable sterile reservoir for containing bodily fluids, including a sample reservoi r as described in the incorporated '420 patent. In some embodiments, the second volume can be any suitable volume of bodily fluid and it need not be a predetermined volume. In other e

mbodiments, the transfer of bodily fluid to the first sample reservoir 180 and/or the second sa mple reservoir 190 can be metered or the like such that the second volume is a second predet ermined volume.

[1084

] The second sample reservoir 190 can be any suitable sample reservoir. In some embodiment s, the second sample reservoir 190 can be substantially similar to the first sample reservoir 1 80 described above. A second sample reservoir 190 can be fluidly coupled to the second outle t port 126 as described above. The fluidic coupling of the second outlet port 126 to the second sample reservoir 190 can be substantially similar to the fluidic coupling of the second outlet p ort 126 to the first sample reservoir 180, as detailed above. Accordingly, such portions are not described in further detail herein and should be considered substantially similar unless explicit ly described to the contrary. Additionally, additional outlet ports and sample reservoirs of flow diverter 120 (not shown in FIG. 1) may be substantially similar to second outlet port 126 and first sample reservoir 180 .

[0032]

[1085] In some embodiments, the pre-sample reservoir 170, the first sample reservoir 180 a nd the second sample reservoir 190 can be similarly coupled to (or formed with) the flow dive rting mechanism 120. FIG. In other embodiments, pre-sample reservoir 170 , first sample res ervoir 180 and second sample reservoir 190 need not be similarly coupled to flow diverting m echanism 120 . For example, in some embodiments, the pre-sample reservoir 170 can be inte grally formed with the flow diverting mechanism 120 (eg, the first outlet port 124) and the fir st sample reservoir 180 and/or the second sample reservoir 190. can be operably coupled to f low diverting mechanism 120 (eg, second outlet port 126) via an intervening structure such a s flexible sterile tubing or any combination thereof.

[0033]

[1086] In some embodiments, the collection device 100 includes an actuator (not shown in FI G. 1) and a first fluid flow path 142, a second fluid flow path 144 and optionally (not shown in FIG. 1). and a flow controller 140 that defines additional fluid flow paths. In some embodimen ts, an actuator may be included in or otherwise operably coupled to the flow diverting mechan ism 120 . As such, actuators can be configured to control fluid movement (eg, between differe nt configurations) within flow controller 140 . For example, the actuator may be movable betw een a first position corresponding to a first configuration of flow controller 140, a second positi on different from the first position corresponding to a second configuration of flow controller 1 40, and so on. In some embodiments, the actuator can be configured to move in one directio n. For example, an actuator can be moved from its first position to its second position, but ca nnot be moved from its second position to its first position. Similarly, the actuator can be mov ed from its second position to its third position, but cannot be moved from its third position ba ck to its second position. In this manner, flow controller 140 is prevented from moving to its s econd or third configuration before its first configuration, thus directing a first volume of bod

y fluid to pre-sample reservoir 170 for medical diagnosis. and/or sample reservoirs 180 and/o r 190 designed to contain a second and/or third volume of withdrawn fluid used as a biological sample, such as for testing for therapeutic purposes. It is necessary not to be directed to

[0034]

[1087] The flow controller 140 has a first fluid flow path 142 fluidly coupling the inlet port 121 to the first outlet port 125 when in the first configuration and a second fluid flow path 142 wh en in the second configuration. 144 is configured to fluidly couple inlet port 121 to second outl et port 126 . In some embodiments, actuators such as those described above are incorporate d into the flow controller 14

0 can be configured to move in translation between the first and second configurations, and o ptionally between the third or fourth configurations. For example, in some embodiments, flow controller 140 may be in a first configuration when in a distal position relative to collection de vice 100 . In such embodiments, the actuator can be actuated to move flow controller 140 pro ximally to a proximal position relative to collection device 100, thereby placing flow controller 130 in the second configuration. In other embodiments, the actuator can be actuated to move the flow controller 140 between the first and second configurations, or optionally between the third or fourth configurations, in a rotary motion. .

[1088

] Thus, when the flow controller 140 is in the first configuration, the second outlet port 126 (a nd optionally an additional outlet port coupled to the sample reservoir) is fluidly routed from t he inlet port 121. isolated to Similarly, first outlet port 125 is fluidly isolated from inlet port 12 1 when flow controller 140 is in the second configuration. Optionally, first outlet port 125 and second outlet port 126 are fluidly isolated from inlet port 121 when flow controller 140 is in a third configuration (not shown in FIG. 1). Thus, the flow controller 140 can direct or divert a fi rst volume of bodily fluid through the first outlet port 125 to the pre-sample fluid reservoir 17 0 when in the first configuration and in the second configuration. A second volume of bodily fl uid can then be directed or diverted to the first sample fluid reservoir 180 via the second outl et port 126 .

[0036]

[1089] In some embodiments, at least a portion of the actuator can be operably coupled to th e pre-sample fluid reservoir 170. As shown in FIG. In this manner, the actuator (or at least a portion of the actuator) causes or otherwise facilitates the creation of a vacuum within the "pr e-sample" fluid reservoir 170, thereby causing the flow diverter mechanism 120 to assume its first configuration. At some point, it can be configured to initiate flow through the bodily fluid collection device 100 and into the pre-sample fluid reservoir 170 . Actuators may be any suita ble mechanism for driving bodily fluid flow into collection device 100, such as, for example, ro tating discs, plungers, slides, dials, buttons, handles, levers, and/or any other suitable mecha nism or combination thereof. can include Examples of suitable actuators are described in more detail herein with reference to specific embodiments.

[0037]

[1090] In some embodiments, the flow diverter mechanism 120 is configured such that the fl ow of the second volume of bodily fluid is transported through the flow diverter mechanism 12 0 to the first sample fluid reservoir 180 and/or to the second sample fluid reservoir 190. can b e configured such that a first volume of bodily fluid needs to be transported to the pre-sample fluid reservoir 170 before allowing for . In this manner, the flow diverting mechanism 120 can be used by a healthcare professional to collect a first predetermined amount of bodily fluid (e. g., a pre-sample) before collecting a second amount and/or a third amount of bodily fluid (e. g., a sample). can be characterized as requiring compliance with respect to Similarly, the flow diverter mechanism 120 can be used by a medical practitioner to transfer a second volume of bodily fluid, i.e., a sample, into a first sample fluid reservoir without first diverting the first vol ume of bodily fluid, i.e., a pre-sample, into a pre-sample reservoir 170. It can be configured t o prevent collection within 180 . In this manner, a healthcare professional may (intentionally o r not) add a first volume of bodily fluid that is more likely to contain surface microbes and/or other undesirable external contaminants into the bodily fluid sample used for analysis. (either unintentionally or unintentionally). In other embodiments, the fluid collection device 100 need not include mandatory compliance features or components.

[1091

] In some embodiments, the flow diverter mechanism 120 can have a fourth configuration (no t shown in FIG. 1) that is different from the first, second, and third configurations. When in th e fourth configuration, the flow diverter mechanism 120 can simultaneously fluidly isolate the inlet port 121 from the first outlet port 125, the second outlet port 126 and, optionally, the thi rd outlet port. Therefore, the shunting

When mechanism 120 is in its fourth configuration, body fluid is prevented from flowing from i nlet port 121 to pre-sample fluid reservoir 170, first sample fluid reservoir 180 and second sa mple fluid reservoir 190. FIG. In use, for example, the flow diverter mechanism 120 is placed (eg, manually or automatically) in a first configuration such that bodily fluid can flow from the inlet port 121 to the pre-sample fluid reservoir 170 . actuated and then moved to a second co nfiguration such that bodily fluids can flow from inlet port 121 to first sample fluid reservoir 1 80 and, optionally, bodily fluids can flow from inlet port 121 to second sample fluid reservoir 1 90 It can be moved to a third configuration so that it can be used, and then moved to a fourth configuration so as to stop the flow of bodily fluids into and/or through the flow diverting mec hanism 120 . In this manner, the device is effectively "cleaned" such that any residual bodily fl uids within the device 100 are prevented from becoming contaminated and/or otherwise expo sing medical personnel and/or patients to potentially hazardous fluids. Locked" and self-contai ned in the fourth form. This optional safety feature can prevent possible exposure to bodily flu id samples that may be infected with pathogens such as HIV, Hepatitis C, and the like.

[0039]

[1092] In some embodiments, one or more portions of the collection device 100 are dispose

within a housing (not shown in FIG. 1). For example, in some embodiments, at least a portion of one or more of flow diverting mechanism 120, first pre-sample reservoir 170 and sample reservoirs 180 and 190 can be disposed within the housing. In such embodiments, at least a portion of the flow diverter mechanism 120 is configured so that the user can activate the flow controller 140 to control the flow of bodily fluid from the patient (e.g., vein) to the collection device 100. Accessible through the housing. Examples of suitable housings are described in more detail herein with reference to specific embodiments.

[0040]

[1093] In some embodiments, the collection device 100 can optionally include one or more flow metering devices that can meter the flow of bodily fluid through the collection device. For example, a flow metering device can be in fluid communication with the first fluid flow path 142 and/or the second fluid flow path 144 to meter the flow of bodily fluid therethrough. In other embodiments, a flow metering device can be in fluid communication with and/or otherwise disposed in first port 125 and/or second port 126 . The flow metering device can be configured to provide the user with an indication related to the predetermined volume being transferred to the pre-sample reservoir 170, the first sample reservoir 180 and/or the second sample reservoir 190, such as an indicator (For example, electrical signal output devices such as dials, displays, colors, tactile output devices, wireless radio signals, Bluetooth radio signals, etc.). In some embodiments, a flow metering device can be operably coupled to an actuator, such as, for example, those described above. In such embodiments, the flow metering device operates an actuator to move flow controller 140 between its first configuration and its second configuration based on the desired volume of bodily fluid that has flowed through the flow metering device. may be operable as such. Thus, using the flow metering device, a desired volume of bodily fluid is transferred to the pre-sample reservoir 170, the first sample reservoir 180 and/or the second sample reservoir 190, thereby providing an insufficient volume, such as in microbiological testing, for example on patient samples. Incorrect and/or erroneous results can be prevented.

[0041]

[1094] Referring now to FIGS. Includes reservoir 290 . As further described herein, the collection device 200 is used to deliver a bodily fluid stream that is substantially free of extracorporeal microbes, such as microbes present on the skin and/or other undesirable external contaminants. It can be moved between a first configuration, a second configuration and a third configuration. collection de

Vise 200 may be of any suitable shape, size or configuration. For example, while sample reservoirs 280 and/or 290 are shown oriented perpendicular to housing 201 in FIGS. 2-13, collection device 200 is oriented planar to housing 201. It can have sample reservoirs 280 and/or 290, such as or arranged conically with respect to housing 201 .

[0042]

[1095] The flow diverter mechanism 220 includes a housing 201 and movable members 250

nd 250'. As shown in FIGS. 2-4, housing 201 is coupled to pre-sample reservoir 270 , first sa mple reservoir 280 and second sample reservoir 290 . Housing 201 includes an inlet port 221, a first outlet port 230, a second outlet port 231, a third outlet port 232, and an internal flow p ath 235 that can define a fluid flow path for collecting bodily fluids from a patient. stipulated. Inlet port 221 can be selectively placed in fluid communication with internal flow path 235 . M ore specifically, inlet port 221 defines an inlet lumen 202 that can be placed in fluid communic ation with internal flow path 235 . Inlet port 221 is thus part of housing 201 such that internal flow path 235 can be placed in fluid communication with a space substantially outside housing 201 via inlet lumen 202 . extends from Inlet port 221 can be fluidly coupled to a medical devi ce (not shown) that defines a fluid flow path for drawing bodily fluid from a patient and/or tra nsporting it to collection device 200 . For example, entry port 221 can be fluidly coupled to a needle or other lumen defining device (eg, flexible sterile tubing) directly or indirectly via ada pter 204 . Similarly, inlet lumen 202 defined by inlet port 221 is arranged to be in fluid comm unication with the lumen defined by the lumen-defining device when the lumen-defining devic e is coupled to inlet port 221 . . More specifically, when the lumen defining device is positione d within a portion of a patient's body (e.g., within a patient's vein or spinal space), the interior passageway 235 of the housing 201 is aligned with that portion of the patient's body. It can b e arranged in fluid communication with the portion.

[0043]

[1096] The internal passageway 235 defined by the housing 201 is a central lumen that exten ds along the length of the housing 201 and is used for venipuncture (fluid access) as describe d herein. (other methods employed to enable the patient to be placed in fluid communication with the patient's bodily fluids). Internal channels 235 form fluid flow paths that transport bod ily fluids between inlet port 221 and first, second, and third outlet ports 230 , 231 , and 232 . More specifically, when the internal flow path 235 is placed in fluid communication with a pati ent (eg, via a medical device coupled to the inlet port 221), the first outlet port 230, the seco nd outlet port 231 are and third outlet port 232 are selectively placed in fluid communication with internal flow path 235 to allow bodily fluids to flow into at least one of pre-sample reserv oir 270 , first sample reservoir 280 or second sample reservoir 290 . can be allowed to flow. I n some embodiments, bodily fluid is prevented from flowing to second outlet port 231 and thir d outlet port 232 before a predetermined volume of bodily fluid has been collected in pre-sam ple reservoir 270 . In some embodiments, the second outlet port 231 and the third outlet port 232 can be placed in fluid communication with the internal flow path 235 at the same time. In some embodiments, the second outlet port 231 and the third outlet port 232 can be arranged in fluid communication with the internal flow path 235 sequentially.

[0044]

[1097] Movable members 250, 250' are actuated (eg, moved) by a user from first and second positions relative to housing 201 to direct fluid flow to first sample reservoir 280 and second s ample reservoir. 290. Movable members 250 and 250 ′ are substantially identical and therefo

e will be described with respect to a single movable member 250 . As shown in FIG. 5, movea ble member 250 includes a boss 251 defining an interior cavity 252 , an inlet port 253 , a first outlet port 254 , and lumen 25 fluidly coupled to interior cavity 252 .

and a piercing member 255 defining 6. Inlet port 253 and outlet port 254 extend through the wall of boss 251 that defines interior chamber 252 of movable member 250 . Movable membe r 250 is positioned within support 257 (see FIG. 4) of housing 201 such that boss 251 is dispo sed within bore 258 (see FIG. 4) and at least a portion of movable member 250 is disposed wi thin annular chamber 260 (see FIG. 4). configured to be attached to the Optionally, a biasing member 259 (eg, a spring) can be disposed within the annular chamber 260 to return the mo vable member 250 to its first position after actuation by the user. In some embodiments, mov able member 250, annular chamber 260, bore 258 or boss 251 are configured to retain mova ble member 250 in a second position (e.g., depressed position) after being actuated by a user. A mechanical locking mechanism can be included.

[0045]

[1098] As described herein, in the first configuration, the movable member 250 is arranged to be spaced apart from the internal channel 235. As shown in FIG. In such configurations, a flui d flow path cannot be established between a portion of the patient's body (eg, a vein, spinal c avity, etc.) and sample reservoirs 280 and/or 290 . In other words, when movable member 25 0 is in its first configuration, first sample reservoir 280 and second sample reservoir 290 are fl uidly isolated from internal flow path 235 defined by housing 201 . Movable member 250 can be actuated by a user to move movable member 250 from the first configuration to the secon d configuration and into alignment with internal channel 235 . The force applied by the user m ay be sufficient to deform (eg, compress) biasing member 259, thereby inserting piercing me mber 255 into sample reservoirs 280 and/or 290. can be done. In the second configuration, in let port 253 and outlet port 254 are substantially aligned with internal flow path 235 to place i nternal cavity 252 in fluid communication with internal flow path 235 . Thus, when movable m ember 250 is in the second configuration, a fluid flow path is established between internal cha nnel 235 , internal cavity 252 , lumen 256 of piercing member 255 and sample reservoir 280 . In other words, in such a configuration, bodily fluids flow from the patient (eg, veins, spinal s paces, etc.) through the flow diverting mechanism 220 into the first sample reservoir 280 an d/or the second sample reservoir 280, as described in further detail herein. It can flow into th e sample reservoir 290 .

[0046]

[1099] The pre-sample reservoir 270 can be any suitable reservoir for containing bodily fluids, such as, for example, a single-use disposable collection tube, a vacuum-assisted collection tub e, and the like. Pre-sample reservoir 270 is configured to be fluidly coupled in any suitable ma nner (either directly or via an intervening structure such as sterile flexible tubing) to first outl et port 230 of collection device 200. . For example, in some embodiments, a portion of pre-sa mple reservoir 270 can form a friction fit within a portion of first outlet port 230 . In other er

bodiments, pre-sample reservoir 270 can be coupled to first outlet port 230 via threaded coup ling, adhesives, snap fits, mechanical fasteners and/or any other suitable coupling method. . I n some embodiments, pre-sample reservoir 270 can be integrally formed with housing 201 . P re-sample reservoir 270 is subjected to a negative pressure condition (vacuum condition) that can enable bodily fluid to be drawn into pre-sample reservoir 270 via vacuum suction from inl et port 221 through outlet port 230 (pre-sample reservoir 270) can be configured to be maint ained internally. Pre-sample reservoir 270 is configured to contain a first volume of bodily flui d, where the first volume of bodily fluid can be a predetermined volume or an unquantified vol ume, thereby is fluidly isolated from a second and/or a third volume of bodily fluid subsequent ly withdrawn from the patient.

[1100

] Sample reservoirs 280 and/or 290 may be single-use disposable collection tubes, vacuum dr iven collection tubes, sample reservoirs such as those described in the '420 patent incorporate d herein by reference above, or the like. It can be any suitable reservoir for containing bodily fluids, including: In some embodiments, sample reservoirs 280 and/or 290 include, for examp le

It can be substantially similar or identical to known sample containers, such as the Vacutainer ®. Sample reservoirs 280 and 290 include sample vessels 282 and 292, respectively, and vac uum seals 284 and 294, respectively. A vacuum seal 284 or 294 can allow bodily fluid to be dr awn into the sample container 282 or 292, respectively, from the internal channel 235 via vac uum suction into the sample container 282 or 292, respectively. state). Sample containers 28 0 and/or 290 are fluidically connected in any suitable manner (directly or via an intervening st ructure such as sterile flexible tubing) to second and third outlet ports 231 and 232, respectiv ely, of collection device 200. It can be configured to be coupled. Sample reservoirs 280 and/or 290 can be moved relative to exit ports 231 and/or 232 so as to be placed in fluid communica tion with exit ports 231 and/or 232 . Sample reservoirs 280 and 290 can be configured to con tain a second volume or a third volume of bodily fluid. The second or third amount of bodily fl uid can be a predetermined amount or an unquantified amount, whereby the second or third amount of bodily fluid is the first amount of bodily fluid withdrawn from the patient. fluidly isol ated from In some configurations, sample reservoirs 280 and/or 290 may be coupled to collec tion device 200 by being integrally formed with housing 201, similar to pre-sample reservoir 2 70, and are therefore not discussed in detail herein. not described in In some cases, the samp le reservoirs 280 and/or 290 can be transparent so that the user has visual feedback to confir m the flow of bodily fluid into the sample reservoirs 280 and/or 290. can be done.

[0048]

[1101] In some embodiments, sample reservoirs 280 and 290 and flow diverter mechanism 2 20 (and/or portions of collection device 200 other than sample reservoirs 280 and 290) are in dependently formed (e.g., integrally formed) and bonded together during the manufacturing p rocess, for example. In some cases, sample reservoirs 280 and 290 can be coupled to flow d

erter mechanism 220 in a substantially sterile or sealed environment (eg, filled with ethylene oxide or the like). Accordingly, the interface between sample reservoirs 280 and 290 and flow diverter 220 is substantially sterile prior to use. Further, collection device 200 can be transported and/or stored pre-assembled, such as to maintain a substantially sterile interface between sample reservoirs 280 and 290 and flow diverting mechanism 220 .

[0049]

[1102] As shown in FIGS. First member 241 is configured to be disposed within recess 266 (see, eg, FIG. 4) of housing 201 and is made of, for example, titanium, graphite, pyrolytic carbon, polyester, polycarbonate, polyurethane, or the like. , elastomeric materials, etc., that are biocompatible. In some embodiments, second member 245 acts as an actuator to move first member 241 from the first configuration to the second configuration. More specifically, once the first member 241 is positioned within the recess 266, the second member 245 is moved between the first and second positions to move the flow controller 240 from the first configuration to the second configuration. It can be moved between two forms. In some embodiments, housing 201 can selectively restrict movement of second member 245 from its first position to its second position. In some embodiments, the housing 201 can be configured to prevent movement of the second member 245 moved to the second position. In other words, housing 201 can include a locking mechanism that prevents second member 245 from moving back from the second position to the first position. Second member 245 and/or housing 201 may also include mechanical detents and/or other indicators that provide visual or tactile feedback to ensure correct positioning of second member 245. is.

[1103

] The first member 241 is used for venipuncture (and/or other methods of accessing a patient's bodily fluids).

A plurality of channels can be included to direct fluid flow subsequent to the . For example, as shown in FIGS. 6 and 7, first member 241 includes first channel 242 and second channel 244 . When the second member 245 is in the first position (see, for example, FIGS. 8 and 9), the flow controller 240 is arranged in the first configuration and the first channel 242 connects the inlet port 221 from the internal channel 235. Fluid communication is established between inlet port 221 and first outlet port 230 while being fluidly isolated. When the second member 245 is in the second position (see, eg, FIGS. 10-13), the flow controller 240 is disposed in the second configuration and the second flow path 244 connects the inlet port 221 to the first outlet port 230. Fluid communication is established between the inlet port 221 and the internal channel 235 while being fluidly isolated from the . The position of the additional second member 245 corresponding to the flow path of the additional first member 241 and/or the configuration of the flow controller 240 to further direct/isolate the fluid flow between the patient and the collection device 200. can be included. For example, the second member 245 can have a third position corresponding to a third configuration of the flow controller 240 that substantially prevents fluid flow between the patient and the collection device 200 as a whole. In other words,

some embodiments, after all bodily fluid samples have been removed from the patient, movin g the dial to the third position substantially seals the sample within the collection device 200 f rom the external environment. can be done.

[0051]

[1104] In operation, the collection device 200 can be used to collect bodily fluids (eg, blood) f rom a patient with reduced contamination from microorganisms present on the skin and/or ot her undesirable external contaminants. can. For example, inlet port 221 of collection device 2 00 is fluidly coupled via adapter 204 to a needle or other lumen defining device (eg, flexible st erile tubing). Following venipuncture (or other fluid access method), second member 245 is ro tated until it reaches the first position, as shown in FIGS. Alternatively, the second member 2 45 can be preset to the first position and the collection device 200 is otherwise sealed to main tain the vacuum within the pre-sample reservoir 270 and the sterility of the collection device 200. can do. For example, inlet port 221 and/or adapter 204 can include a valve that opens w hen collection device 200 is coupled to a needle or other lumen defining device.

[0052]

[1105] As described above, when the second member 245 is in the first position, the flow con troller 240 is disposed in the first configuration and the first passageway 242 of the first mem ber 241 connects the inlet port 221 to the internal passageway. Fluid communication is establi shed between inlet port 221 and first outlet port 230 while being fluidly isolated from 235 . Fu rther, the first sample reservoir 280 and the second sample reservoir 290 are fluidly isolated f rom the inlet port 221 in the first configuration and are located in a portion of the patient's bo dy (eg, a vein), as indicated by arrows AA in FIG. and a pre-sample reservoir 270 are defined. As described above, the fluid reservoirs used in collection device 200, such as pre-sample res ervoir 270 and sample reservoirs 280 and 290, are exposed to a negative pressure (i.e., the p ressure of the body part from which collection device 200 is used to draw bodily fluids). press ure less than the fluid pressure), thereby establishing fluid communication between a portion of the patient's body (e.g., a vein) and pre-sample reservoir 270, the negative pressure within pre-sample reservoir 270 causes , the pressure differential between the pre-sample reservoir 270 and that portion of the patient's body causes fluid to be drawn into the pre-sample reserv oir 270 . In this first configuration, flow controller 240 also fluidly isolates pre-sample reservoi r 270 from internal flow path 235 . Thus, a first volume (predetermined or unquantified) of bo dily fluid can be received in pre-sample reservoir 270 (for example) immediately after venipun cture and isolated from subsequent samples. Thus, with the collection device 200, a first volu me of bodily fluid most likely to contain surface microorganisms and/or other undesirable exte rnal contaminants may be diagnosed or affected by the contaminants. Subsequent volumes of bodily fluid samples collected and used for other tests can be uncontaminated.

[0053]

[1106] Following collection of the body fluid pre-sample volume in the pre-sample reservoir 2 70,



, the second member 245 can be rotated until it reaches a second position as shown in FIGS. When the second member 245 is in the second position, the flow controller 240 is placed in th e second configuration and the second flow path 244 of the first member 241 enters the first outlet port 230 (i.e., the pre-sample reservoir 270). Fluid communication is established betwe en inlet port 221 and internal channel 235 while being fluidly isolated from port 221 . In other words, in the second configuration, the flow controller 240 provides flow between a portion of the patient's body (eg, a vein) and the internal flow path 235 via the second flow path 244, as indicated by arrow BB in FIG. establish a fluid flow path in the

[0054]

[1107] With flow controller 240 in the second configuration, movable member 250 and/or 25 0' is actuated (i.e., depressed) by a user from a first position to a second position to move the patient's body. Fluid communication can be established between a portion (eg, a vein) and the first sample reservoir 280 and/or the second sample reservoir 290 . More specifically, movable member 250 moves from its first position to its second configuration such that piercing memb er 255 pierces vacuum seal 284 of first sample reservoir 280, as indicated by arrow CC in FI G. The piercing member 255 passes through the exit port 231 so that it can be opened and pl aced inside the sample container 282 . When in the second position, inlet port 253 and outlet port 254 of movable member 250 are substantially aligned with and in fluid communication wi th internal channel 235 such that bodily fluids flow from internal channel 235 to the movable member. It can flow into the internal cavity 252 of 250 and out of the lumen 256 of the pierci ng member 255 into the first sample reservoir 280 . A pressure differential between sample r eservoir 280 (eg, vacuum or negative pressure) and internal channel 235 draws bodily fluid in to sample reservoir 280 . In other words, in the second configuration, movable member 250 e stablishes a fluid flow path between internal flow path 235 and first sample reservoir 280, as i ndicated by arrow DD in FIG. Once a desired amount of bodily fluid (eg, a second amount) ha s been collected in first sample reservoir 280, the user releases movable member 250 such th at biasing member 259 returns the button to its first position. can be enabled to move to Whe n movable member 250 returns to its first position, piercing member 255 is removed from firs t sample reservoir 280 and seal 284 (e.g., a self sealing septum) opens first sample reservoir 280 to internal flow. It is fluidly isolated from channel 235 .

[0055]

[1108] Similarly, while the flow controller 240 is in the second configuration, the movable me mber 250' is actuated (depressed) by a user from its first position to its second position, as in dicated by arrow EE in FIG.)be able to. Thus, in a manner similar to the movable member 25 0 and the first sample reservoir 280 described above, a portion of the patient's body (eg, a ve in) and the second sample reservoir 290 (via the exit port 232). Fluid communication is establ ished. In other words, in the second configuration, movable member 250' establishes a fluid fl ow path between internal flow path 235 and second sample reservoir 290, as indicated by arr ow FF in FIG. Once a desired amount of bodily fluid (eg, a third amount) has been collected

second sample reservoir 290, the user releases movable member 250' such that biasing mem ber 259' causes button 250' to move to its third position. It can be allowed to move back to o ne position. Although shown and described as being a sequential process, the order and/or se quencing of filling is not necessary (i.e., sample reservoir 280 may not necessarily fill before s ample reservoir 290, etc.). . In other words, when the flow controller 240 is moved to the sec ond configuration, the first sample reservoir 280 and the second sample reservoir 290 (and a ny additional sample reservoirs) are activated in any order at the same time (eg, simultaneou sly) and/or Or they can be filled in overlapping time intervals. For example, a user can initiate filling of the first sample reservoir 280, and then after the first sample reservoir 280 is partiall y filled, the user presses the movable member 250' to Filling of the second sample reservoir 2 90 can begin while the first sample reservoir 280 finishes filling. Additionally, adjustment of th e volume of bodily fluid collected in sample reservoirs 280 and/or 290 can be achieved by mo ving member 2

It can be enabled by repeatedly actuating (inserting) 50 and/or 250'. As noted above, the sec ond member 245 can have a third position corresponding to the third configuration of the flow controller 240, thereby substantially reducing fluid flow between the patient and the collection device 200 as a whole. to substantially seal the sample within the collection device 200 from t he external environment.

[1109

] Although not shown in FIGS. 2-13, the collection device 200 meters the volume of bodily flui d transferred to the pre-sample reservoir 270, the first sample reservoir 280 and/or the secon d sample reservoir 290. A flow metering device or the like can be included that can be configu red to. For example, in some embodiments, first member 241 of flow controller 240 can includ e a flow metering device in fluid communication with first flow path 242 and second flow path 244 . In other embodiments, a flow metering device can be positioned within the internal cavi ty 252 of the moveable member 250 and/or 250'. Accordingly, the volume of the bodily fluid s ample transferred to and placed in the first sample reservoir 280 and the second sample reser voir 290 may be such that the volume of the bodily fluid sample placed in each sample reserv oir 280 and 290 is e.g. It can be metered and/or controlled to have a predetermined volume, such as 30 mL.

[0057]

[1110] Although the collection device 200 is shown and described as including a first sample r eservoir 280 and a second sample reservoir 290, other embodiments may include any number of pre-sample reservoirs and/or sample reservoirs. can contain. For example, Figures 14 and 15 show a collection device 300 according to embodiments. As shown, some aspects of the co llection device 300 may be substantially similar to corresponding aspects of the collection devi ce 200 described above with reference to FIGS. 2-13. Accordingly, similar aspects are not des cribed in further detail herein.

[0058]

[1111] As shown in Figs. A fourth sample reservoir 390' is included. Pre-sample reservoir 370 may be substantially similar to pre-sample reservoir 270 described in detail above. In some e mbodiments, sample reservoirs 380, 380', 390 and 390' can be substantially similar to sample reservoirs 280 and 290 described in detail above. In some embodiments, sample reservoirs 3 80, 380', 390 and 390' can have substantially the same shape and size, eg, contain substanti ally the same medium. In other embodiments, sample reservoirs 380, 380', 390 and 390' can have substantially the same shape and size and contain one of aerobic or anaerobe media. ca n be done. For example, in some embodiments, the first sample reservoir 380 and the third s ample reservoir 390 can contain an aerobic culture medium, and the second sample reservoir 380' and the fourth sample reservoir 390' can contain an anaerobe culture medium. A culture medium can be included. In other embodiments, sample reservoirs 380, 380', 390 and 390' m ay each contain aerobic or anaerobe media in any arrangement or combination.

[0059]

[1112] The flow diverter mechanism 320 includes a housing 301 and a set of moveable memb ers 350, 350', 350'' and 350'''. Movable members 350, 350', 350'' and 350''' are substantially similar to movable member 250 described above with reference to FIG. 5, for example. Accor dingly, movable members 350, 350', 350'' and 350''' are positioned in a first position relative t o housing 301 such that they are placed in fluid communication with sample reservoirs 380, 3 80', 390 and 390', respectively. and a second position. The housing 301 is in fluid communicat ion with an inlet port 321 , a first outlet port 330 configured to be arranged in fluid communic ation with a pre-sample reservoir 370 , and a first sample reservoir 380 .

a second outlet port 331 configured to be arranged to be in fluid communication with a secon d sample reservoir 380' and a third outlet port 332 configured to be arranged in fluid commun ication with a third sample reservoir 390'; and a fifth outlet port 334 configured to be placed i n fluid communication with a fourth sample reservoir 390'. Further, housing 301 can be selecti vely placed in fluid communication with inlet port 321 and outlet ports 331 , 332 , 333 and 33 4 in a manner similar to that described above with respect to interior passageway 235 of hous ing 201 . An internal channel 335 is defined.

[1113

] The flow controller 340 is substantially similar to the flow controller 240 described above, e g, with reference to FIGS. 6-13. Accordingly, the flow controller 340 is rotated between the fir st and second configurations to provide a portion of the fluid flow path between the patient an d the pre-sample reservoir 370 or the sample reservoirs 380, 380', 390 and 390'. can be sele ctively defined. In this manner, a user can operate collection device 300 in a manner similar t o that described above with respect to collection device 200 in FIGS. 8-13. Thus, a first volum e of bodily fluid can be transferred to and placed in pre-sample reservoir 370, and subsequent volumes of bodily fluid can be transferred to and placed in sample reservoirs 380, 380', 390 a nd 390'. can be placed.

[0061]

[1114] FIGS. 16-22 illustrate a collection device 400 according to an embodiment. Collection device 400 includes flow diverter mechanism 420, flow controller 440 and sample reservoirs 480, 480', 490 and 490'. As further described herein, the collection device 400 can be moved between first, second, third, fourth and fifth configurations to, for example, collect microorganisms and/or microorganisms present on the skin. or a body fluid stream that is substantially free of extracorporeal microorganisms, such as other undesirable external contaminants. Collection device 400 may be of any suitable shape, size or configuration. For example, although sample reservoirs 480, 480', 490 and 490' are shown oriented perpendicular to housing 401 in FIGS. It is possible to have the sample reservoirs 480, 480', 490 and 490' oriented in a plane, arranged conically with respect to the housing 401, or the like.

[0062]

[1115] The sample reservoirs 480, 480', 490 and 490' are substantially similar or identical in form and function to the sample reservoirs 280 and/or 290 of the collection device 200; No details are given. As described above, the sample reservoirs 480, 480', 490 and 490' are negative pressure conditions that can allow fluid to be drawn from the patient into the sample reservoirs 480, 480', 490 and 490' via suction. (vacuum state) is maintained. In some embodiments, sample reservoirs 480 and 480′ can be aerobe culture bottles, sample reservoirs 490 and 490′ can be anaerobe culture bottles, and collection device 400 can be used to Thus, multiple aerobic and multiple anaerobic blood culture samples can be collected from a single venipuncture. As described in further detail herein, sample reservoirs 480, 480', 490 and 490' are each arranged in fluid communication with at least a portion of flow diverting mechanism 420 to receive a volume of bodily fluid sample. can do. The volume of the bodily fluid sample can be either predetermined or unquantified. Further, once a desired volume of bodily fluid has been placed within sample reservoirs 480, 480', 490, 490', each sample reservoir 480, 480', 490 and 490' will be displaced as described in further detail herein. can be fluidly isolated from at least a portion of flow diverting mechanism 420 .

[1116

] Flow diverting mechanism 420 includes housing 401 and distribution member 429 . Housing 401 of flow diverter mechanism 420 is physically and fluidly coupled to distribution member 429 to provide patient-to-body flow.

It provides and/or defines a set of fluid flow paths for collecting liquid. Housing 401 defines a recess 466 and a set of exit openings 403 . Recess 466 is configured to receive seal member 441 included in flow controller 440, as described in further detail herein. The set of outlet openings 403 is configured to define a different fluid flow path, each of which is in fluid communication with a different portion of the distribution member 429, a first outlet opening 403a, a second outlet opening 403b. , a third exit opening 403c, a fourth exit opening 403d and a fifth exit opening 403e. More specifically, distribution member 429 includes at least a portion of pre-sample reservoir 470 in fluid communication with first outlet opening 403a and a first channel 435a in fluid communication with second outlet opening 403b. , a second channel 435b in flu

d communication with the third outlet opening 403, a third channel 435c in fluid communicati on with the fourth outlet opening 403d, and a third channel 435c in fluid communication with the fifth outlet opening 403e. defines and/or forms four channels 435;

[0064]

[1117] As shown in FIGS. Pre-sample reservoir 470 is configured to contain bodily fluids such as, for example, blood, plasma, urine, and the like. A first outlet opening 403a of housing 401 can be substantially aligned with an open portion of pre-sample reservoir 470 to allow pre-sa mple reservoir 470 to receive the flow of bodily fluid from the patient. For example, pre-sampl e reservoir 470 can receive and contain a first amount or first volume of bodily fluid, where th e first amount of bodily fluid can be a predetermined amount or an unquantified amount. Addi tionally, the arrangement of the flow diverter mechanism 420 may be such that the pre-sampl e reservoir 470 may be configured to allow fluid from the flow paths 435a, 435b, 435c and 43 5d and/or subsequent volumes of bodily fluid withdrawn from the patient, as described in furt her detail herein. can be maintained in a systematically isolated manner. Although pre-sample reservoirs 270 and 370 are described above as maintaining a negative pressure, pre-sample r eservoir 470 does not maintain a negative pressure (vacuum) and therefore uses other mecha nisms such as gravity for example. can be used to draw bodily fluid into the pre-sample reser voir 470 .

[0065]

[1118] Channels 435a-435d extend radially from the center of distribution member 429 such that each channel 435a, 435b, 435c and 435d is fluidly isolated from pre-sample reservoir 47 0 and the other channels. are placed in In this manner, channels 435a, 435b, 435c and 435d are fluid flow channels between first and second ends substantially aligned with outlet openin gs 403b, 403c, 403d and 403e, respectively. can be oriented and/or otherwise defined. As sho wn in FIGS. 17 and 18, the distribution member 429 has a first outlet port 431 located at the second end of the first flow path 435a and a second outlet port 431 located at the second end of the second flow path 435b. defining a second outlet port 432, a third outlet port 433 positio ned at the second end of the third flow path 435c, and a fourth outlet port 434 positioned at t he second end of the fourth flow path 435d; are doing. Further, the distribution member 429 i ncludes a first piercing member 455a, a second piercing member 455b, a third piercing memb er 455c and a fourth piercing member 455d, which are the first outlet port 431, the second ou tlet port 432, the third It is physically and fluidly coupled to outlet port 433 and fourth outlet port 434, respectively. Thus, as described in further detail herein, piercing members 455a-355 d can be used to pierce the vacuum seals of sample reservoirs 480, 480', 490 and 490', there by allowing bodily fluids to flow. Flow can be started. Although not shown in Figures 17 and 1 8, sample reservoirs 480, 480', 490 and 490' are in fluid communication with outlet ports 43 1, 432, 433 and 434, respectively. can be physically coupled (either directly or via an interven ing structure such as a sterile flexible tube) to a portion of distribution member 429 in any sui table manner that can allow the can.

[0066]

[1119] The flow controller 440 includes a dial 445 and a seal member 441 . C
Lel member 441 is positioned within recess 466 of housing 401 (see, eg, FIG. 20). More partic ularly, coupling flow controller 440 to housing 401 such that seal member 441 is positioned be tween and in contact with the surface of housing 401 defining recess 466 and the surface of di al 445 . can be done. In addition, seal member 441 may be positioned against the surface of housing 401 defining dial 445 and recess 466 when flow controller 440 is coupled to housing 401, as described in further detail herein. can be sized and shaped to form a substantially flui d-tight seal with. The sealing member 441 is made of, for example, silicone, polylactic acid, p olyglycolic acid, polylactic-co-glycolic acid (PLGA), polyanhydride, polyorthoester, polyetherest er, polycaprolactone, polyesteramide, poly(butyric acid).), poly(valeric acid), polyurethanes, nylons, polyesters, polycarbonates, polyacrylates, polymers of ethylene-vinyl acetate and othe r acyl-substituted cellulose acetates, polystyrene, polyvinyl chloride, polyvinyl fluoride, poly(vi nylimidazole), chloro It can be made from any material that is biocompatible, such as sulfonat e polyolefins, polyethylene oxides and/or mixtures and copolymers thereof.

[0067]

[1120] As shown in FIG. 17, the sealing member 441 defines a set of openings 444 through w hich the flow of bodily fluids can be directed following venipuncture (or other method of acces sing bodily fluids). . For example, the set of openings 444 defined by the seal member 441 inc ludes a first opening 444a, a second opening 444b, a third opening 444c, a fourth opening 44 4d and a fifth opening 444e. The arrangement of the sealing member 441 is such that when t he sealing member 441 is arranged in the recess 446, the first opening 444a, the second ope ning 444b, the third opening 444c, the fourth opening 444d, and the fifth opening 444e are , t he first outlet opening 403a, the second outlet opening 403b, the third outlet opening 403c, t he fourth outlet opening 403d and the fifth outlet opening 403e of the housing 401, respectiv ely. is.

[0068]

[1121] The dial 445 of the flow controller 440 is rotatably coupled to the housing 401 and is movable between a first position, a second position, a third position, a fourth position and a fif th position relative to the housing 401. . Dial 445 includes an entry port 421 that defines lume n 402 . Inlet port 421 can be fluidly coupled to a medical device (not shown) that defines a flu id flow path for withdrawing and/or transporting bodily fluid from the patient's body to collecti on device 400 . For example, entry port 421 can be fluidly coupled to a needle or other lumen defining device (eg, flexible sterile tubing) either directly or indirectly via adapter 404 . Simila rly, inlet lumen 402 defined by inlet port 421 is arranged to be in fluid communication with th e lumen defined by the lumen-defining device when the lumen-defining device is coupled to in let port 421 . be. Inlet port 421 thus connects to pre-sample reservoir 470, first sample reser voir 480, second sample reservoir 480', third sample reservoir 490 and fourth sample reservoi r 490, as described in further detail herein. ' can be configured to be selectively placed in flu

communication with a patient.

[0069]

[1122] As described above, the dial 445 is movable between a first position, a second positio n, a third position, a fourth position, and a fifth position. When the dial 445 is in the first posit ion, the flow controller 440 is arranged in a first configuration, aligning the inlet port 421 subs tantially with the first opening 444 a of the seal member 441 and the first outlet opening 403 a of the housing 401 . can be combined. Thus, the first opening 444a of the seal member 441 fluidly isolates the inlet port 421 from the outlet openings 403b, 403c, 403d and 403e, thereb y fluidly isolating the inlet port 421 from the flow paths 435a-335d. Fluid communication is es tablished between the inlet port 421 and the first outlet opening 403a while isolating to the fir st outlet port 403a. When the first outlet port 403a is aligned with the open portion of the pre -sample reservoir 470, the first opening 444a and the first outlet port 403a are aligned. Mouth opening 403 a establishes fluid communication between inlet port 421 and pre-sample reservoir 470 . When the dial 445 is rotated (or driven) to the second position, the flow contro ller 440 is placed in the second configuration and the second outlet opening 444b connects th e inlet port 421 to the outlet openings 403a, 403c, 403d and 403e. Fluid communication is est ablished between inlet port 421 and second outlet opening 403b while being fluidly isolated fr om. When the second outlet opening 403b is aligned with the first end of the first flow path 4 35a, the second opening 444b and the second outlet opening 403b are between the inlet port 421 and the first flow path 435a. establish fluid communication with the

[0070]

[1123] The collection device 400 operates similarly when the dial 445 is rotated to the third, f ourth and fifth positions. Thus, when inlet lumen 402 is placed in fluid communication with a p atient (eg, via a medical device coupled to inlet port 421), first outlet port 430, second outlet port 431, third outlet Port 432, fourth outlet port 433, and fifth outlet port 434 are selectively placed in fluid communication with inlet lumen 402 so that all body fluids are present in at lea st one of pre-sample reservoirs 470 or sample. It can be enabled to flow into one or more of r eservoirs 480, 480'490 and 490'. In some embodiments, additional seal outlet openings and/o r additional dials 445 corresponding to the configuration of the flow controller 440 are provide d to further direct/isolate fluid flow between the patient and the collection device 400. Can inc lude location. For example, dial 445 can have a sixth position corresponding to a sixth configu ration of flow controller 440 that substantially prevents fluid flow between the patient and coll ection device 400 as a whole. In other words, in some embodiments, after all bodily fluid sam ples have been removed from the patient, dial 445 can be moved to the sixth position to subs tantially seal the sample within collection device 400 from the external environment. can.

[0071]

[1124] In some embodiments, until after a predetermined volume of bodily fluid has been coll ected in the pre-sample reservoir 470, the bodily fluid does not flow to the outlet ports associ ated with the sample reservoir (eg, outlet ports 431-434). prevented. In some embodiments

the exit ports associated with the sample reservoirs (eg, exit ports 431-434) can be placed in fluid communication with the entrance lumen 402 only sequentially (eg, exit ports 431-434). 431 must be in fluid communication with the inlet lumen 402 before the outlet port 432, etc.). In some embodiments, outlet ports associated with subsequent sample reservoirs (eg, outlet ports 432-434) are placed in fluid communication with inlet lumen 402 only after a defined vol ume of bodily fluid has been collected. can be placed. In some embodiments, the outlet ports associated with the sample reservoirs (eg, outlet ports 431-434) can be arranged in fluid com munication with the inlet lumen 402 in any random manner without any order preference. (e g, outlet port 434 can be in fluid communication with inlet lumen 402 before outlet port 431, outlet port 432 can be in fluid communication with inlet lumen 402 before outlet port 433, et c.)).

[0072]

[1125] In some embodiments, the housing 401 can selectively restrict movement of the dial 4 45 from its first position to its second, third, fourth and fifth positions. . In some embodiment s, housing 401 can be configured to prevent movement of dial 445 moved to the fifth positio n. In other words, housing 401 may include a locking mechanism that prevents dial 445 from moving back from the fifth position to the first position. Dial 445 and/or housing 401 may also include mechanical detents and/or other detents that provide visual or tactile feedback to ens ure correct positioning of dial 445 relative to exit openings 403a-403e of housing 401. It is als o possible to include an indicator.

[0073]

[1126] In operation, the collection device 400 can be used to collect bodily fluids (eg, blood, p lasma, urine, etc.) from a patient with reduced contamination. For example, entry port 421 of collection device 400 can be fluidly coupled to a needle or other lumen defining device (eg, fle xible sterile tubing). Following venipuncture (or other method of accessing bodily fluids), dial 445 is actuated (or turned) until it reaches the first position, as shown in FIGS. Alternatively, dial 445 can be preset to the first position and collection device 400 can be otherwise sealed t o maintain sterility of collection device 400 . For example, inlet port 421 can include a valve t hat opens when collection device 400 is coupled to a needle or other lumen defining device.

[0074]

[1127] As described above, when the dial 445 is in the first position, the flow controller 440 is disposed in the first configuration, and the first opening 444a of the seal member 441 connect s the inlet port 421 to the four flow paths 435a through 435a. Fluid communication is establis hed between inlet port 421 (contained within housing 401) and first outlet port 430 while bein g fluidly isolated from 335d. Further, sample reservoirs 480, 480', 490 and 490' are fluidly isol ated from inlet port 421 in the first configuration and are part of the patient's body (e.g., A flu id flow path is defined between the vein) and the pre-sample reservoir 470 . In this first confi guration, bodily fluid passes from that portion of the patient's body through the inlet lumen 4 02 of the inlet port 421, the first opening 444a of the seal member 441, the first outlet port

30, and into the pre-sample reservoir 470 (for example, by gravity, vacuum, etc.). In the firs t form, flow controller 440 also fluidly isolates pre-sample reservoir 470 from channels 435a-3 35d. Accordingly, a first volume (predetermined or unquantified) of bodily fluid can be receive d in pre-sample reservoir 470 immediately after venipuncture and isolated from subsequent s amples. Thus, with the collection device 400, a first volume of bodily fluid most likely to conta in surface microorganisms and/or other undesirable external contaminants may be diagnosed or affected by the contaminants. Subsequent volumes of bodily fluid samples collected and us ed for other tests can be uncontaminated.

[0075]

[1128] Following the collection of the bodily fluid pre-sample into the pre-sample reservoir 47 0, the dial 445 can be actuated (rotated) until it reaches the second position, as shown in FIG S. When dial 445 is in the second position, flow controller 440 is disposed in the second config uration, and second opening 444b of seal member 441 fluidly isolates pre-sample reservoir 47 0 from inlet port 421 while allowing inlet port 421 to flow. Establish fluid communication betw een 421 and channel 435a. In other words, in the second configuration, flow controller 440 es tablishes a fluid flow path between a portion of the patient's body (eg, a vein) and flow path 4 35a, as indicated by arrow HH in FIG. With flow controller 440 in the second configuration, sa mple reservoir 480 is actuated by the user from the first configuration to the second configura tion (e.g., by pushing piercing member 455a) into a portion of the patient's body (e.g., A vei n) and the first sample reservoir 480 can be in fluid communication.

[0076]

[1129] As described above, the piercing member 455a is positioned inside the sample reservo ir 480 by piercing the vacuum seal of the sample reservoir 480 by moving the sample reservoi r 480 to the second configuration. In this second configuration, a portion of the patient's body (eg, a vein) is exposed to a vacuum suction force from the sample reservoir 480 due to the ne gative pressure (vacuum) within the sample reservoir 480 . A pressure differential between th e sample reservoir 480 (eg, vacuum or negative pressure) and that portion of the patient's bo dy draws fluid into the sample reservoir 480 . Bodily fluid passes from that portion of the pati ent's body through the inlet lumen 402 of the inlet port 421, the second opening 444b of the seal member 441, the second outlet opening 403b of the housing 401, and into the first flow path 435a. flow in. Vacuum suction draws the flow of bodily fluid through first channel 435a a nd into sample reservoir 480 via second outlet port 431 and piercing member 455a.

. In other words, in the second configuration, flow controller 440 establishes a fluid flow path between inlet port 421 and sample reservoir 480 . Once a desired amount of bodily fluid (eg, a second amount) has been collected in sample reservoir 480, the user actuates (rotates) flow controller 440 to a third position and/or rotates sample reservoir 480 to its The first sample re servoir 480 can be isolated from the channel 435a by moving it back to the first configuration. When sample reservoir 480 returns to the first configuration, piercing member 455a is remov ed from sample reservoir 480 and a seal (eg, self-sealing membrane) in sample reservoir 48

isolates first sample reservoir 480 from flow path 435a. Filling of the other sample reservoirs i s done similarly with the flow controller 440 positioned in the third, fourth and fifth configurati ons, respectively.

[0077]

[1130] It should be noted that the order and/or sequencing of filling is not necessary (ie, sam ple reservoir 480 does not necessarily need to be filled before sample reservoir 490, etc.). In other words, first sample reservoir 480 and second sample reservoir 490 (and any additional sample reservoirs) can be filled in any order. For example, the user can start filling the first sa mple reservoir 480, and then after the first sample reservoir 480 is partially filled, the user ca n fill the second sample reservoir 490. . Further, adjustment of the volume of bodily fluid colle cted in sample reservoirs 480 and/or 490 can be enabled by repeated filling of sample reservo irs 480 and/or 490 . However, in other embodiments, the order of filling is such that the secon d sample reservoir cannot be accessed until it is verified that a specified amount of bodily flui d has been placed in the first reservoir. It can be operated mechanically. As described above, t he dial 445 can substantially prevent fluid flow between the patient and the collection device 400 as a whole, substantially sealing the sample within the collection device 400 from the ext ernal environment. A sixth position for a sixth configuration of the flow controller 440 can be provided.

[0078]

[1131] The collection device 400 includes a set of four sample reservoirs (eg, a first sample re servoir 480, a second sample reservoir 480', a third reservoir 490 and a fourth reservoir 490') and/or to which other Although shown and described above as being coupled in a manner, in o ther embodiments the collection device may include and/or be coupled to any suitable numbe r of sample reservoirs. For example, Figures 23-25 show a collection device 500 according to an embodiment. As shown, some aspects of the collection device 500 can be substantially sim ilar to corresponding aspects of the collection device 500 described above with reference to FI GS. 16-22. Accordingly, similar aspects are not described in further detail herein.

[1132

] The collection device 500 includes a flow diverter mechanism 520 , a flow controller 540 , a f irst sample reservoir 580 and a second sample reservoir 590 . Sample reservoirs 580 and 590 can be substantially similar to the sample reservoirs described in detail above. In some embo diments, sample reservoirs 580 and 590 can have substantially the same shape and size and contain substantially the same medium. In other embodiments, sample reservoirs 580 and 59 0 can have substantially the same shape and size and can contain one of an aerobe medium o r an anaerobe medium. In still other embodiments, first sample reservoir 580 can have a first size that is substantially larger than the size of second sample reservoir 590 .

[0080]

[1133] As shown in FIGS. Housing 501 of flow diverter mechanism 520 is physically and fluidl y coupled to distribution member 529 to provide a set of fluid flow paths for collecting bodily

luids from a patient and/or

stipulates. As described above with respect to housing 401, housing 501 can define a recess a nd first, second, and third outlet openings 503a, 503b, and 503c. The recess is configured to r eceive a seal member 541 included in flow controller 540, as described in detail above. First o utlet opening 503a, second outlet opening 503b and third outlet opening 503c correspond to f irst outlet opening 403a, second outlet opening 403b and third outlet opening 403c defined by housing 401, respectively. They can be substantially similar in form and function. Similarly, di stribution member 529 includes pre-sample reservoir 470 , first flow channel 435 a and secon d flow channel 435 a that are substantially similar to pre-sample reservoir 470 , first flow cha nnel 435 a and second flow channel 435 b included in flow diverter member 429 . Two flow pa ths 435b are defined. Thus, pre-sample reservoir 570 is in fluid communication with first outle t opening 503a, first channel 535a is in fluid communication with second outlet opening 503b, and as described above with respect to flow diverter mechanism 420; The second flow path 5 35b is in fluid communication with the third outlet opening 503c. As shown in FIG. 25, distribu tion member 529 is in fluid communication with first outlet port 531, which is in fluid commun ication with first channel 535a and first piercing member 555a, and second channel 535b, wit h second piercing member 555b. A second outlet port 532 is defined. As described above, pier cing members 555a and 555b can be used to pierce the vacuum seals of sample reservoirs 58 0 and 590, thereby initiating bodily fluid flow, as described in further detail herein. can do.

[0081]

[1134] The flow controller 540 includes a dial 545 and a seal member 541 . The seal member 541 is positioned within the recess of the housing 501 as described above. Thus, when flow co ntroller 540 is coupled to housing 501, seal member 541 forms a substantially fluid-tight seal with the surface of dial 545 and the surface of housing 501 that defines the recess. As shown in FIGS. 24 and 25, seal member 541 is substantially configured with first outlet opening 503 a, second outlet opening 503b and third outlet opening 503c, respectively, as described in det ail above with respect to seal member 441. defines a first opening 544a, a second opening 54 4b and a third opening 544c, which are aligned with each other.

[0082]

[1135] The dial 545 of the flow controller 540 may be substantially similar in form and functio n to the dial 445 while having a suitable size to be coupled to the housing 501 . Accordingly, d ial 545 may be rotatably coupled to housing 501 and movable relative to housing 501 betwee n first, second and third positions. Dial 545 includes an entry port 521 defining lumen 502 tha t defines a fluid flow path for withdrawing and/or transporting bodily fluid from a patient to col lection device 500. Medical device (not shown) can be fluidly coupled to In this way, inlet port 521 can be configured to selectively locate pre-sample reservoir 570 , first sample reservoir 5 80 and second sample reservoir 590 . More specifically, when the dial 545 is in the first positio n, the flow controller 540 is arranged in the first configuration and the inlet port 521 communi cates with the first opening 544a of the seal member 541 and the first outlet opening 503a c

the housing 501. is substantially aligned with Thus, as described in detail above with respect t o collection device 400, first opening 544a of seal member 541 establishes fluid communicatio n between inlet port 521 and first outlet opening 503a, and thus the inlet port. 521 is placed i n fluid communication with pre-sample reservoir 570 . Similarly, when the dial 545 is turned (or driven) to the second position, the flow controller 540 is placed in the second configuratio n and the second outlet opening 544b is connected to the inlet port 521 and the second outlet opening 503b. , thus establishing fluid communication with the first flow path 535a, and when the dial 545 is turned to the third position, the flow controller 540 is disposed in the third conf iguration, and the third outlet opening 544c communicates with the inlet port. Fluid communic ation is established between 521 and the third outlet opening 503c and thus the second flow path 535a. Thus, the collection device 500 is applied to the pre-sample 570 as described in de tail above with respect to the collection device 400 .

It can be used to transfer second and third volumes of bodily fluid to reservoir 580 and secon d sample reservoir 590, respectively.

[1136

] Figures 26-33 show a collection device 600 according to an embodiment. Collection device 6 00 includes flow diverter mechanism 620, flow controller 640 and sample reservoirs 680, 68 0', 690 and 690'. As further described herein, the collection device 600 can be moved betwee n first, second, third, fourth and fifth configurations to, for example, collect microorganisms a nd/or microorganisms present on the skin. A fluid stream can be delivered that is substantiall y free of extracorporeal microorganisms, such as or other undesirable external contaminants. Collection device 600 may be of any suitable shape, size or configuration. For example, aspect s and/or portions of collection device 600 may be similar in form and/or function to correspon ding aspects and/or portions of any of collection devices 100, 200, 300, 400 and/or 500 descr ibed above. . Accordingly, such similar aspects and/or parts will not be described in further de tail herein. By way of example, in some embodiments sample reservoirs 680, 680′, 690 and 6 90′ of collection device 600 are similar to sample reservoirs 480, 480′, 490 and 490′ included in collection device 400 of FIGS. may be substantially similar and/or the same in form and/or function as each.

[0084]

[1137] The flow diverting mechanism 620 includes a distribution member 629 and a set of co upling members 637a, 637b, 637c and 637d (see, eg, FIG. 27). Distribution member 629 is in fluid communication with coupling members 637a, 637b, 637c and 637d and is configured to provide and/or define a set of fluid flow paths for collecting bodily fluid from a patient. As sho wn in FIGS. 27 and 28, distribution member 629 includes a first outlet port 630 in fluid comm unication with pre-sample reservoir 670, a second outlet port 631 in fluid communication with first coupling member 637a; A third outlet port 632 in fluid communication with the second co upling portion 637b, a fourth outlet port 633 in fluid communication with the third coupling po rtion 637c, and a fifth outlet in fluid communication with the fourth coupling portion 637d. d

ines and/or forms a port 634;

[0085]

[1138] As shown in FIG. Pre-sample reservoir 670 is configured to contain bodily fluids such a s, for example, blood, plasma, urine, and the like. For example, the pre-sample reservoir 670 can receive and contain a first amount or volume of bodily fluid from a patient, where the first amount of bodily fluid can be a predetermined amount or an unquantified amount. Additionall y, the arrangement of flow diverter mechanism 620 and flow controller 640 allows pre-sample reservoir 670 to follow coupling portions 637a, 637b, 637c and 637d and/or bodily fluids with drawn from the patient, as described in further detail herein. It may be maintained fluidly isol ated from the volume. Thus, outlet ports 631, 632, 633 and 634 direct fluid flow paths betwe en flow controller 640 and coupling members 637a, 637b, 637c and 637d, respectively, as des cribed in further detail herein. may be attached and/or otherwise defined. In some embodime nts, the arrangement of first exit port 630 and pre-sample reservoir 670 can be substantially similar in form and function to pre-sample reservoirs 470 and/or 570 . Accordingly, pre-sampl e reservoir 670 will not be described in further detail herein.

[0086]

[1139] As shown in FIG. 29, the first coupling member 637a defines a channel 638a that is flu idly coupled to the piercing member 655a. Coupling member 637a can be physically and fluidl y coupled to distribution member 629, as described above. For example, channel 638a can re ceive a portion of distribution member second outlet port 631 and coupling member 637a can be physically and fluidically coupled thereto. In some embodiments, the surface of the second outlet port 631 forms a substantially fluid-tight seal (e.g., fluid-tight seal) with the inner surfa ce of the coupling portion 637a that defines the flow path 638a.

(e.g., a friction fit) that can form a substantially hermetic seal. The piercing member 655a of t he coupling portion 637a can be substantially similar in form and function to the piercing me mber 455a included in the collection device 400 of FIGS. 16-22. Accordingly, piercing member 655a will not be further described herein. The second coupling member 637b, the third coupli ng member 637c and the fourth coupling member 637d are similarly arranged. Accordingly, th e second coupling member 637b, the third coupling member 637c and the fourth coupling me mber 637d each include piercing members 655b, 655c and 655d respectively and define chan nels 638b, 638c and 638d respectively. As described in further detail herein, first coupling me mber 637a, second coupling member 637b, third coupling member 637c and fourth coupling member 637d are used to connect flow diverting mechanism 620 to first sample reservoir 68 0, It can be selectively placed in fluid communication with each of the second sample reservoi r 680', the third sample reservoir 690 and the fourth sample reservoir 690'.

[0087]

[1140] The flow controller 640 includes a dial 645 and a seal member 641, as shown in FIGS. A dial 645 of flow controller 640 is rotatably disposed within distribution member 629 (see FI GS. 32 and 33) and is movable between first, second, third and fourth positions. . Dial 645 i

ludes an inlet port 621, a first outlet port 647 and a second outlet port 648, each in fluid com munication with interior space 646 (see, eg, FIG. 30). Interior space 646 is configured to rece ive a portion of seal member 641, as described in further detail herein. Inlet port 621 can be f luidly coupled to a medical device (not shown) that defines a fluid flow path for drawing bodily fluid from a patient and/or transporting it to collection device 600 . For example, inlet port 62 1 may be fluidly coupled to a needle or other lumen-defining device (e.g., flexible sterile tubin g) directly or indirectly via an adapter 604 (see, e.g., FIGS. 26 and 27). can do. First outlet po rt 647 is in fluid communication with pre-sample reservoir 670 . For example, first outlet port 647 can be rotatably disposed within first outlet port 630 of distribution member 629 . When dial 645 is in its first, second, third and fourth positions respectively, second outlet port 648 is connected to second outlet port 631, third outlet port 632, fourth outlet port 633 and It can b e selectively placed in fluid communication with the fifth outlet port 634 . Thus, the interior sp ace 646 of the dial 645 is divided into a pre-sample reservoir 670, a first sample reservoir 68 0, a second sample reservoir 680', a third sample reservoir 690 and a fourth sample reservoir, as described in further detail herein. It can be selectively placed in fluid communication with t he sample reservoir 690'.

[0088]

[1141] At least a portion of the sealing member 641 of the flow controller 640 is rotatably dis posed within an interior space 646 of the dial 645 and is movable between a first position and a second position. Further, seal member 641 can be sized and shaped such that an outer surf ace of seal member 641 forms a substantially fluid-tight seal with an inner surface of dial 645 that defines at least a portion of interior space 646 . As shown in FIG. 31, the sealing member 641 defines a first flow path 642 and a second flow path 644. As shown in FIG. When seal me mber 641 is in its first position within interior space 646 , passage 642 fluidly isolates inlet po rt 621 from second outlet port 648 while allowing inlet port 621 and first outlet port 647 to co mmunicate with each other. establish fluid communication therebetween. Similarly, when seal member 641 is in its second position within interior space 646 , second flow path 644 fluidly is olates inlet port 621 from first outlet port 647 while allowing inlet port 621 and second outlet port 647 to flow through inlet port 621 and second outlet port 647 . Establish fluid communica tion with outlet port 648 . Collection device 600 operates similarly when dial 645 is rotated wit hin dispensing member 629 to second, third and fourth positions. Accordingly, when inlet port 621 is placed in fluid communication with a patient (e.g., via a medical device coupled to inlet port 621 and/or adapter 604), first outlet port 630 of distribution member 629; 2 outlet port 631 , third outlet port 632 , fourth outlet port 633 and fifth outlet port 634 are in fluid commu nication with inlet port 621 .

to allow bodily fluids to flow into pre-sample reservoir 670, first sample reservoir 680, second sample reservoir 680', third sample reservoir 690 and fourth sample reservoir 690', respectiv ely. can be

[1142

] In operation, the collection device 600 can be used to collect bodily fluids (eg, blood, plasm a, urine, etc.) from a patient with reduced contamination. For example, entry port 621 of colle ction device 600 can be fluidly coupled to a needle or other lumen defining device (eg, flexible sterile tubing). Following venipuncture (or other method of accessing bodily fluids), the seal m ember can be actuated (or rotated) to its first position, as shown in FIG. Alternatively, the sea l member 641 can be preset in the first position and the collection device 600 can be otherwis e sealed to maintain the sterility of the collection device 600 . When seal member 641 is in its first position, flow controller 640 causes inlet port 621 and a first outlet port of distribution me mber 629 to flow through inlet port 621 from coupling members 637a, 637b, 637c and 637d while fluidly isolating inlet port 621 from coupling members 637a, 637b, 637c and 637d. 630 t o establish fluid communication. Thus, in a manner similar to that described above with respe ct to collection device 400, as indicated by arrow II in FIG. It can be transferred into pre-sam ple reservoir 670 via first exit port 630 of member 629 .

[0090]

[1143] Following collection of the bodily fluid pre-sample within pre-sample reservoir 670, sea l member 641 may be actuated (rotated) relative to dial 645 from its first position to its secon d position. Similarly, dial 645 can be actuated (or rotated) until it reaches the second position relative to distribution member 629, as shown in FIG. When seal member 641 and dial 645 ar e in their second positions, flow controller 640 is disposed in a second configuration and secon d flow path 644 of seal member 641 fluidly isolates pre-sample reservoir 670 from inlet port 6 21 . while establishing fluid communication between inlet port 621 and channel 638a of first c oupling member 637a. With flow controller 640 in its second configuration, sample reservoir 6 80 is actuated by a user from its first configuration to its second configuration (e.g., by pushin g piercing member 655a) to force a portion of the patient's body (e.g., , vein) and the first sa mple reservoir 680 . By moving the sample reservoir 680 to the second configuration, as desc ribed in detail above, the piercing member 655 a is positioned inside the sample reservoir 680 piercing the vacuum seal of the sample reservoir 680 . In this second configuration, that porti on of the patient's body (eg, a vein) is exposed to a vacuum suction force from the sample re servoir 680 due to the negative pressure (vacuum) within the sample reservoir 680 . Thus, as shown by arrows JJ in FIG. 33, body fluid is directed from that portion of the patient's body th rough inlet port 621, second channel 644, second outlet port 631 and channel 638a and throu gh the piercing member of first coupling member 637a. It can be forced through 655a into th e first sample reservoir 680. FIG.

[0091]

[1144] Once a desired volume of bodily fluid (eg, a second amount) has been collected in sam ple reservoir 680, the user may actuate (rotate) flow controller 640 to a third position and/or can be moved back to its first configuration to isolate the first sample reservoir 680 from the s econd flow path 644 . When the sample reservoir 680 returns to the first configuration, the pi ercing member 655a is removed from the sample reservoir 680 and the seal (eg, self-sealing

membrane) of the sample reservoir 680 fluidly removes the first sample reservoir 680 from th e flow path 635a. isolate to Filling of the other sample reservoirs is similarly performed with t he flow controller 640 positioned in the third, fourth and fifth configurations, respectively.

[1145

] Figures 34-40 show a collection device 700 according to an embodiment. The collection devi ce 700 includes a flow diverter 720, a flow controller 740 and sample reservoirs 780 and 780. 90 (although there are holders for four sample reservoirs, only two sample reservoirs are incl uded in the figure for clarity, and as part of the collection device 700 additional sample reserv oirs (e.g. 5th, 6th, etc.). As further described herein, the collection device 700 can be moved between first, second, third, fourth and fifth configurations to, for example, collect microorgan isms and/or microorganisms present on the skin. A bodily fluid stream can be delivered that is substantially free of extracorporeal microorganisms, such as other undesirable external conta minants. Collection device 700 may be of any suitable shape, size or configuration. For examp le, aspects and/or portions of collection device 700 may be substantially similar in form and/o r function to corresponding aspects and/or portions of any of collection devices 100, 200, 300, 400, 500 and/or 600 described above. can be similar to Accordingly, such similar aspects and/ or parts will not be described in further detail herein. By way of example, in some embodimen ts, sample reservoirs 780 and 790 of collection device 700 are substantially similar and/or sim ilar in form and function to sample reservoirs 480 and 490, respectively, included in collection device 400 of FIGS. or may be the same.

[0093]

[1146] The flow diverter mechanism 720 includes a housing 701, a distribution member 729 a nd a base plate 771. As shown in FIG. As described above with respect to collection device 40 0, housing 701 has a first outlet opening 703a, a second outlet opening 703b, a second outlet opening 703a, a second outlet opening 703b, and a second outlet opening 703a, each configu red to be in fluid communication with a different portion of distribution member 729. It define s three exit openings 703c, a fourth exit opening 703d and a fifth exit opening 703e. More spe cifically, distribution member 729 includes at least a portion of pre-sample reservoir 770 in flu id communication with first outlet opening 703a and a first fluid chamber 735a in fluid commu nication with second outlet opening 703b. , a second fluid chamber 735b in fluid communicati on with the third outlet opening 703b, a third fluid chamber 735c in fluid communication with the fourth outlet opening 703d, and a second fluid chamber 735c in fluid communication with the fifth outlet opening 703e. defines and/or forms four fluid chambers 735d. Additionally, ho using 701 defines a recess 766 configured to movably receive at least a portion of flow control ler 740, as described further herein.

[0094]

[1147] As shown in FIG. Pre-sample reservoir 770 is configured to contain bodily fluids such a s, for example, blood, plasma, urine, and the like. The first outlet opening 703a of the housin g 701 is substantially aligned with the open portion of the pre-sample reservoir 770 so that t

e pre-sample reservoir 770 can receive the flow of bodily fluid from the patient, as described i n detail above. be able to. More specifically, distribution member 729 includes a set of walls 7 36 that can, for example, divide the interior space of distribution member 729 into portions a nd/or spaces that are fluidly isolated from one another. For example, as shown in FIG. 36, a s et of walls 736 divides the interior space of distribution member 729 into pre-sample reservoir 770, first fluid chamber 735a, second fluid chamber 735b, third fluid chamber 735c and fourth fluid chamber 735c. It can be divided into chambers 735d. In some embodiments, wall 736 ca n equally define and/or form pre-sample reservoir 770 and fluid chambers 735a-735d. In othe r embodiments, pre-sample reservoir 770 can define a space that is different than the space d efined by fluid chambers 735a-735d.

[0095]

[1148] The distribution member 729 is in fluid communication with the first piercing member 755a, the second piercing member 755b, respectively, with the first fluid chamber 735a, the s econd fluid chamber 735b, the third fluid chamber 735c and the fourth fluid chamber 735d. , a third piercing member 755c and a fourth piercing member 755d. Thus, piercing members 7 55a-355d can be used to pierce sample reservoirs 780 and 790 (and corresponding sample re servoirs not shown in FIGS. 34-40), as described in further detail herein. , thereby initiating b odily fluid flow.

[1149

] The flow controller 740 of the collection device 700 includes a dial 745 and a seal member 7 41 . Seal member 741 is positioned within recess 766 of housing 701 (see, eg, FIGS. 38 and 40). More particularly, coupling flow controller 740 to housing 701 such that seal member 741 is positioned between and in contact with the surface of housing 701 defining recess 766 and the surface of dial 745 . can be done. Seal member 741 may be configured to form a substant ially fluid-tight seal with the surface of dial 745 and the surface of housing 701 defining recess 766, as described in detail above. As shown in FIG. 35, the sealing member 741 defines a first opening 744a, a second opening 744b, a third opening 744c, a fourth opening 744d and a fift h opening 744e. The arrangement of the sealing member 741 is such that when the sealing m ember 741 is arranged in the recess 766, the first opening 744a, the second opening 744b, th e third opening 744c, the fourth opening 744d, and the fifth opening 744e are formed. , the fi rst outlet opening 703a, the second outlet opening 703b, the third outlet opening 703c, the fo urth outlet opening 703d and the fifth outlet opening 703e of the housing 701, respectively. i s.

[0097]

[1150] The dial 745 of the flow controller 740 is rotatably coupled to the housing 701 and is movable relative to the housing 701 between a first position, a second position, a third positio n, a fourth position, and a fifth position. be. Dial 745 includes an entry port 721 that connects entry port 721 to a medical device (either directly or indirectly via adapter 704) that defines a fluid flow path for withdrawing bodily fluid from a patient and/or transporting it to collection

evice 700.) can be fluidly coupled. Inlet port 721 thus connects to pre-sample reservoir 770, first sample reservoir 780, second sample reservoir 780', third sample reservoir 790 and fourt h sample reservoir 790, as described in further detail herein. ' can be configured to be selectiv ely placed in fluid communication with a patient. When dial 745 is in the first position, flow co ntroller 740 is disposed in a first configuration, aligning inlet port 721 substantially with first o pening 744 a of seal member 741 and first outlet opening 703 a of housing 701 . can be comb ined. Thus, the first opening 744a of the seal member 741 fluidly isolates the inlet port 721 fr om the outlet openings 703b, 703c, 703d and 703e, thereby fluidly isolating the inlet port 721 from the fluid chambers 735a-335d. Fluid communication is established between the inlet port 721 and the first outlet opening 703a while isolating to the first outlet port 703a. When the di al 745 is turned (or driven) to the second position, the flow controller 740 is placed in the sec ond configuration and the second outlet opening 744b connects the inlet port 721 to the pre-s ample reservoir 770 and the fluid chambers 735b-735b. Fluid communication is established b etween inlet port 721 and second outlet opening 703b while being fluidly isolated from 735d. Collection device 700 operates similarly when dial 745 is turned to the third, fourth and fifth p ositions. Accordingly, inlet port 721 is in fluid communication with the patient (eg, via a medic al device coupled to inlet port 721).

[1151

] In some embodiments, housing 701 selectively limits movement of dial 745 from its first pos ition to its second, third, fourth and fifth positions. be able to. In some other embodiments, th e housing 701 can be configured to prevent movement of the dial moved to the fifth position. In other words, housing 701 can include a locking mechanism that prevents dial 745 from mo ving back from the fifth position to the first position. This feature allows flow chambers 735a-735d and/or

This reduces the risk that bodily fluids collected in pull reservoirs 780 and 790 are contaminat ed from bodily fluids contained in pre-sample reservoir 770 (which has a high risk of containin g surface-bound microorganisms and/or other undesirable external contaminants). can be red uced. This locking mechanism can also protect medical personnel from exposure to blood-bor ne pathogens in patient samples, which may include HIV, hepatitis C, and the like. Dial 745 an d/or housing 701 may also have mechanical detents that provide visual or tactile feedback to ensure correct alignment of dial 745 with respect to exit port 703a and exit openings 703a-70 3d in housing 701. and/or other indicators may also be included.

[0099]

[1152] Similar to the embodiment of the collection device 400 shown in FIGS. The pre-sample reservoir 770 can contain bodily fluids such as, for example, blood, plasma, urine, and the lik e. Pre-sample reservoir 770 is configured to be fluidly coupled to first outlet port 703a of colle ction device 700 (located within housing 701). During operation of the collection device 700, when the flow controller 740 is in the first position, body fluid flows from a portion of the patie nt's body (eg, a vein) through the inlet port 721, into the pre-sample reservoir 770, into the

eal member 741. is drawn into the opening for the pre-sample reservoir 744a and the first exi t port 703a located at . Pre-sample reservoir 770 is configured to contain a first volume of flui d to be drawn from a patient, where the first volume of bodily fluid can be a predetermined vo lume or an unquantified volume. Thereby the first volume of bodily fluid is fluidly isolated fro m a second and/or third and/or fourth and/or fifth volume of bodily fluid subsequently withdra wn from the patient.

[0100]

[1153] In operation, the collection device 700 can be used to collect bodily fluids (eg, blood, p lasma, urine, etc.) from a patient with reduced contamination. For example, entry port 721 of collection device 700 can be fluidly coupled to a needle or other lumen defining device (eg, fle xible sterile tubing). Following venipuncture, dial 745 is turned until it reaches the first positio n, as shown in FIGS. Alternatively, the dial 745 can be preset in the first position and the colle ction device 700 can be otherwise sealed to maintain the sterility of the collection device 700, as described above. With the dial 745 in the first position, the flow controller 740 is placed in a first configuration and the first outlet opening 744a of the seal member 741 fluidly connects the inlet port 721 from the four sample flow paths 735a-735d. While in isolation, fluid commu nication is established between inlet port 721 (contained within housing 701) and first outlet port 741 . In this first configuration, bodily fluids are directed from that portion of the patien t's body, as indicated by arrows KK in FIG. through and into the pre-sample reservoir 770 defi ned by the distribution member 770 . Accordingly, as described in detail above, a first volume (predetermined or unquantified) of bodily fluid can be received in pre-sample reservoir 770 im mediately after venipuncture and segregated from subsequent samples.

[0101]

[1154] Following the collection of the bodily fluid pre-sample within the pre-sample reservoir 770, the dial 745 can be actuated (or rotated) until it reaches the second position, as shown i n FIGS. When dial 745 is in the second position, flow controller 740 is placed in a second confi guration, and second outlet opening 744 a of seal member 741 fluidly isolates pre-sample res ervoir 770 from inlet port 721 while allowing inlet port 721 to flow. Fluid communication is est ablished between port 721 and first fluid chamber 735a. Once the first fluid chamber 735a is f illed with bodily fluid, the flow controller 740 can be moved to the third position to isolate and seal the first flow path 735a from the external environment. Additionally, the sample reservoir 780 is actuated from the first configuration to the second configuration to transfer bodily fluid from the first fluid chamber 735a to the sample reservoir 780.

can be sent. For example, sample reservoir 780 may be user or automatically actuated from a first configuration to a second configuration (pressing piercing member 755a) to allow a portio n of the patient's body (e.g., a vein) to move between sample reservoir 780 and sample reser voir 780. can establish fluid communication with the As described above, moving the sample r eservoir 780 to the second configuration causes the piercing member 755a to pierce the vacu um seal of the sample reservoir 780 and be positioned inside the sample reservoir 780 . In a

second configuration, that portion of the patient's body (eg, a vein) is subjected to vacuum su ction from the sample reservoir 780 due to the negative pressure (vacuum) existing within th e sample reservoir 780 in some embodiments. Thus, as indicated by arrow LL in FIG. 40, bodil y fluids flow from that portion of the patient's body through inlet port 721, second outlet open ing 744b in seal member 741, second outlet opening 703b in housing 701, second It flows int o the first sample reservoir 780 through the fluid chamber 735b.

[1155

] Once a desired amount of bodily fluid (eg, a second amount) has been collected in sample r eservoir 780, the user may actuate (rotate) flow controller 740 to a third position and/or The sample reservoir 780 can be moved back to its first configuration to isolate the first sample re servoir 780 from the inlet port 721 . When the sample reservoir 780 returns to the first config uration, the piercing member 755a is removed from the sample reservoir 780 and the seal (e g, self-sealing membrane) of the sample reservoir 780 allows the first sample reservoir 780 to enter the second fluid chamber 735b and the exterior. Fluid isolation from the environment. Fi lling of the other sample reservoirs is done in the same manner with the flow controller 740 in the third, fourth and fifth configurations respectively.

[0103]

[1156] In some embodiments, the collection device 700 can be configured such that there is no set of walls 736 separating the different fluid chambers 735a-735d within the distribution member 729 (detailed in FIG. 16). (see cross section). In such embodiments, the distribution member 729 is divided between the pre-sample reservoir 770 and the associated fluid chamb er 735 (ie, the fluid chamber is not separated into four separate portions by wall 736). In suc h embodiments, the user can fill all four sample reservoirs at once by actuating (rotating) dial 745 to either the second, third, fourth or fifth position. can be done.

[0104]

[1157] Any of the embodiments described herein can be used, for example, to meter (e.g., qu antify) the flow of bodily fluid into a pre-sample reservoir and/or a sample reservoir. Can be u sed with metering devices. In some cases, laboratory standard practice limits the exact inocul ation volume of bodily fluids (e.g., blood samples) due to the fact that fill volumes are judged visually by clinicians and/or phlebotomists and are therefore subject to human error. Consiste nt compliance is not ensured. The volume indicator on the blood collection bottle is difficult to read when held, and the fact that the collection bottle is not held upright during the withdraw al procedure contributes to the inaccurate volume of the bodily fluid sample received from the patient. could be a factor. Insufficient sample volume (eg, less than the manufacturer's recom mendation) can reduce the sensitivity of the culture test and lead to false-negative results. In addition, briefing materials and instructions for certain types of test supplies and equipment (e.g., blood culture bottles designed for use with automated microbial detection systems prod uced by manufacturers such as Becton Dickinson of Franklin Lakes, NJ). Filling volumes in exc ess of the manufacturer's recommendations, as indicated in the literature, may result in fals

positives. Thus, flow metering and volume display capabilities allow laboratory technicians an d/or medical personnel (e.g., phlebotomists) to transfer sample reservoirs to incubators or oth er laboratories, depending on how the sample needs to be processed. The volume of bodily flu id collected in each individual sample reservoir can be verified prior to placement within the te sting device. The laboratory technician and/or phlebotomist may also provide accurate volume tric information (e.g., in medical records, databases, spreadsheets, etc.) for clinician evaluatio n when results are received.

), which helps reduce the likelihood of misinterpretation of false negative and/or false positive results.

[1158

] By way of example, FIGS. 41-45 illustrate a collection device 800 that can include one or mo re metering devices. Collection device 800 includes flow diverter mechanism 820 , flow contro ller 840 , display 875 and sample reservoir 880 . As further described herein, the collection de vice 800 can be moved between first, second and third configurations to remove, for example, microorganisms present on the skin and/or other undesirable external contaminants, and the l ike. , can deliver a body fluid stream that is substantially free of extracorporeal microorganis ms. Collection device 800 may be of any suitable shape, size or configuration. For example, as pects and/or portions of collection device 600 may be similar in form and/or function to corres ponding aspects and/or portions of any of collection devices 100, 200, 300, 400, 500, 600 an d/or 700 described above. can be substantially similar. Accordingly, such similar aspects and/o r parts will not be described in further detail herein. By way of example, in some embodiment s, sample reservoir 880 of collection device 800 is substantially similar and/or identical in for m and function to sample reservoir 480 included in collection device 400 of FIGS. could be.

[0106]

[1159] As shown in FIGS. 41-43, the flow diverter mechanism 820 includes an actuator portio n 822 (eg, a first portion), an intermediate portion 823 (eg, a second portion) and a coupling portion 824 (eg, a third portion). including. Actuator portion 822 of flow diverter mechanism 8 20 is substantially cylindrical including a set of actuator walls that define interior space 806 . More specifically, actuator portion 822 has a first end that is substantially closed and an oppos ite end that is substantially open to allow access to interior space 806 . a side second end. As such, actuator portion 822 can movably receive at least a portion of flow controller 840, as de scribed in further detail herein. Actuator portion 822 further includes inlet port 821 and outlet port 831 . Inlet port 821 is fluidly connected (either directly or indirectly via adapter 804) to a medical device that defines a fluid flow path for withdrawing bodily fluid from a patient and/or transporting it to collection device 800, as described in detail above. can be linked together.

[0107]

[1160] The outlet port 831 of the actuator portion 822 may be selectively positioned to place a portion of the interior space 806 of the actuator portion 822 in fluid communication with the interior space 807 defined by the intermediate portion 823. As shown in FIG. 43, intermedia

portion 823 is positioned between actuator portion 822 and coupling portion 824 . Although n ot shown in FIGS. 41-45, intermediate portion 823 can include a metering device that can be configured to meter a volume of bodily fluid transferred to sample reservoir 880, for example. For example, in some embodiments, a flow metering device can be fluidly coupled to outlet po rt 831 to meter the flow of bodily fluid therethrough. As shown in FIGS. 41 and 42, the interm ediate portion 823 includes a display 875 that provides a user with visual indicators and/or inf ormation related to the volume of bodily fluid that has flowed through the outlet port 831, for example. can provide. In other embodiments, the flow metering device may be placed at any other suitable location within or along the flow diverter 820 .

[1161

] The coupling portion 824 can be physically and fluidly coupled to the intermediate portion 82 3 . For example, in some embodiments, coupling portion 824 is partially disposed within interi or space 807 of intermediate portion 823 and attached thereto at least temporarily via a fricti on fit, press fit, snap fit, threaded connection, adhesive, or the like. can be linked together. Co upling portion 824 is configured to receive a portion of sample reservoir 880, as described in detail above, so that it can puncture the vacuum seal of sample reservoir 880, thereby initiati ng bodily fluid flow. includes a piercing member 855 that can be used to

[1162

] The flow controller 840 of the collection device 800 is disposed at least partially within the in terior space 806 defined by the actuator portion 822 and is movable between first, second an d third configurations. is. As shown in FIGS. 42 and 43, the flow controller 840 includes a mov able member 850 having a first sealing member 861, a second sealing member 862 and a thir d sealing member 863, and a biasing member 859 (eg, a spring or the like). including. Seal m embers 861 , 862 and 863 are in contact with the inner surface of actuator portion 822 that d efines interior space 806 . Accordingly, as described in further detail herein, each of the seal members 861, 862 and 863 has an inner surface that can, for example, divide the interior spa ce 806 of the actuator portion 822 into fluidly isolated portions; A fluid-tight seal can be form ed.

[0110]

[1163] The movable member 850 is movable within the interior space 806 between a first pos ition, a second position and a third position. The arrangement of movable member 850 is such that seal members 861, 862 and 863 selectively move within interior space 806 as movable m ember 850 moves between its first, second and third positions. It can be. More specifically, th e first sealing member 861 can move simultaneously with the movable member 850 as the m ovable member 850 moves between its first, second and third positions. A second seal memb er 862 and a third seal member 863 can be fixedly coupled to each other (eg, positioned at a fixed distance from each other) and slidably disposed about a portion of the movable member 850, which This causes movable member 850 to move from its first position (see, eg, FIG. 4 3) to its first position while second sealing member 862 and third sealing member 863 rema

in a substantially fixed position relative to actuator portion 822 . It may be possible to move t o two positions (see, eg, FIG. 44). For example, as movable member 850 moves between its f irst and second positions, second sealing member 862 and third sealing member 863 can rem ain in a substantially fixed position, thereby providing an inlet port. Port 821 is located on a fir st side of second sealing member 862 and exit port 831 is located on a second side of second sealing member 862 opposite the first side. Thus, when movable member 850 is in its first po sition (FIG. 43) and its second position (FIG. 44), inlet port 821 is in contact with first sealing member 861, as described in further detail herein. is in fluid communication with a portion of the interior space 806 defined between the second seal member 862 and the exit port is in th e interior space 806 defined between the second seal member 862 and the third seal member 863. in fluid communication with the part.

[0111]

[1164] The arrangement of the flow controller 840 is such that the first sealing member 861 moves relative to the second sealing member 862 and the third sealing member 863 when th e movable member 850 moves from its first position to its second position. , can be Movemen t of first seal member 861 relative to second seal member 862 can enlarge the space defined therebetween, thereby forming and/or otherwise defining pre-sample reservoir 870 . can do. I n addition, seal members 861 and 862 form a substantially fluid-tight seal with the inner surf ace of actuator portion 822 such that pre-sample reservoir 870 defined between first seal me mber 861 and second seal member 862 is , are fluidly isolated from the rest of the interior sp ace 806 . Thus, inlet port 821 can be in fluid communication with pre-sample reservoir 870 w hen moveable member 850 moves from its first position to its second position. As movable m ember 850 moves from its second position (see, eg, FIG. 44) to its third position (see, eg, FI G. 45), a portion of movable member 850 contacts third sealing member 863. , the first sealin g member 861 , the second sealing member 862 and the third sealing member 863 can be m oved substantially simultaneously within the interior space 806 . Accordingly, both the inlet po rt 821 and the outlet port 831 provide fluid communication to the portion of the interior space 806 defined between the second sealing member 862 and the third sealing member 863, as d escribed in further detail herein. A second sealing member 862 can be moved relative to the i nlet port 821 in communication.

[0112]

[1165] In operation, the collection device 800 can be used to collect bodily fluids (eg, blood, p lasma, urine, etc.) from a patient with reduced contamination. For example, entry port 821 of collection device 800 can be fluidly coupled to a needle or other lumen defining device (eg, fle xible sterile tubing). With inlet port 821 coupled to the lumen defining device, flow controller 840 can be moved from its first configuration to its second configuration. Thus, a user can app ly a force to move movable member 850 from its first position to its second position, as indica ted by arrow MM in FIG. As described above, the first sealing member 861 moves simultaneou sly with the movable member 850, thereby enlarging the space defined between the first sea

ng member 861 and the second sealing member 862, thereby A sample reservoir 870 is form ed and/or defined. First sealing member 861 and second sealing member 862 form a substant ially fluid-tight seal with the inner surface of actuator portion 822 that defines interior space 8 06 such that first sealing member 861 and second sealing member 862 are in contact with ea ch other. A negative pressure is created in the pre-sampling reservoir 870 by the increase in v olume between . Accordingly, once fluid communication is established between a portion of th e patient's body (eg, a vein) and the pre-sample reservoir 870 (eg, via inlet port 821 in FIG. 4 4), indicated by arrows NN in FIG. As such, the negative pressure differential between pre-sa mple reservoir 870 and that portion of the patient's body draws fluid into pre-sample reservoir 870 through inlet port 821 . In this first configuration, flow controller 840 also fluidly isolates pre-sample reservoir 870 from outlet port 831 . Accordingly, a first volume (predetermined or unquantified) of bodily fluid can be received in pre-sample reservoir 870 (for example) immed iately after venipuncture and isolated from subsequent samples. In this manner, the collection device 800 can be used to collect surface microorganisms and/or other undesirable A first vol ume of bodily fluid most likely to contain an external contaminant contaminates a subsequent volume of bodily fluid sample collected and used for diagnosis or other testing that may be aff ected by the contaminant can be prevented. In some embodiments, the metering device can meter a volume of bodily fluid placed in pre-sample reservoir 870 and present a value associa ted with that volume on display 875 .

[0113]

[1166] Following collection of the body fluid pre-sample volume in pre-sample reservoir 870, moveable member 850 is moved from its second position to its third position, as indicated by arrow OO in FIG. It can be arranged in a third configuration. As described above, when movab le member 850 moves from its second position to its third position, a portion of movable mem ber 850 is placed in contact with third sealing member 863 . Accordingly, the movable membe r 850 moves the first sealing member 861 , the second sealing member 862 and the third seal ing member 863 substantially simultaneously within the interior space 806 . Accordingly, the s econd sealing member 862 is positioned such that both the inlet port 821 and the outlet port 831 are in fluid communication with the portion of the interior space 806 defined between the second sealing member 862 and the third sealing member 863 . It can be moved relative to p ort 821 . Furthermore, because the volume of body fluid is fluidly isolated within the pre-sam ple reservoir 870, movement of the second seal member 862 and the third seal member 863 i n the direction of the first seal member 861 is restricted (i.e., body fluid is a substantially inco mpressible fluid). Thus, the pre-sample volume of bodily fluid is sequestered within pre-sampl e reservoir 870 and the space defined between second sealing member 862 and third sealing member 863 is separated by inlet port 821 and outlet port 821 . 831 defines a fluid flow path. Further, flow controller 840 is positioned such that when in its third configuration, first sealing member 861 is in contact with biasing member 859 such that at least a portion of the force ex erted by the user on movable member 850 is The biasing member 859 is operable to deform

compress, bend and/or otherwise reconfigure. Accordingly, the biasing member 859 acts agai nst the first sealing member 861 to resist movement of the flow controller 840 from its secon d configuration to its third configuration, as described in further detail herein. can affect

[1167

] As described in detail above, piercing member 855 provides a vacuum seal for sample reser voir 880.

The sample reservoir 880 can be positioned relative to the collection device 800 such that the hole is pierced and placed inside the sample reservoir. A pressure differential between the sa mple reservoir 880 (eg, vacuum or negative pressure) and that part of the body draws body fl uid into the sample reservoir 880 . In other words, in the second configuration, flow controller 840 and flow diverter mechanism 820 direct body fluid from the patient through inlet port 82 1, second sealing member 862, and third sealing member 863, as indicated by arrow PP in FI G. through the portion of the interior space 806 defined therebetween, and the exit port 831 of the actuator portion 822, through the piercing member 855 of the intermediate portion 823 and the coupling portion 824, and into the sample reservoir 880; Establish a fluid flow path. A s discussed above, a metering device (not shown) can meter the volume of bodily fluid transfe rred, for example, through outlet port 831 and can present a value associated with the volum e of bodily fluid on display 875 .

[0115]

[1168] Once a desired volume of bodily fluid (eg, a second amount) has been collected in the sample reservoir 880, the user can remove and/or reduce the force applied to the movable m ember 850, thereby , a biasing member 859 can move the first sealing member 861 and the movable member 850 from their third position toward their second position. Further, due to th e substantially incompressible nature of the bodily fluid disposed within pre-sample reservoir 870, movement of first sealing member 861 transfers force through the volume of bodily flui d, thereby increasing second sealing member 862 and third sealing member 862. Seal memb ers 863 are moved from their third position toward their second position. In some embodimen ts, the biasing member 859 is operable to move the second seal member 862 relative to the a ctuator portion 822, for example, to a fourth position where the inlet port 821 can be substan tially blocked. The resulting force can be applied to the first sealing member 861 . Accordingl y, inlet port 821 can be fluidly isolated from interior space 806 of actuator portion 822 . Additi onally, the piercing member 855 can be removed from the sample reservoir 880 and a seal (e g, a self-sealing membrane) can fluidly isolate the bodily fluid sample from the space outside t he sample reservoir 880 . Subsequent filling of the sample reservoir is similarly accomplished by placing piercing member 855 into the sample reservoir and moving flow controller 840 to t he third configuration to allow bodily fluid to flow from the patient into the sample reservoir. c an be done.

[0116]

[1169] FIGS. 46-53 illustrate a collection device 900 according to an embodiment. Collection

device 900 includes flow diverter mechanism 920, flow controller 940 and sample reservoirs 9 80, 980', 990 and 990'. As further described herein, the collection device 900 can be moved b etween first, second, third, fourth and fifth configurations to, for example, collect microorgani sms and/or microorganisms present on the skin. or a body fluid stream that is substantially fr ee of extracorporeal microorganisms, such as other undesirable external contaminants. Collec tion device 900 may be of any suitable shape, size or configuration. For example, aspects an d/or portions of collection device 900 may be corresponding aspects and/or portions and confi gurations and/or of any of collection devices 100, 200, 300, 400, 500, 600, 700 and/or 800 d escribed above. They may be substantially similar in function. Accordingly, such similar aspect s and/or parts will not be described in further detail herein. By way of example, in some embo diments, sample reservoirs 980, 980′, 990 and 990′ of collection device 900 are similar to sa mple reservoirs 680, 680′, 690 and 690 included in collection device 600 of FIGS. ' can be sub stantially similar and/or the same in form and function.

[1170

] The flow diverter mechanism 920 includes a housing 901, a distribution member 929 and m ovable members 950a, 950b, 950c and 950d. Housing 901 is physically and fluidly coupled to distribution member 929 to provide and/or define a set of fluid flow paths for collecting bodily fluids from a patient. Housing 901 may be included in a flow metering device and/or otherwis e (e.g., electrically and/or mechanically) as described in further detail herein.

and a set of displays 975' (eg, liquid crystal displays (LCDs), etc.) that can be coupled togethe r. Housing 901 defines recess 966, exit openings 903a, 903b, 903c, 903d, 903e and movable member openings 950a, 950b, 950c, 950d (also referred to herein as "openings"). Recess 966 is configured to receive seal member 941 included in flow controller 940, as described in furth er detail herein. First outlet opening 903a, second outlet opening 903b, third outlet opening 9 03c, fourth outlet opening 903d and fifth outlet opening 903e are each in fluid communication with different portions of distribution member 929. It is configured to define different fluid flo w paths. More specifically, distribution member 929 includes at least a portion of pre-sample r eservoir 970 in fluid communication with first outlet opening 903a and a first channel 935a in fluid communication with second outlet opening 903b. , a second passageway 935b in fluid co mmunication with the third outlet opening 903b, a third passageway 935c in fluid communicat ion with the fourth outlet opening 903d, and a second passageway 935c in fluid communicatio n with the fifth outlet opening 903e. defines and/or forms four channels 935;

[0118]

[1171] As shown in FIGS. Pre-sample reservoir 970 is configured to contain bodily fluids such as, for example, blood, plasma, urine, and the like. As described in detail above with respect t o pre-sample reservoir 470 in FIGS. 16-22, first outlet opening 903a of housing 901 is pre-mo unted to allow pre-sample reservoir 970 to receive a flow of bodily fluid from the patient. It ca n be substantially aligned with the open portion of sample reservoir 970 . Channels 935a-935 d extend radially from the center of distribution member 929 and are arranged such that eac

channel 935a, 935b, 935c and 935d is fluidly isolated from pre-sample reservoir 970 and the other channels. ing. Thus, channels 935a, 935b, 935c and 935d have first ends defining openi ngs substantially aligned with outlet openings 903b, 903c, 930d and 903e, respectively, and movable members 950a, 950b, A fluid flow path may be directed and/or otherwise defined bet ween the second ends defining openings or ports configured to receive 950c and 950d, respec tively. Although distribution member 929 is shown in FIGS. 47 and 48 as including channels 9 35a-935d that are substantially closed, in other embodiments, with respect to distribution me mber 429 of FIGS. Channels 935a-935d can be substantially open as shown and described ab ove. Accordingly, distribution member 929 of collection device 900 can function substantially s imilar to distribution member 429 of collection device 400 .

[0119]

[1172] Movable members 950a, 950b, 950c and 950d are movably disposed in respective ope nings 905a, 905b, 905c and 905d of housing 901 and corresponding openings defined by the second end of distribution member 929. be. Although not shown in FIGS. 46-53, in some emb odiments moveable members 950a, 950b, 950c and 950d are biased members, as described i n detail above with respect to moveable members 250 and 250′ of collection device 200. etc. can be operatively coupled. Thus, movable members 950a, 950b, 950c and 950d are actuated (moved) by a user from first and second positions relative to housing 901 and distribution me mber 929 to direct fluid flow to a first sample. It can be directed into each of reservoir 980, se cond fluid reservoir 980', third fluid reservoir 990 and fourth sample reservoir 990'. Movable members 950a, 950b, 950c and 950d are substantially identical and therefore will be describe d with respect to a single movable member 950 in FIG. Additionally, some portions of movable member 950 may be substantially similar to movable members 250 and 350 described above. Accordingly, some portions of movable member 950 are not described in further detail herein. Movable member 950 defines an internal cavity 952 in fluid communication with inlet port 953 and piercing member 955 . The piercing member is substantially similar to that detailed abov e. The inlet port 953 extends through a set of walls that define the interior space 952 of the movable member 950 with corresponding passages 935a, 935b, 935c.

Alternatively, an internal chamber 952 is defined for selective placement in fluid communicatio n with 935d.

[1173

] As shown in FIG. The flow metering mechanism 967 can be, for example, a wheel or the like that can include a set of spokes or fins. In this manner, bodily fluid can enter inlet port 953 of movable member 950 and flow past flow metering device 967 , thereby allowing flow meterin g device 967 to rotate relative to movable member 950 . Accordingly, the rotational features o f the flow metering device 967 may be usable in determining the volume of bodily fluid transf erred to the interior space 952 of the movable member 950, the volumetric flow rate, and the like. Although not shown in FIGS. 46-53, flow control mechanism 967 of movable member 95 0 is operably coupled to display 975 ′ of housing 901 . Accordingly, as bodily fluids are trans

rred to sample reservoirs 980, 980', 990 and/or 990', for example, volumetric information rel ated to the flow of bodily fluids can be presented on display 975'. In this way, a user can oper ate the collection device 900 to collect a bodily fluid sample from a patient, e.g. One can be vi sualized.

[0121]

[1174] The flow controller 940 of the collection device 900 includes a dial 945 and a seal me mber 941 . Seal member 941 is disposed within recess 966 of housing 901 . More particularly, flow controller 940 is coupled to housing 901 such that seal member 941 is positioned betwee n and in contact with the surface of housing 901 defining recess 966 and the surface of dial 9 45 . be able to. As described in detail herein, sealing member 941 can be configured to form a substantially fluid-tight seal with the surface of dial 945 and the surface of housing 901 defini ng recess 966 . As shown in FIG. 47, the sealing member 941 defines a first opening 944a, a second opening 944b, a third opening 944c, a fourth opening 944d and a fifth opening 944e. As for the arrangement of the sealing member 941, when the sealing member 941 is arrange d in the recess 966, the first opening 944a, the second opening 944b, the third opening 944c, the fourth opening 944d, and the fifth opening 944e are opened. , the first outlet opening 903 a, the second outlet opening 903b, the third outlet opening 903c, the fourth outlet opening 90 3d and the fifth outlet opening 903e of the housing 901, respectively. is.

[0122]

[1175] The dial 945 of the flow controller 940 is rotatably coupled to the housing 901 and is movable relative to the housing 901 between a first position, a second position, a third positio n, a fourth position, and a fifth position. be. Dial 945 includes an entry port 921 that connects entry port 921 to a medical device (either directly or indirectly via adapter 904) that defines a fluid flow path for drawing bodily fluid from a patient and/or transporting it to collection devic e 900.) can be fluidly coupled. Inlet port 921 thus connects to pre-sample reservoir 970, first sample reservoir 980, second sample reservoir 980', third sample reservoir 990 and fourth sa mple reservoir 990, as described in further detail herein. ' can be configured to be selectively placed in fluid communication with a patient. configuring dial 945 to rotate through first, seco nd, third, fourth and fifth positions in a manner substantially similar to that described above w ith respect to dial 445 of collection device 400; , and therefore will not be described in further detail here.

[1176

] As shown, the dial 945 can further include a display 975 that can be configured to present v olumetric information related to the flow of bodily fluids. For example, although not shown in FIGS. 46-53, a dial may be a flow metering device included in movable member 950
967, can include flow metering devices and the like. Thus, the flow metering device can, for e xample, meter the flow of bodily fluid through inlet port 921 such that volumetric information associated with the flow of bodily fluid through inlet port 921 is presented on display 975 of di al 945. , may be operatively coupled to the display 975 .

[1177

] In operation, the collection device 900 can be used to collect bodily fluids (eg, blood, plasm a, urine, etc.) from a patient with reduced contamination. For example, entry port 921 of colle ction device 900 can be fluidly coupled to a needle or other lumen defining device (eg, flexible sterile tubing). Following venipuncture (or other method of accessing bodily fluids), dial 945 is actuated (or turned) until it reaches the first position, as shown in FIGS. Alternatively, dial 94 5 can be preset to the first position and collection device 900 can be otherwise sealed to main tain sterility of collection device 900 .

[0125]

[1178] As described above, when the dial 945 is in the first position, the flow controller 940 is disposed in the first configuration, and the first opening 944a of the seal member 941 connect s the inlet port 921 to the four flow paths 935a to 935a. Fluid communication is established b etween inlet port 921 (contained within housing 901) and first outlet port 930 while being flui dly isolated from 335d. Further, sample reservoirs 980, 980', 990 and 990' are fluidly isolated from inlet port 921 in the first configuration and are part of the patient's body (e.g., A fluid flo w path is defined between the vein) and the pre-sample reservoir 970 . In this first configurati on, bodily fluids are forced (e.g., by gravity, vacuum, etc.) from that portion of the patient's b ody through inlet port 921, first opening 944a in seal member 941, and first outlet port 903a i n housing 901. through and into the pre-sample reservoir 970 . In the first form, flow controll er 940 also fluidly isolates pre-sample reservoir 970 from flow paths 935a-935d. Accordingly, a first volume (predetermined or unquantified) of bodily fluid can be received in pre-sample re servoir 970 immediately after venipuncture and isolated from subsequent samples. In this wa y, using the collection device 900, a first volume of bodily fluid most likely to contain surface microorganisms and/or other undesirable contaminants may be diagnosed or otherwise affect ed by the contaminant. Subsequent amounts of bodily fluid samples collected and used for tes ting can be avoided from contaminating. Additionally, the display 975 can present information received from a flow control mechanism (not shown) related to, for example, the volume of b odily fluid transferred to the pre-sample reservoir 970 . Thus, a precise volume of bodily fluid can be transferred to and fluidly isolated within the pre-sample reservoir.

[0126]

[1179] Following the collection of the bodily fluid pre-sample within the pre-sample reservoir 970, the dial 945 can be actuated (or rotated) until it reaches the second position, as shown i n FIGS. When the dial 945 is in the second position, the flow controller 940 is disposed in the second configuration, and the second opening 944b of the seal member 941 fluidly isolates th e pre-sample reservoir 970 from the inlet port 921 while allowing the inlet port 921 to flow. Fl uid communication is established between 921 and channel 935a. With flow controller 940 in t he second configuration, movable member 950a is actuated (i.e., depressed) by a user from a first position to a second position to allow patient (eg, vein) and first sample reservoir 880 to move. can establish fluid communication between the More specifically, as indicated by arrow

RR in FIG. to be placed in the first sample reservoir 980 .

[1180

] While in the second position, the inlet port 953 of the movable member 950 is substantially aligned with and in fluid communication with the first flow path 935a, thereby allowing body fl uid to flow through the first flow path 935a. can flow from into the internal cavity 952 of the working member 950 and out of the piercing member 955 into the first sample reservoir 980 . Sample reservoir 980 (e.g. vacuum or negative pressure)

) and the first channel 935 a draws bodily fluid into the sample reservoir 980 . In other words, in the second configuration, flow controller 940 and movable member 950a establish a fluid fl ow path between inlet port 921 of dial 945 and first sample reservoir 980, as indicated by arr ow SS in FIG. In addition, flow of bodily fluids through movable member 950 a causes flow m etering mechanism 967 to rotate relative to movable member 950 . Thus, rotation of flow met ering mechanism 967 may be usable in determining the volume of bodily fluid sample transfer red to sample reservoir 980 . Additionally, display 975 ′ can present information received from flow control mechanism 967 related to, for example, the volume of bodily fluid transferred to sample reservoir 980 . Therefore, a precise volume of bodily fluid can be transferred to the sa mple reservoir 980 . For example, in some cases, collection device 900 is used to collect three sample volumes of 20 mL each in first sample reservoir 980, second sample reservoir 980', an d third sample reservoir 990 (i.e., a total of 60 mL of sample volume is collected).

[0128]

[1181] Once a desired volume of bodily fluid (eg, a second amount) has been collected in the first sample reservoir 980, the user releases the movable member 950 to cause the biasing m ember (not shown) to It can be allowed to move back to the first position. When movable me mber 950 returns to its first position, piercing member 955 is removed from first sample reser voir 980 and a seal (eg, a self-sealing membrane) fluidly disconnects first sample reservoir 98 0 from internal flow path 935 . isolate to Using the collection device 900, transfer the second sample volume to the second sample reservoir 980' and the third sample volume to the third sample by rotating the dial 945 to its third, fourth and fifth positions, respectively. A fourth sa mple volume can be similarly transferred to reservoir 990 to fourth sample reservoir 990'.

[0129]

[1182] In some cases, the fluid collection device 900 allows the clinician and/or phlebotomist to open the package containing the fluid collection device 900, remove only the housing 901 (including the dispensing member 929), and remove the housing 901. It can be carried by the patient's bedside. The clinician and/or phlebotomist performs a venipuncture (or employs any other method of accessing the patient's bodily fluids) into a portion of the patient's body (e.g., a vein) using any standardized technique be able to. Following venipuncture, the clinician an d/or phlebotomist can collect the total blood volume required for all samples. For example, a c linician and/or phlebotomist can collect a 2.5 mL pre-sample diversion volume and a 10 mL sa mple volume for each of the four sample reservoirs, whereby the collected bodily fluid (e.g.,

lood) totals 42.5 mL. Following collection of a desired amount of bodily fluid, the hypodermic needle can be removed from that portion of the patient's body (e.g., a vein) and the clinician and/or phlebotomist can access the housing 901 (which contains the bodily fluid). can be plac ed on top of 4-pack (or 2-pack) pre-sterilized sample reservoirs with the membrane tops pre-placed in custom trays that match the shape of housing 901. By using such pre-sterilized pack s of sample reservoirs, the clinician does not have to perform the process step of "wiping" the sample reservoir tops with a sterilant, thereby, for example, sterilizing the reservoir tops. Red uced potential for contamination if inappropriate and/or insufficient. A clinician and/or phlebot omist can then trigger automatic inoculation of a sample reservoir containing bodily fluid with precise volume control. In some embodiments, after inoculation of the sample reservoirs is co mplete, the entire device 900 with volume information displayed for each individual sample re servoir can be sent to a laboratory for analysis. In other embodiments, sample reservoirs 980 and/or 990 are individually

[1183

] The collection device 900, with reference to FIGS.

Although shown and described as including 975 and 975', in other embodiments the collection device can include any suitable flow metering mechanism with any suitable output indicator. F or example, Figures 54 and 55 show a flow diverter 1020 and a flow controller 1040 according to embodiments. Flow diverter 1020 and flow controller 1040 may be substantially similar in f orm and function to flow diverter 920 and flow controller 940, respectively. Accordingly, simila r parts will not be described further herein. However, flow diverter 1020 and flow controller 10 40 may differ in the placement of set of displays 1075 . For example, flow diverting mechanis m 1020 includes housing 1001 configured to movably receive a set of movable members 1050 a, 1050b, 1050c and 1050d, each of which can include a flow metering mechanism, as describ ed above with respect to movable member 950. include. Accordingly, movable members 1050 a, 1050b, 1050c and 1050d can be used to determine the precise volume of bodily fluid that i s transported through them. As shown in FIG. 55, the display 1075 of the housing 1001 provi des a first illumination for a small volume (eg, 5 mL), a second illumination associated with an intermediate volume (eg, 20 mL), and an acceptable and/or large volume. A set of three light s can be included, including a third light associated with (eg, 40 mL). In this manner, when th e flow of bodily fluid is transferred through the flow controller 1040 and the flow diverter mec hanism 1020, for example into the first movable member 1050a, the flow metering mechanis m contained therein can send a signal or the like to the display. , the display is operable to illu minate the first light, the second light and/or the third light according to the volume of bodily fluid transferred through the movable member 1050 .

[0131]

[1184] In other embodiments, movable members 1050a, 1050b, 1050c, and 1050d can be m oved from a first position to a second position, a third position, or a fourth position relative to housing 1001 . In such embodiments, their positions can be associated with, for example, th

intended volume of bodily fluid to be transferred to the sample reservoir. For example, in som e embodiments, a user can actuate (eg, move) movable member 1050a from its first position to its second position. In such embodiments, the second position can be associated with, for e xample, a small volume (eg, 10 mL) of bodily fluid to be transferred to the sample reservoir. I n some embodiments, housing 1001 and/or moveable member 1050a can temporarily hold m oveable member 1050a in a second position until a low volume of sample has been transferre d to the sample reservoir. , locks, fasteners, protrusions, recesses, and the like. Further, when positioned in the second position, display 1075 is configured to illuminate a first illumination a ssociated with the smaller volume to indicate to the user the preset volume of bodily fluid to b e transferred to the sample reservoir. can do. Once a desired volume of bodily fluid has been t ransferred to and fluidly isolated within the sample reservoir, the flow diverter mechanism 102 0 can be configured to automatically return the movable member 1050a to its first position. I n this manner, flow diverter mechanism 1020 and flow controller 1040 can be physically and fl uidly coupled to any number of sample reservoirs and used to transfer precise volumes of bod ily fluid to each sample reservoir.

[0132]

[1185] FIG. 56 is a flowchart illustrating a method 1190 of obtaining a predetermined sample volume of bodily fluid from a patient using a flow metering transfer device. A flow metering tr ansfer device can be any of the transfer devices described herein (also referred to herein as a "collection device"). By way of example, in some embodiments the transfer device can be the collection device 900 described above with reference to FIGS. 46-53. Thus, the transfer devic e includes an inlet port configured to be selectively placed in fluid communication with a patie nt, a pre-sample reservoir and a sample reservoir, and fluid flow from the patient to the pre-s ample reservoir and to the sample reservoir. and a flow metering mechanism configured to m eter the flow of bodily fluid. The method 1190 includes, at 1191, establishing fluid communica tion between a patient and a port of a flow metering transfer device. For example, the port m ay be connected to a needle or other lumen-defining device (e.g., a flexible

A needle or other lumen-defining device can be inserted into the patient's body (eg, a venipun cture event or other method of accessing bodily fluids).

[1186

] With the port in fluid communication with the patient, at 1192, fluid communication is establ ished between the port and the pre-sample reservoir. In some embodiments, the flow meterin g transfer device can include a flow controller or the like (eg, flow controller 940 included in c ollection device 900) that provides fluid communication between the port and the pre-sample reservoir. It can be actuated and/or manipulated (eg rotated) to an established position (eg fir st position). In some embodiments, actuation of the flow controller may cause the flow contro ller and flow diversion mechanism to collectively define at least a portion of a fluid flow path b etween the port and the pre-sample reservoir. In some embodiments, the pre-sample reservoi r can include negative pressure or the like that can initiate the flow of bodily fluid from the p

ient to the pre-sample reservoir. In other embodiments, bodily fluid flow can be initiated in an y other suitable manner (eg, gravity, etc.).

[0134]

[1187] At 1193, the flow of bodily fluid transferred from the patient to the pre-sample reservo ir is metered. For example, in some embodiments, the port has a flow control mechanism that can meter the flow of bodily fluid through the port (eg, in a manner similar to that described a bove with respect to flow control mechanism 967 of collection device 900). can contain. Thus, a pre-sample volume of bodily fluid is transferred to the pre-sample reservoir. The method 11 90 includes, at 1194, verifying, via the flow metering mechanism of the flow metering transfer device, that the pre-sample volume of bodily fluid disposed within the pre-sample reservoir is a predetermined pre-sample volume of bodily fluid. For example, the flow metering mechanis m can include and/or be operably coupled to a display or the like (eg, display 975 and/or 975′ of collection device 900). The flow metering mechanism can be configured to present volumet ric information on a display, as described above.

[0135]

[1188] Once the pre-sample volume of bodily fluid is disposed within the pre-sample reservoi r, at 1195, the pre-sample reservoir is fluidly isolated from the port to seal the pre-sample vol ume of bodily fluid within the pre-sample reservoir. For example, in some cases, the flow cont roller and/or flow diverter mechanism can be actuated (or rotated) from a first position and/or configuration to a second position and/or configuration. When the flow controller and/or flow diverter mechanism are in the second configuration, the pre-sample reservoir is fluidly isolate d from the space outside the pre-sample reservoir. In some embodiments, when the flow cont roller and/or flow diversion mechanism is driven to its second position and/or configuration, at 1196 fluid communication is established between the port and the sample reservoir. For exam ple, in some embodiments, the flow metering transfer device can include a piercing member (e.g., movable member 950) configured to pierce a portion of the sample reservoir (e.g., me mbrane, etc.) etc. Thus, when the flow controller and/or flow diverter mechanism is in its sec ond position and/or second configuration, the perforation of that portion of the sample reserv oir places the sample reservoir in fluid communication with the port. As noted above, the sam ple reservoir can contain, for example, a negative pressure or the like that can initiate the flo w of bodily fluid from the patient to the sample reservoir.

[0136]

[1189] At 1197, the flow of bodily fluid transferred from the patient to the pre-sample reservo ir is metered. For example, as described above, the port may include a flow control mechanis m capable of metering the flow of bodily fluid through the port (eg, in a manner similar to tha t described above with respect to flow control mechanism 967 of collection device 900). can b e done. In some embodiments, the flow control mechanism can be included in a movable me mber, such as, for example, movable member 950 in FIG. A sample volume of bodily fluid is t hus transferred to the sample reservoir. The method 1190 includes, at 1198, removing the b

dy disposed within the sample reservoir via the flow metering mechanism of the flow meterin g transfer device.

This includes verifying that the sample volume of liquid is a predetermined sample volume of volume. For example, as described above, a display or the like can be configured to present v olumetric information.

[0137]

[1190] In this manner, a predetermined pre-sample volume of bodily fluid is collected, which may include, for example, externally present microorganisms. For example, in some embodim ents, the predetermined pre-sample volume is about 0.1 mL, about 0.3 mL, about 0.5 mL, ab out 1.0 mL, about 2.0 mL, about 3.0 mL, about 4.0 mL, It can be about 5.0 mL, about 10 mL, about 20 mL, about 50 mL, and/or any volume or volume fraction value therebetween. In oth er embodiments, the pre-sample volume can be greater than 50 mL or 0.1 mL. In other embo diments, the predetermined pre-sample volume can be between about 2 mL and about 5 mL. In one embodiment, the predetermined pre-sample volume can be approximately 3 mL. Additi onally, by collecting the predetermined pre-sample volume, the predetermined sample volume disposed within the one or more sample reservoirs can be substantially free of externally pres ent microorganisms. In some embodiments, the predetermined sample volume can be betwee n 10 mL and 60 mL. In other embodiments, the predetermined sample volume can be betwee n 30 mL and 60 mL. In still other embodiments, the predetermined sample volume can be 60 mL. Although described above as transferring a sample volume of bodily fluid to a single samp le reservoir, in other embodiments, a flow metering transfer device can be used to transfer a given sample volume to two or more sample reservoirs. For example, in some embodiments, a predetermined pre-sample volume of bodily fluid can be collected in and fluidly isolated with in a pre-sample reservoir, as described above. A predetermined sample volume into a first sa mple reservoir, a predetermined sample volume into a second sample reservoir, and a predete rmined sample volume into a third sample reservoir using a flow metering transfer device whil e the pre-sample volume is fluidly isolated. can be transferred to In such a case, the predeter mined sample volume can be, for example, 20 mL, so that the total sample volume placed in t he first, second and third reservoirs is 60 mL.

[0138]

[1191] Various embodiments of the bodily fluid collection devices described herein enable coll ection of two (or more) sets of bodily fluid (e.g., blood) samples from a single venipuncture. c an do. The current standard of care is to perform some tests (e.g., blood cultures) on separat e, independent samples (e.g., via two separate venipunctures, via catheter + venipuncture, a nd/or combinations thereof). They are asked to do so by obtaining it from a fluid access point. Embodiments described herein can facilitate obtaining multiple samples for a given diagnostic test (e.g., blood culture test) from a single bodily fluid access point (e.g., venipuncture); Ther eby, the annual number of venipunctures required to obtain these samples can be reduced by a factor of two. This is advantageous for both patients and medical personnel alike. Reducing

the number of venipunctures (and/or other blood access procedures) significantly reduces the risk of needlestick injuries to health care workers and reduces patient-related complications resulting from these procedures (e.g., hematoma, thrombosis, phlebitis, infection, etc.) can be reduced. Further, reducing the number of fluid access procedures (eg, venipuncture) reduces the supply utilization, labor and waste associated with these procedures. The cost reductions realized by the healthcare system are significant and patient due to improved sample integrity resulting in more accurate patient diagnoses that inform treatment plan development and implementation, as well as more efficient resource consumption. presents an opportunity to promote improved outcomes in The bodily fluid collection device also greatly reduces the incidence of false positives from post-collection analysis. The fluid collection devices described herein can also streamline the fluid collection process, reducing the number of manual steps and "touch points", thereby reducing the chances of external contamination. The devices described herein can also minimize the risk of needle stick injury and infection to the laboratory technician and/or phlebotomist.

[1192

] In some embodiments, the bodily fluid collection devices described herein (eg, 100, 200, 300, 400, 500, 600, 700, 800 and 900) are sterile saturated.

It may include and/or be formed in part from a composite material (eg, housing 401). Current standards rely on medical personnel to place individual antiseptic materials (eg, isopropyl alcohol swabs) on top of individual sample reservoirs (eg, 480, 480', 490 and 490'). To ensure compliance with this protocol, (for example) the device 400 may include antiseptic material disposed within the device 400 so that the housing 401, as shown in FIG. 2 pack), the first point of contact from the top of housing 401 and sample reservoirs 480, 480', 490, 490' is the disinfectant material. In this way, the tops of the sample reservoirs 480, 480', 490, 490' are ensured that proper disinfection is applied before bodily fluids are inoculated into the sample reservoirs.

[0140]

[1193] While various embodiments have been particularly shown and described, various changes in form and detail can be made. For example, although dial 445 (actuator) is shown and described with reference to FIGS. 19-22 as rotating in a single direction, in other embodiments, dial 445 (actuator) rotates in a first direction. and a second direction opposite the first direction. In such embodiments, rotation in the second direction can be configured to move the collection device through any number of configurations. In other embodiments, rotation of the actuator in the second direction can be restricted. In some embodiments, the dial can include a mechanical stop or lock to fluidly isolate the first volume of bodily fluid received from the patient (ie, the contaminated sample). In other words, when the first reservoir (pre-sample reservoir) is filled with a predetermined volume of bodily fluid and the user rotates the dial (actuator) to start drawing in additional sample, the dial (actuator) is turned to (It cannot be moved back to establish fluid communication with the first sample volume (contained within the pre

ample reservoir).

[0141]

[1194] While several embodiments have been described above, it should be understood that t hey have been presented by way of example only and not limitation. Although various embodi ments have been described as including combinations of particular features and/or component s, any combination or sub-combination of any feature and/or component from any of the emb odiments described herein may be described. Other embodiments with combinations are possi ble. For example, with reference to FIGS. 34-40, although collection device 700 is shown and described as having a first, second, third, fourth or fifth configuration, other implementations are possible. In form, the collection devices described herein can have more or fewer forms. F urther, while the collection device 200 is shown and described with reference to FIGS. 2-13 as having a vacuum-assisted collection tube as the pre-sample reservoir 270, in other embodime nts, the collection device 200 includes a dispensing member. The collection device 400 of the embodiment presented in FIGS. 16-22 can have chambers housed in a housing 201 similar to the collection device 400 of the embodiment presented in FIGS. It is possible.

[0142]

[1195] It is also possible to vary the specific arrangement of the various components. For exa mple, the sizes and specific shapes of various components may differ from the illustrated emb odiments while still providing functionality as described herein. More specifically, the sizes and shapes of the various components can be specifically selected for the desired flow rate of bodil y fluid flow into the fluid reservoir. For example, although flow metering mechanism 967 is sp ecifically shown in FIG. 49, any of the collection devices described herein can be used with an y suitable flow metering mechanism. For example, in some embodiments, the collection devic e includes a flow metering mechanism and/or, for example, pressure sensors, voltage sensor s, optical sensors, velocity sensors, flow meters, strain gauges, valves, turbines, floats, displa cement analysis, Density Analysis, Gravimetric Analysis, Optical Analysis, Ultrasound Analysis, Thermal Analysis, Doppler Analysis, Electromagnetic Field (emf) Analysis, Reflection Analysis, Obstacle Analysis, Area Analysis, Venturi Analysis, Coriolis Analysis, Visual Analysis and/or an y other suitable sensor, analysis and/or

(e.g., applying and/or using Boyle's law, the ideal gas law, force calculations (force = mass x acceleration), etc., as examples), other Any mechanism, device or method can be included.

drawing open ----

[Fig. 1]

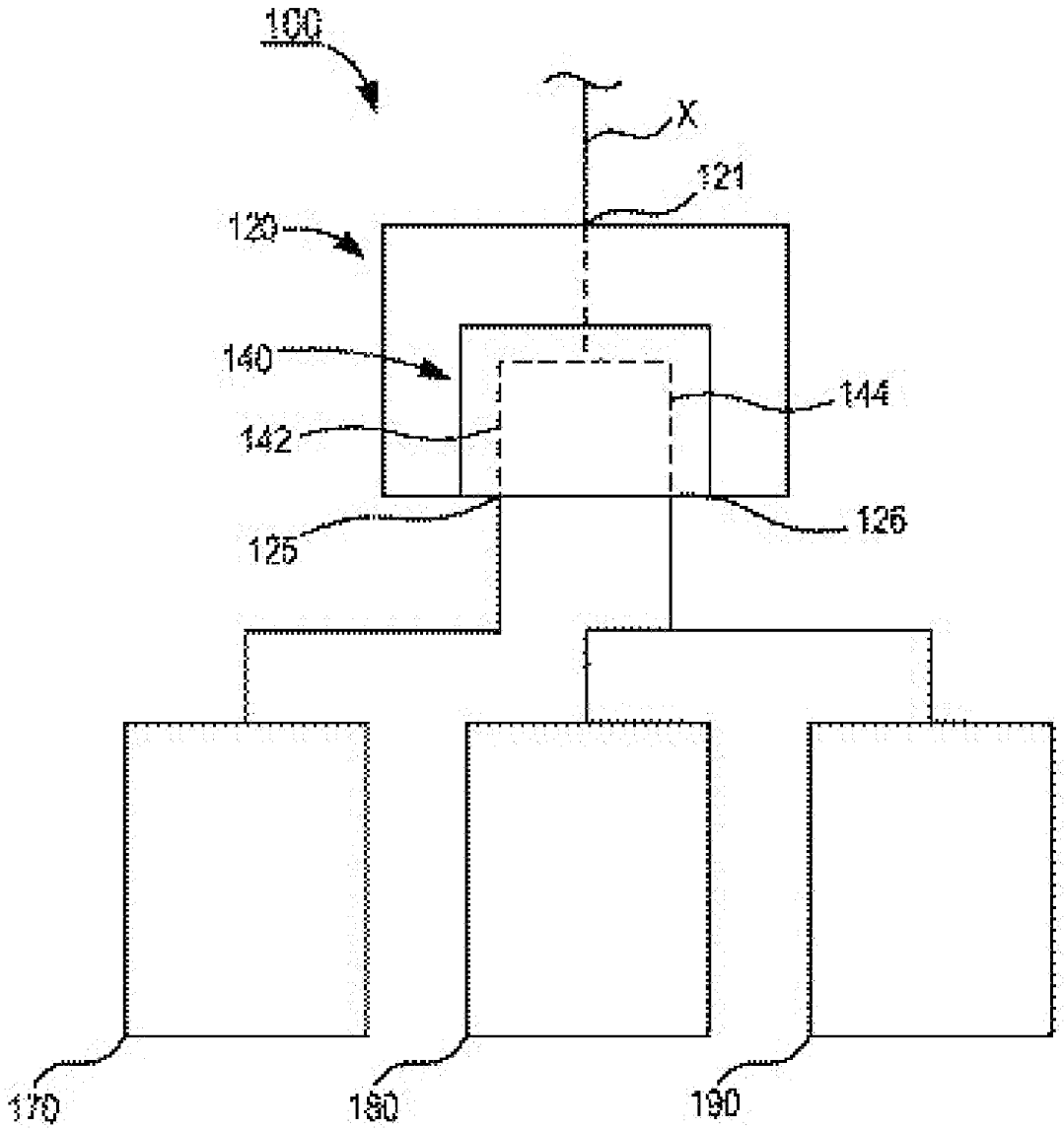


FIG. 1

[Figure 2]

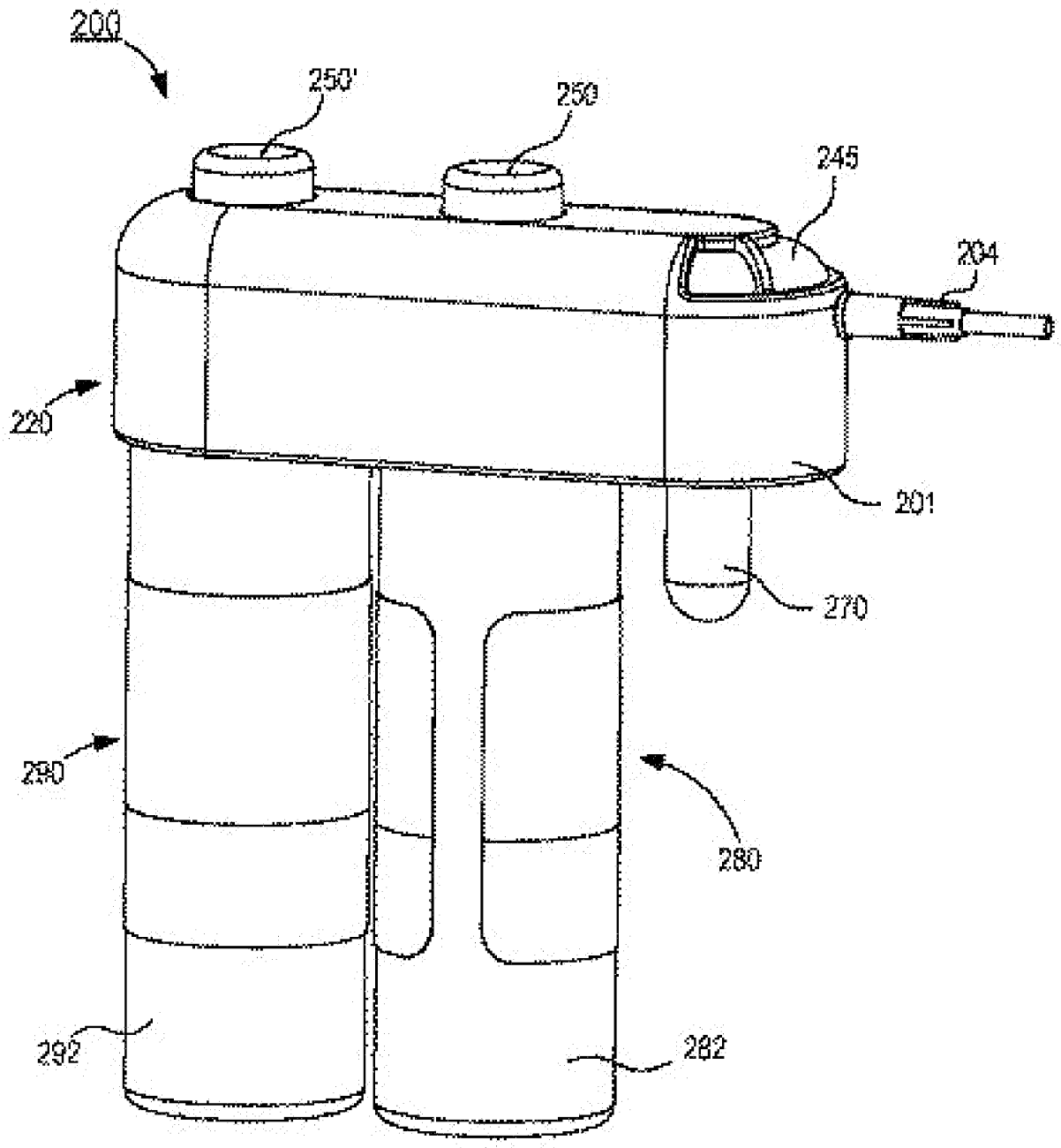
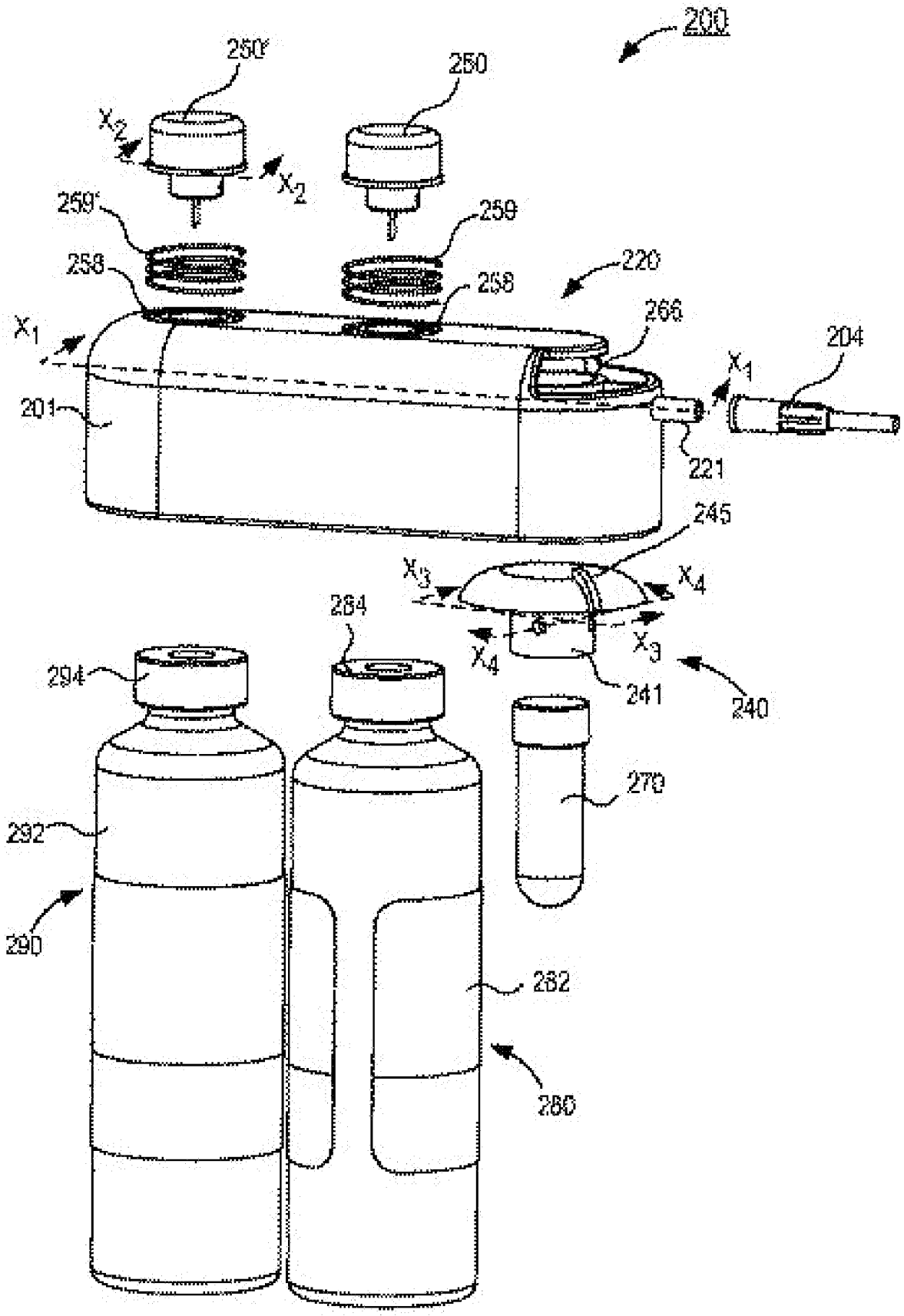


FIG. 2

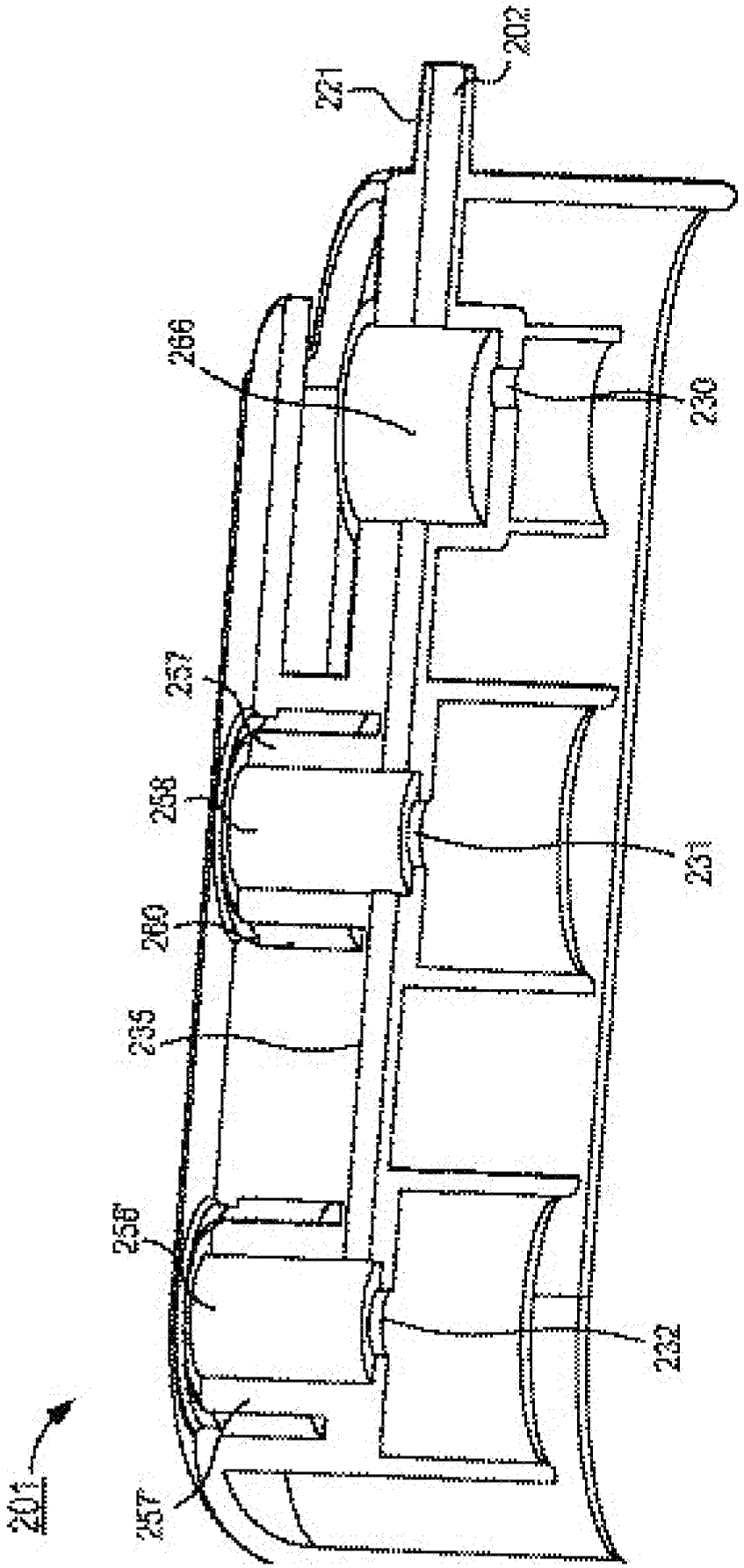
[Figure 3]


200
250'
250
X2
X2
259'
259
258
258
220
266
204
X1
X1
201
221
245
X3
X4
264
X4
X3
294
241
240
270
292
290
282
280

[Figure 4]

FIG. 3

FIG. 4



[Figure 5]

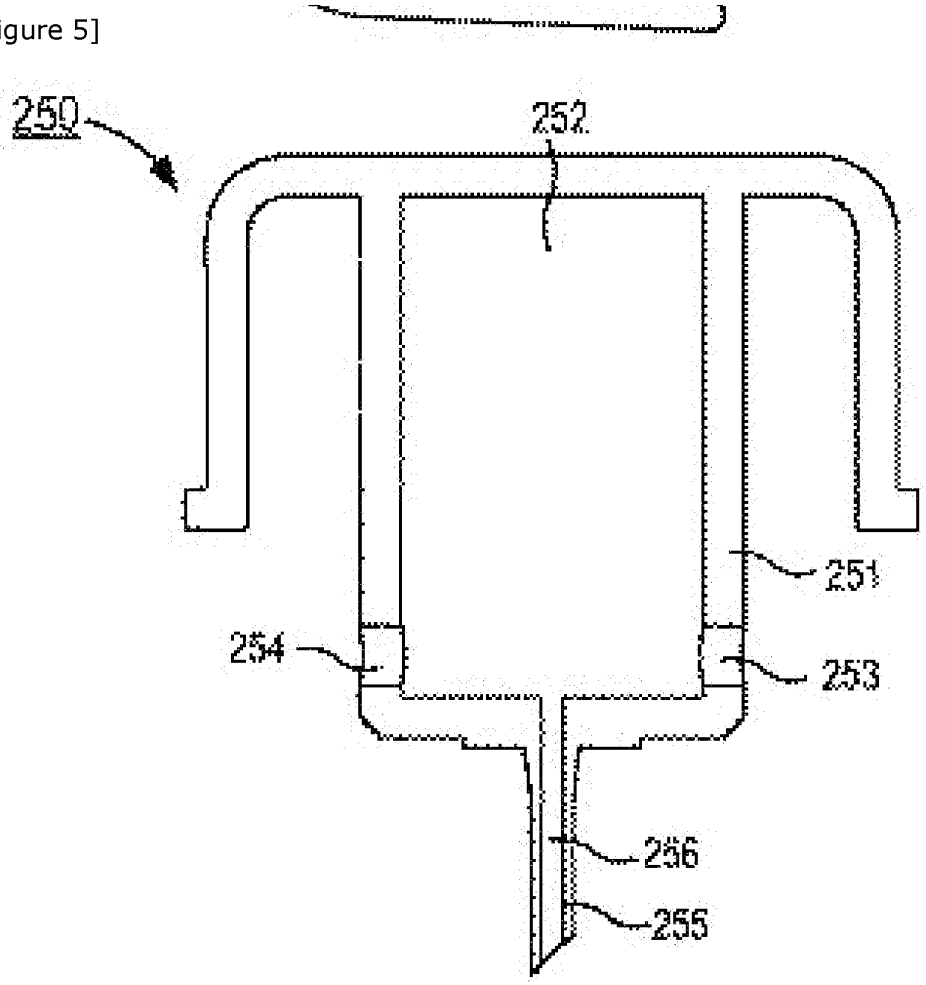


FIG. 5

[Fig. 6]

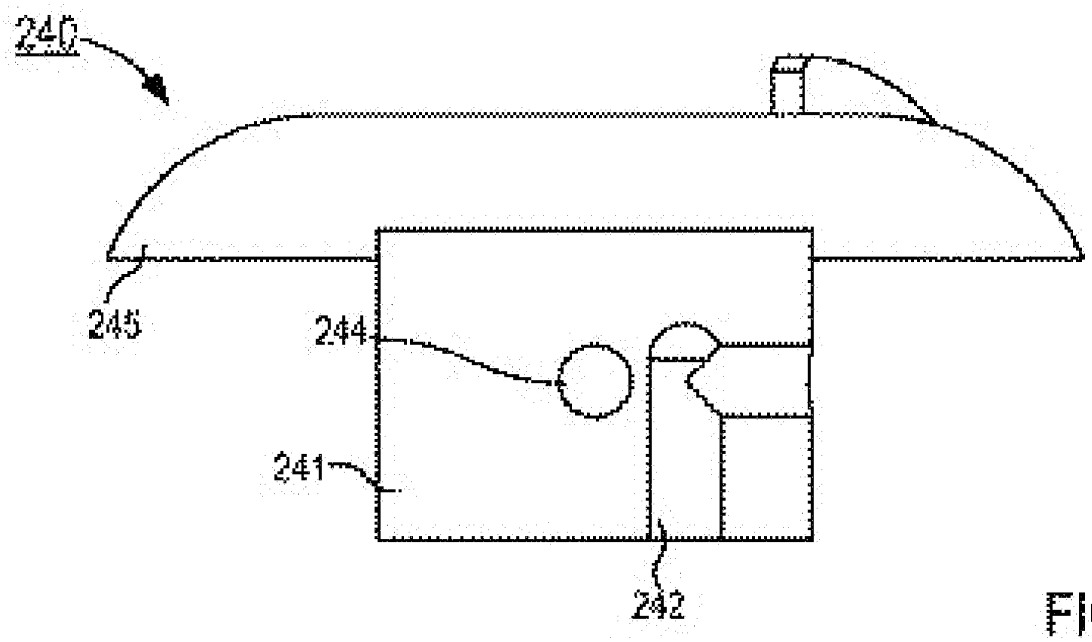


FIG. 6

[Fig. 7]

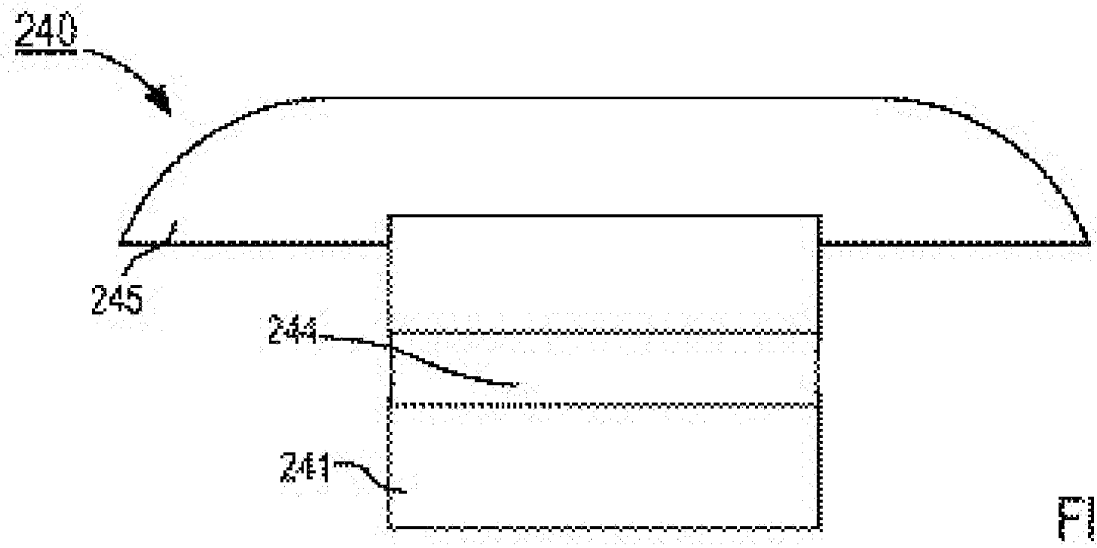


FIG. 7

[Fig. 8]

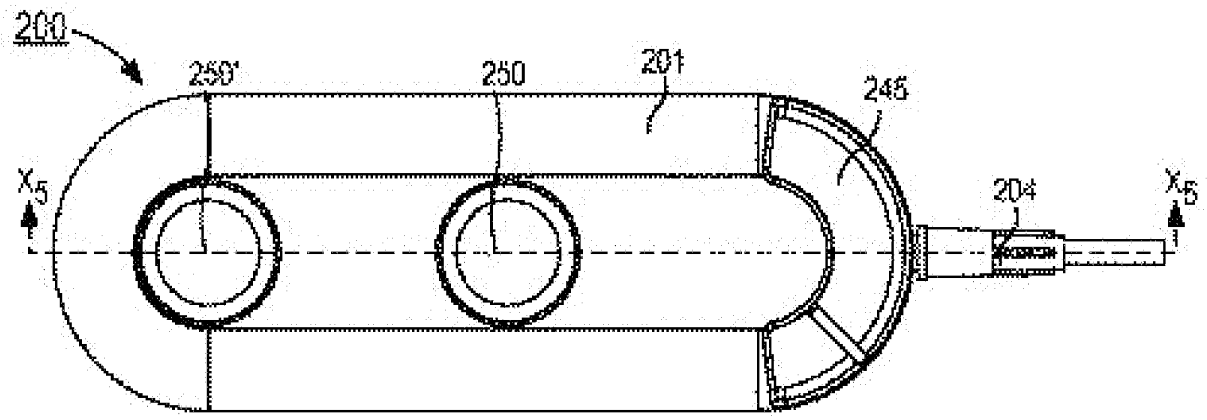


FIG. 8

[Fig. 9]

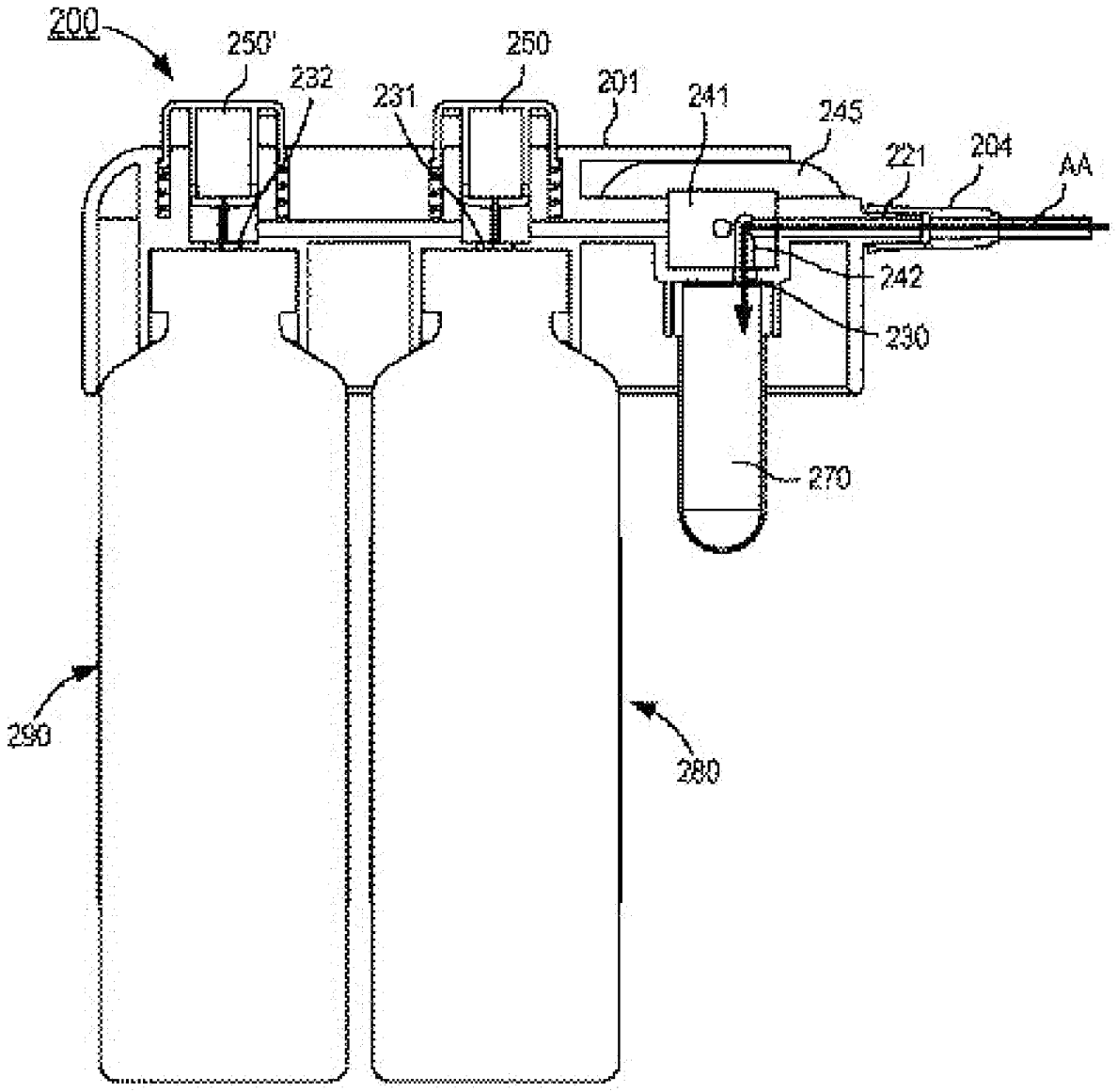


FIG. 9

[Fig. 10]

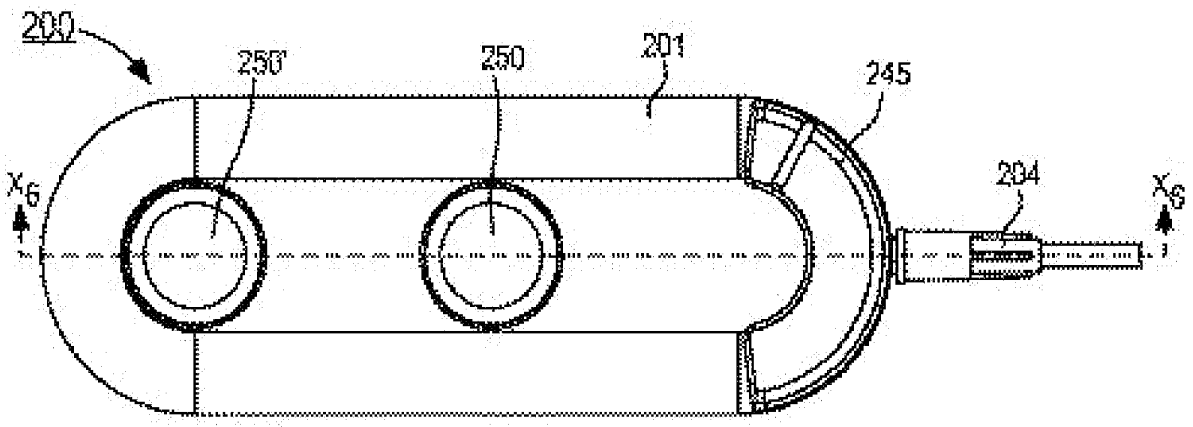


FIG. 10

[Fig. 11]

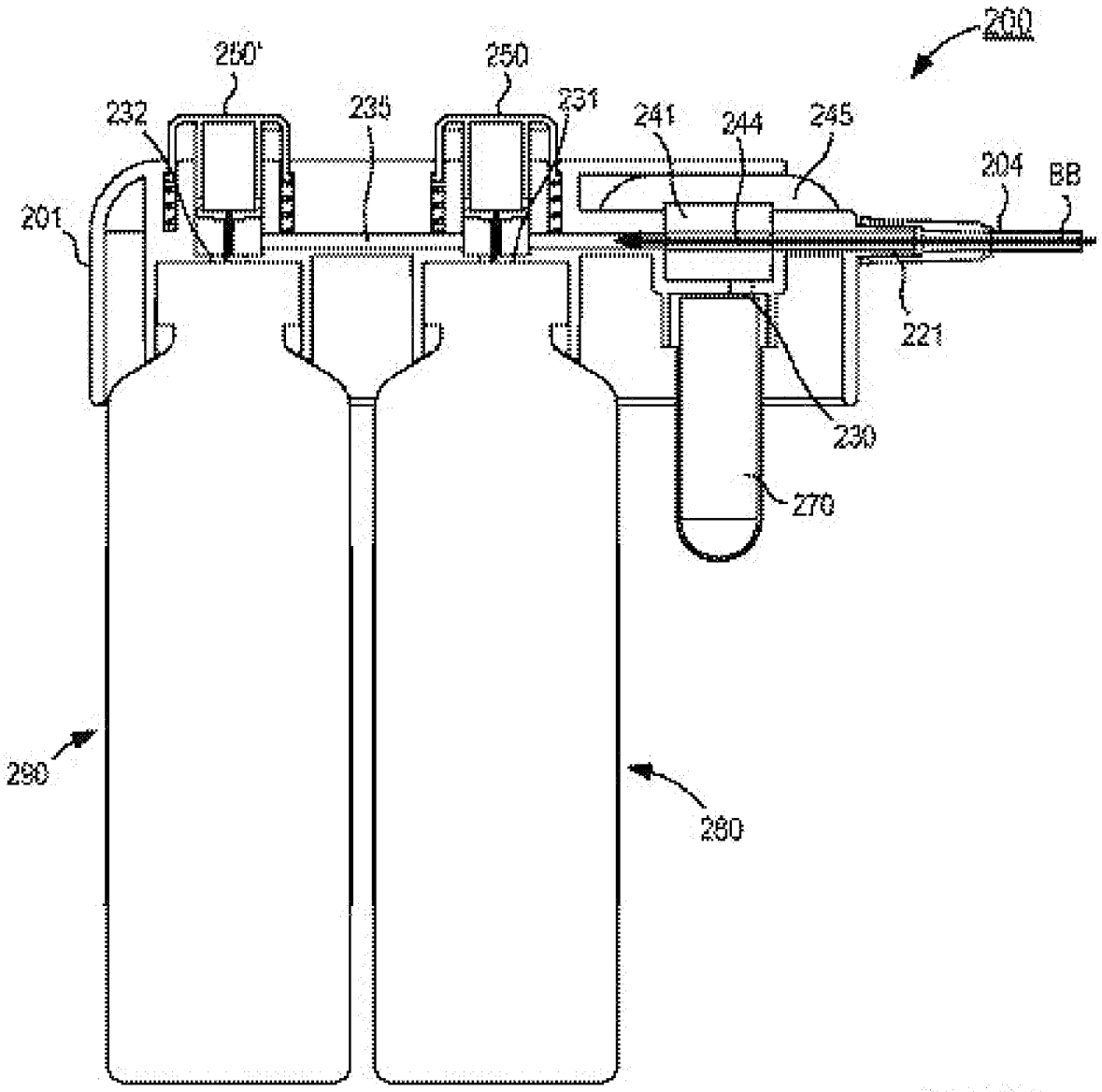

200
250'
250
232
235
231
241
244
245
204
BB
201
221
230
270
280
280

FIG. 11

[Fig. 12]

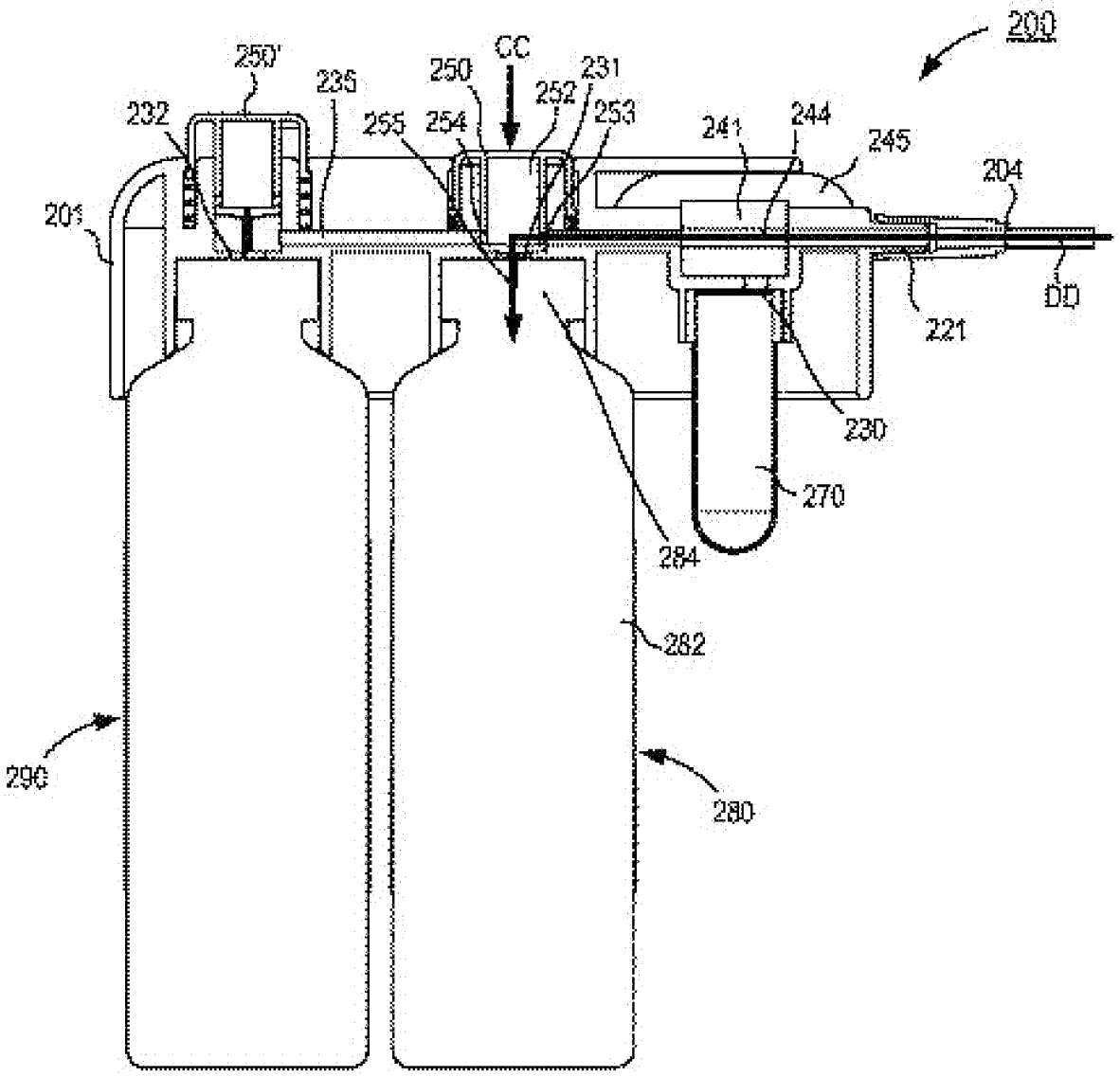

200
250'
236
250
CC
231
232
255
254
252
253
241
244
245
204
201
DD
221
230
270
284
282
290
280

FIG. 12

[Fig. 13]

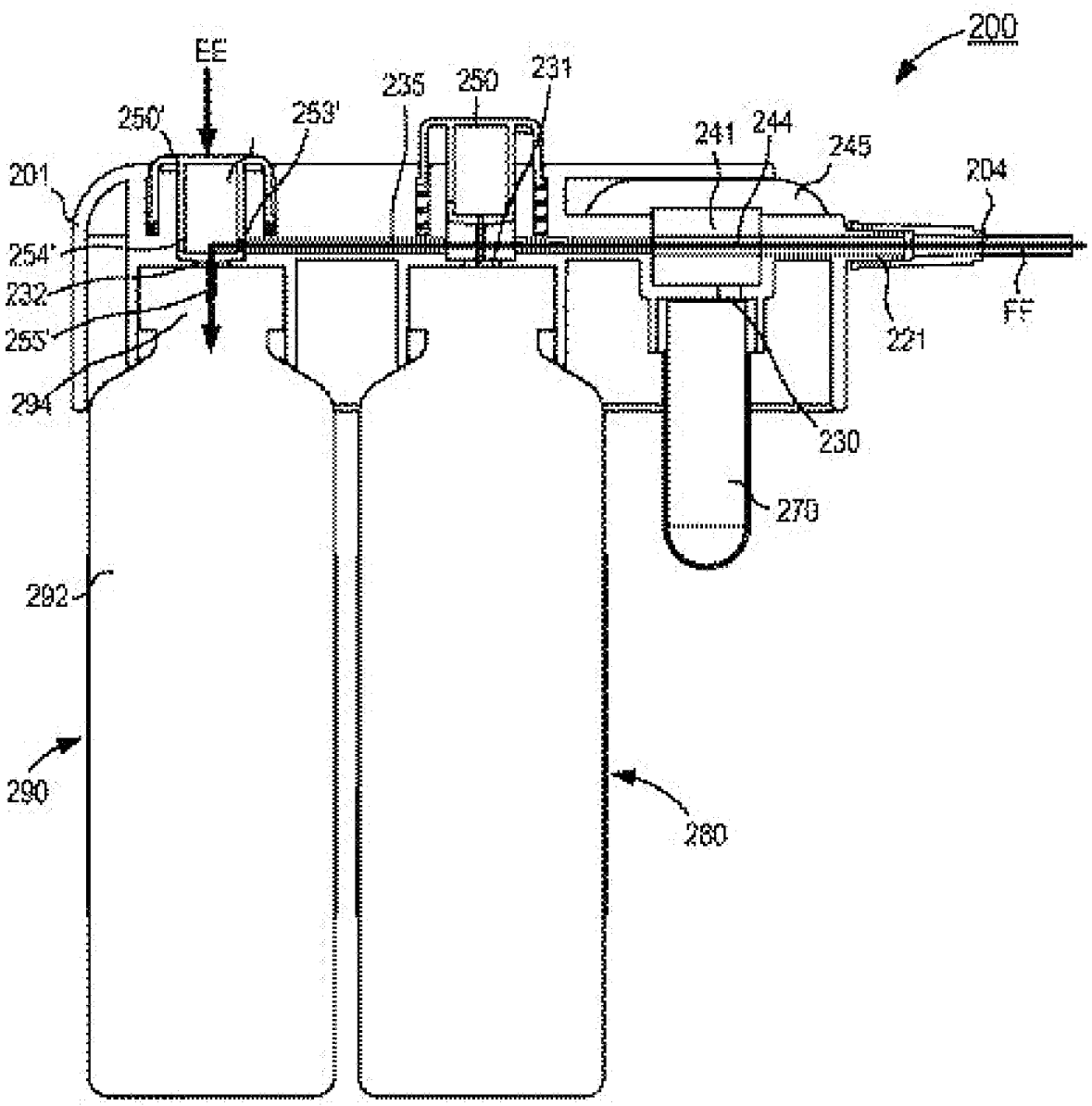

200
EE
250'
253'
235
250
231
241
244
245
204
201
254'
232
255'
294
221
FF
230
270
292
290
280

FIG. 13

[Fig. 14]

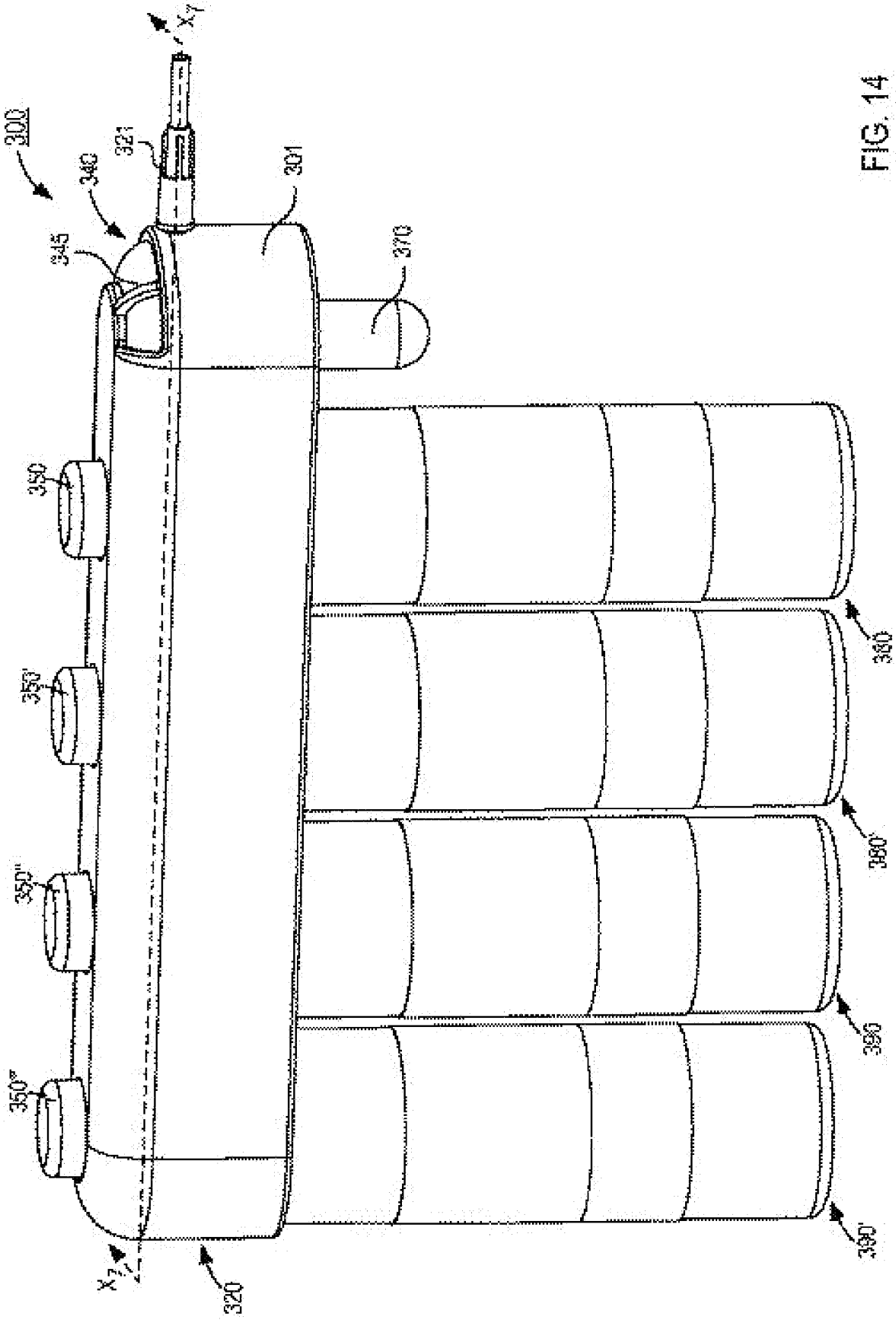
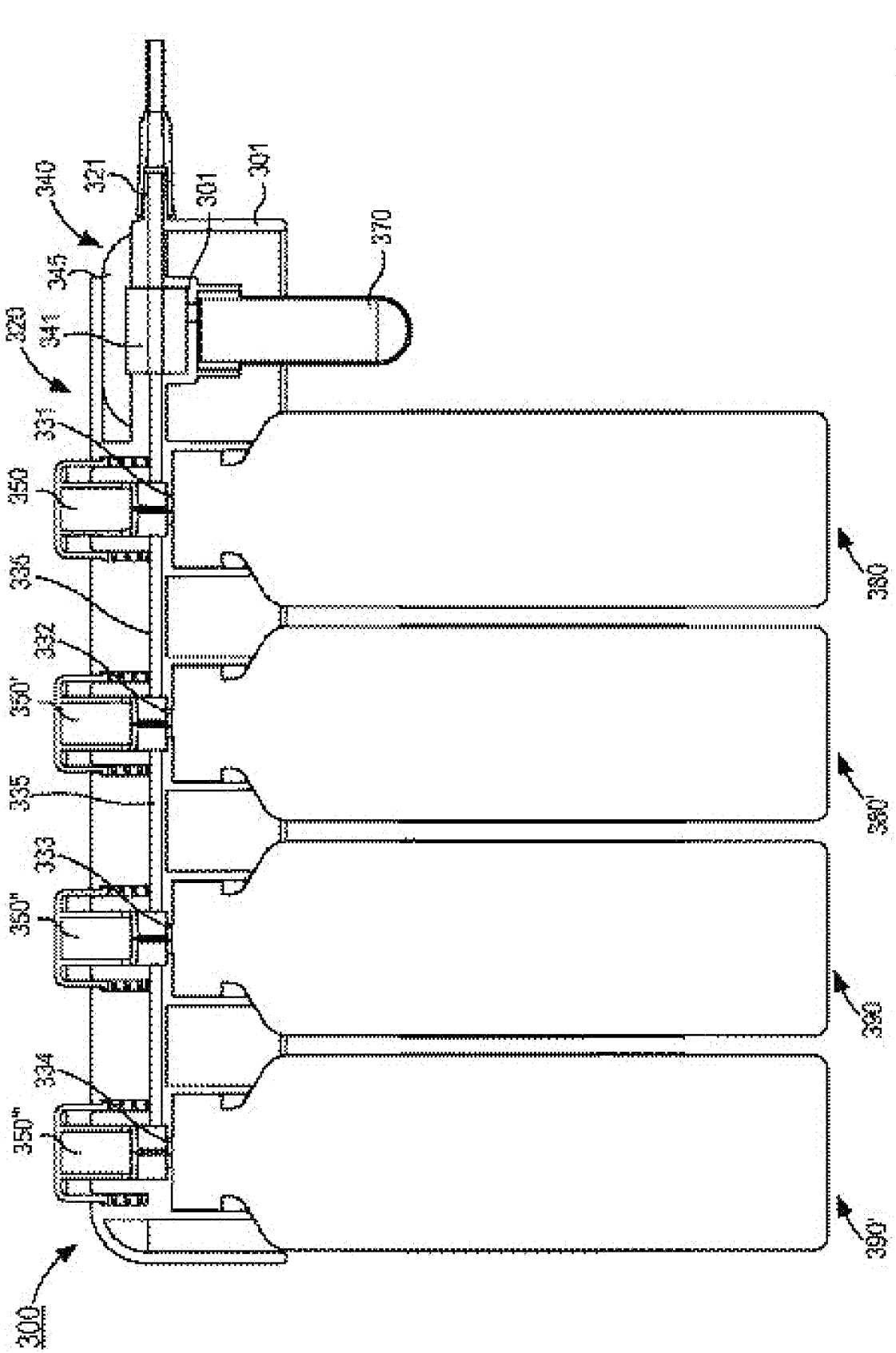
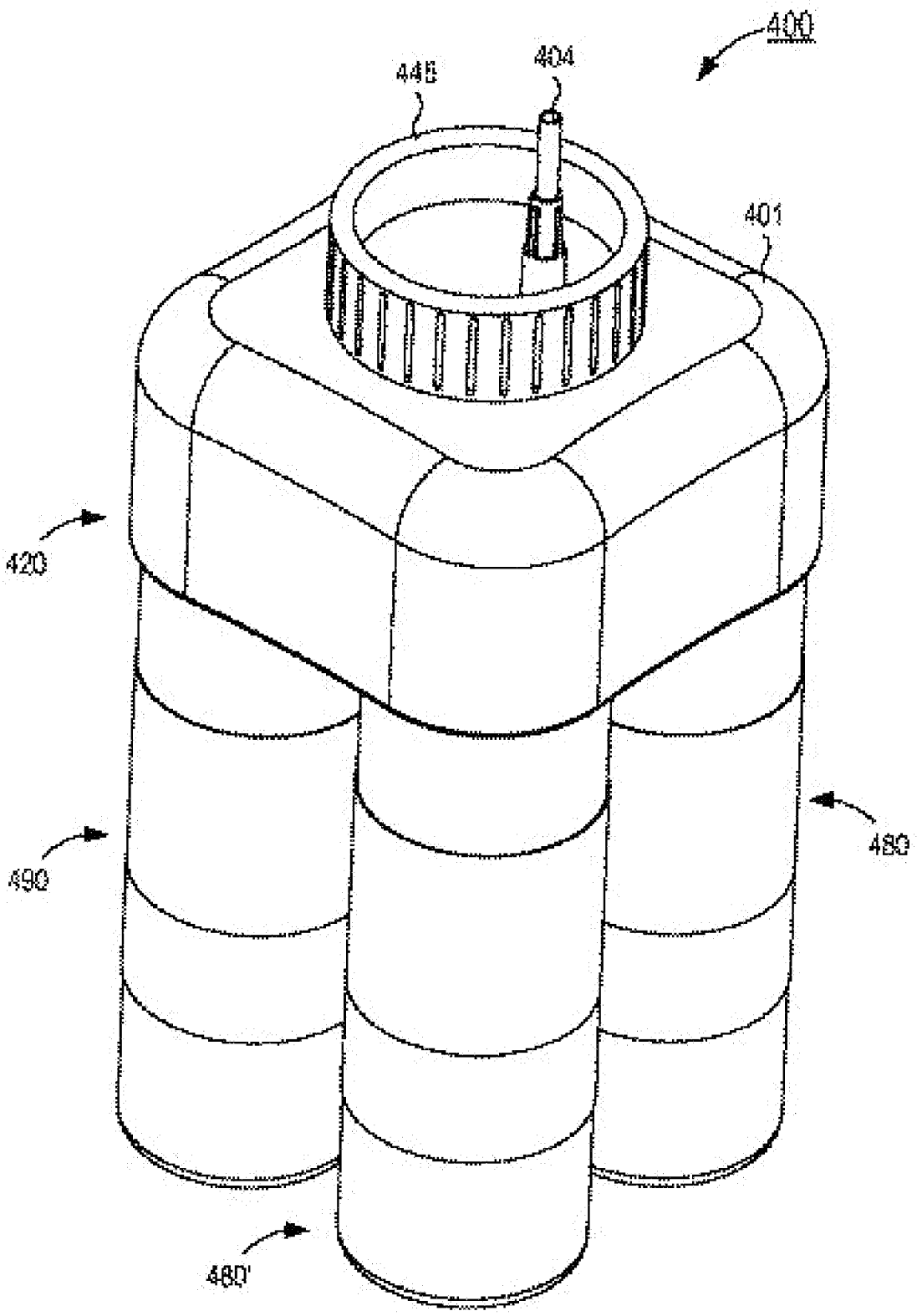

300
321
340
345
301
370
350
350'
350''
350'''
360
360'
360''
360'''
320
X_1
X_2
X_3

FIG. 14

[Fig. 15]

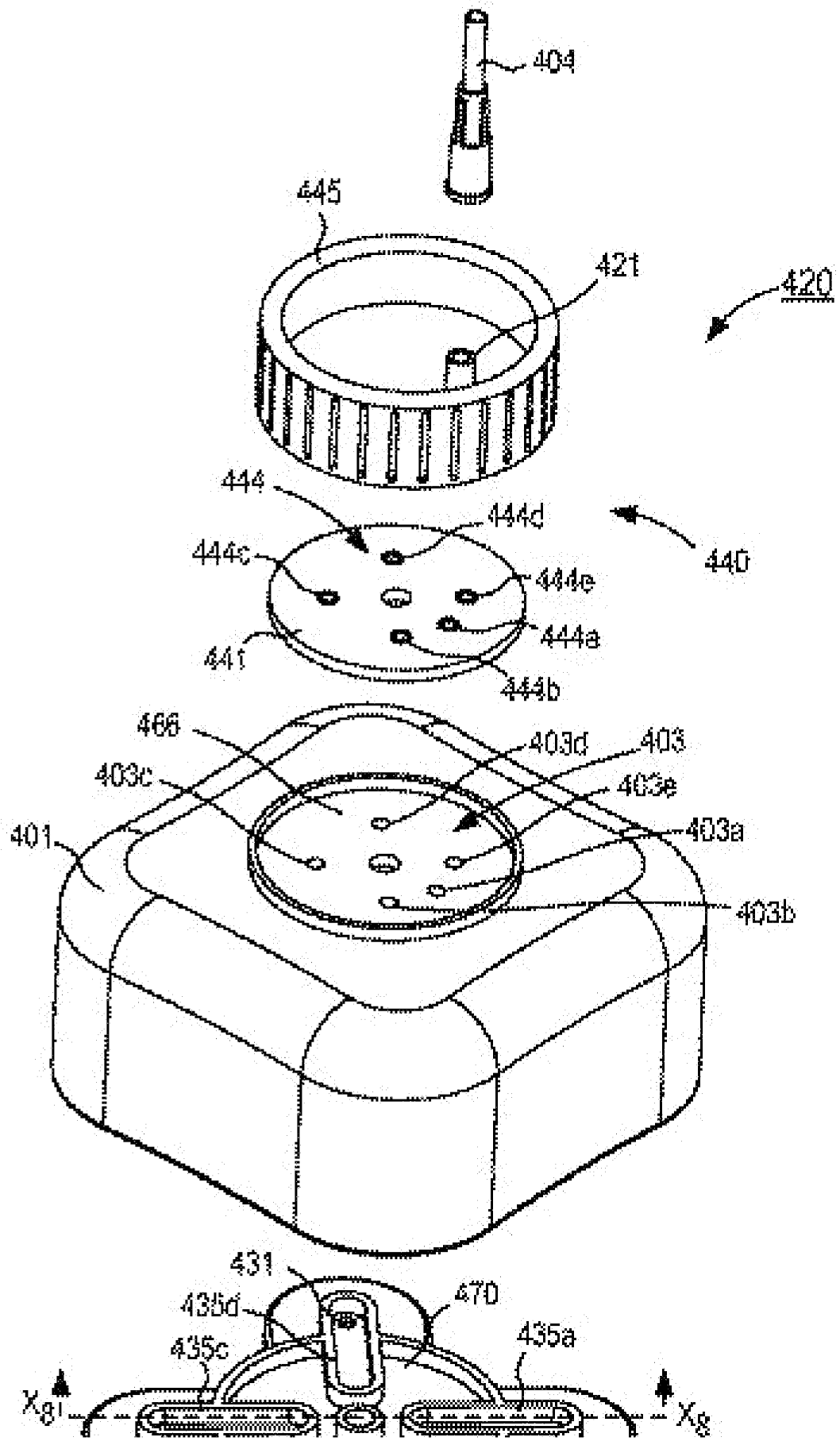

FIG. 15
340
321
301
301
370
345
329
348
331
350
336
332
350'
335
333
350"
334
350"
300
380
380'
390
390'

[Fig. 16]


400
404
401
420
490
480
480'

[Fig. 17]

FIG. 16


404
445
421
420
444
444d
444c
444e
440
444a
441
444b
466
403d
403
403c
403e
401
403a
403b
431
470
435d
435a
435c
X8
X8

[Fig. 18]

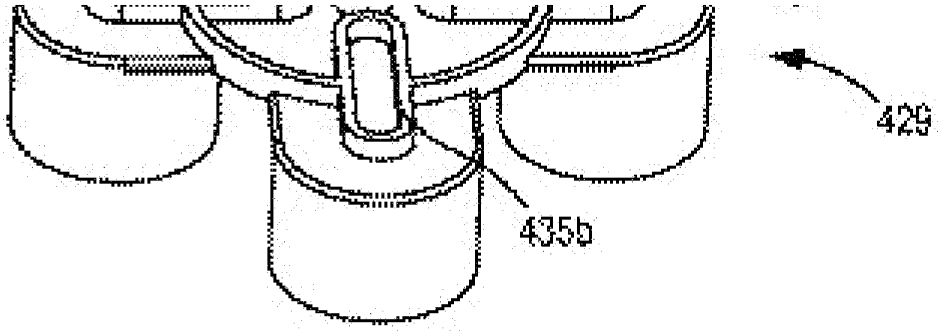


FIG. 17

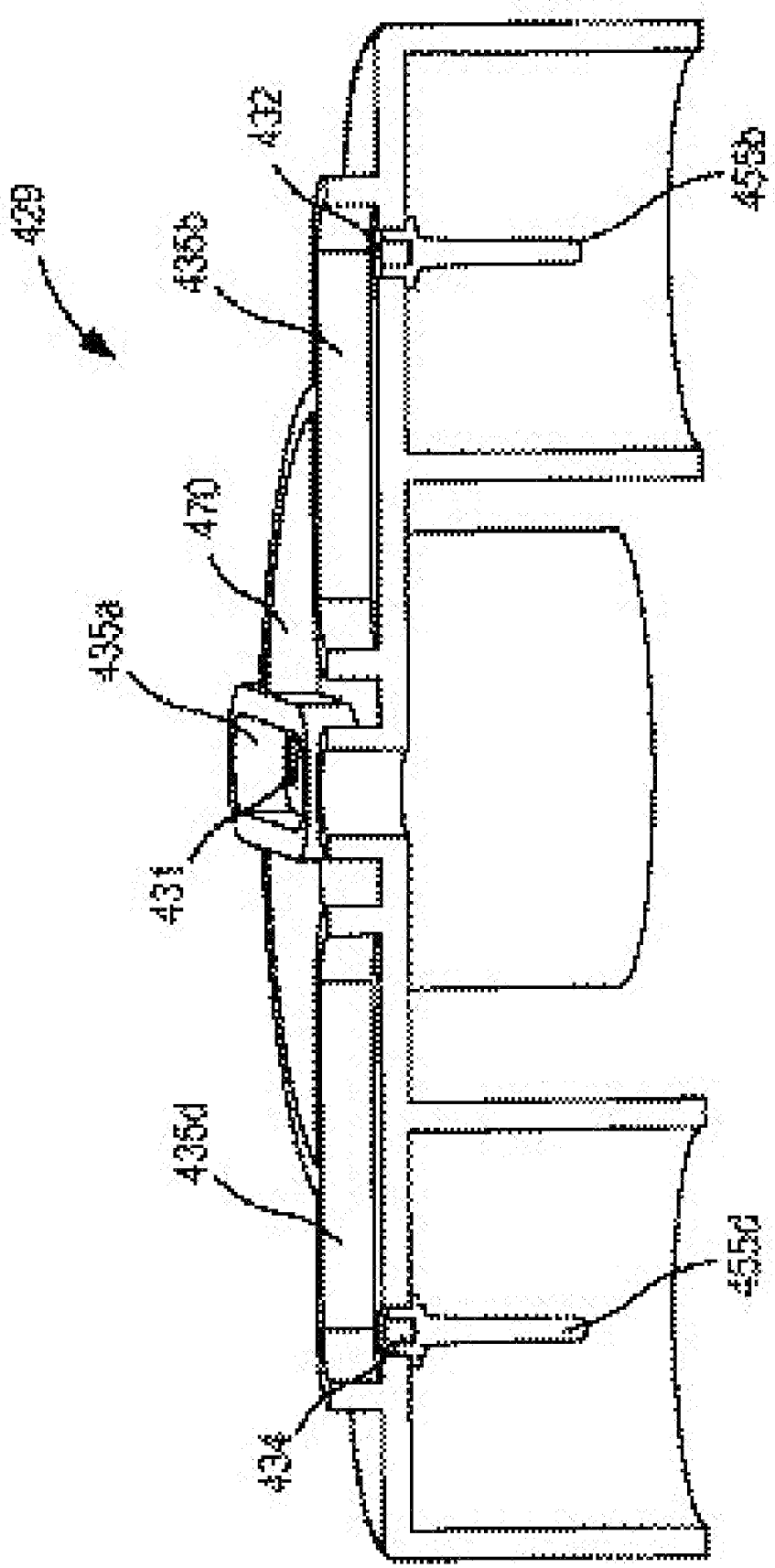


FIG. 18

[Fig. 19]

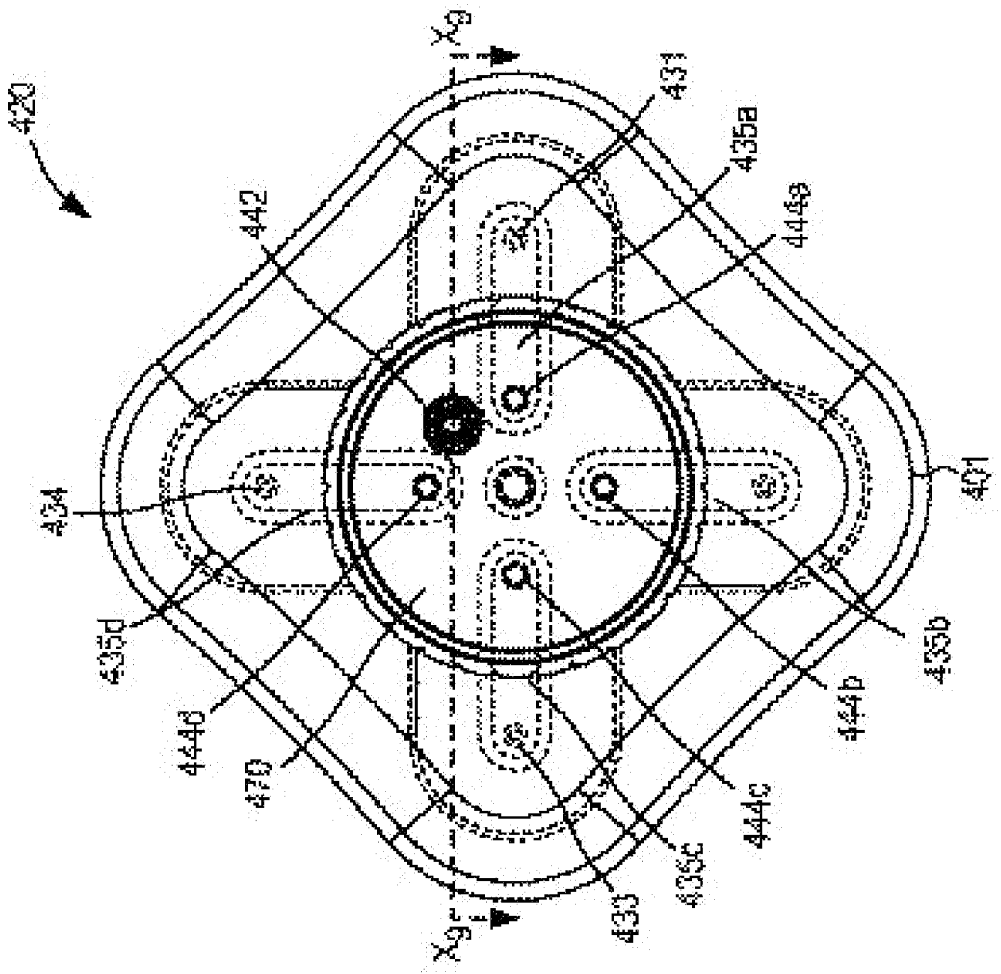


FIG. 19

[Fig. 20]

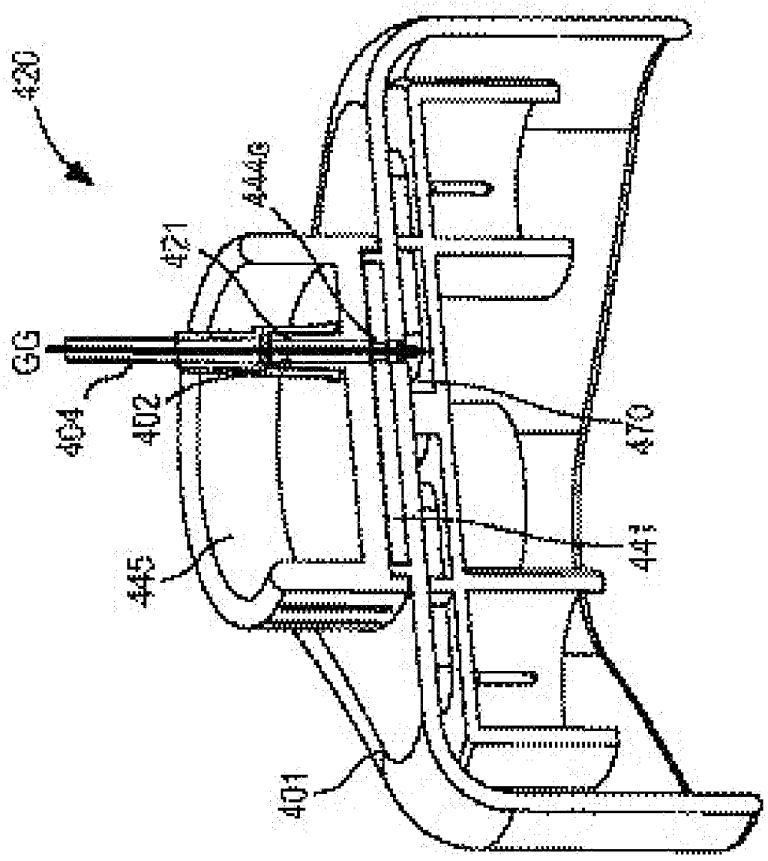


FIG. 20

[Fig. 21]

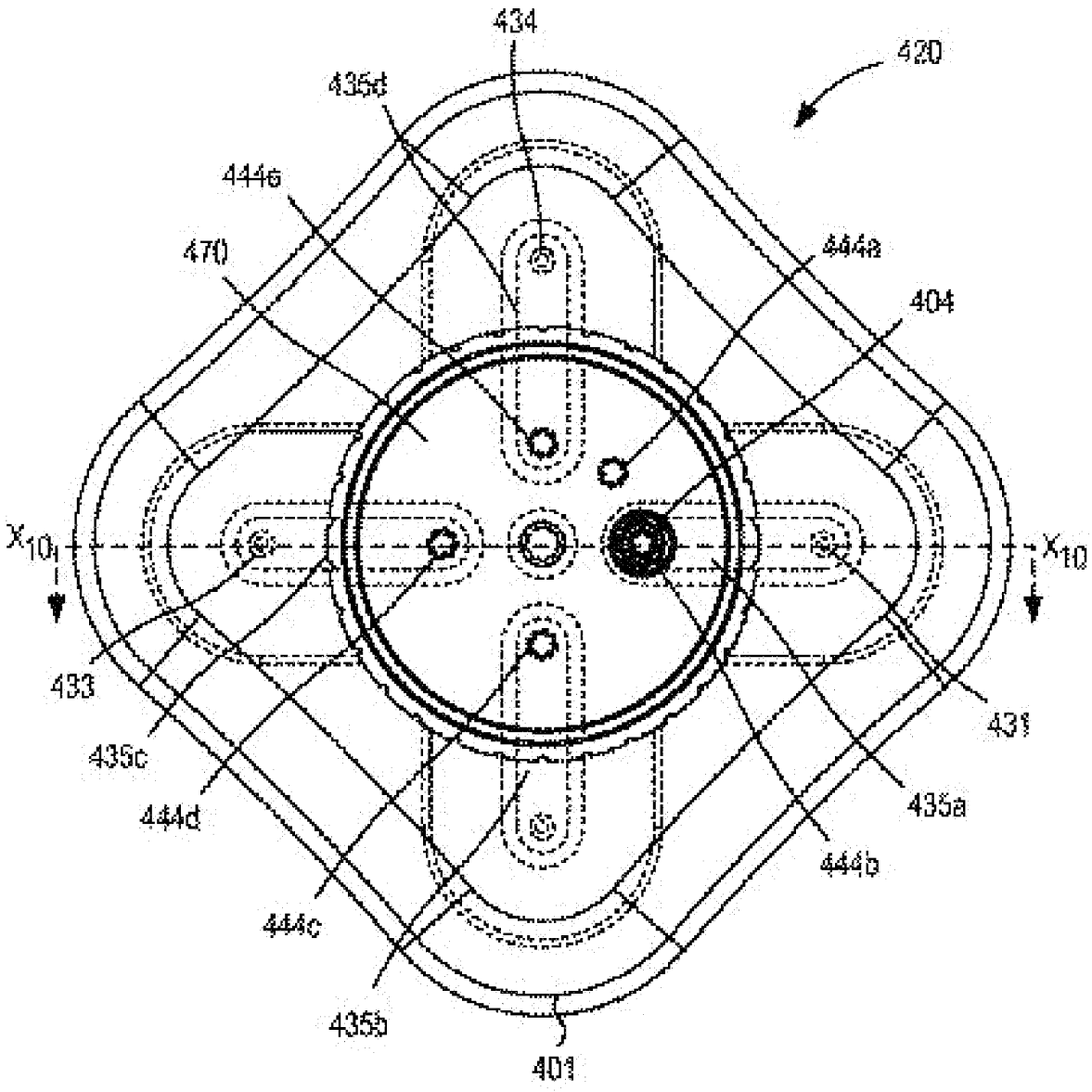
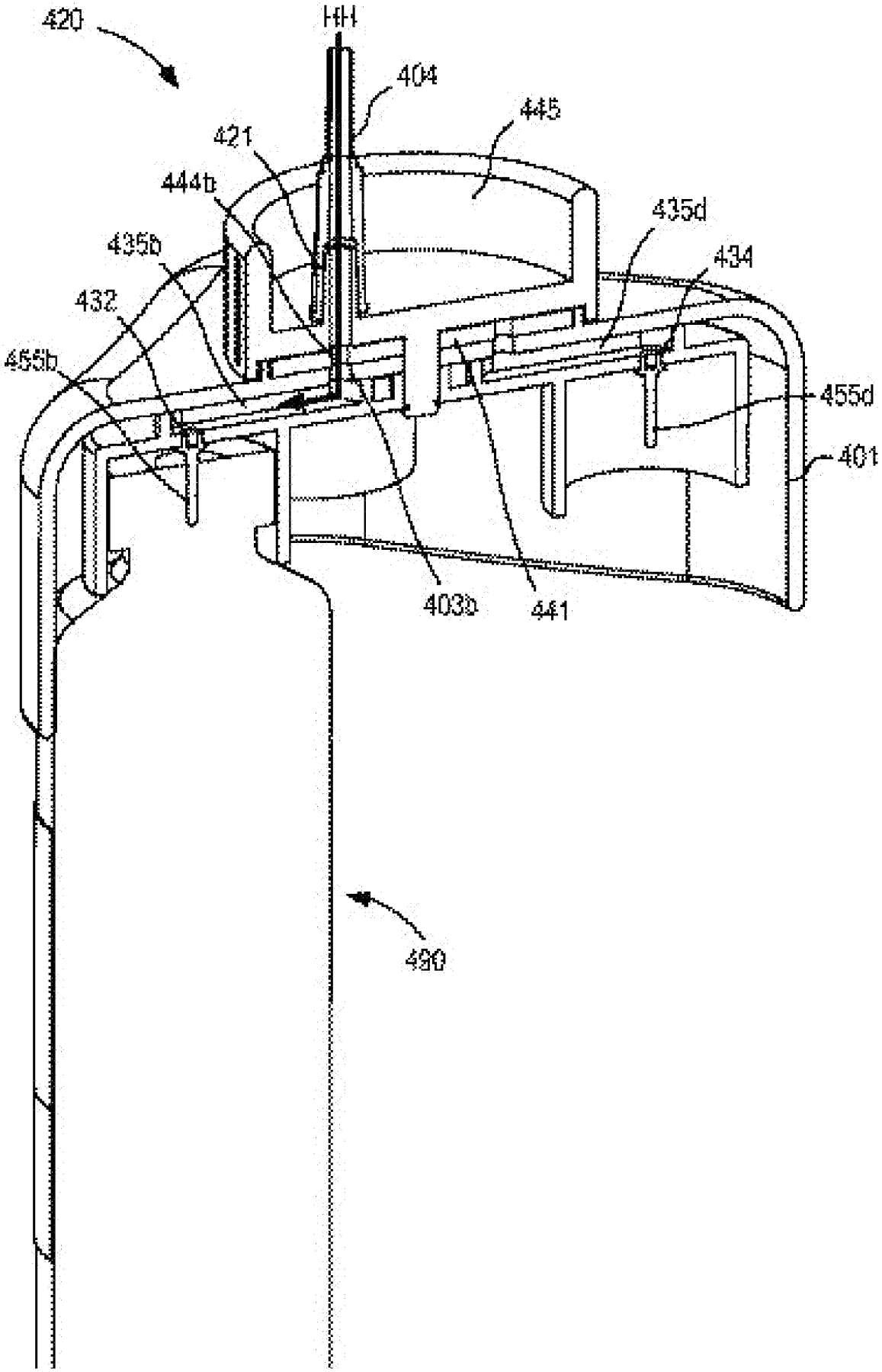

434
420
435d
444e
470
444a
404
X_{10}
X_{10}
433
439c
444d
431
435a
444b
444c
435b
401

FIG. 21

[Fig. 22]


420
HH
404
445
421
444b
435d
435b
434
432
455b
455d
401
403b
441
490

[Fig.23]

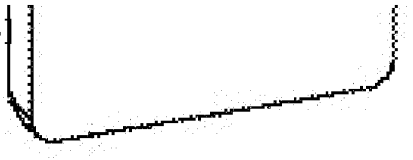
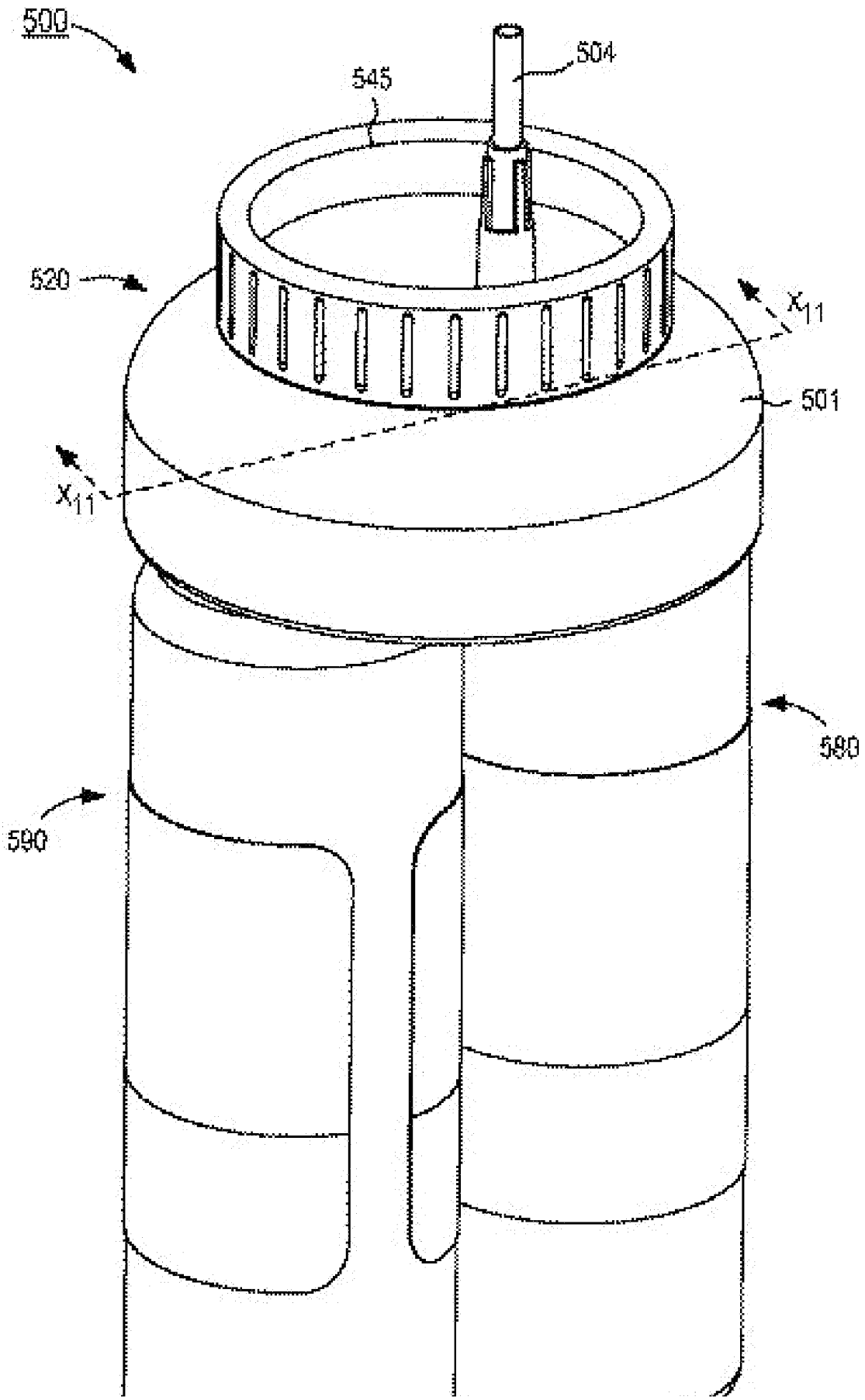


FIG. 22


500
504
545
520
X_{11}
501
X_{11}
580
590

[Fig.24]

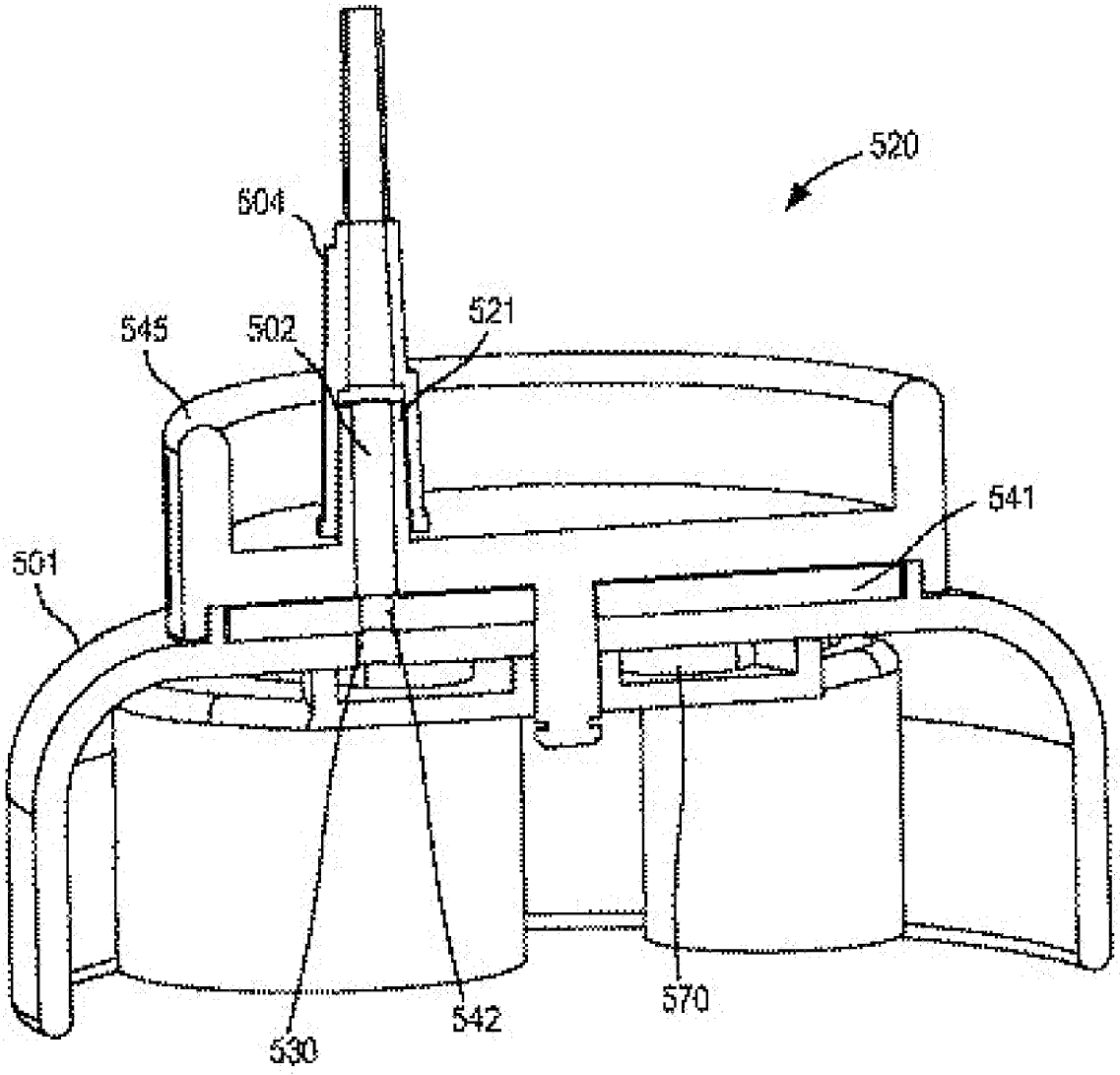
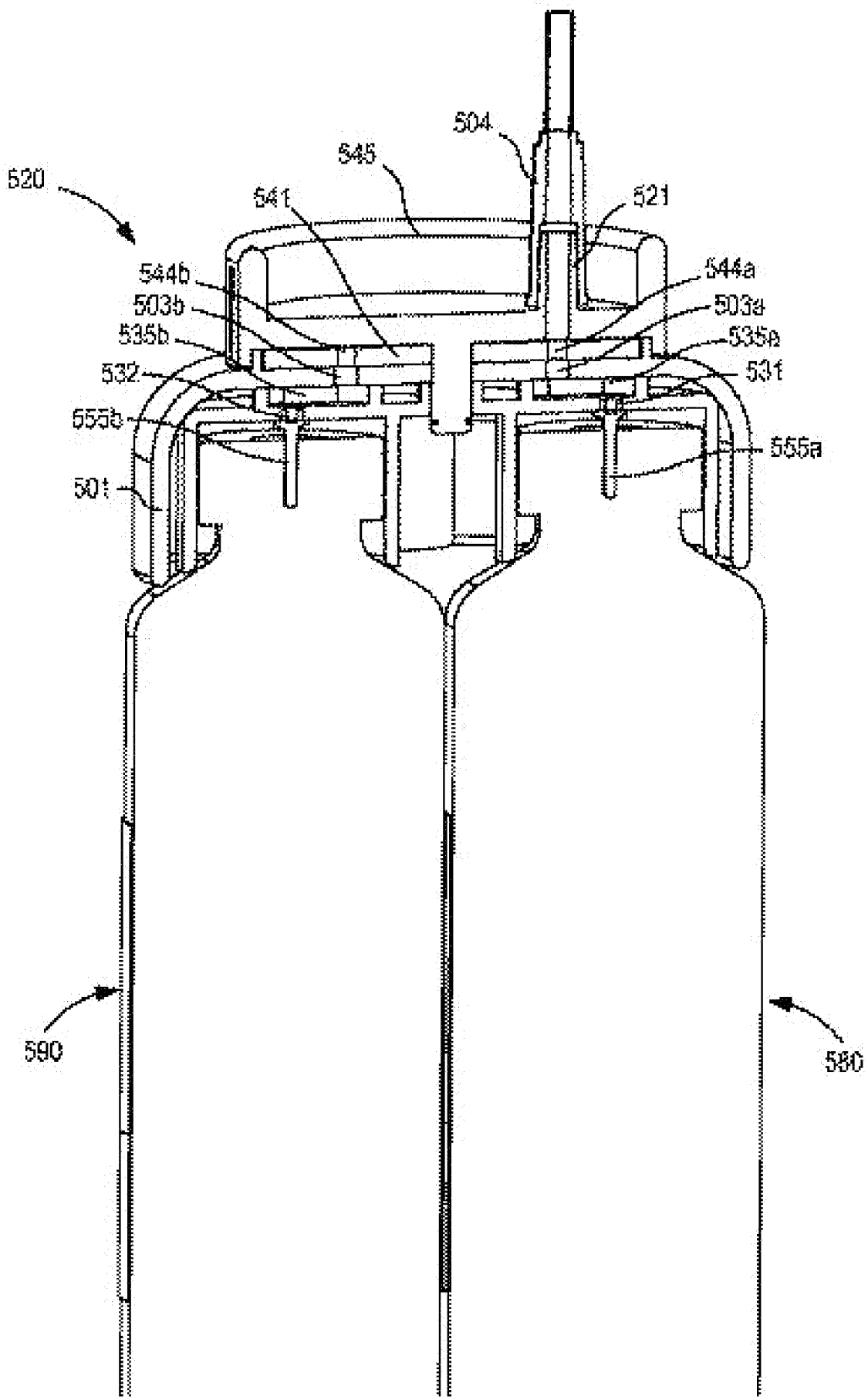


FIG. 24

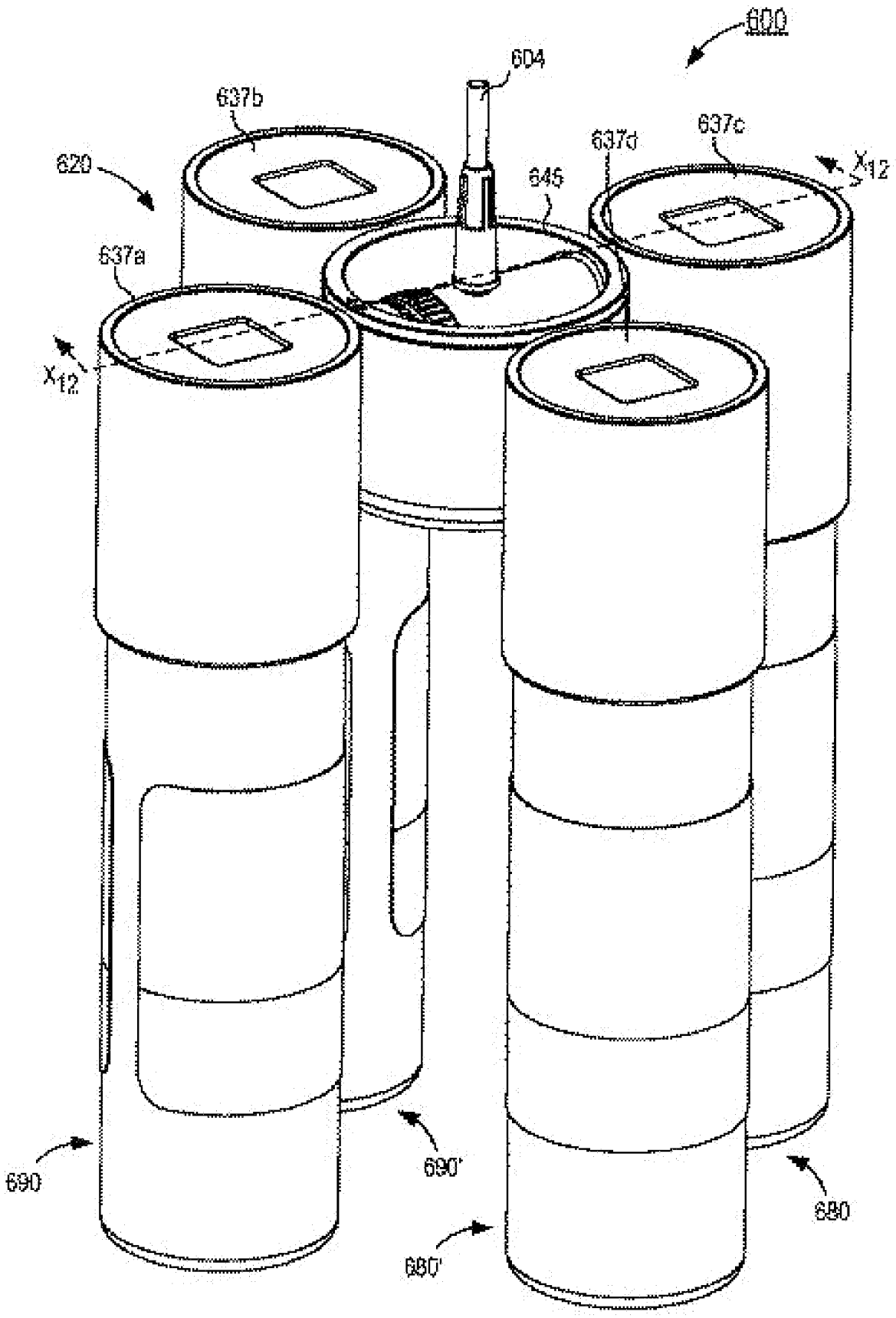
[Fig.25]


504
545
520
541
521
544b
544a
503b
503a
535b
535a
532
531
555b
555a
501
590
580

[Fig.26]



FIG. 25


600
604
637b
637d
637c
620
645
637a
X_{12}
X_{12}
690
690'
680
680'

[Fig.27]

FIG. 26

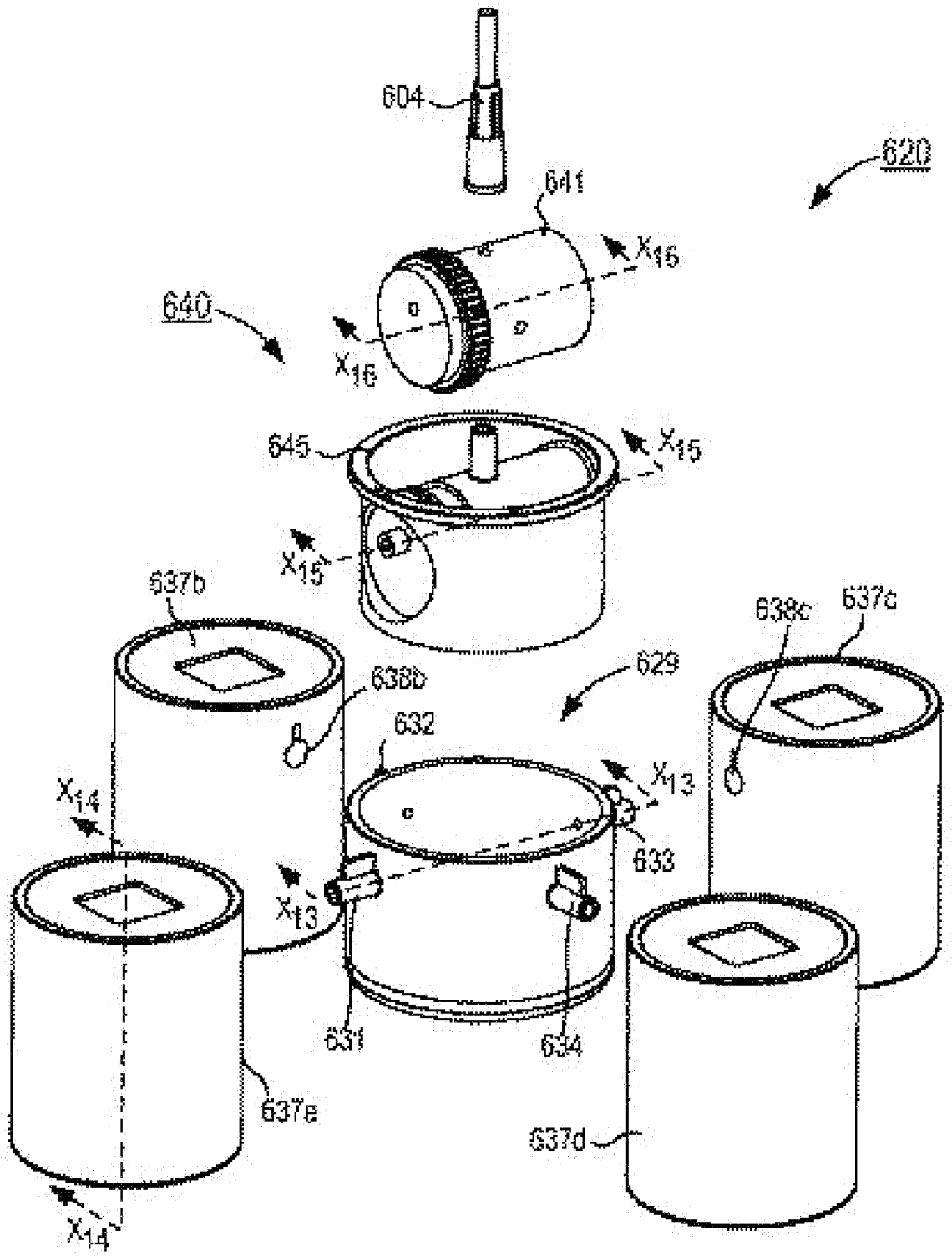
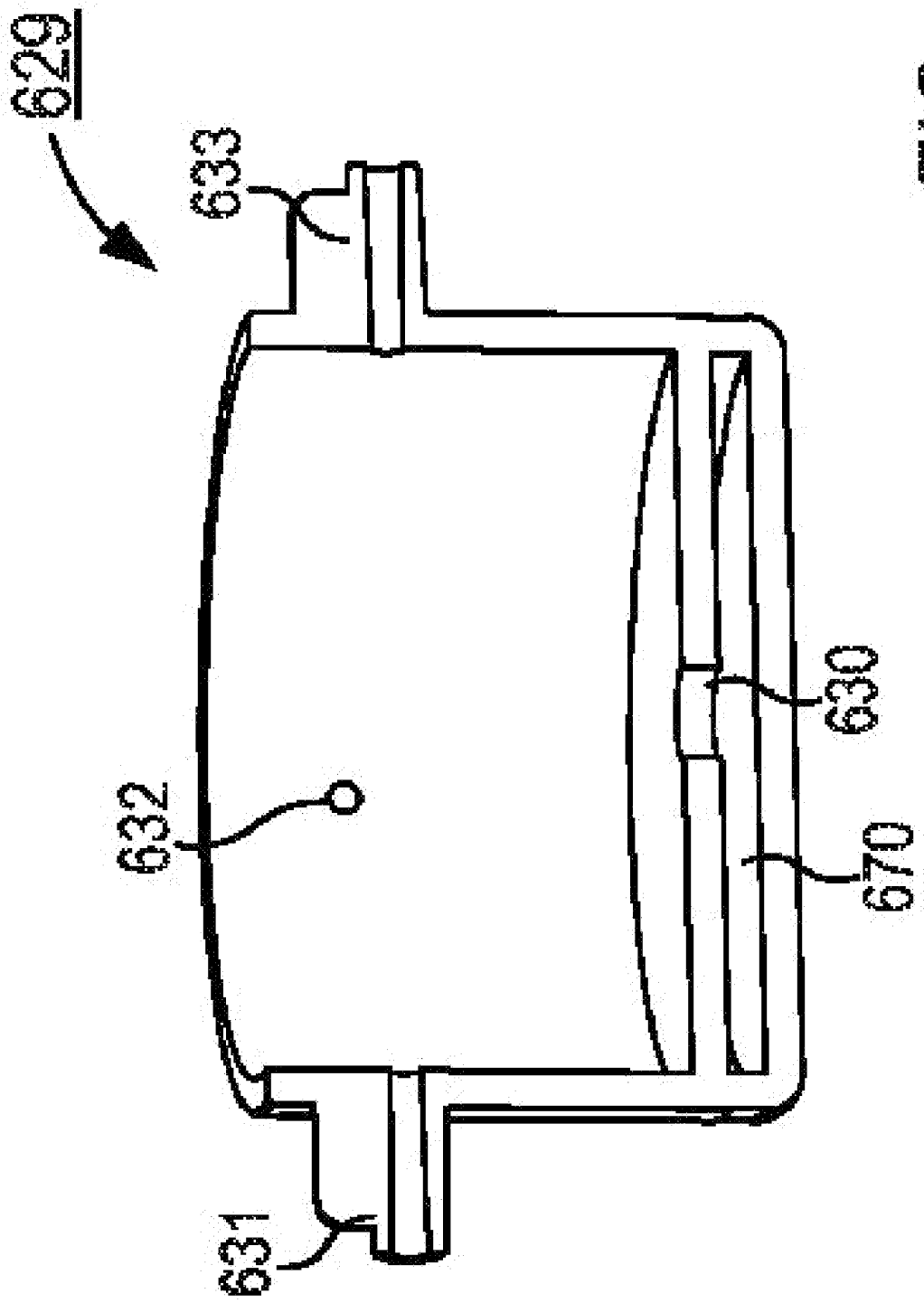

604
620
641
X_{16}
640
X_{16}
645
X_{15}
X_{15}
637b
638c
637c
638b
629
632
X_{14}
X_{13}
633
X_{13}
631
634
637e
637d
X_{14}

FIG. 27

[Fig.28]

FIG. 28



[Fig.29]

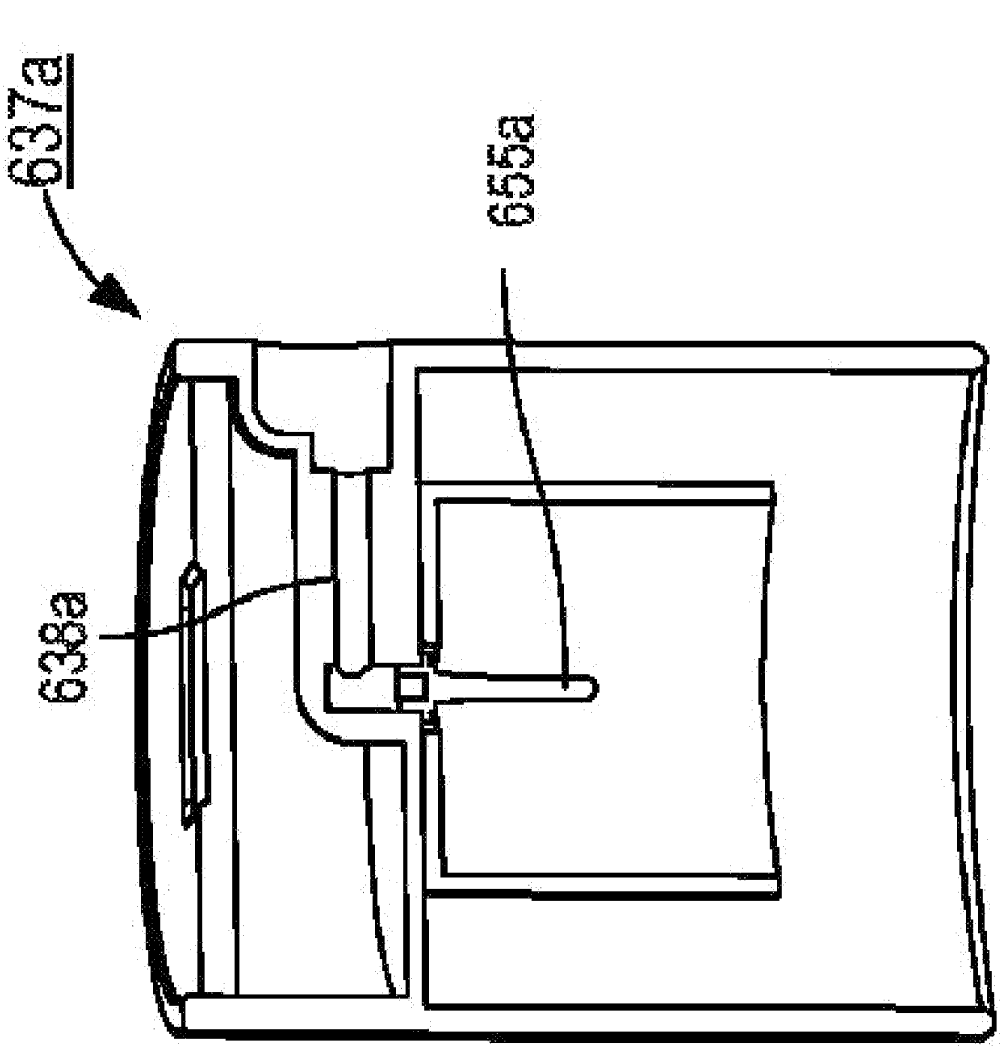
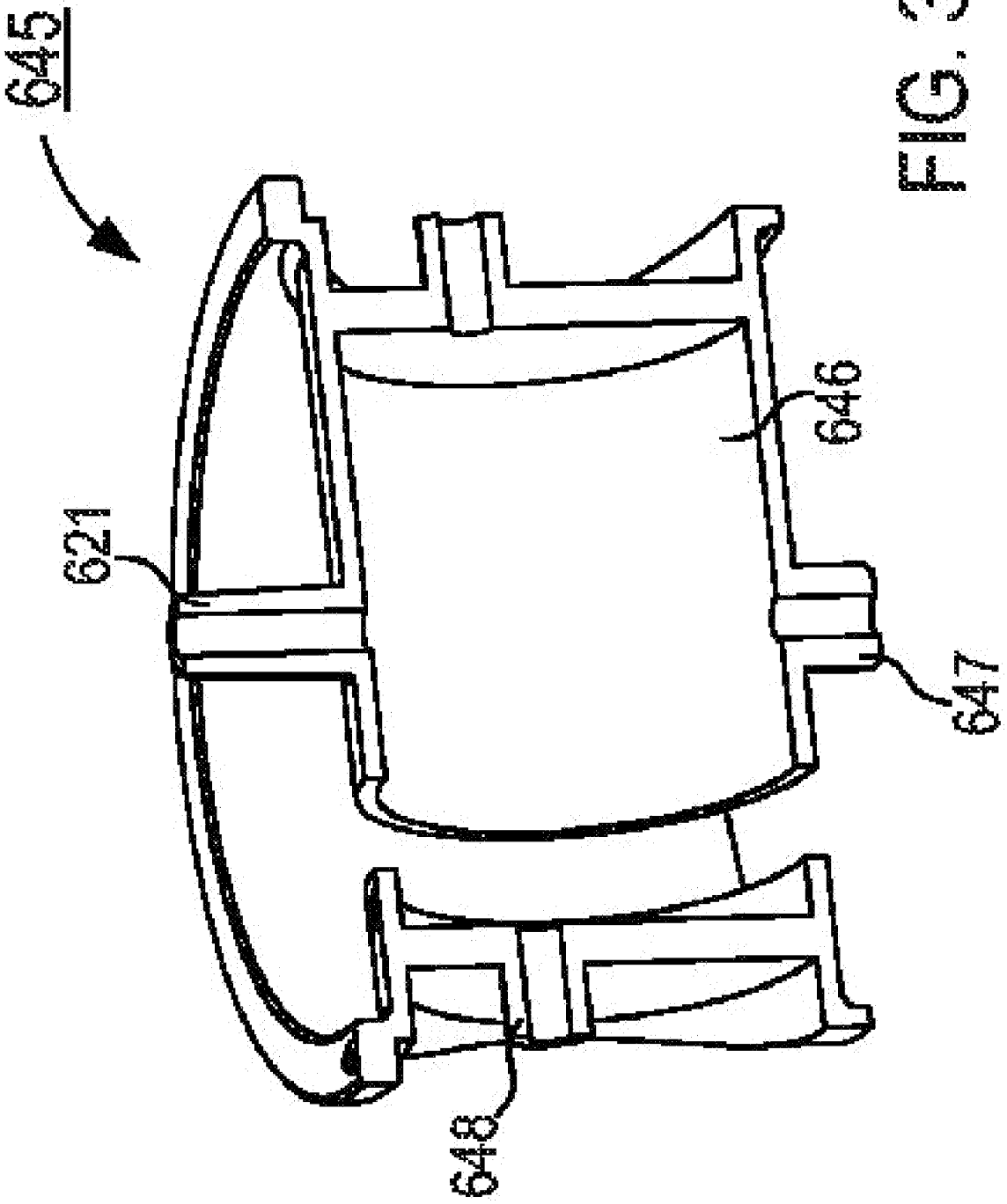


FIG. 29

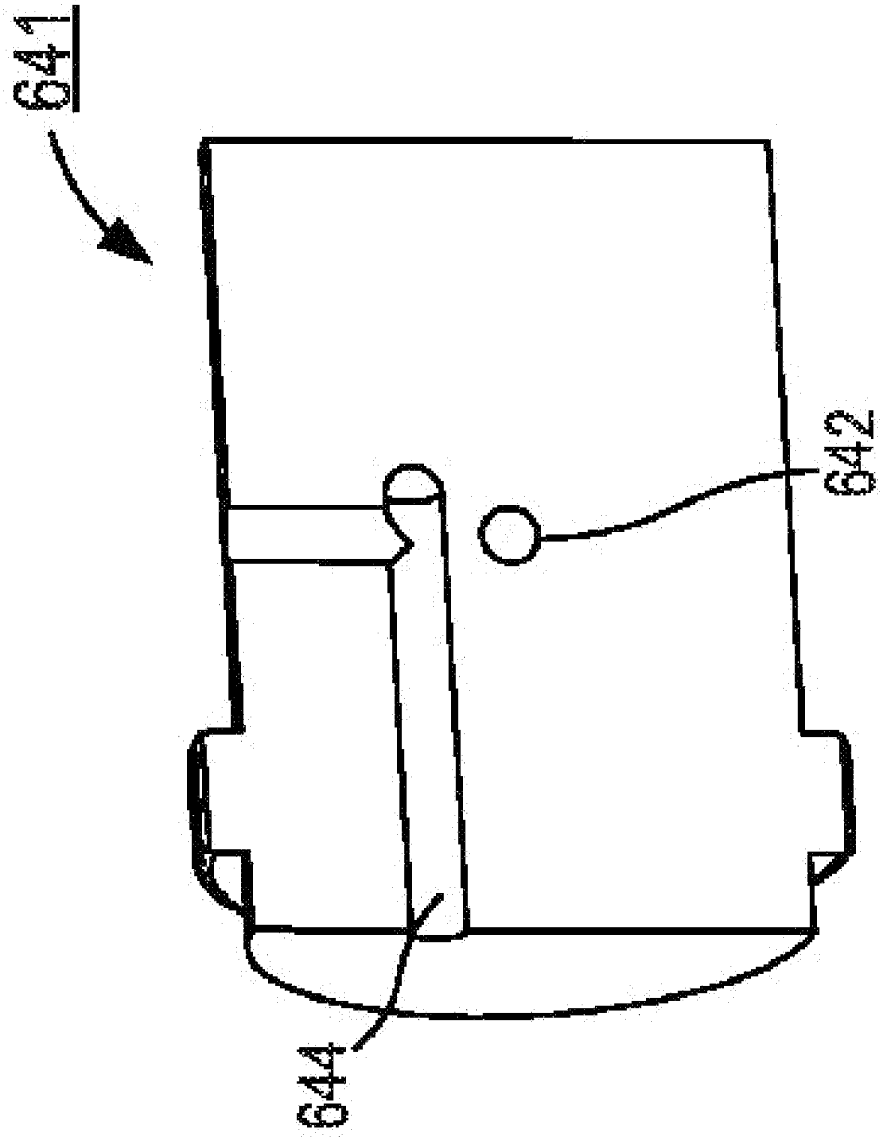
[Fig. 30]

FIG. 30



[Fig. 31]

FIG. 31



[Fig. 32]

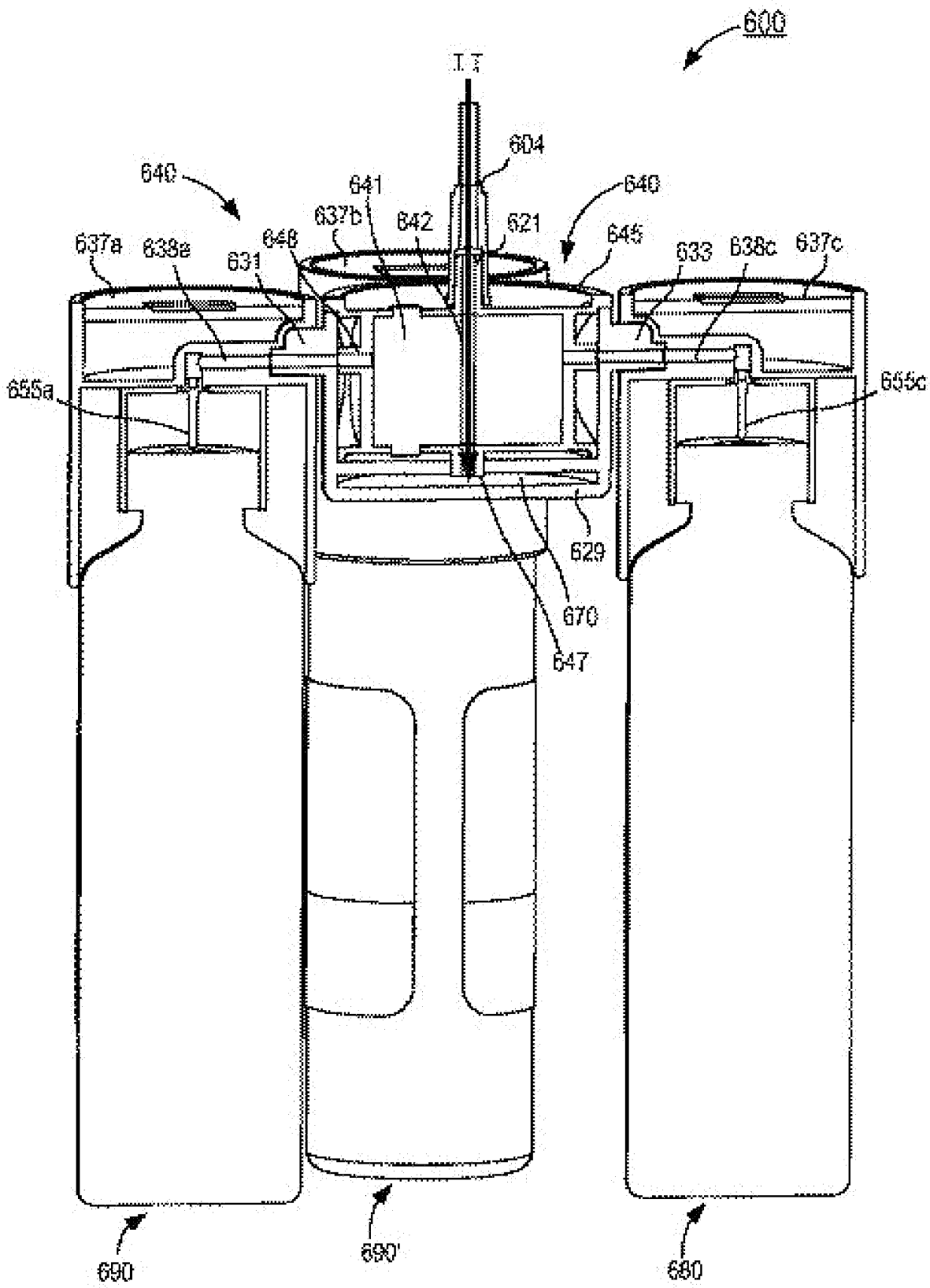

600
T.T
604
640
641
637b
642
621
640
637a
638a
648
631
645
633
638c
637c
655a
655c
629
670
647
690
690'
680

FIG. 32

[Fig. 33]

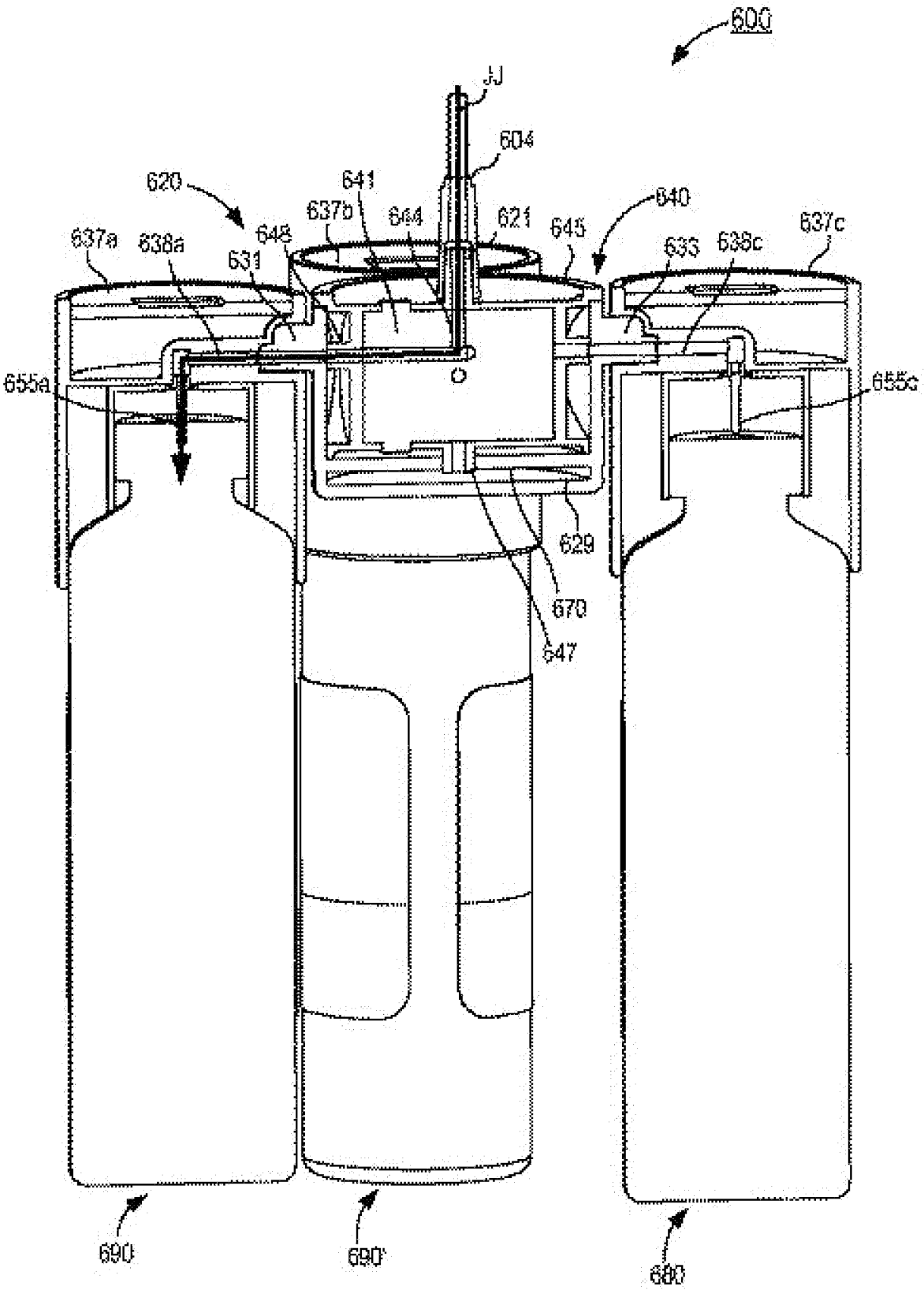
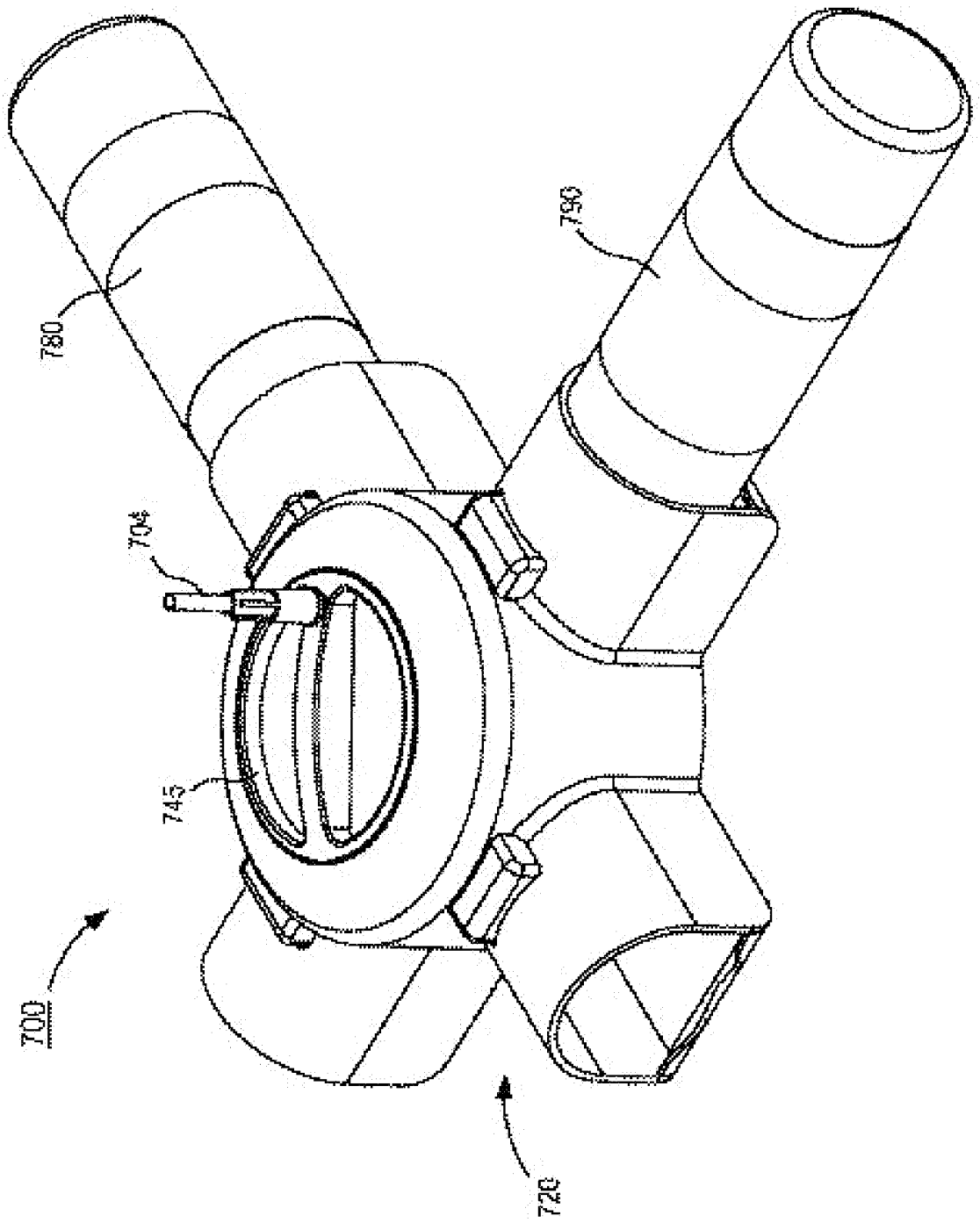

600
JJ
604
620
641
637b
644
621
645
640
637c
637a
638a
648
631
633
638c
655a
655c
629
670
647
690
690'
680

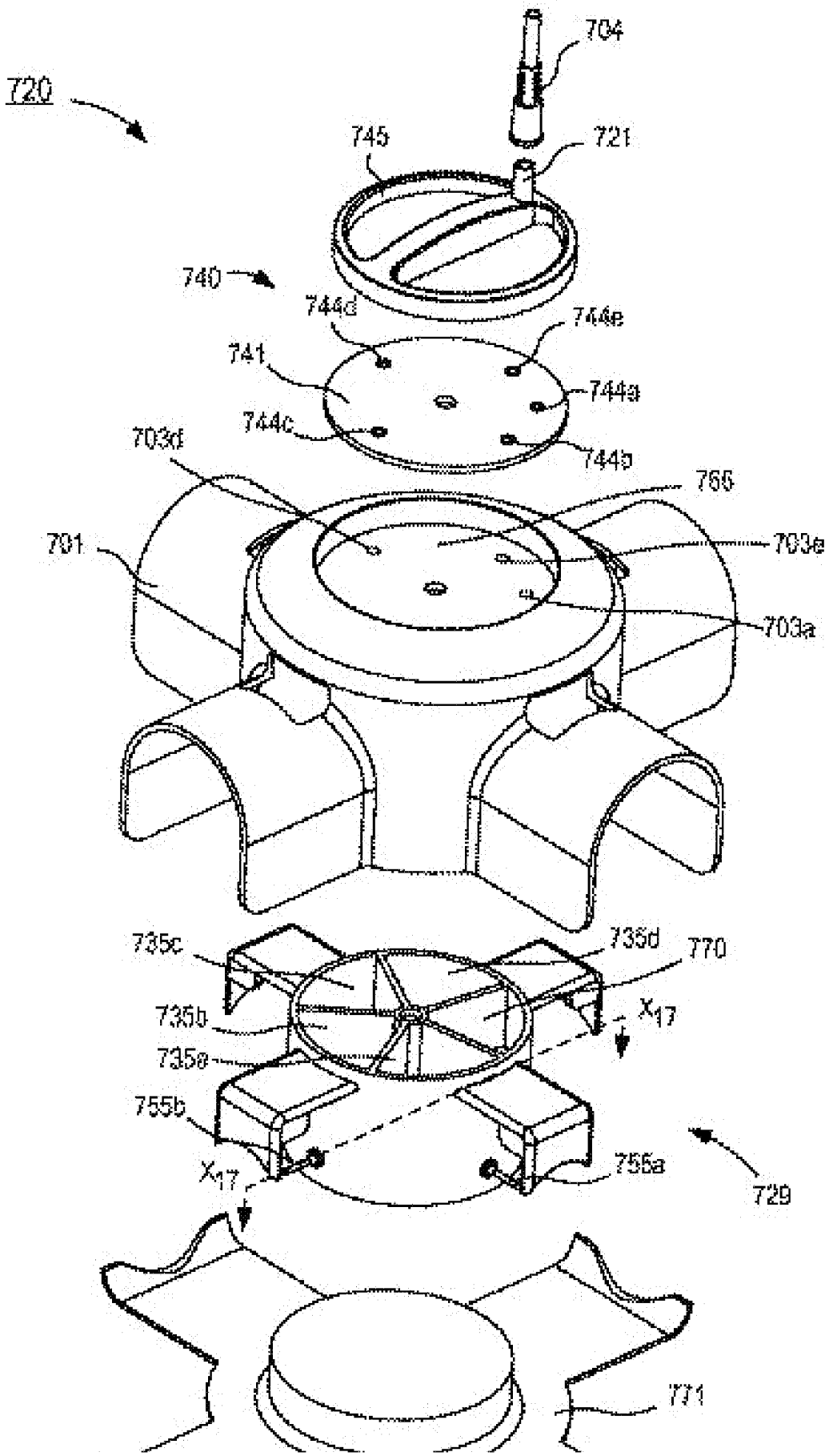
FIG. 33

[Fig. 34]

FIG. 34



[Fig.35]


720
704
745
721
740
744d
744e
741
744a
744c
744b
703f
766
701
703e
703a
735c
735d
770
735b
735a
X_{17}
755b
755a
729
771

[Fig. 36]

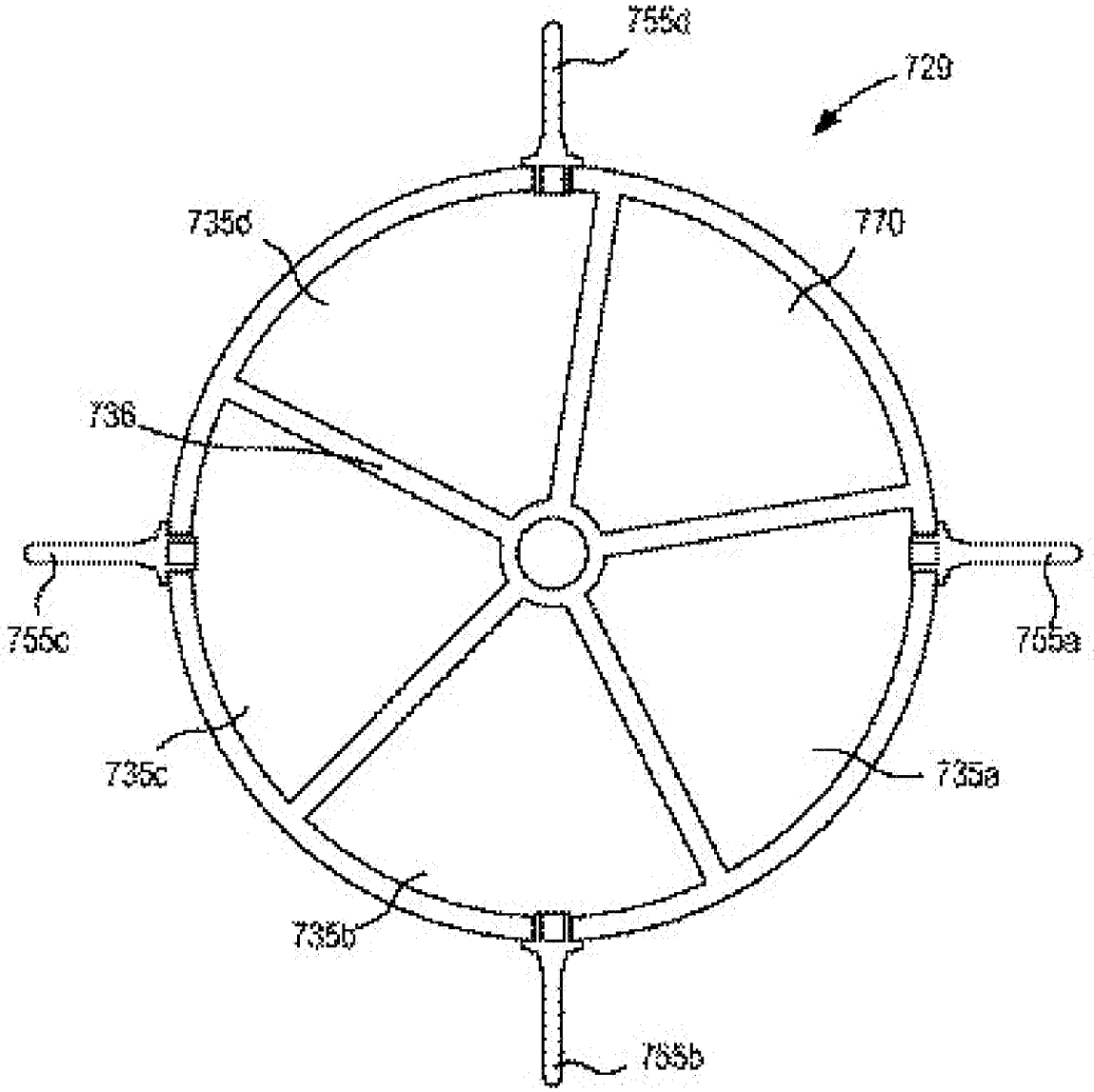


FIG. 36

[Fig. 37]

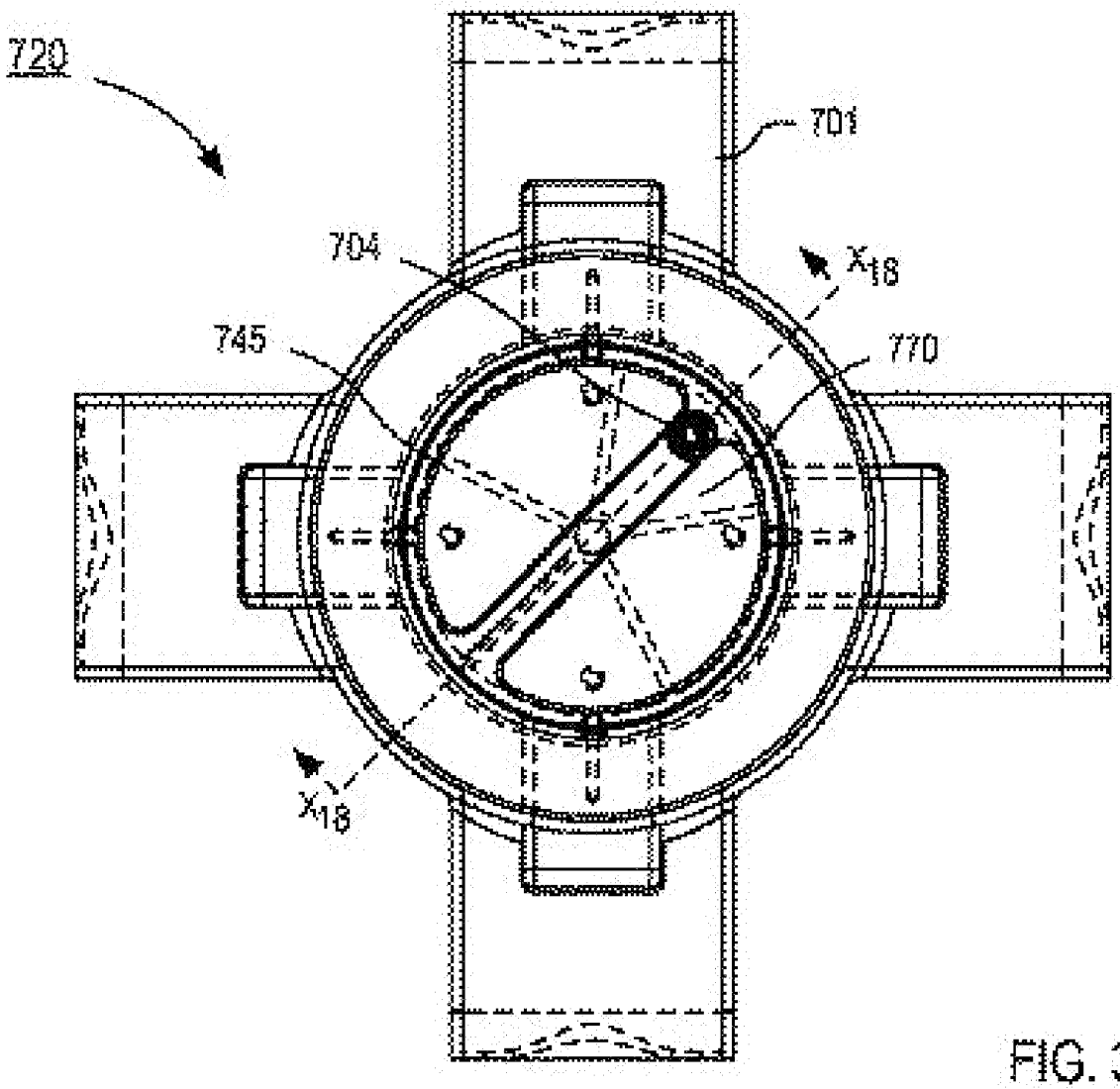


FIG. 37

[Fig. 38]

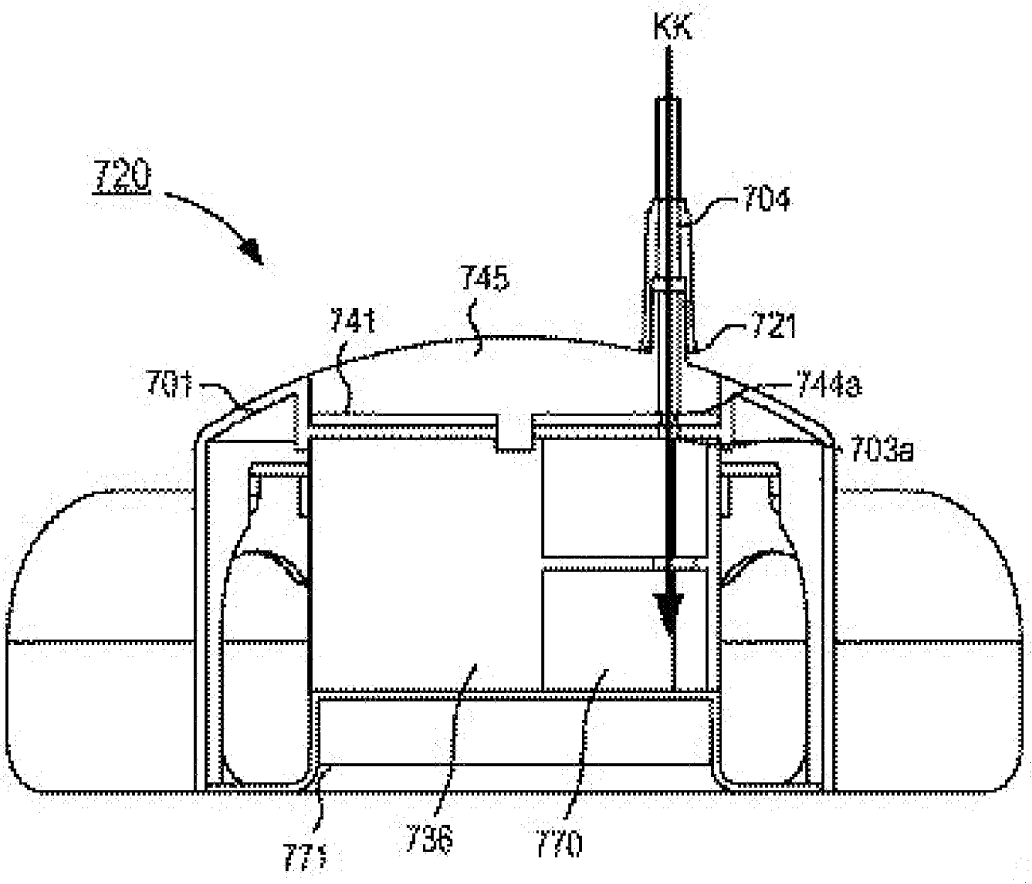


FIG. 38

[Fig.39]

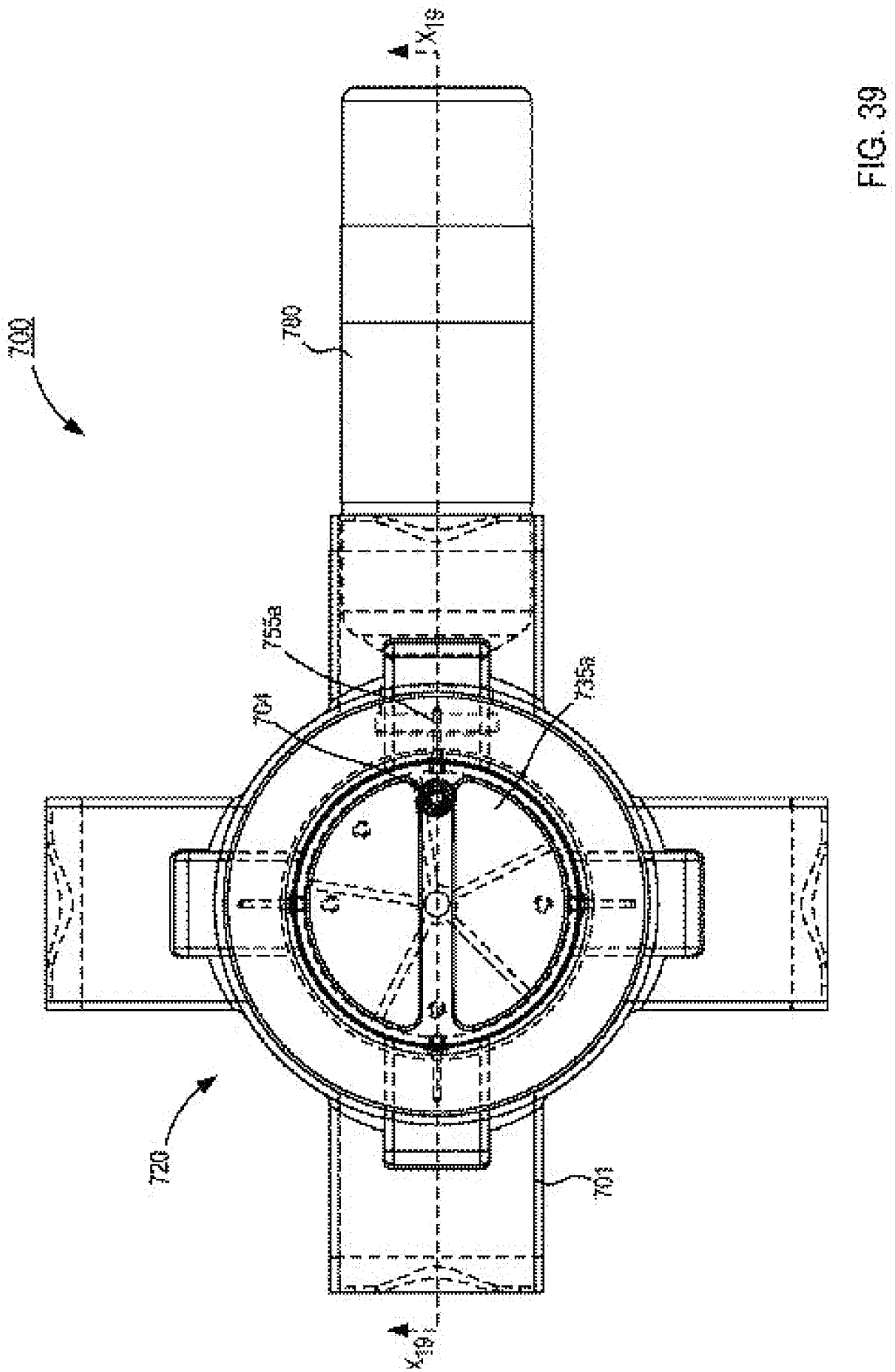


FIG. 39

[Fig. 40]

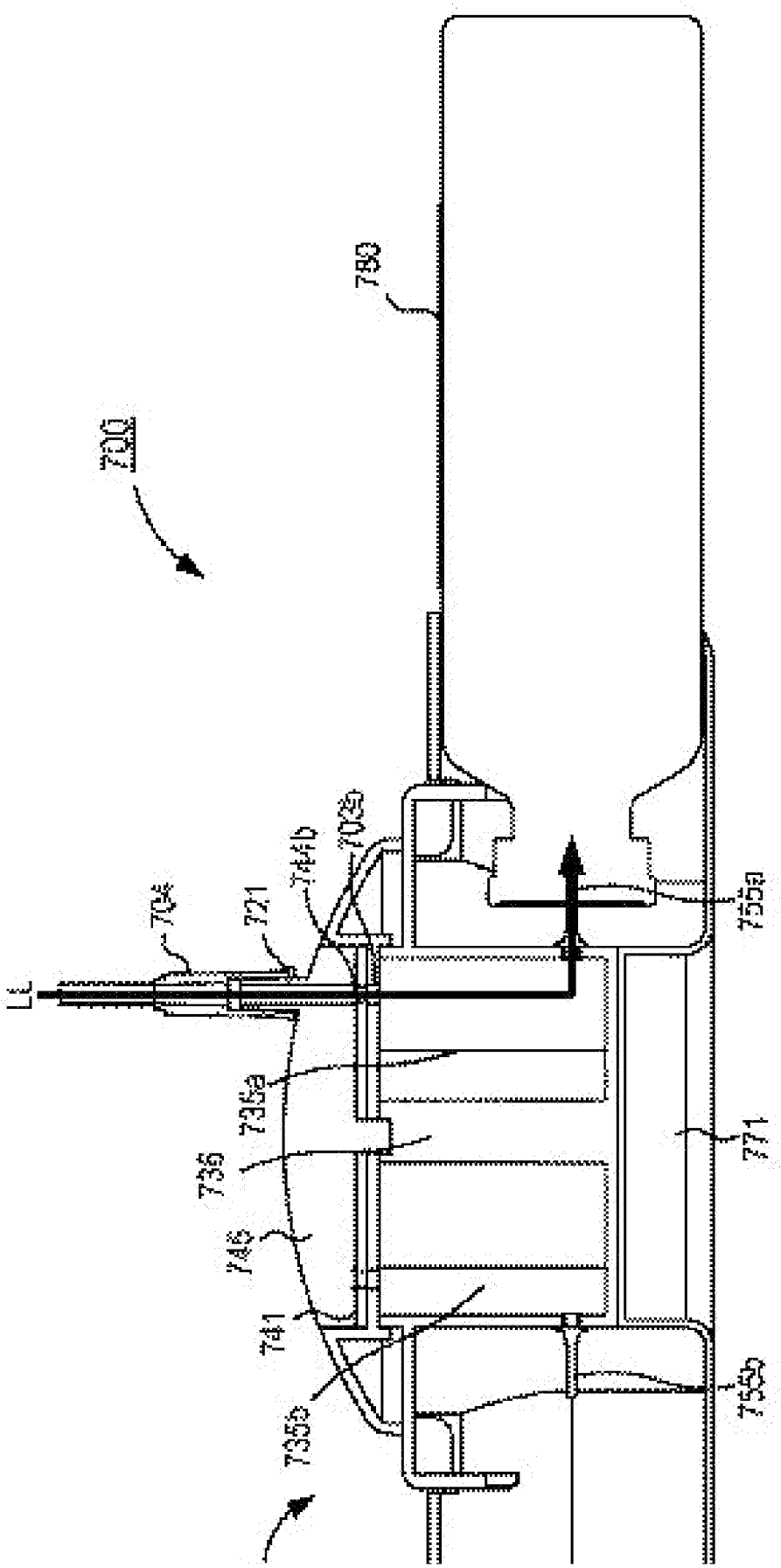
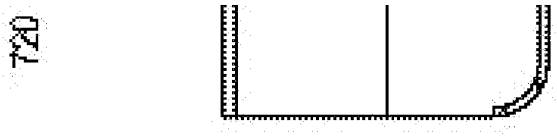
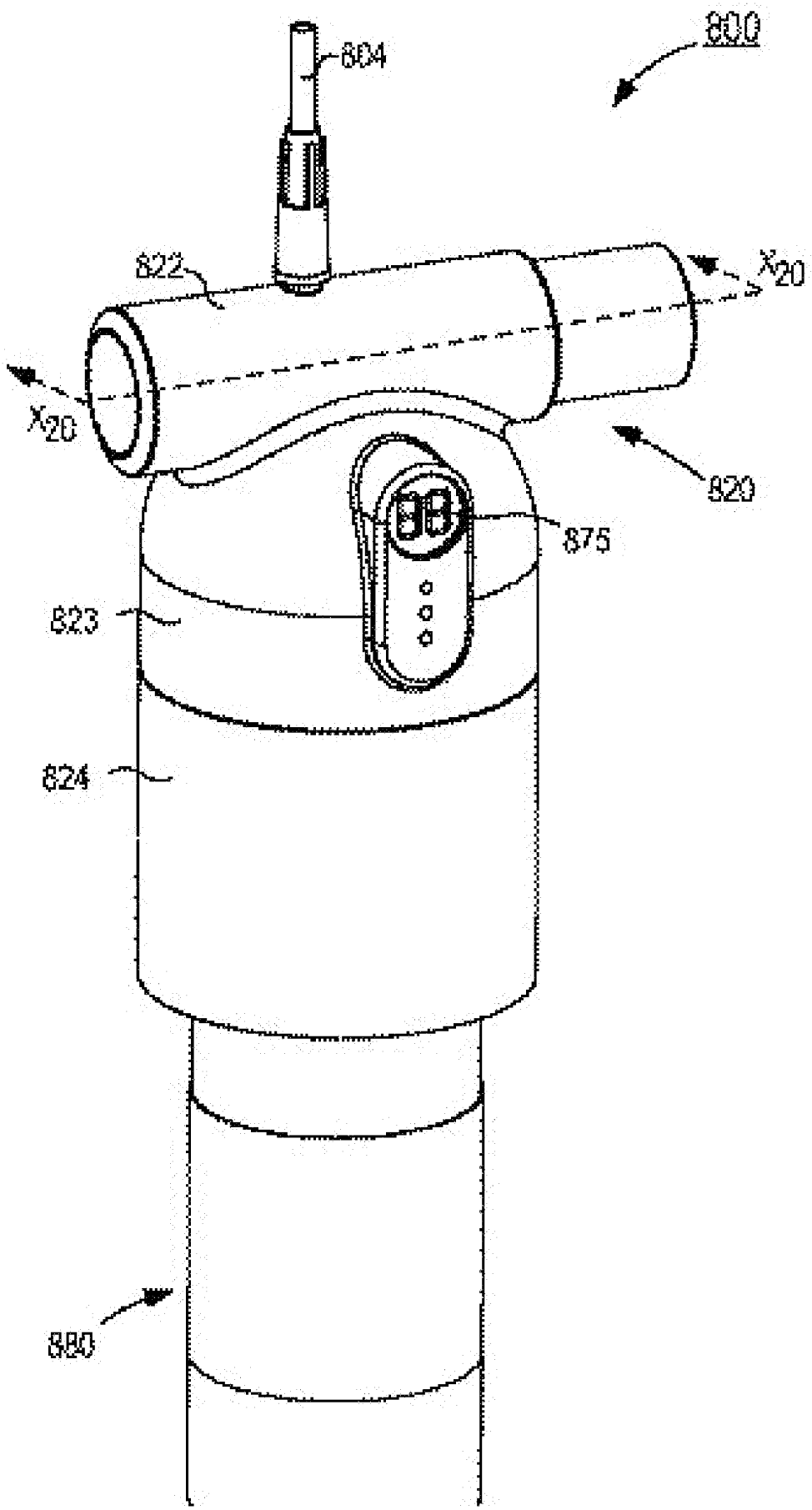

700
780
703a
744b
721
704
LL
735a
735
746
741
735b
735a
771
755b

FIG. 40

[Fig. 41]




800
804
822
X20
X20
820
875
823
824
880

[Fig. 42]

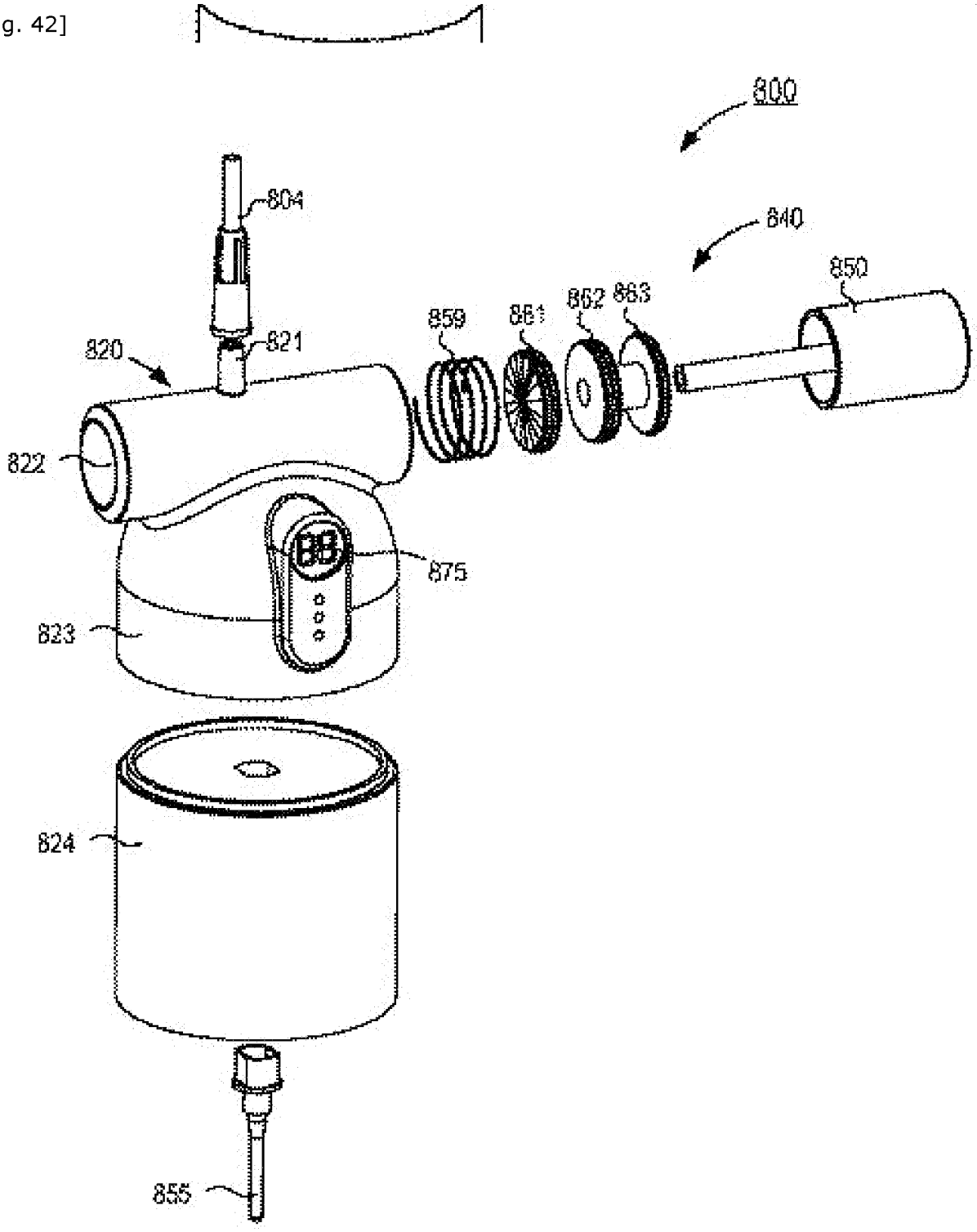
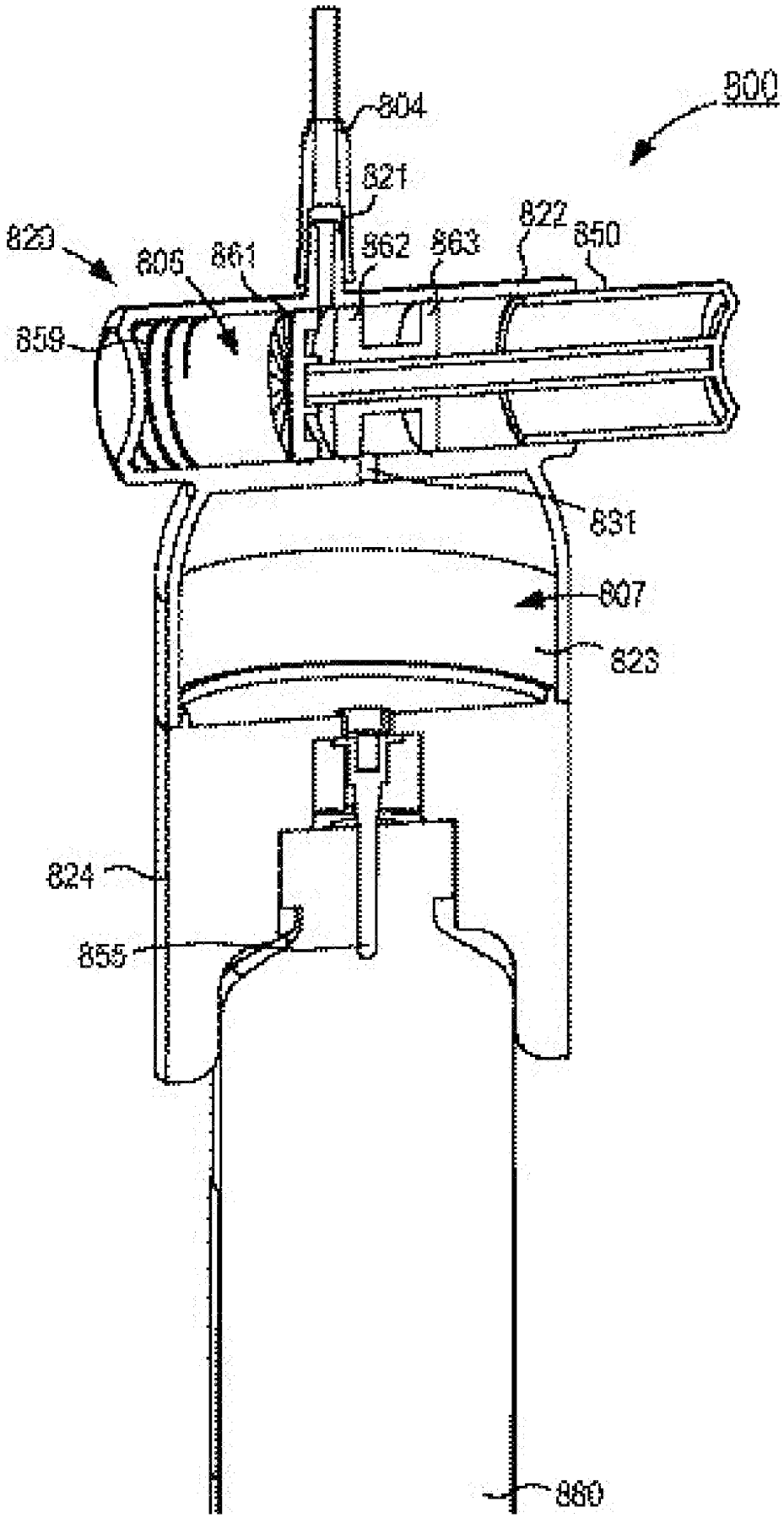


FIG. 42

[Fig. 43]


800
804
821
822
850
820
805
861
862
863
859
831
807
823
824
855
860

[Fig. 44]

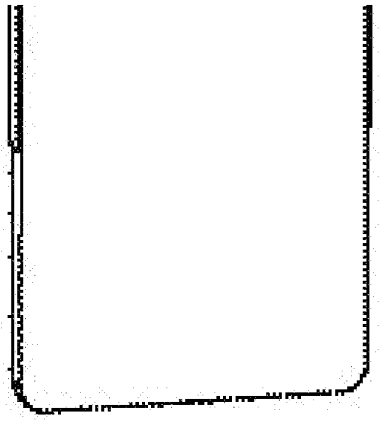
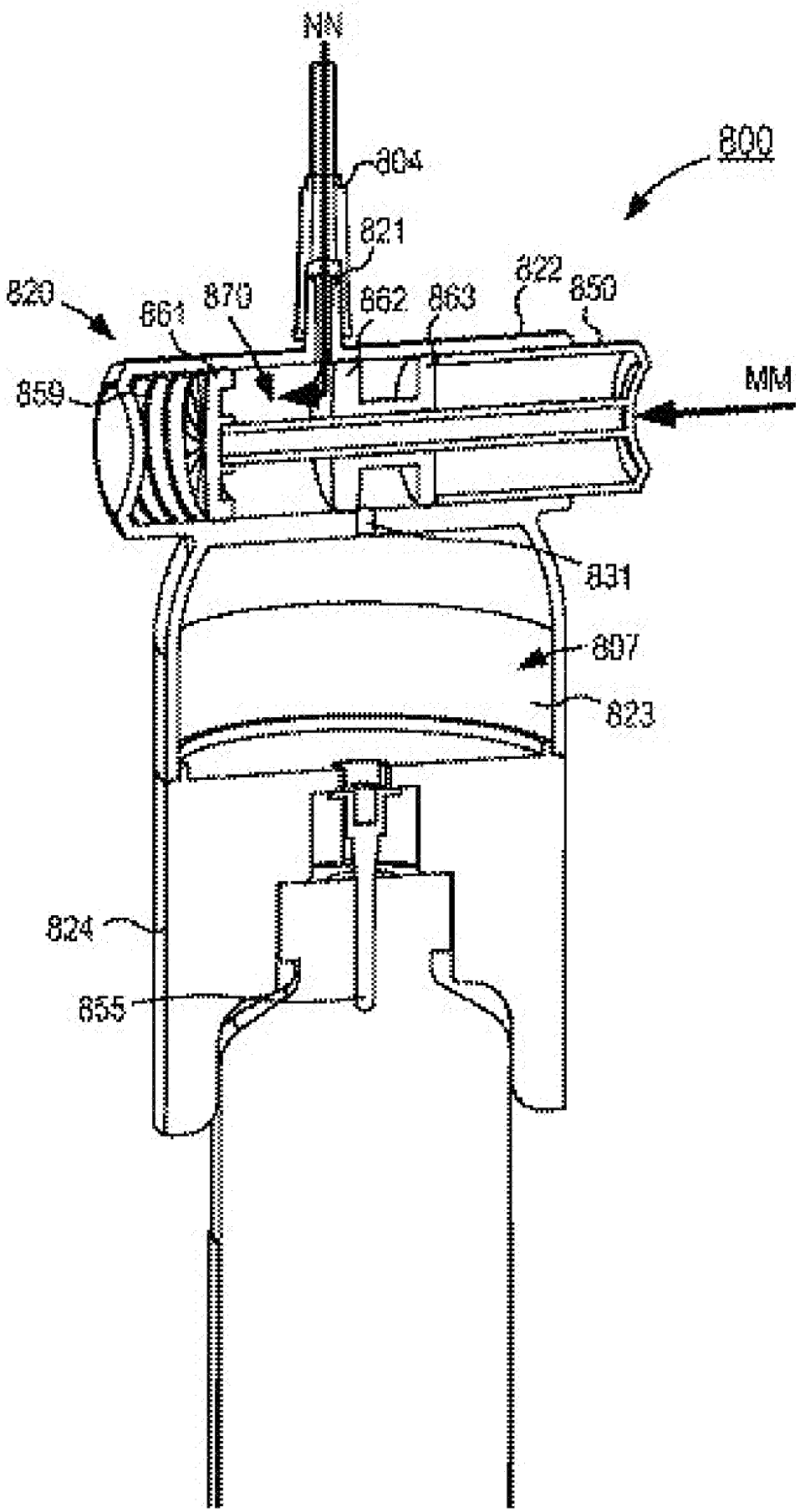


FIG. 43


NN
800
804
821
822
850
820
661
870
862
863
859
MM
831
807
823
824
855

[Fig. 45]

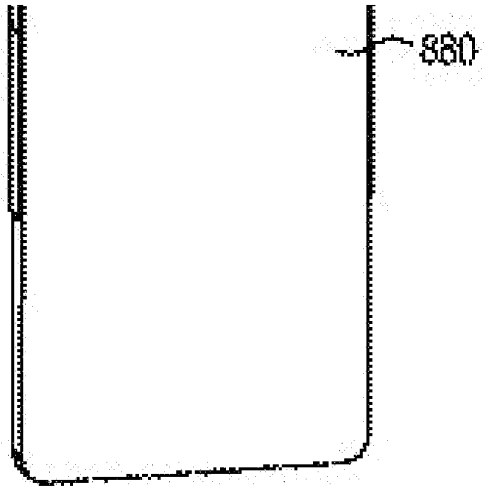
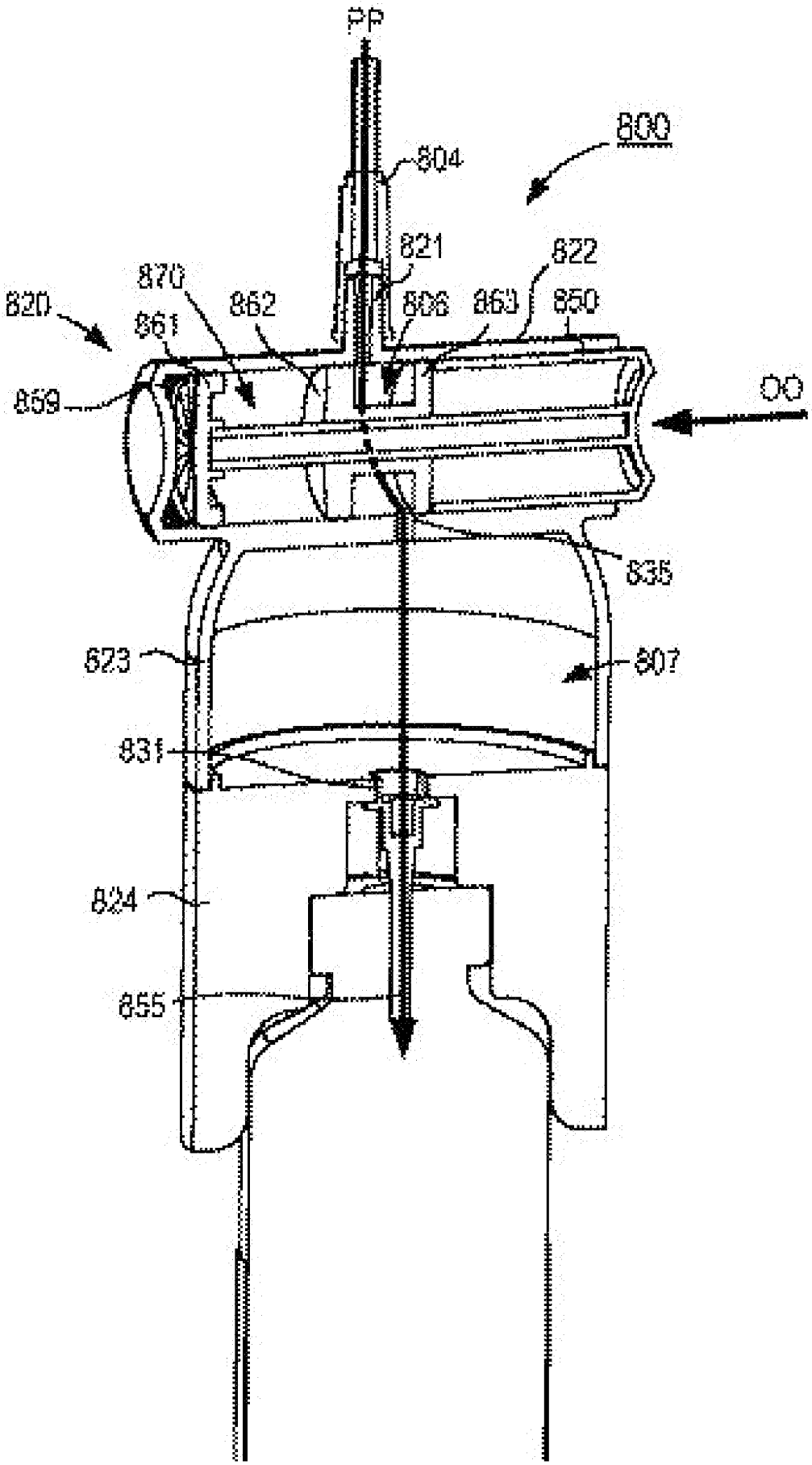


FIG. 44


PP
800
804
821
822
870
820
862
806
863
850
861
859
OO
835
823
807
831
824
855

[Fig. 46]

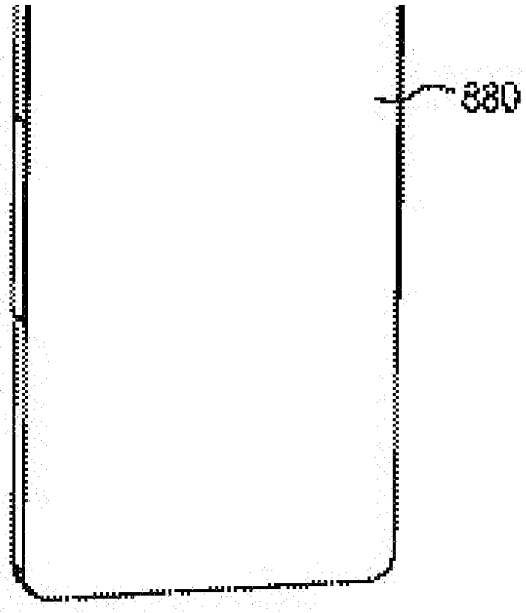
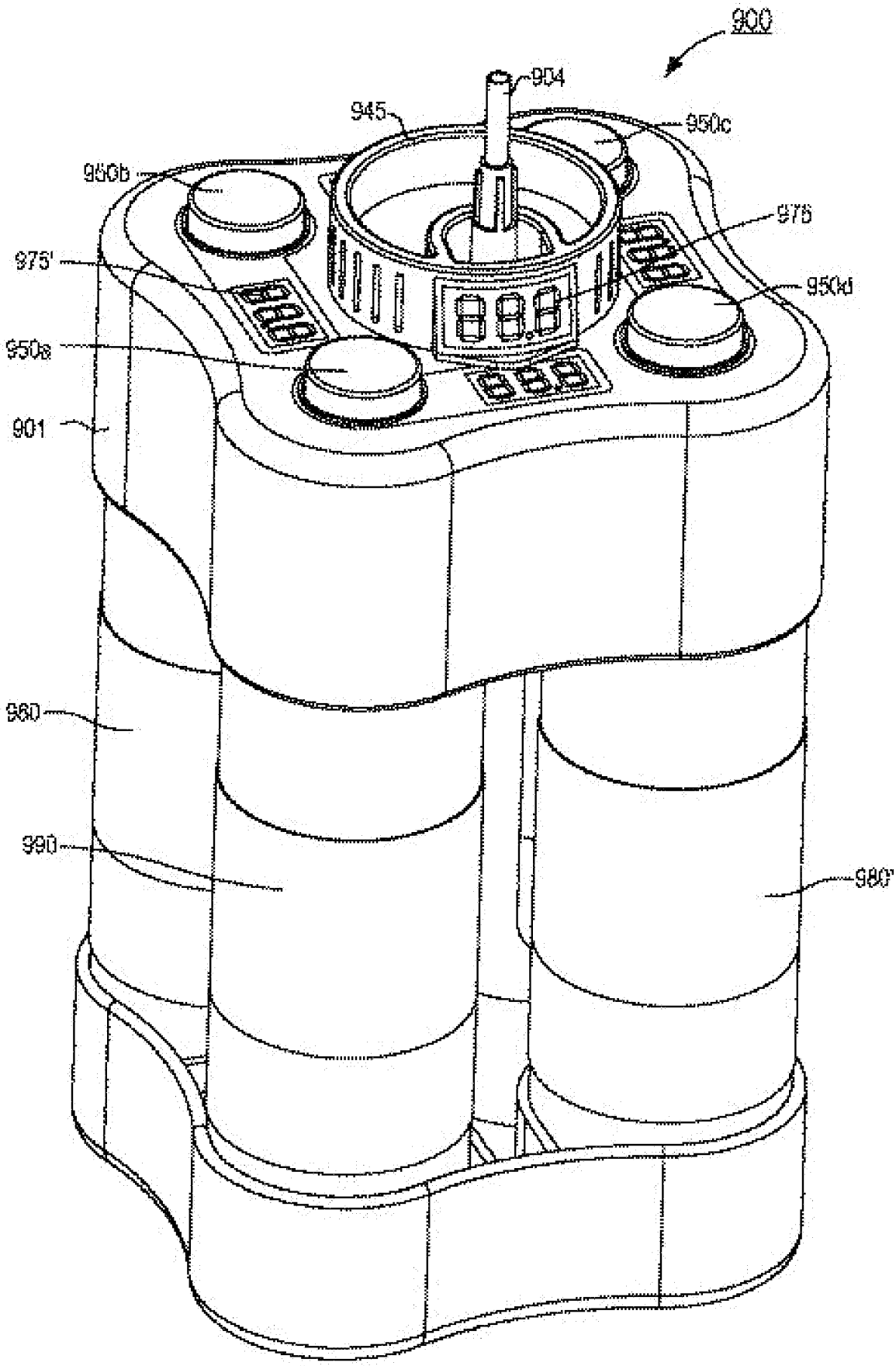
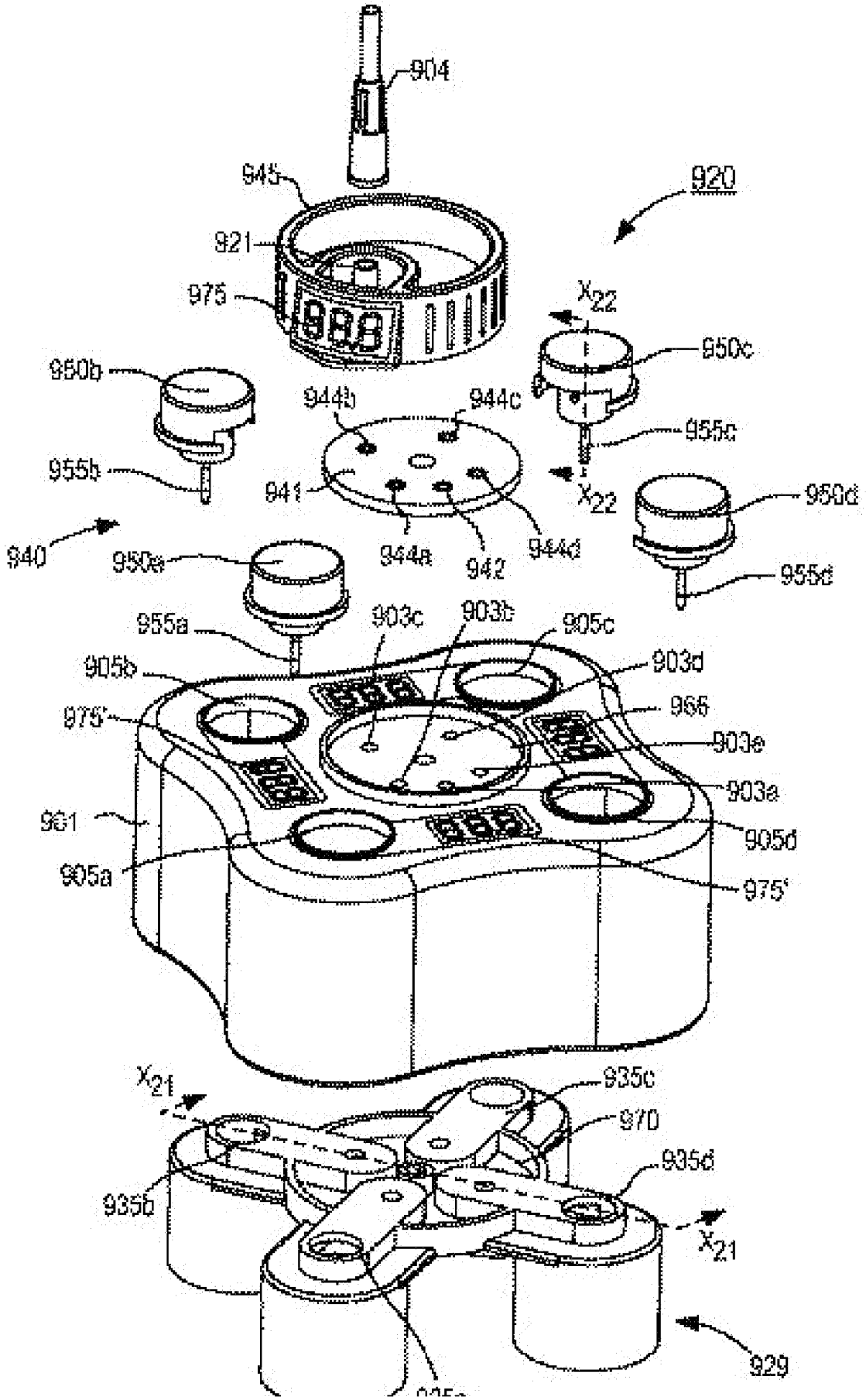


FIG. 45


900
904
945
950c
950b
975
975'
950d
950a
901
980
990
980'

[Fig. 46]


904
945
920
921
975
X22
950c
950b
944b
944c
955c
955b
941
X22
950d
940
944a
942
944d
950a
955d
955a
903c
903b
905c
905b
903d
975'
966
903e
903a
961
905d
905a
975'
X21
935c
970
935d
935b
X21
929

[Fig. 48]

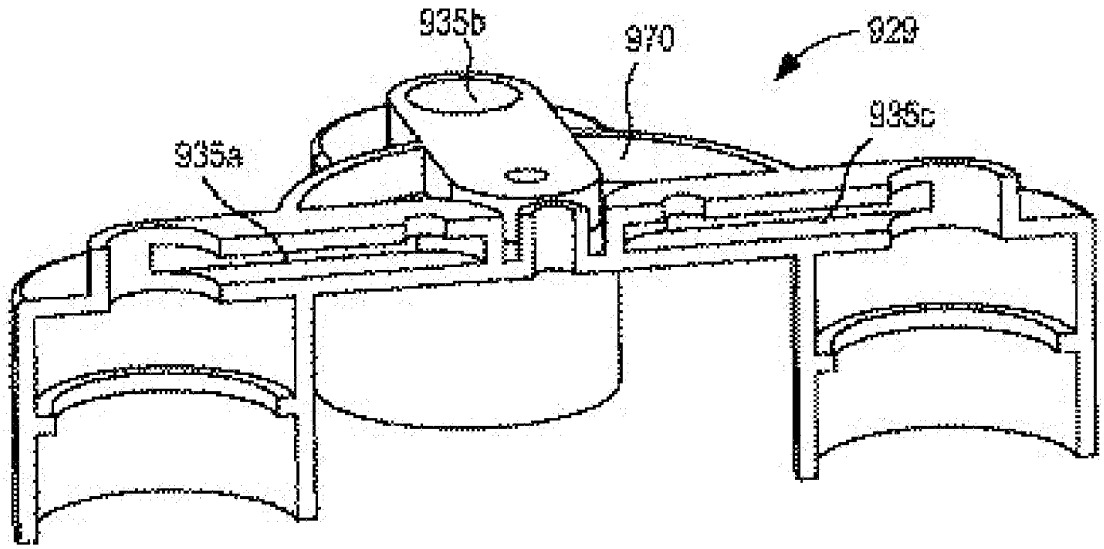


FIG. 48

[Fig. 49]

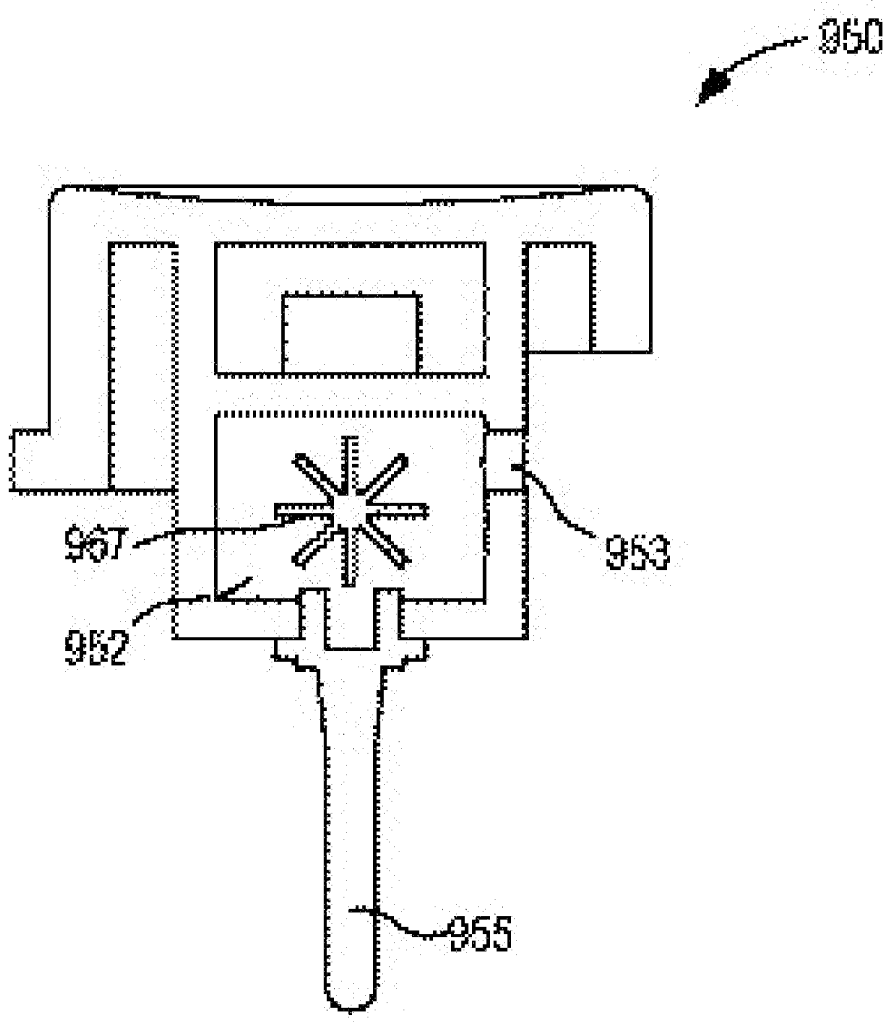


FIG. 49

[Fig. 50]

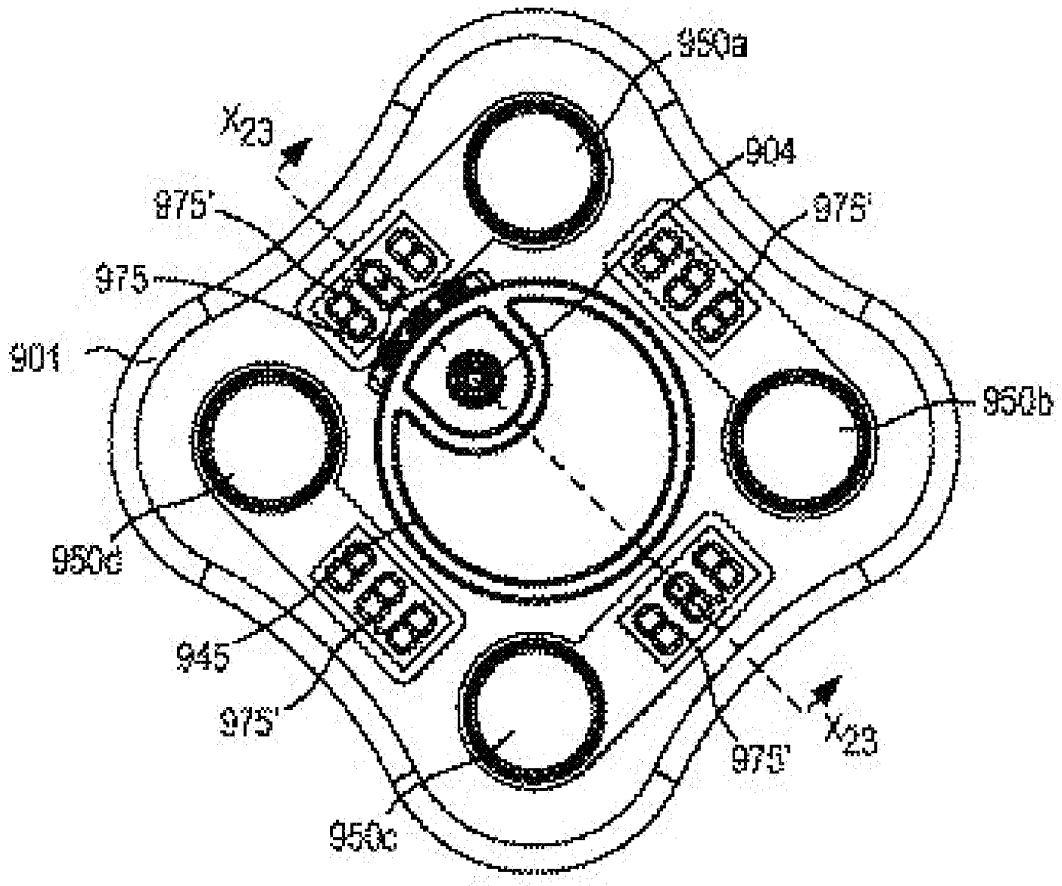


FIG. 50

[Fig. 51]

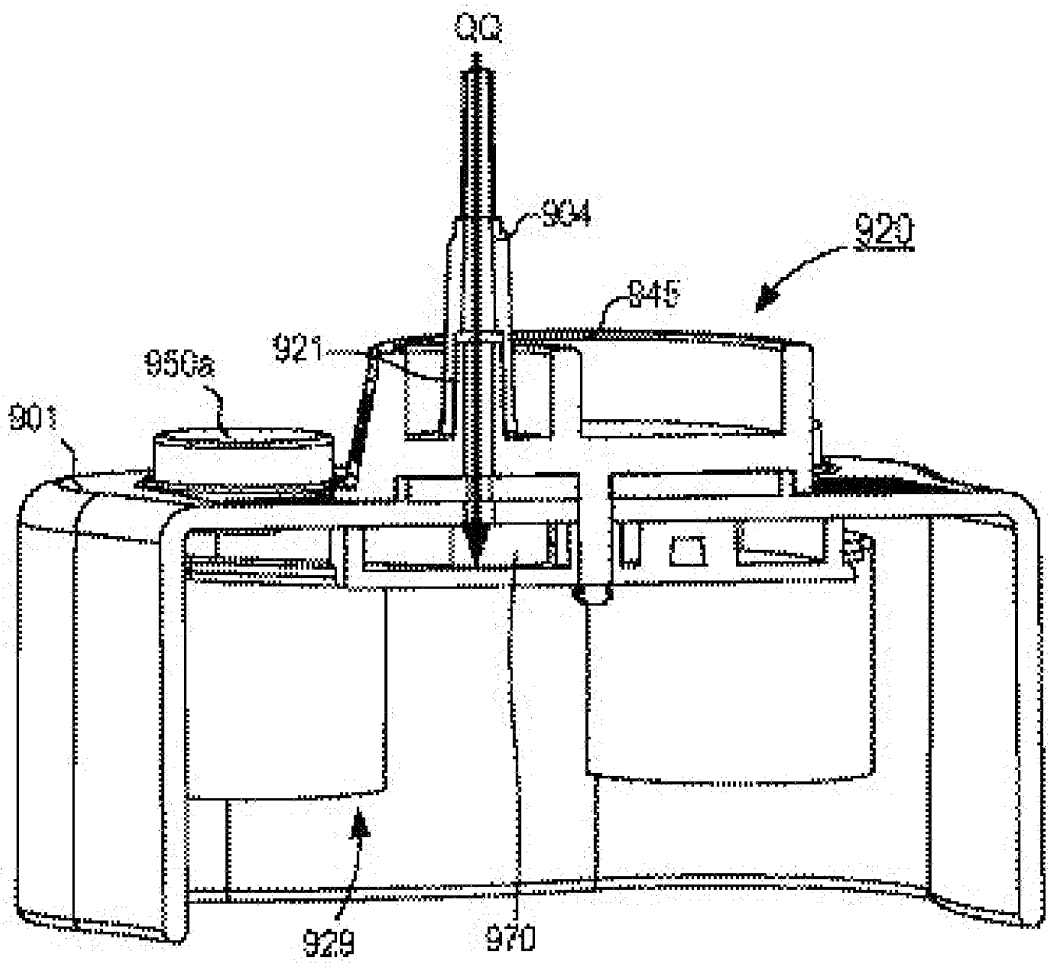


FIG. 51

[Fig. 52]

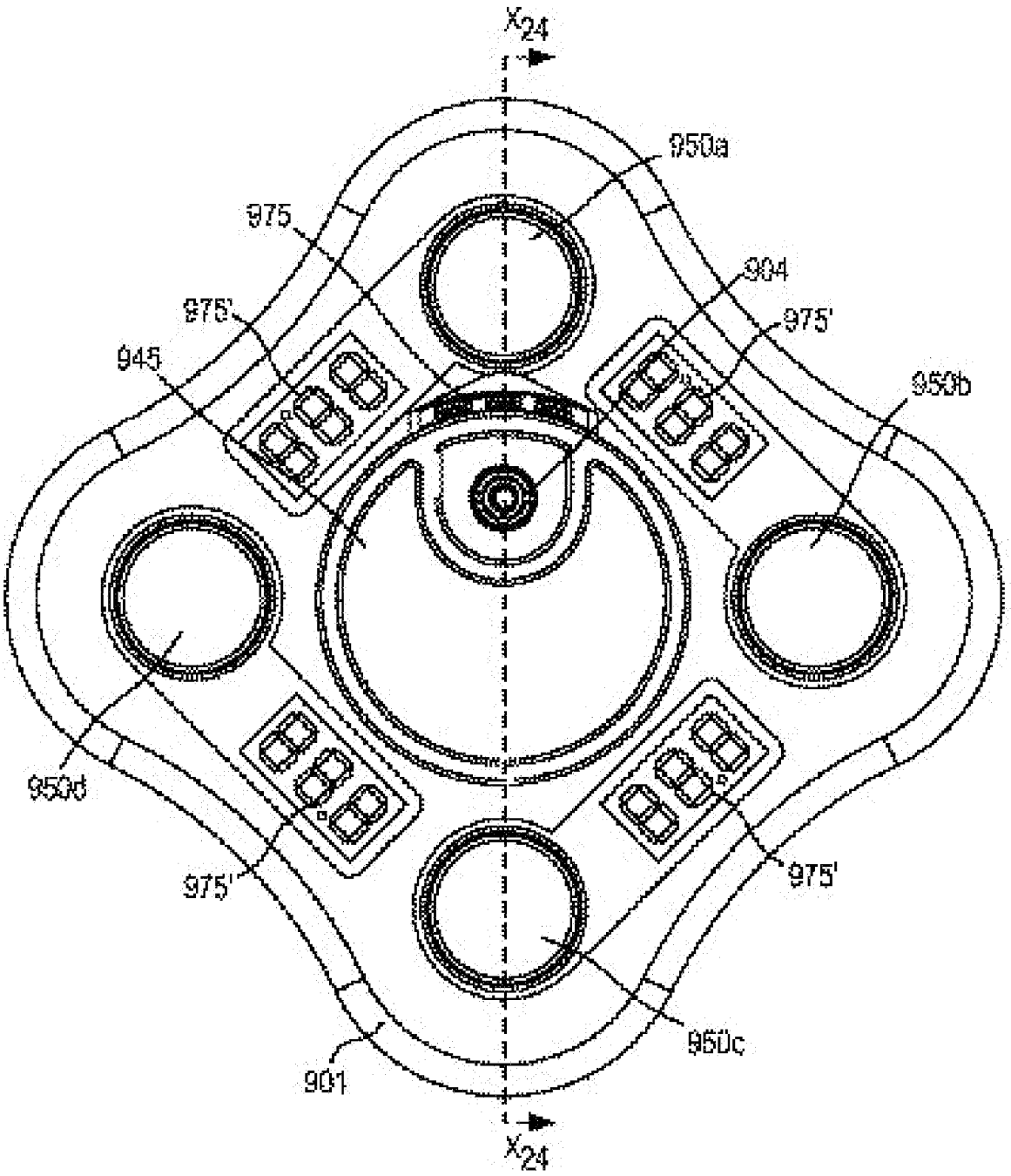
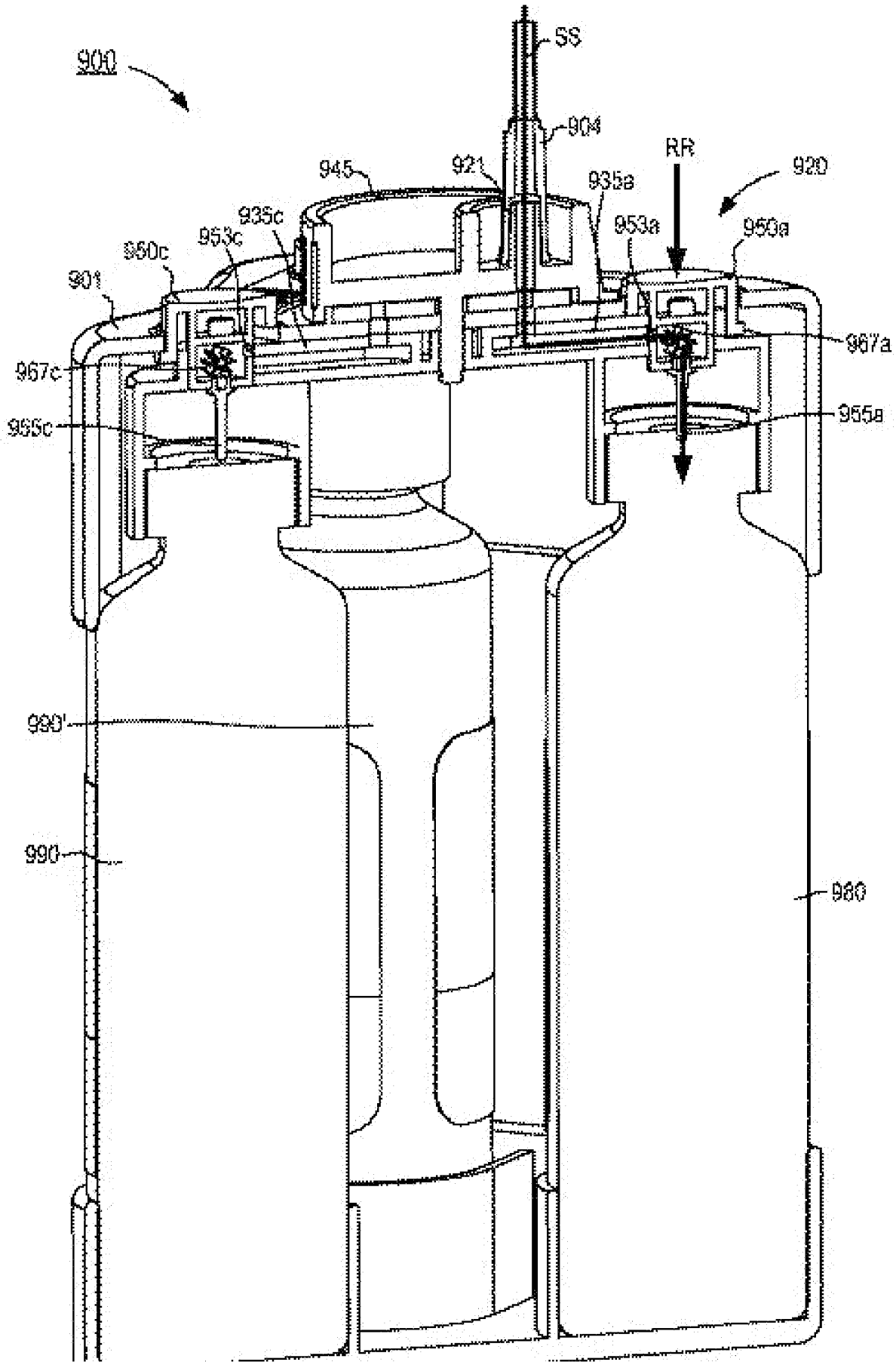
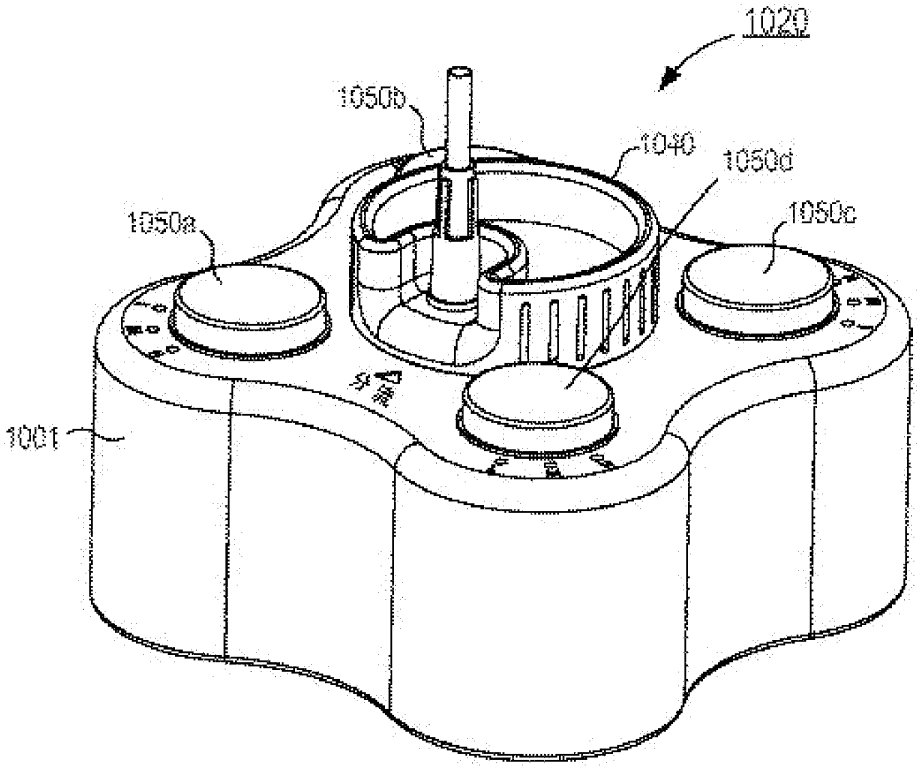


FIG. 52

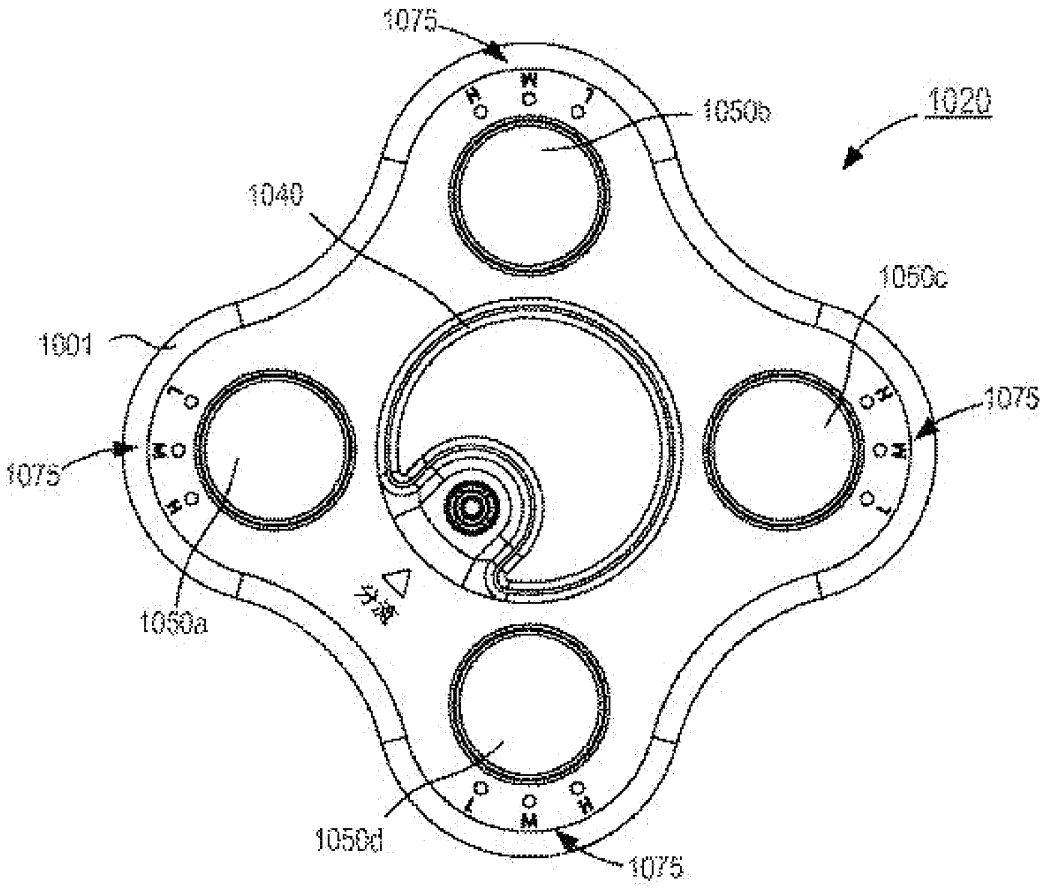
[Fig. 53]


900
SS
904
RR
920
945
921
935a
935c
953c
953a
950a
950c
901
967a
967c
955a
955c
990'
990
980

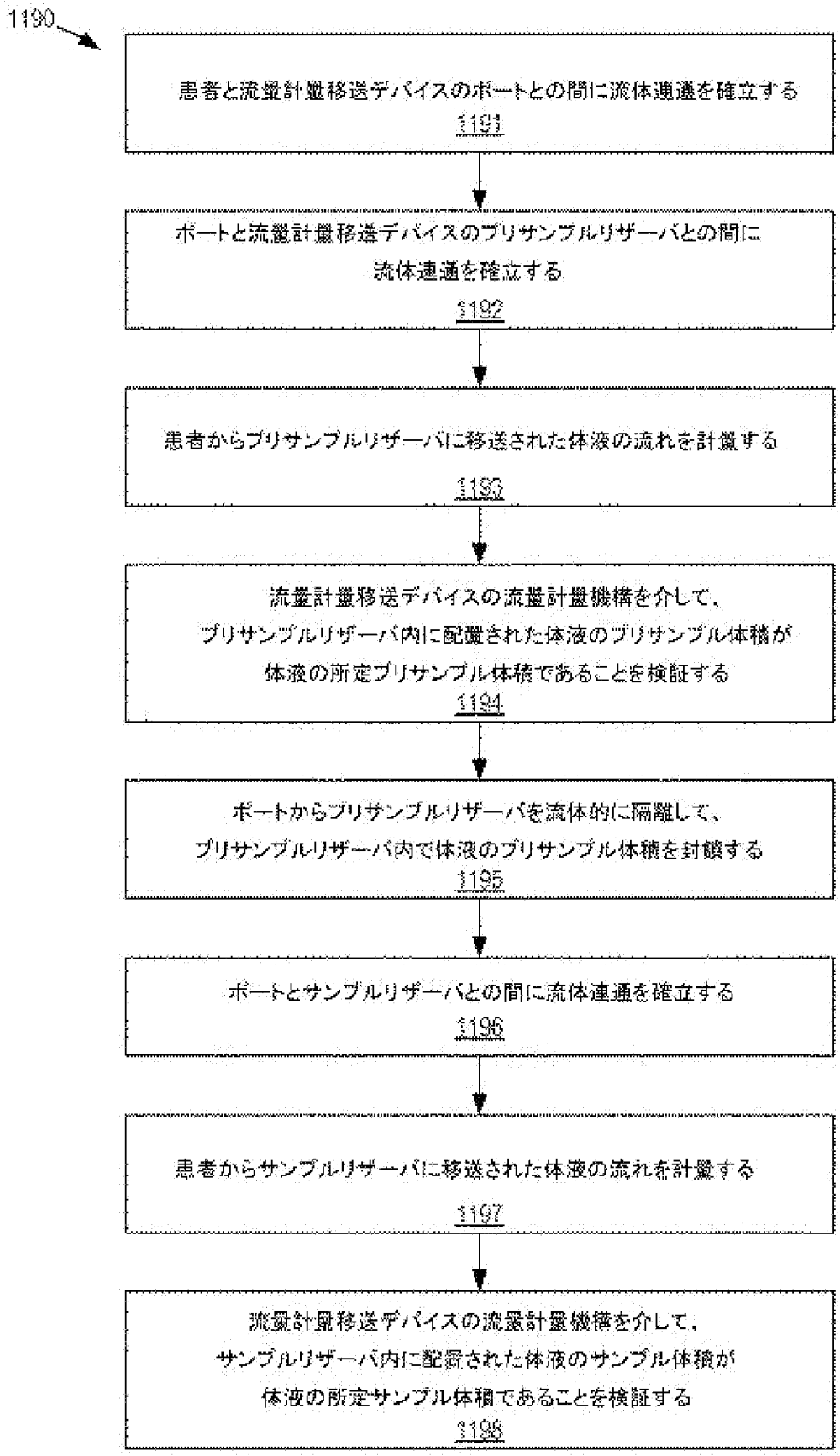
[Fig. 54]



[Fig. 55]



[Fig. 56]


1190
患者と流量計量移送デバイスのポートとの間に流体連通を確立する
1191
ポートと流量計量移送デバイスのプリサンプルリザーバとの間に
流体連通を確立する
1192
患者からプリサンプルリザーバに移送された体液の流れを計量する
1193
流量計量移送デバイスの流量計量機構を介して、
プリサンプルリザーバ内に配置された体液のプリサンプル体積が
体液の所定プリサンプル体積であることを検証する
1194
ポートからプリサンプルリザーバを流体的に隔離して、
プリサンプルリザーバ内で体液のプリサンプル体積を封鎖する
1195
ポートとサンプルリザーバとの間に流体連通を確立する
1196
患者からサンプルリザーバに移送された体液の流れを計量する
1197
流量計量移送デバイスの流量計量機構を介して、
サンプルリザーバ内に配置された体液のサンプル体積が
体液の所定サンプル体積であることを検証する
1198

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drawing open —

Representative drawing | 1 | 2 | 3 | Four | Five | 6 | 7 | 8 | 9 | ...

Magnify and Rotate

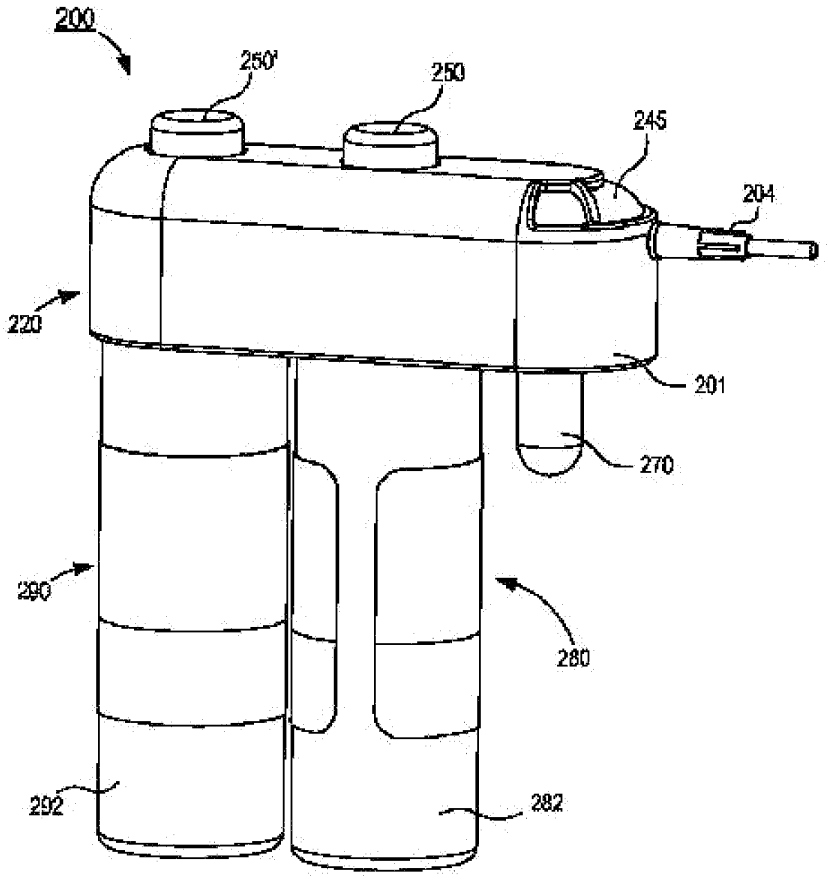


FIG. 2

Representative drawing

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最終頁に続く

(54)【発明の名称】滅菌体液収集デバイス及び方法

(57)【要約】
装置は、プリサンプルリザーバ、分流機構及び流量計量機構を含む。分流機構は、患者から体液を受け取るように内腔規定デバイスに結合可能な入口ポートと、プリサンプルリザーバに流体的に結合可能な第１出口ポートと、サンプルリザーバに流体的に結合可能な第２出口ポートと、を有する。分流機構は、第１出口ポート及び第２出口ポートをそれぞれ入口ポートに流体連通するように配置するように構成された第１流体流路及び第２流路を規定する。流量計量機構は、体液の所定体積の第１流体流路を通るプリサンプルリザーバへの流れを計量し、体液の第２体積の第２流体流路を通るサンプルリザーバへの流れを計量し、所定体積及び第２体積に関連する体積インジケータを表示するように構成される。
【選択図】図２

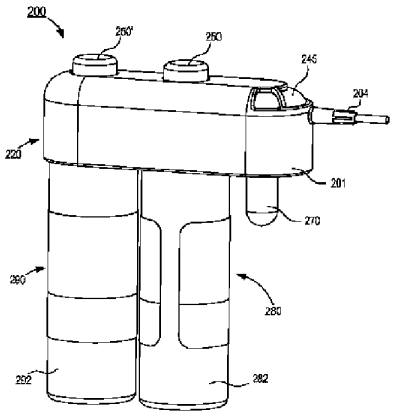


FIG. 2

【特許請求の範囲】
【請求項１】
患者から体液サンプルを取得する装置であって、
前記患者から抜き取られる体液の第１体積を受け取るように構成されたプリサンプルリザーバと、
入口ポート、第１出口ポート及び第２出口ポートを含む分流機構であって、前記入口ポートが、患者から体液を受け取るように内腔規定デバイスに結合されるように構成され、前記第１出口ポートが、前記分流機構に前記プリサンプルリザーバを流体的に結合するように構成され、前記第２出口ポートが、前記分流機構にサンプルリザーバを流体的に結合するように構成され、前記分流機構が、前記第１出口ポートを前記入口ポートに流体連通するように配置するように構成された第１流体流路と、前記第２出口ポートを前記入口ポートに流体連通するように配置するように構成された第２流体流路と、を規定する、分流機構と、
前記第１流体流路及び前記第２流体流路に流体連通する流量計量機構であって、体液の第１体積の前記第１流体流路を通る前記プリサンプルリザーバ内への流れを計量し、体液の第２体積の前記第２流体流路を通る前記サンプルリザーバ内への流れを計量するように構成され、前記第１体積及び前記第２体積に関連する体積インジケータを表示するように構成された流量計量機構と、を備える装置。
【請求項２】
前記体液の第１体積が、第１期間中に前記第１流体流路内で流れ、前記体液の第２体積が、前記第１期間の後、第２期間中に前記第２流体流路内で流れる、請求項１に記載の装置。
【請求項３】
前記体液の第１体積が、皮膚に存在する汚染物質を含み、前記体液の第２体積には、皮膚に存在する汚染物質が実質的にない、請求項１に記載の装置。
【請求項４】
前記プリサンプルリザーバが、前記分流器機構の一部によって少なくとも部分的に規定される、請求項１に記載の装置。
【請求項５】
前記体積インジケータが視覚的インジケータである、請求項１に記載の装置。
【請求項６】
前記分流機構が、前記第２出口ポートを通って移動して前記サンプルリザーバを前記第２流体流路に流体連通するように配置するように構成された可動部材を含む、請求項１に記載の装置。
【請求項７】
前記流量計量機構が、前記可動部材の一部の中に少なくとも部分的に配置される、請求項６に記載の装置。
【請求項８】
前記分流機構が、前記血液の第１体積が前記プリサンプルリザーバ内に配置されると、前記プリサンプルリザーバ及び前記第１流体流路の少なくとも一部を流体的に隔離するように構成される、請求項１に記載の装置。
【請求項９】
前記分流機構が、第２サンプルリザーバを前記分流機構に流体的に結合するように構成された第３出口ポートを含み、前記第３出口ポートを前記入口ポートに流体連通するように配置するように構成された第３流体流路を規定する、請求項１に記載の装置。
【請求項１０】
第１内腔及び第２内腔を規定する流量コントローラであって、前記第１内腔が前記第１流体流路を前記入口ポートに流体連通するように配置する第１形態と、前記第２内腔が前記第２流体流路を前記入口ポートに流体連通するように配置する第２形態との間で移動するように構成された流量コントローラをさらに備える、請求項１に記載の装置。

【請求項１１】
前記流量コントローラが、前記体液の第１体積が前記プリサンプルリザーバ内に配置された後、前記第１形態から前記第２形態に移動するように構成される、請求項１０に記載の装置。
【請求項１２】
患者から体液サンプルを取得する装置であって、
前記患者から抜き取られる体液の第１体積を受け取るように構成されたプリサンプルリザーバと、
入口ポート、第１出口ポート及び第２出口ポートを含む分流機構であって、前記入口ポートが、患者から体液を受け取るように内腔規定デバイスに結合されるように構成され、前記第１出口ポートが前記プリサンプルリザーバを前記分流機構に流体的に結合するように構成され、前記第２出口ポートが、サンプルリザーバを前記分流機構に流体的に結合するように構成される、分流機構と、
前記分流機構内に少なくとも部分的に配置された流量コントローラであって、前記流量コントローラが前記入口ポートと前記第１出口ポートとの間に流体流路の少なくとも一部を規定する第１形態と、前記流量コントローラが前記入口ポートと前記第２出口ポートとの間に流体流路の少なくとも一部を規定する第２形態との間で移動するように構成された流量コントローラと、
前記分流機構に移動可能に結合された可動部材であって、前記サンプルリザーバが前記入口ポートと前記第２出口ポートとの間の流体流路から流体的に隔離される第１形態と、前記サンプルリザーバが前記入口ポートと前記第２出口ポートとの間の前記流体流路に流体連通する第２形態との間で、前記第２出口ポートを通して移動するように構成され、前記サンプルリザーバが、前記流量コントローラがその第２形態にあり、前記可動部材がその第２形態にある時、前記患者から抜き取られる体液の第２体積を受け取るように構成される、可動部材と、を含む装置。
【請求項１３】
前記体液の第１体積が、皮膚に存在する汚染物質を含み、前記体液の第２体積には、皮膚に存在する汚染物質が実質的にない、請求項１２に記載の装置。
【請求項１４】
前記流量コントローラが、前記分流機構に対してその第１形態とその第２形態との間で回転する、請求項１２に記載の装置。
【請求項１５】
前記流量コントローラが、前記分流機構に対して線形運動で移動する、請求項１２に記載の装置。
【請求項１６】
前記流量コントローラが、その第２形態にある時に、前記プリサンプルリザーバを流体的に隔離するように構成される、請求項１２に記載の装置。
【請求項１７】
前記可動部材が、その第２形態にある時、前記サンプルリザーバの一部を穿孔するように構成された穿孔部材を含む、請求項１２に記載の装置。
【請求項１８】
前記可動部材が、前記可動部材をその第１形態で少なくとも一時的に維持するように構成された付勢部材に結合されている、請求項１２に記載の装置。
【請求項１９】
前記分流機構が、第２サンプルリザーバを前記分流機構に流体的に結合するように構成された第３出口ポートを含む、請求項１２に記載の装置。
【請求項２０】
前記可動部材が第１可動部材であり、前記装置が、
第２可動部材であって、前記第２サンプルリザーバが前記入口ポートと前記第３出口ポートとの間に規定された流体流路から流体的に隔離される第１形態と、前記第２サンプル

リザーバが前記入口ポートと前記第３出口ポートとの間に規定された前記流体流路に流体連通する第２形態との間で、前記第３出口ポートを通して移動するように構成され、前記第２サンプルリザーバが、前記流量コントローラがその第２形態にあり、前記第２可動部材がその第２形態にある時、前記患者から抜き取られる体液の第３体積を受け取るように構成される、第２可動部材をさらに含む、請求項１９に記載の装置。

【請求項２１】

患者から体液サンプルを取得する装置であって、

前記患者から抜き取られる体液の第１体積を受け取るように構成されたプリサンプルリザーバと、

ハウジング及び分配部材を含む分流機構であって、前記ハウジングが第１開口部及び第２開口部を規定し、前記第１開口部が前記プリサンプルリザーバに流体連通しており、前記分配部材が、前記ハウジング内に少なくとも部分的に配置され、かつ前記第２開口に流体連通している流体流路を規定し、前記分配部材が、前記流路に流体連通しかつサンプルリザーバに物理的にかつ流体的に結合されるように構成された結合部分を含む、分流機構と、

前記患者から体液を受け取るように内腔規定デバイスに結合されるように構成された入口ポートを含む流量コントローラであって、前記分流機構に回転可能に結合され、かつ前記入口ポートが前記第１開口部に流体連通する第１形態と、前記入口ポートが前記第２開口部に流体連通する第２形態との間で移動するように構成された流量コントローラと、を備える装置。

【請求項２２】

前記体液の第１体積が、皮膚に存在する汚染物質を含み、前記体液の第２体積には、皮膚に存在する汚染物質が実質的にない、請求項２１に記載の装置。

【請求項２３】

前記プリサンプルリザーバが、前記分配部材の一部によって少なくとも部分的に規定される、請求項２１に記載の装置。

【請求項２４】

前記結合部分が、前記サンプルリザーバの一部を穿孔して前記サンプルリザーバを前記流体流路に流体連通するように配置するように構成された穿孔部材を含む、請求項２１に記載の装置。

【請求項２５】

前記穿孔部材による前記サンプルリザーバの前記一部の前記穿孔が、前記流量コントローラがその第２形態にある時、体液の前記患者から前記入口ポート及び前記流路を通る前記サンプルリザーバ内への流れを開始する、請求項２４に記載の装置。

【請求項２６】

前記体液の第１体積が、体液の第１所定体積であり、前記流体流路が、体液の第２所定体積を受け取るように構成され、前記体液の第２所定体積がサンプル体積に関連する、請求項２１に記載の装置。

【請求項２７】

前記サンプル体積が、約１０ミリリットルと約５０ミリリットルとの間である、請求項２６に記載の装置。

【請求項２８】

前記サンプル体積が約３０ミリリットルである、請求項２６に記載の装置。

【請求項２９】

前記分流機構がシール部材を含み、前記流量コントローラが前記分流機構に結合された時に、前記シール部材が、前記流量コントローラの表面及び前記ハウジングの表面と実質的流体密封シールを形成するように、前記ハウジングと前記流量コントローラとの間に配置され、前記シール部材が第１開口部及び第２開口部を規定し、前記シール部材の前記第１開口部が、前記ハウジングの前記第１開口部と実質的に同軸であり、前記シール部材の前記第２開口部が、前記ハウジングの前記第２開口部と実質的に同軸である、請求項２１

に記載の装置。
【請求項３０】
流量計量移送デバイスを用いて患者から体液の所定サンプル体積を取得する方法であって、前記流量計量移送デバイスが、プリサンプルリザーバ及びサンプルリザーバに流体連通するように選択的に配置されるように構成された入口ポートを含む分流機構と、前記患者からの体液の前記プリサンプルリザーバへの流れ及び前記サンプルリザーバへの流れを計量するように構成された流量計量機構とを含む、方法であり、
前記患者と前記流量計量移送デバイスの前記ポートとの間に流体連通を確立するステップと、
前記ポートと前記プリサンプルリザーバとの間に流体連通を確立するステップと、
前記患者から前記プリサンプルリザーバに移送された体液の流れを計量するステップと、
前記流量計量移送デバイスの前記流量計量機構を介して、前記プリサンプルリザーバ内に配置された体液のプリサンプル体積が体液の所定プリサンプル体積であることを検証するステップと、
前記プリサンプルリザーバを前記ポートから流体的に隔離して、前記プリサンプルリザーバ内で前記体液のプリサンプル体積を封鎖するステップと、
前記ポートと前記サンプルリザーバとの間に流体連通を確立するステップと、
前記患者から前記サンプルリザーバに移送された体液の流れを計量するステップと、
前記流量計量移送デバイスの前記流量計量機構を介して、前記サンプルリザーバ内に配置された体液のサンプル体積が体液の所定サンプル体積であることを検証するステップと、を含む方法。
【請求項３１】
前記流量計量移送デバイスが、前記患者と前記プリサンプルリザーバとの間に流体連通が確立される第１形態と、前記患者と前記サンプルリザーバとの間に流体連通が確立される第２形態との間で移動するように構成された流量コントローラを含む、請求項３０に記載の方法。
【請求項３２】
前記体液が血液である、請求項３０に記載の方法。
【請求項３３】
前記サンプルリザーバが、好気性菌用培地又は嫌気性菌用培地のうちの少なくとも一方を含む、請求項３２に記載の方法。
【請求項３４】
前記所定プリサンプル体積が、約１ミリリットルと約１０ミリリットルとの間である、請求項３０に記載の方法。
【請求項３５】
前記所定サンプル体積が、約２０ミリリットルと約６０ミリリットルとの間である、請求項３０に記載の方法。
【請求項３６】
前記所定サンプル体積が約６０ミリリットルである、請求項３０に記載の方法。
【請求項３７】
前記サンプルリザーバが第１サンプルリザーバであり、前記サンプル体積が第１サンプル体積であり、
前記第１サンプルリザーバ内の前記第１サンプル体積が前記所定サンプル体積であることを検証した後、前記ポートと第２サンプルリザーバとの間に流体連通を確立するステップと、
前記患者から前記第２サンプルリザーバに移送された体液の流れを計量するステップと、
前記流量計量移送デバイスの前記流量計量機構を介して、前記第２サンプルリザーバ内に配置された体液の第２サンプル体積が体液の前記所定サンプル体積であることを検証す

るステップと、をさらに含む、請求項３０に記載の方法。
【請求項３８】
前記第１サンプル体積及び前記第２サンプル体積が、まとめて、約２０ミリリットルと約６０ミリリットルとの間に等しい、請求項３７に記載の方法。
【請求項３９】
前記第２サンプルリザーバ内の前記第２サンプル体積が前記所定サンプル体積であることを検証した後、前記ポートと第３サンプルリザーバとの間に流体連通を確立するステップと、
前記患者から前記第３サンプルリザーバに移送された体液の流れを計量するステップと、
前記流量計量移送デバイスの前記流量計量機構を介して、前記第３サンプルリザーバ内に配置された体液の第３サンプル体積が体液の前記所定サンプル体積であることを検証するステップと、をさらに含む、請求項３７に記載の方法。
【請求項４０】
前記第１サンプル体積、前記第２サンプル体積及び前記第３サンプル体積が、まとめて、約３０ミリリットルと約６０ミリリットルとの間に等しい、請求項３９に記載の方法。
【請求項４１】
前記第１サンプル体積、前記第２サンプル体積及び前記第３サンプル体積が、まとめて、約６０ミリリットルに等しい、請求項３９に記載の方法。
【発明の詳細な説明】
【技術分野】
【０００１】
関連出願の相互参照
[1001] 本出願は、２０１２年１２月４日に出願された「滅菌体液収集デバイス及び方法（Sterile Bodily-Fluid Collection Device and Methods）」と題する米国仮特許出願第６１，７３３，１９９号に対する優先権及びその利益を主張し、その出願の開示内容は、全体として参照により本明細書に組み込まれる。
【０００２】
[1002] 本明細書に記載する実施形態は、概して体液サンプルの非経口的獲得（parenteral procurement）に関し、より詳細には、皮膚に存在する微生物等、体液源の外部の微生物又は他の汚染物質からの汚染を低減して、体液サンプルを非経口的に獲得するデバイス及び方法に関する。
【背景技術】
【０００３】
[1003] 医療従事者は、日常的に、非経口的に取得された体液を用いて患者に対してさまざまなタイプの微生物検査を行う。場合によっては、患者サンプル（例えば、体液）は、細菌、真菌又は酵母菌（例えば、カンジダ）等、１種又は複数種の望ましくない可能性がある微生物が存在するか検査される。微生物検査は、微生物増殖を促進する培地を収容する１つ又は複数の滅菌容器において患者サンプルを培養すること、リアルタイム診断及び／又は分子ＰＣＲに基づく手法を含む場合がある。一般に、こうした微生物が患者サンプルに存在する場合、それら微生物は、培地において経時的に繁殖する。可変時間（例えば数時間から数日間）の後、自動化された連続モニタリングにより、生物体の成長を検出することができる。こうした自動化モニタリングは、生物体の増殖によって生成される二酸化炭素を検出することができる。そして、培地に対して、微生物が存在するか検査することができる。培地に微生物が存在する場合、それは、患者サンプルに同じ微生物が存在することを示唆し、それはさらに、サンプルを取得した患者の体液に同じ微生物が存在することを示唆する。従って、培地に微生物が存在すると判断された場合、患者は、患者から望ましくない微生物を処置するか又は他の方法で除去するように特に設計された１種あるいは複数種の抗生物質又は他の処置が処方される可能性がある。
【０００４】

[1004] しかしながら、患者サンプルは、獲得中に汚染される可能性がり、及び／又は、他の方法で偽陽性結果が出やすい可能性がある。患者サンプルの汚染が発生する可能性がある１つの過程は、患者の体内への針の挿入中に取り除かれ後に患者サンプルとともに培地に移送された体表からの微生物（例えば、皮膚に存在する微生物）の移送による。体表微生物及び／又は他の望ましくない外部微生物は、直接、又は取り除かれた組織片、毛包、汗腺及び他の皮膚付属器構造を介して取り除かれる可能性がある。別のあり得る汚染源は、患者サンプルを抜き取る人から来る。例えば、医師、瀉血専門医、看護師等が、自身の身体（例えば、指、腕等）から患者サンプルに及び／又は患者サンプルを収容している機器に汚染物質を移送する可能性がある。さらに詳述すると、患者サンプル獲得プロセス（例えば、患者から針、針／管からサンプル容器等）の間に使用される機器及び／又はデバイスは、各々が有り得る汚染の箇所を生じさせる可能性がある複数の流体インタフェースを含むことが多い。こうした機器及び／又はデバイスの使用は、通常、さまざまなインタフェースを接続し及び／又は流体的に結合するための手作業による介入を含む。これらのインタフェースは、単一の流体的に結合されたシステムとして事前に組み立てられかつ滅菌されないため、使用者（例えば、医師、瀉血専門医等）及び／又は他の汚染源（例えば、周囲空気、病室のテーブル及びカウンタの表面の汚染物質、リネン又は衣類から移送された微生物等）を介して患者サンプルに導入される可能性がある。場合によっては、こうした汚染物質は、培地で生育し、最終的に陽性の微生物検査結果をもたらす可能性があり、それにより、体内におけるこうした微生物の存在を誤って示す。

【０００５】

[1005] 場合によっては、偽陽性結果及び／又は偽陰性結果は、患者サンプルの所定体積に起因する可能性がある。例えば、体積に影響されやすい血液培養ボトルを過充填することにより、こうした培養ボトル及び関連する自動連続モニタリング微生物検出システムの製造業者からの使用説明書及び／又は警告ラベルにおいて注記されているように、偽陽性結果に至る可能性がある。一方、別の例として、培地内における患者サンプルの体積が不十分であることにより、偽陰性結果がもたらされる可能性がある。例として、Journal of Clinical Microbiologyの２０１１年１２月号に記載された「Optimized Pathogen Detection with 30- Compared to 20-Milliliter Blood Culture Draws」と題するMayo Clinicによって行われた研究において、２０ミリリットル（ｍＬ）の患者サンプル体積により、患者サンプルに存在する菌血症の約８０％の存在を検出することができ、４０ｍＬの患者サンプル体積により、菌血症の約８８％を検出することができ、６０ｍＬの患者サンプル体積により、菌血症の約９９％を検出することができる。

【０００６】

[1006] 汚染、不十分な患者サンプル体積等の結果としてのこうした不正確な結果は、疑いのある病気又は健康状態を診断するか又は治療しようとする時に問題である。例えば、微生物検査からの偽陰性結果により、患者の病気が誤診され及び／又は治療が遅れることになる可能性があり、それによって場合によっては、患者の死に至る可能性がある。逆に、微生物検査からの偽陽性結果により、患者が１つ又は複数の抗微生物療法を不必要に受けることになる可能性があり、それにより、例えば死を含む患者の深刻な副作用が引き起こされるとともに、患者の入院の期間の延長及び／又は間違った治療に関連する他の合併症のために医療制度に対する不必要な負担及び出費がもたらされる可能性がある。さらに、これらの偽陽性結果に起因する診断撮像機器の使用はまた、コストとともに、種々の撮像処置（例えば、ＣＴスキャン）に関連する高濃度放射線の不必要な照射が長期の患者の健康に対して多くの既知の悪影響を及ぼすため、患者の安全性の観点からも問題である。

【０００７】

[1007] 従って、例えば、患者サンプル及び／又は流体インタフェースの周囲の非滅菌状態及び／又は他の外部汚染源への暴露を最小限にすることにより、体液検査サンプルにおける微生物汚染を低減する、滅菌「一体型」体液収集デバイス及び方法が必要とされている。さらに、こうした体液収集デバイスが、患者サンプルを実質的にリアルタイムに（例えば、患者のベッドわきで）獲得している医療従事者に視覚的に、計算された方法で、又

は他の方法で通信することができる、患者からサンプルリザーバ又は培地に移送された体液の体液を正確に計量し、測定し、及び／又は、他の方法で評価する手段を含むことが必要とされている。

【発明の概要】

【０００８】

[1008] 本明細書では、皮膚に存在する微生物及び／又は他の望ましくない外部汚染物質等、体液源の外部の微生物からの汚染を低減して体液サンプルを非経口的に獲得するデバイスについて記載されている。いくつかの実施形態では、患者から体液サンプルを取得する装置は、プリサンプルリザーバ、分流機構及び流量計量機構を含む。プリサンプルリザーバは、患者から抜き取られる体液の第１体積を受け取るように構成されている。分流機構は、入口ポート、第１出口ポート及び第２出口ポートを含み、第１流体流路及び第２流体流路を規定している。入口ポートを、患者から体液を受け取るように内腔規定デバイスに結合することができる。第１出口ポート及び第２出口ポートは、プリサンプルリザーバ及びサンプルリザーバそれぞれを分流機構に流体的に結合するように構成されている。第１流体流路は、第１出口ポートを入口ポートに流体連通するように配置するように構成され、第２流体流路は、第２出口ポートを入口ポートに流体連通するように配置するように構成されている。流量計量機構は、第１流体流路及び第２流体流路に流体連通している。流量計量機構は、体液の第１体積の第１流体流路を通るプリサンプルリザーバ内への流れを計量し、体液の第２体積の第２流体流路を通るサンプルリザーバ内への流れを計量するように構成されている。流量計量機構は、第１体積及び第２体積に関連する体積インジケータを表示するように構成されている。

【図面の簡単な説明】

【０００９】

【図１】実施形態による体液収集デバイスの概略図である。

【図２】実施形態による体液収集デバイスの斜視図である。

【図３】図２の体液収集デバイスの組立分解斜視図である。

【図４】図２の体液収集デバイスに含まれるハウジングの図３の線X_1－X_1に沿って取り出された側断面図である。

【図５】図２の体液収集デバイスに含まれる可動部材の図３の線X_2－X_2に沿って取り出された断面図である。

【図６】図２の体液収集デバイスに含まれる流量コントローラの図３の線X_3－X_3に沿って取り出された断面図である。

【図７】図２の体液収集デバイスに含まれる流量コントローラの図３の線X_4－X_4に沿って取り出された断面図である。

【図８】第１形態にある図２の体液収集デバイスの上面図である。

【図９】第１形態にある図２の体液収集デバイスの図８の線X_5－X_5に沿って取り出された断面図である。

【図１０】第２形態にある図２の体液収集デバイスの上面図である。

【図１１】第２形態にある図２の体液収集デバイスの図１０の線X_6－X_6に沿って取り出された断面図である。

【図１２】第３形態にある図２の体液収集デバイスの図１０の線X_6－X_6に沿って取り出された断面図である。

【図１３】第４形態にある図２の体液収集デバイスの図１０の線X_6－X_6に沿って取り出された断面図である。

【図１４】実施形態による体液収集デバイスの斜視図である。

【図１５】図１４の体液収集デバイスの線X_7－X_7に沿って取り出された側断面図である。

【図１６】実施形態による体液収集デバイスの斜視図である。

【図１７】図１６の体液収集デバイスに含まれる分流機構の組立分解斜視図である。

【図１８】図１６の体液収集デバイスに含まれる分配部材の図１６の線X_8－X_8に沿っ

て取り出された側断面図である。
【図１９】第１形態にある図１６の体液収集デバイスの上面図である。
【図２０】第１形態にある図１６の一部体液収集デバイスの図１９の線X_9－X_9に沿って取り出された断面図である。
【図２１】第２形態にある図１６の体液収集デバイスの上面図である。
【図２２】第２形態にある図１６の体液収集デバイスの図２１の線X_{10}－X_{10}に沿って取り出された断面図である。
【図２３】実施形態による体液収集デバイスの斜視図である。
【図２４】第１形態にある、図２３の体液収集デバイスの一部の線X_{11}－X_{11}に沿って取り出された断面図である。
【図２５】第２形態にある、図２３の体液収集デバイスの線X_{11}－X_{11}に沿って取り出された断面図である。
【図２６】実施形態による体液収集デバイスの斜視図である。
【図２７】図２６の体液収集デバイスに含まれる分流機構の組立分解斜視図である。
【図２８】図２７の体液収集デバイスに含まれる分配部材の図２７の線X_{13}－X_{13}に沿って取り出された断面図である。
【図２９】図２６の体液収集デバイスに含まれる結合部材の図２７の線X_{14}－X_{14}に沿って取り出された断面図である。
【図３０】図２６の体液収集デバイスに含まれるダイヤルの図２７の線X_{15}－X_{15}に沿って取り出された断面図である。
【図３１】図２６の体液収集デバイスに含まれる弁の図２７の線X_{16}－X_{16}に沿って取り出された断面図である。
【図３２】第１形態にある図２６の体液収集デバイスの線X_{12}－X_{12}に沿って取り出された断面図である。
【図３３】第２形態にある図２６の体液収集デバイスの線X_{12}－X_{12}に沿って取り出された断面図である。
【図３４】実施形態による体液収集デバイスの斜視図である。
【図３５】図３４の体液収集デバイスに含まれる分流機構の組立分解斜視図である。
【図３６】図３５の分流機構に含まれる分配部材の線X_{17}－X_{17}に沿って取り出された断面図である。
【図３７】第１形態にある図３４の体液収集デバイスの一部の上面図である。
【図３８】第１形態にある図３７の一部体液収集デバイスの線X_{18}－X_{18}に沿って取り出された断面図である。
【図３９】第２形態にある図３３の体液収集デバイスの上面図である。
【図４０】第２形態にある図３３の体液収集デバイスの図３９の線X_{19}－X_{19}に沿って取り出された断面図である。
【図４１】実施形態による第１形態にある体液収集デバイスの斜視図である。
【図４２】図４１の体液収集デバイスの一部の組立分解斜視図である。
【図４３】第１形態にある図４１の体液収集デバイスの線X_{20}－X_{20}に沿って取り出された断面図である。
【図４４】第２形態にある図４１の体液収集デバイスの線X_{20}－X_{20}に沿って取り出された断面図である。
【図４５】第３形態にある図４１の体液収集デバイスの線X_{20}－X_{20}に沿って取り出された断面図である。
【図４６】実施形態による第１形態にある体液収集デバイスの斜視図である。
【図４７】図４５の体液収集デバイスの一部の組立分解斜視図である。
【図４８】図４６の体液収集デバイスに含まれる分配部材の図４７の線X_{21}－X_{21}に沿って取り出された側断面図である。
【図４９】図４６の体液収集デバイスに含まれる可動部材の図４７の線X_{22}－X_{22}に沿って取り出された側断面図である。

【図５０】第１形態にある図４６の体液収集デバイスの上面図である。
【図５１】第１形態にある図４６の一部体液収集デバイスの図５０の線$X_{23}-X_{23}$に沿って取り出された断面図である。
【図５２】第２形態にある図４６の体液収集デバイスの上面図である。
【図５３】第２形態にある図４６の体液収集デバイスの図５２の線$X_{24}-X_{24}$に沿って取り出された断面図である。
【図５４】実施形態による体液収集デバイスの斜視図である。
【図５５】図５４の体液収集デバイスの上面図である。
【図５６】実施形態による収集デバイスを用いて、汚染を低減して体液サンプルを取得する方法を示すフローチャートである。
【発明を実施するための形態】
【００１０】
[1063] 本明細書では、皮膚に存在する微生物及び／又は他の望ましくない外部汚染物質等、体液源の外部の微生物からの汚染を低減して体液サンプルを非経口的に獲得するデバイスについて記載されている。いくつかの実施形態では、患者から体液サンプルを取得する装置は、プリサンプルリザーバ、分流機構及び流量計量機構を含む。プリサンプルリザーバは、患者から抜き取られる体液の第１体積を受け取るように構成されている。分流機構は、入口ポート、第１出口ポート及び第２出口ポートを含み、第１流体流路及び第２流体流路を規定している。入口ポートを、患者から体液を受け取るように内腔規定デバイスに結合することができる。第１出口ポート及び第２出口ポートは、プリサンプルリザーバ及びサンプルリザーバそれぞれを分流機構に流体的に結合するように構成されている。第１流体流路は、第１出口ポートを入口ポートに流体連通するように配置するように構成され、第２流体流路は、第２出口ポートを入口ポートに流体連通するように配置するように構成されている。流量計量機構は、第１流体流路及び第２流体流路に流体連通している。流量計量機構は、体液の第１体積の第１流体流路を通るプリサンプルリザーバ内への流れを計量し、体液の第２体積の第２流体流路を通るサンプルリザーバ内への流れを計量するように構成されている。流量計量機構は、第１体積及び第２体積に関連する体積インジケータを表示するように構成されている。
【００１１】
[1064] いくつかの実施形態では、患者から体液サンプルを取得する装置は、プリサンプルリザーバ、分流機構、流量コントローラ及び可動部材を含む。プリサンプルリザーバは、患者から抜き取られる体液の第１体積を受け取るように構成されている。分流機構は、入口ポート、第１出口ポート及び第２出口ポートを含む。入口ポートは、患者から体液を受け取るように内腔規定デバイスに結合可能である。第１出口ポートは、プリサンプルリザーバを分流機構に流体的に結合し、第２出口ポートは、サンプルリザーバを分流機構に流体的に結合する。流量コントローラは、分流機構内に少なくとも部分的に配置され、流量コントローラを、流量コントローラが入口ポートと第１出口ポートとの間に流体流路の少なくとも一部を規定する第１形態と、流量コントローラが入口ポートと第２出口ポートとの間に流体流路の少なくとも一部を規定する第２形態との間で移動させることができる。可動部材は、分流機構に移動可能に結合され、サンプルリザーバが入口ポートと第２出口ポートとの間の流体流路から流体的に隔離される第１形態と、サンプルリザーバが入口ポートと第２出口ポートとの間の流体流路に流体連通する第２形態との間で、第２出口ポートを通して移動可能である。サンプルリザーバは、流量コントローラがその第２形態にあり、可動部材がその第２形態にある時、患者から抜き取られる体液の第２体積を受け取るように構成されている。
【００１２】
[1065] いくつかの実施形態では、患者から体液サンプルを取得する装置は、プリサンプルリザーバ、分流機構及び流量コントローラを含む。プリサンプルリザーバは、患者から抜き取られる体液の第１体積を受け取るように構成されている。分流機構は、ハウジング及び分配部材を含む。ハウジングは、プリサンプルリザーバに流体連通している第１開口

部と第２開口部とを規定している。分配部材は、ハウジング内に少なくとも部分的に配置され、かつ第２開口に流体連通している流体流路を規定している。分配部材は、流路に流体連通しかつサンプルリザーバに物理的にかつ流体的に結合されるように構成された結合部分を含む。流量コントローラは、患者から体液を受け取るように内腔規定デバイスに結合されるように構成された入口ポートを含む。流量コントローラは、分流機構に回転可能に結合され、かつ入口ポートが第１開口部に流体連通する第１形態と、入口ポートが第２開口部に流体連通する第２形態との間で移動可能である。

【００１３】

[1066] いくつかの実施形態では、プリサンプルリザーバ及びサンプルリザーバに流体連通するように選択的に配置されるように構成された入口ポートを含む分流機構と、患者からの体液のプリサンプルリザーバへの流れ及びサンプルリザーバへの流れを計量するように構成された流量計量機構とを有する流量計量移送デバイスを用いる方法は、患者と流量計量移送デバイスの入口ポートとの間に流体連通を確立するステップを含む。そして、ポートとプリサンプルリザーバとの間に流体連通が確立される。患者からプリサンプルリザーバに移送された体液の流れが計量される。本方法は、流量計量移送デバイスの流量計量機構を介して、プリサンプルリザーバ内に配置された体液のプリサンプル体積が体液の第１プリサンプル体積であることを検証するステップを含む。プリサンプルリザーバ内にプリサンプル体積が配置された状態で、プリサンプルリザーバがポートから流体的に隔離されて、プリサンプルリザーバ内で体液のプリサンプル体積が封鎖される。プリサンプルリザーバが流体的に隔離された状態で、本方法は、ポートとサンプルリザーバとの間に流体連通を確立するステップを含む。患者からサンプルリザーバに移送された体液の流れが計量される。本方法は、流量計量移送デバイスの流量計量機構を介して、サンプルリザーバ内に配置された体液のサンプル体積が体液の第１サンプル体積であることを検証するステップを含む。

【００１４】

[1067] いくつかの実施形態では、装置は、分流機構及び流量コントローラを含む。分流機構は、入口ポート、第１出口ポート、第２出口ポート及び第３出口ポートを規定することができる。第１出口ポートは、プリサンプルリザーバに流体的に結合され、第２出口ポートは、第１サンプルリザーバに流体的に結合され、第３出口ポートは、第２サンプルリザーバに流体的に結合され、等である。流体リザーバのすべてを、互いから流体的に隔離することができる。流量コントローラはさまざまな流体チャネルを含み、流体チャネルは、指定された方向における流体移動を可能にすることができ、分流機構に動作可能に結合されるように構成され得る。使用時、分流機構が第１形態にある時、流量コントローラは、体液の流れがプリサンプルリザーバに入るのを可能にすることができる。分流機構を第２形態に移動させることができ、そこでは、流量コントローラは、体液の流れが第１サンプルリザーバに入るのを可能にすることができる。さらに、分流機構を、その後、第３形態に移動させることができ、それにより、流量コントローラは、体液の流れが第２サンプルリザーバに入るのを可能にすることができる。

【００１５】

[1068] いくつかの実施形態では、体液収集デバイスを、体液の第２体積の第１サンプルリザーバ内への流れ及び／又は体液の第３体積の第２サンプルリザーバ内への流れを可能にする前に、体液の第１の所定体積をプリサンプルリザーバに選択的に分流させるように構成することができる。このように、体液の第２体積及び／又は第３体積を、診断又は他の検査に使用することができ、一方で、体表又はサンプルを獲得する患者の外部の他の微生物源からの微生物を含む可能性がある体液の第１体積が隔離される。いくつかの実施形態では、体液収集デバイスは、行われる分析プロトコル及び／又は検査プロトコルに応じて追加のサンプルリザーバ（例えば、３、４、５、６以上）を含むことができる。

【００１６】

[1069] いくつかの実施形態では、体液収集デバイスは、体液の適切な体積が患者から収集され及び／又は所定のプリサンプルリザーバ及び／又はサンプルリザーバに移送される

のを確実にするために、流量計量を含むことができる。体液収集デバイスを、体液の計量された体積が収集された後に、流体流を自動的に分流させ及び／又は制御するように構成することができる。例えば、第１計量プリサンプル体積が収集されると、分流機構を、体液流を第１サンプルリザーバに分流させるように構成することができ、その後、第１計量サンプル体積が収集された後、分流機構を、体液流を第２サンプルリザーバに分流させるように構成することができ、等である。いくつかの実施形態では、体液収集デバイスは、例えば液晶ディスプレイ（ＬＣＤ）等の計量された体積のディスプレイを含み、どれだけの体液が各所定の個々のサンプルリザーバ内に収集されたかの視覚的指示を使用者に提供することができる。いくつかの実施形態では、カスタマイズされたプリサンプル及び／又はサンプル体積収集を可能にするように、複数のディスプレイを設けることができる。

【００１７】

[1070] 本明細書及び添付の特許請求の範囲で用いる単数形「１つの（a、an）」及び「その（the）」は、文脈に明示的に述べられていない限り、複数の指示対象を含む。従って、例えば、「（１つの）部材」という用語は、単一部材又は部材の組合せを意味するように意図され、「（１つの）材料」は、１つあるいは複数の材料又はそれらの組合せを意味するように意図されている。

【００１８】

[1071] 本明細書で用いる「体液」は、限定されないが、血液、髄液、尿、胆汁、リンパ液、唾液、滑液、漿液、胸膜液、羊水等又はそれらのあらゆる組合せを含む、患者の体内から得られるあらゆる流体を含むことができる。

【００１９】

[1072] 本明細書で用いる「第１の所定量」、「第１量」及び「第１体積」という用語は、第１リザーバ又はプリサンプルリザーバによって受け取られるか又は収容されるように構成された体液の量を述べる。「第１量」及び「第１体積」という用語は、所定量を明示的に述べないが、明示的に異なるように述べられていない限り、第１量は第１の所定量であることが理解されるべきである。

【００２０】

[1073] 本明細書で用いる「第２量」及び「第２体積」という用語は、第２リザーバ又はサンプルリザーバによって受け取られるか又は収容されるように構成された体液の量を述べる。第２量を、体液のあらゆる好適な量とすることができ、それは所定量である必要はない。逆に、そのように明示的に述べられる場合、第２リザーバ又はサンプルリザーバによって受け取られかつ収容される第２量は、第２の所定量であり得る。

【００２１】

[1074] 本明細書で用いる「組」という用語は、複数の機構又は複数の部品を含む単一の機構を指すことができる。例えば、壁の組と言う場合、壁の組を、別個の部分を含む１つの壁とみなすことができ、又は壁の組を、複数の壁とみなすことができる。同様に言えば、一体的に構成された物品は一組の壁を含むことができる。こうした一組の壁は、例えば、互いに不連続である複数の部分を含むことができる。一組の壁を、別個に製造され、後に（例えば、溶接、接着剤又はあらゆる好適な方法を介して）互いに接合される複数の物品から製造することも可能である。

【００２２】

[1075] 本明細書で用いる「近位」及び「遠位」という用語は、デバイスを患者に接触するように配置する使用者に対してそれぞれ近い方の方向及び離れる方向を指す。従って、例えば、患者の身体に最初に接触するデバイスの端部は遠位端となり、デバイスの反対側の端部（例えば、使用者が操作しているデバイスの端部）はデバイスの近位端となる。

【００２３】

[1076] 本明細書で用いる「約」、「およそ」及び「実質的に」という用語は、数値と関連して用いられる場合、そのように定義される値が名目上示されている値であることを意味するように意図されている。言い換えれば、約、およそ及び実質的にという用語は、数値に関連して用いられる場合、概して、示されている値プラスマイナス所与の許容差を含

む。例えば、場合によっては、好適な許容差は、示されている値の±１０％である可能性があり、従って、約０．５は０．４５及び０．５５を含み、約１０は９～１１を含み、約１０００は９００～１１００を含む。他の場合では、好適な許容差は、プラスマイナス示されている値の最後の有効数字の許容可能な割合であり得る。例えば、好適な許容差は、最後の有効数字の±１０％である可能性があり、従って、約１０．１は１０．０９及び１０．１１を含み、およそ２５は２４．５及び２５．５を含む。こうした変動は、製造公差又は他の実際的な考慮事項（例えば、測定器具に関連する公差、許容可能な人的ミス等）からもたらされ得る。

【００２４】

[1077] 体液の所定体積と体液の収集された体積との関係について述べる場合、それらの値は、上述したものの等の好適な許容差を含むことが理解されるべきである。例えば、体液の収集された体積が体液の所定体積と実質的に等しいと述べる場合、収集された体積及び所定体積は、名目上、好適な許容差の範囲内で等しい。場合によっては、許容差を、体液の収集された体積の意図された使用によって求めることができる。例えば、場合によっては、血液培養のアッセイは、血液の収集された体積が製造業者の（又はエビエンスに基づく最適な実践）推奨体積の１．０％から５．０％の範囲内である時、約９９％正確であり得る。例として、体液のアッセイに対する製造業者の推奨体積は、約９９％の信頼度のために、合計４本又は６本の収集ボトルが使用される場合、１本のサンプル収集ボトル当り１０ミリリットル（ｍＬ）（すなわち、総体積は４０ｍｌ～６０ｍｌ）±５％であり得る。従って、１０．５ｍＬの収集体積により、約９９％を超える信頼度での結果が提供され、１１ｍＬの収集体積により、約９９％未満の信頼度の結果が提供される。他の場合では、好適な許容差は、０．１％、０．５％、１．０％、２．０％、３．０％、４．０％、５．０％、６．０％、７．０％、８．０％、９．０％、１０．０％又はそれらの間のあらゆる分数値であり得る。さらに他の場合では、許容差は１０．０％を上回る可能性がある。従って、本明細書に記載する実施形態のいずれも、好適な許容差の範囲内で体液の流量を計量し及び／又は体液の体積を他の方法で測定するように構成されたあらゆる好適な流量測定機構及び／又はデバイスを含み及び／又はそれとともに使用することができる。さらに、流量計量機構及び／又はデバイスを、不正確な測定、人的ミス等の組合せからもたらされる可能性がある公差の蓄積を最小限にするか又はなくすように配置することができる。

【００２５】

[1078] 図１は、実施形態による体液収集デバイス１００の一部の概略図である。概して、体液収集デバイス１００（本明細書では、「流体収集デバイス」又は「収集デバイス」とも呼ぶ）は、患者から体液を抜き取ることを可能にし、その際、抜き取られた体液の第１部分又は第１量が、医療診断及び／又は治療の目的で検査されるため等、生物学的サンプルとして使用される、抜き取られた体液の第２部分あるいは体積及び／又は第３部分あるいは体積から離れるように分流されるように構成されている。言い換えれば、本明細書においてより詳細に記載するように、収集デバイス１００は、体液の第１の所定体積をプリサンプル収集リザーバに、体液の第２体積及び第３体積（又は、いくつかの実施形態では、第４、第５等）を、プリサンプルリザーバから流体的に隔離された１つ又は複数のサンプル収集リザーバ（例えば、サンプルリザーバ）に移送するように構成されている。

【００２６】

[1079] 収集デバイス１００は、分流機構１２０、流量コントローラ１４０、プリサンプルリザーバ１７０、第１サンプルリザーバ１８０、及び第１サンプルリザーバ１８０とは異なる第２サンプルリザーバ１９０を含む。分流機構１２０は、図１に示すように、入口ポート１２１と、第１出口ポート１２５及び第２出口ポート１２６等、少なくとも２つの出口ポートとを含む。いくつかの実施形態では、分流機構１２０は、プリサンプルリザーバ及びサンプルリザーバの総数に等しい一組の出口ポートを含むことができる。例えば、収集デバイス１００が１つのプリサンプル及び４つのサンプリリザーバを有する場合、分流機構１２０は５つの出口ポートを含むことができる。いくつかの実施形態では、分流機

構１２０を、複数の形態の間の分流機構１２０の移動を容易にすることができる（図１には示さない）アクチュエータに動作可能に結合することができる。入口ポート１２１は、患者から体液を抜き取り及び／又は収集デバイス１００に輸送するための経路Ｘを規定している医療デバイスに流体的に結合されるように構成されている。例えば、入口ポート１２１を、針又は他の内腔規定デバイス（例えば、可撓性滅菌管）に流体的に結合することができる。このように、分流機構１２０は、針又は他のあらゆる内腔規定デバイスを介して患者から体液を受け取ることができる。

【００２７】

[1080] 分流機構１２０の第１出口ポート１２５を、プリサンプルリザーバ１７０に流体的に結合することができる。いくつかの実施形態では、プリサンプルリザーバ１７０は、第１出口ポート１２５及び／又は分流機構１２０の一部と一体的に形成されている。他の実施形態では、プリサンプルリザーバ１７０を、接着剤、抵抗嵌め（resistance fit）、機械的締結具、あらゆる数の嵌合凹部、ねじ結合及び／又は他のあらゆる好適な結合あるいはその組合せを介して、分流機構１２０に機械的に及び／又は流体的に結合することができる。同様に言えば、プリサンプルリザーバ１７０を、分流機構１２０に物理的に（例えば、機械的に）結合することができ、それにより、プリサンプルリザーバ１７０によって規定される内部空間（volume）が分流機構１２０の第１出口ポート１２５に流体連通する。さらに他の実施形態では、プリサンプルリザーバ１７０を、可撓性滅菌管等の（図１には示さない）介在構造を介して、分流機構１２０の第１出口ポート１２５に動作可能に結合することができる。より詳細には、介在構造は、プリサンプルリザーバ１７０を、第１出口ポート１２５に流体連通するように配置するように構成された内腔を規定することができる。

【００２８】

[1081] プリサンプルリザーバ１７０は、体液の第１の所定体積を受け取りかつ収容するように構成されている。いくつかの実施形態では、プリサンプルリザーバ１７０は、体液の第１体積を、患者から後に抜き取られる（体液の第１体積と同じである場合もあれば異なる場合もある）体液の第２体積及び／又は第３体積から流体的に隔離するように収容するように構成されている。プリサンプルリザーバ１７０は、全体として参照により本明細書に組み込まれる、「汚染を低減して体液サンプルを非経口的に獲得するシステム及び方法（Systems and Methods for Parenterally Procuring Bodily-Fluid Samples with Reduced Contamination）」と題する米国特許第８，１９７，４２０号に詳細に記載されているプリサンプルリザーバ等、体液を収容するあらゆる好適なリザーバであり得る。

【００２９】

[1082] いくつかの実施形態では、分流機構１２０の第２出口ポート１２６は、第１サンプルリザーバ１８０及び第２サンプルリザーバ１９０に結合することができる内腔規定デバイスに流体的に結合されるように構成されている。任意選択的に、他の実施形態では、分流機構１２０の第２出口ポート１２６を、第１サンプルリザーバ１８０に結合することができ、分流機構１２０は、第２サンプルリザーバ１９０に結合された（図示せず）第３出口ポートを有することができる。いくつかの実施形態では、第１サンプルリザーバ１８０を、第２出口ポート１２６及び／又は分流機構１２０の一部と一体的に形成することができる。他の実施形態では、第１サンプルリザーバ１８０を、プリサンプルリザーバ１７０に関して上述したような介在構造を介して、第２出口ポート１２６に機械的に結合し、又は第２出口ポート１２６に動作可能に結合することができる。第１サンプルリザーバ１８０は、体液の第２体積を受け取りかつ収容するように構成されている。例えば、体液の第２体積は、第１プリサンプル体積の抜取りに続いて患者から抜き取られた量であり得る。いくつかの実施形態では、第１サンプルリザーバ１８０は、第２体積がプリサンプル体液の第１体積から流体的に隔離されるように、体液の第２体積を収容するように構成されている。

【００３０】

[1083] 第１サンプルリザーバ１８０及び第２サンプルリザーバ１９０は、例えば、上で

参照により組み込んだ‘４２０特許に記載されているようなサンプルリザーバを含む、体液を収容するあらゆる好適な滅菌リザーバであり得る。いくつかの実施形態では、第２体積を、体液のあらゆる好適な体積とすることができ、それは所定体積である必要はない。他の実施形態では、第１サンプルリザーバ１８０及び／又は第２サンプルリザーバ１９０への体液の移送を、第２体積が第２の所定体積であるように、計量等することができる。

【００３１】

[1084] 第２サンプルリザーバ１９０は、あらゆる好適なサンプルリザーバであり得る。いくつかの実施形態では、第２サンプルリザーバ１９０は、上述した第１サンプルリザーバ１８０と実質的に同様であり得る。第２サンプルリザーバ１９０を、上述したように、第２出口ポート１２６に流体的に結合することができる。第２出口ポート１２６の第２サンプルリザーバ１９０への流体的結合は、詳細に上述したように、第２出口ポート１２６の第１サンプルリザーバ１８０への流体的結合と実質的に同様であり得る。従って、こうした部分については、本明細書ではそれ以上詳細には記載せず、明示的に異なるように記載されていない限り、実質的に同様であるとみなすべきである。さらに、（図１には示さない）分流機構１２０の追加の出口ポート及びサンプルリザーバは、第２出口ポート１２６及び第１サンプルリザーバ１８０と実質的に同様であり得る。

【００３２】

[1085] いくつかの実施形態では、プリサンプルリザーバ１７０、第１サンプルリザーバ１８０及び第２サンプルリザーバ１９０を、分流機構１２０に同様に結合する（又はともに形成する）ことができる。他の実施形態では、プリサンプルリザーバ１７０、第１サンプルリザーバ１８０及び第２サンプルリザーバ１９０は、分流機構１２０に同様に結合される必要はない。例えば、いくつかの実施形態では、プリサンプルリザーバ１７０を、分流機構１２０（例えば、第１出口ポート１２４）と一体的に形成することができ、第１サンプルリザーバ１８０及び／又は第２サンプルリザーバ１９０を、可撓性滅菌管又はそのあらゆる組合せ等の介在構造を介して、分流機構１２０（例えば、第２出口ポート１２６）に動作可能に結合することができる。

【００３３】

[1086] いくつかの実施形態では、収集デバイス１００は、（図１には示さない）アクチュエータと、第１流体流路１４２、第２流体流路１４４及び任意選択的に（図１には示さない）追加の流体流路を規定する流量コントローラ１４０と、をさらに含むことができる。いくつかの実施形態では、アクチュエータを、分流機構１２０に含めるか又は他の方法で動作可能に結合することができる。このように、アクチュエータを、流量コントローラ１４０内の（例えば、異なる形態の間の）流体移動を制御するように構成することができる。例えば、アクチュエータは、流量コントローラ１４０の第１形態に対応する第１位置、流量コントローラ１４０の第２形態に対応する、第１位置とは異なる第２位置等の間で移動可能であり得る。いくつかの実施形態では、アクチュエータを、単方向に移動するように構成することができる。例えば、アクチュエータを、その第１位置からその第２位置に移動させることができるが、その第２位置からその第１位置に移動させることはできない。同様に、アクチュエータを、その第２位置から第３位置に移動させることができるが、その第３位置からその第２位置に戻るように移動させることはできない。このように、流量コントローラ１４０は、その第１形態の前にその第２形態又は第３形態に移動することが防止され、従って、体液の第１量がプリサンプルリザーバ１７０に向けられ、医療診断及び／又は治療の目的での検査のため等、生物学的サンプルとして使用される抜き取られた流体の第２体積及び／又は第３体積を収容するように設計されたサンプルリザーバ１８０及び／又は１９０に向けられないことが必要である。

【００３４】

[1087] 流量コントローラ１４０は、第１形態にある時、第１流体流路１４２が入口ポート１２１を第１出口ポート１２５に流体的に結合し、第２形態にある時、第２流体流路１４４が入口ポート１２１を第２出口ポート１２６に流体的に結合するように構成されている。いくつかの実施形態では、上述したようなアクチュエータを、流量コントローラ１４

０を第１形態及び第２形態、任意選択的に第３形態又は第４形態の間で、並進運動で移動させるように構成することができる。例えば、いくつかの実施形態では、流量コントローラ１４０は、収集デバイス１００に対して遠位位置にある時に第１形態であり得る。こうした実施形態では、アクチュエータを、流量コントローラ１４０を収集デバイス１００に対して近位位置まで近位方向に移動させ、それにより流量コントローラ１３０を第２形態に配置するように作動させることができる。他の実施形態では、アクチュエータを、流量コントローラ１４０を第１形態及び第２形態又は任意選択的に第３形態あるいは第４形態の間で、回転運動で移動するように作動させることも可能である。

【００３５】

[1088] 従って、流量コントローラ１４０が第１形態にある時、第２出口ポート１２６（及び任意選択的に、サンプルリザーバに結合された追加の出口ポート）は、入口ポート１２１から流体的に隔離される。同様に、流量コントローラ１４０が第２形態にある時、第１出口ポート１２５は入口ポート１２１から流体的に隔離される。任意選択的に、流量コントローラ１４０が（図１には示さない）第３形態にある場合、第１出口ポート１２５及び第２出口ポート１２６は、入口ポート１２１から流体的に隔離される。このように、流量コントローラ１４０は、第１形態にある時、体液の第１量を、第１出口ポート１２５を介してプリサンプル流体リザーバ１７０に仕向け又は分流させることができ、第２形態にある時、体液の第２量を、第２出口ポート１２６を介して第１サンプル流体リザーバ１８０に仕向け又は分流させることができる。

【００３６】

[1089] いくつかの実施形態では、アクチュエータの少なくとも一部を、プリサンプル流体リザーバ１７０に動作可能に結合することができる。このように、アクチュエータ（又はアクチュエータの少なくとも一部）を、「プリサンプル」流体リザーバ１７０内における真空の発生を引き起こすか又は他の方法で促進し、それにより、分流機構１２０がその第１形態にある時、体液の収集デバイス１００を通りプリサンプル流体リザーバ１７０に入る流れを開始するように構成することができる。アクチュエータは、例えば、回転ディスク、プランジャ、スライド、ダイヤル、ボタン、ハンドル、レバー及び／あるいは他のあらゆる好適な機構又はそれらの組合せ等、収集デバイス１００内への体液の流れを駆動するあらゆる好適な機構を含むことができる。好適なアクチュエータの例については、本明細書において具体的な実施形態を参照してより詳細に記載する。

【００３７】

[1090] いくつかの実施形態では、分流機構１２０を、体液の第２量の流れが分流機構１２０を通って第１サンプル流体リザーバ１８０に及び／又は第２サンプル流体リザーバ１９０に輸送されるのを可能にする前に、体液の第１量をプリサンプル流体リザーバ１７０に輸送する必要があるように構成することができる。このように、分流機構１２０を、医療従事者による、体液の第２量及び／又は第３量（例えば、サンプル）を収集する前に体液の第１の所定量（例えば、プリサンプル）を収集することに関するコンプライアンスを必要とするものとして特徴付けることができる。同様に言えば、分流機構１２０を、医療従事者が、体液の第１量、すなわちプリサンプルをプリサンプルリザーバ１７０に最初に分流させることなく、体液の第２量すなわちサンプルを第１サンプル流体リザーバ１８０内に収集するのを防止するように構成することができる。このように、医療従事者は、体表微生物及び／又は他の望ましくない外部汚染物質を含む可能性がより高い体液の第１量を、分析に使用される体液サンプル内に（意図的であっても無意図的であっても）含めることが防止される。他の実施形態では、流体収集デバイス１００は、強制的コンプライアンスの特徴又は構成要素を含む必要はない。

【００３８】

[1091] いくつかの実施形態では、分流機構１２０は、第１形態、第２形態及び第３形態とは異なる（図１には示さない）第４形態を有することができる。第４形態にある時、分流機構１２０は、入口ポート１２１を、第１出口ポート１２５、第２出口ポート１２６及び任意選択的に第３出口ポートから同時に流体的に隔離することができる。従って、分流

機構１２０がその第４形態にある時、入口ポート１２１からプリサンプル流体リザーバ１７０、第１サンプル流体リザーバ１８０及び第２サンプル流体リザーバ１９０に体液が流れることが防止される。使用時、例えば、分流機構１２０を、体液が入口ポート１２１からプリサンプル流体リザーバ１７０に流れることができるように分流機構１２０を第１形態に配置するように（例えば、手動で又は自動的に）作動させ、その後、体液が入口ポート１２１から第１サンプル流体リザーバ１８０に流れることができるように第２形態まで移動させ、任意選択的に、体液が入口ポート１２１から第２サンプル流体リザーバ１９０に流れることができるように第３形態に移動させることができ、その後、体液の分流機構１２０内への及び／又はそこを通る流れを停止させるように第４形態に移動させることができる。このように、デバイスは、デバイス１００内のいかなる残留体液も汚染され及び／又は他の方法で医療従事者及び／又は患者をあり得る危険な流体にさらすことが防止されるように、有効に「ロックされ」かつ第４形態で自己完結する。この任意選択的な安全機能により、ＨＩＶ、Ｃ型肝炎等の病原体が感染している可能性がある体液サンプルへのあり得る暴露を防止することができる。

【００３９】

[1092] いくつかの実施形態では、収集デバイス１００の１つ又は複数の部分は、（図１には示さない）ハウジング内に配置されている。例えば、いくつかの実施形態では、分流機構１２０、第１プリサンプルリザーバ１７０並びにサンプルリザーバ１８０及び１９０のうちの１つ又は複数の少なくとも一部を、ハウジング内に配置することができる。こうした実施形態では、分流機構１２０の少なくとも一部は、使用者が、患者（例えば、静脈）から収集デバイス１００への体液の流れを制御するように流量コントローラ１４０を作動させることができるように、ハウジングを通してアクセス可能である。好適なハウジングの例については、本明細書において具体的な実施形態を参照してより詳細に記載する。

【００４０】

[1093] いくつかの実施形態では、収集デバイス１００は、任意選択的に、収集デバイスを通して体液の流れを計量することができる１つ又は複数の流量計量デバイスを含むことができる。例えば、流量計量デバイスは、第１流体流路１４２及び／又は第２流体流路１４４に流体連通してそこを通る体液の流れを計量することができる。他の実施形態では、流量計量デバイスは、第１ポート１２５及び／又は第２ポート１２６に流体連通し及び／又は他の方法でそこに配置されることが可能である。流量計量デバイスは、プリサンプルリザーバ１７０、第１サンプルリザーバ１８０及び／又は第２サンプルリザーバ１９０に移送されている所定体積に関連する指示を使用者に提供するように構成することができるインジケータ等（例えば、ダイヤル、ディスプレイ、色、触覚出力デバイス、ワイヤレス無線信号、Bluetooth（登録商標）無線信号等の電気信号出力デバイス）を含むことができる。いくつかの実施形態では、流量計量デバイスを、例えば、上述したもののようなアクチュエータ等に動作可能に結合することができる。こうした実施形態では、流量計量デバイスは、流量計量デバイスを通して流れた体液の所望の体積に基づいて、流量コントローラ１４０をその第１形態とその第２形態との間で移動させるようにアクチュエータを作動させるように、動作可能であり得る。従って、流量計量デバイスを用いて、体液の所望の体積がプリサンプルリザーバ１７０、第１サンプルリザーバ１８０及び／又は第２サンプルリザーバ１９０に移送され、それにより、例えば患者サンプルに対する微生物検査等において不十分な、不正確な及び／又は誤った結果を防止することができることを確実にすることができる。

【００４１】

[1094] ここで図２～図１３を参照すると、収集デバイス２００は、分流機構２２０、流量コントローラ２４０、プリサンプルリザーバ２７０、第１サンプルリザーバ２８０、及び第１サンプルリザーバ２８０とは異なる第２サンプルリザーバ２９０を含む。本明細書においてさらに記載するように、収集デバイス２００を、例えば皮膚に存在する微生物及び／又は他の望ましくない外部汚染物質等、体外の微生物が実質的にない体液の流れを送出するために、第１形態、第２形態及び第３形態の間で移動させることができる。収集デ

バイス２００は、いかなる好適な形状、サイズ又は構成でもあり得る。例えば、図２～図１３ではサンプルリザーバ２８０及び／又は２９０がハウジング２０１に対して垂直に向けられているように示されているが、収集デバイス２００は、ハウジング２０１に対して平面に向けられているか又はハウジング２０１に対して円錐状に配置されている等のサンプルリザーバ２８０及び／又は２９０を有することができる。

【００４２】

[1095] 分流機構２２０は、ハウジング２０１及び可動部材２５０及び２５０’を含む。図２～図４に示すように、ハウジング２０１は、プリサンプルリザーバ２７０、第１サンプルリザーバ２８０及び第２サンプルリザーバ２９０に結合されている。ハウジング２０１は、入口ポート２２１、第１出口ポート２３０、第２出口ポート２３１、第３出口ポート２３２を含み、患者から体液を収集するための流体流路を規定することができる内部流路２３５を規定している。入口ポート２２１を、内部流路２３５に流体連通するように選択的に配置することができる。より具体的には、入口ポート２２１は、内部流路２３５に流体連通するように配置することができる入口内腔２０２を規定している。このように、入口ポート２２１は、内部流路２３５を、入口内腔２０２を介してハウジング２０１の実質的に外側の空間に流体連通するように配置することができるように、ハウジング２０１の一部から延在している。入口ポート２２１を、患者から体液を抜き取り及び／又は収集デバイス２００に輸送するための流体流路を規定する（図示せず）医療デバイスに流体的に結合することができる。例えば、入口ポート２２１を、アダプタ２０４を介して直接又は間接的に針又は他の内腔規定デバイス（例えば、可撓性滅菌管）に流体的に結合することができる。同様に言えば、入口ポート２２１によって規定された入口内腔２０２は、内腔規定デバイスが入口ポート２２１に結合された時に内腔規定デバイスによって規定される内腔に流体連通するように配置される。さらに詳述すると、内腔規定デバイスが患者の身体の一部の中に（例えば、患者の静脈又は脊椎腔内に）配置されると、ハウジング２０１の内部流路２３５を、患者の身体のその部分に流体連通するように配置することができる。

【００４３】

[1096] ハウジング２０１によって規定される内部流路２３５は、ハウジング２０１の長さに沿って延在する中心内腔であり、それを、本明細書に記載するように静脈穿刺（体液へのアクセスを可能にするために採用される他の方法）に続いて患者の体液に流体連通するように配置することができる。内部流路２３５は、入口ポート２２１と第１出口ポート２３０、第２出口ポート２３１及び第３出口ポート２３２との間で体液を移送する流体流経路を形成する。より具体的には、内部流路２３５が（例えば、入口ポート２２１に結合された医療デバイスを介して）患者に流体連通するように配置されると、第１出口ポート２３０、第２出口ポート２３１及び第３出口ポート２３２を、内部流路２３５に流体連通するように選択的に配置して、体液がプリサンプルリザーバ２７０、第１サンプルリザーバ２８０又は第２サンプルリザーバ２９０のうちの少なくとも１つに流れ込むのを可能にすることができる。いくつかの実施形態では、体液は、体液の所定体積がプリサンプルリザーバ２７０内に収集される前に、第２出口ポート２３１及び第３出口ポート２３２に流れるのが防止される。いくつかの実施形態では、第２出口ポート２３１及び第３出口ポート２３２を、同時に内部流路２３５に流体連通するように配置することができる。いくつかの実施形態では、第２出口ポート２３１及び第３出口ポート２３２を、逐次内部流路２３５に流体連通するように配置することができる。

【００４４】

[1097] 可動部材２５０、２５０’は、使用者によって、ハウジング２０１に対して第１位置及び第２位置から作動（例えば、移動）させて、流体流を第１サンプルリザーバ２８０及び第２サンプルリザーバ２９０内に向けるように構成されている。可動部材２５０及び２５０’は、実質的に同じであり、従って、単一の可動部材２５０に関して記載する。図５に示すように、可動部材２５０は、内部空洞２５２を規定するボス２５１と、入口ポート２５３と、第１出口ポート２５４と、内部空洞２５２に流体的に結合された内腔２５

６を規定する穿孔部材２５５とを含む。入口ポート２５３及び出口ポート２５４は、可動部材２５０の内部チャンバ２５２を規定するボス２５１の壁を通って延在している。可動部材２５０は、ボス２５１がボア２５８（図４参照）内に配置され、可動部材２５０の少なくとも一部が環状チャンバ２６０内に配置されるように、ハウジング２０１の支持体２５７（図４参照）に取り付けられるように構成されている。任意選択的に、可動部材２５０を使用者が作動させた後にその第１位置に戻すように、付勢部材２５９（例えば、ばね）を環状チャンバ２６０内に配置することができる。いくつかの実施形態では、可動部材２５０、環状チャンバ２６０、ボア２５８又はボス２５１は、使用者によって作動された後に可動部材２５０を第２位置（例えば、押下位置）で保持するように構成された機械的係止機構を含むことができる。

【００４５】

[1098] 本明細書に記載するように、第１形態では、可動部材２５０は、内部流路２３５から間隔を空けて配置されるように配置されている。こうした形態では、患者の身体の一部（例えば、静脈、脊椎腔等）とサンプルリザーバ２８０及び／又は２９０との間に、流体流路を確立することができない。言い換えれば、可動部材２５０がその第１形態にある時、第１サンプルリザーバ２８０及び第２サンプルリザーバ２９０は、ハウジング２０１によって規定される内部流路２３５から流体的に隔離される。可動部材２５０を、使用者により、可動部材２５０を第１形態から第２形態にかつ内部流路２３５と整列するように移動させるように作動させることができる。使用者によってかけられる力は、付勢部材２５９を変形させる（例えば、圧縮する）のに十分である可能性があり、それにより、穿孔部材２５５をサンプルリザーバ２８０及び／又は２９０内に挿入することができる。第２形態では、入口ポート２５３及び出口ポート２５４は、内部流路２３５と実質的に位置合せされて、内部空洞２５２を内部流路２３５に流体連通するように配置する。従って、可動部材２５０が第２形態にある場合、内部流路２３５と、内部空洞２５２と、穿孔部材２５５の内腔２５６と、サンプルリザーバ２８０との間に流体流経路が確立される。言い換えれば、こうした形態では、本明細書においてさらに詳細に記載するように、体液は、患者（例えば、静脈、脊椎腔等）から分流機構２２０を通って、第１サンプルリザーバ２８０及び／又は第２サンプルリザーバ２９０内に流れ込むことができる。

【００４６】

[1099] プリサンプルリザーバ２７０は、例えば、単回使用使い捨て収集チューブ、真空による収集チューブ等、体液を収容するあらゆる好適なリザーバであり得る。プリサンプルリザーバ２７０は、収集デバイス２００の第１出口ポート２３０に（直接、又は滅菌可撓性管等の介在構造を介して）あらゆる好適な方法で流体的に結合されるように構成されている。例えば、いくつかの実施形態では、プリサンプルリザーバ２７０の一部は、第１出口ポート２３０の一部の中に摩擦嵌めを形成することができる。他の実施形態では、プリサンプルリザーバ２７０を、ねじ結合、接着剤、スナップフィット、機械的締結具及び／又は他のあらゆる好適な結合方法を介して、第１出口ポート２３０に結合することができる。いくつかの実施形態では、プリサンプルリザーバ２７０を、ハウジング２０１と一体的に形成することができる。プリサンプルリザーバ２７０を、体液を、真空吸引を介して入口ポート２２１から出口ポート２３０を通りプリサンプルリザーバ２７０に引き込むのを可能にすることができる負圧状態（真空状態）を（プリサンプルリザーバ２７０の）内部で維持するように構成することができる。プリサンプルリザーバ２７０は、体液の第１量を収容するように構成されており、そこでは、体液の第１量は所定量であることも未定量であることも可能であり、それにより、体液の第１量は、患者から後に抜き取られる体液の第２量及び／又は第３量から流体的に隔離される。

【００４７】

[1100] サンプルリザーバ２８０及び／又は２９０は、単回使用使い捨て収集チューブ、真空による収集チューブ、上記参照により本明細書に組み込まれる‘４２０特許に記載されているようなサンプルリザーバ等を含む、体液を収容するあらゆる好適なリザーバであり得る。いくつかの実施形態では、サンプルリザーバ２８０及び／又は２９０は、例えば

Vacutainer（登録商標）等、既知のサンプル容器と実質的に同様であるか又は同じであり得る。サンプルリザーバ２８０及び２９０は、それぞれサンプル容器２８２及び２９２を含み、それぞれ真空シール２８４及び２９４を含む。真空シール２８４又は２９４は、サンプル容器２８２又は２９２それぞれ内部に、真空吸引を介して内部流路２３５からサンプル容器２８２又は２９２それぞれに体液が引き込まれるのを可能にすることができる負圧状態（真空状態）を維持する。サンプル容器２８０及び／又は２９０を、収集デバイス２００の第２出口ポート２３１及び第３出口ポート２３２それぞれに（直接、又は滅菌可撓管等の介在構造を介して）あらゆる好適な方法で流体的に結合されるように構成することができる。サンプルリザーバ２８０及び／又は２９０を、出口ポート２３１及び／又は２３２に流体連通するように配置するように、出口ポート２３１及び／又は２３２に対して移動させることができる。サンプルリザーバ２８０及び２９０を、体液の第２量又は第３量を収容するように構成することができる。体液の第２量又は第３量は、所定量であることも未定量であることも可能であり、それにより、体液の第２量又は第３量は、患者から抜き取られる体液の第１量から流体的に隔離される。いくつかの構成では、サンプルリザーバ２８０及び／又は２９０を、プリサンプルリザーバ２７０と同様にハウジング２０１と一体的に形成することによって収集デバイス２００に結合することができ、従って、それらについてはここでは詳細に記載しない。場合によっては、サンプルリザーバ２８０及び／又は２９０を透明とすることができ、それにより、使用者は、サンプルリザーバ２８０及び／又は２９０内への体液の流れを確認するように視覚的フィードバックを得ることができる。

【００４８】

[1101] いくつかの実施形態では、サンプルリザーバ２８０及び２９０と分流機構２２０（及び／又はサンプルリザーバ２８０及び２９０以外の収集デバイス２００の部分）とは、独立して形成され（例えば、一体的に形成されず）例えば製造プロセス中に合わせて結合される。場合によっては、サンプルリザーバ２８０及び２９０を、実質的に滅菌又は密封環境（例えば、エチレンオキシド等で充填された環境）で分流機構２２０に結合することができる。従って、サンプルリザーバ２８０及び２９０と分流機構２２０との間のインタフェースは、使用前に実質的に滅菌される。さらに、収集デバイス２００を、サンプルリザーバ２８０及び２９０と分流機構２２０との間に実質的滅菌インタフェースを維持するため等、事前組立式に輸送及び／又は保管することができる。

【００４９】

[1102] 図６及び図７に示すように、流量コントローラ２４０は、第１部材２４１及び第２部材２４５を含む。第１部材２４１は、ハウジング２０１の凹部２６６（例えば、図４を参照）内に配置されるように構成され、第１部材２４１を、例えば、チタン、グラファイト、熱分解炭素、ポリエステル、ポリカーボネート、ポリウレタン、エラストマー材料等、生体適合性であるあらゆる材料から作製することができる。いくつかの実施形態では、第２部材２４５は、第１部材２４１を第１形態から第２形態に移動させるアクチュエータとしての役割を果たす。より具体的には、第１部材２４１が凹部２６６内に配置されると、第２部材２４５を、第１位置と第２位置との間で移動させて、流量コントローラ２４０を第１形態と第２形態との間で移動させることができる。いくつかの実施形態では、ハウジング２０１は、第２部材２４５のその第１位置からその第２位置への移動を選択的に制限することができる。いくつかの実施形態では、ハウジング２０１を、第２位置に移動した第２部材２４５の移動を防止するように構成することができる。言い換えれば、ハウジング２０１は、第２部材２４５が第２位置から第１位置に戻るように移動するのを防止する係止機構を含むことができる。第２部材２４５及び／又はハウジング２０１はまた、第２部材２４５の正確な位置決めを確実にするように視覚的フィードバック又は触覚フィードバックを提供する機械的戻り止め及び／又は他のインジケータを含むことも可能である。

【００５０】

[1103] 第１部材２４１は、静脈穿刺（及び／又は患者の体液にアクセスする他の方法）

に続いて流体流を方向付ける複数のチャネルを含むことができる。例えば、図６及び図７に示すように、第１部材２４１は第１流路２４２及び第２流路２４４を含む。第２部材２４５が第１位置にある時（例えば、図８及び図９を参照）、流量コントローラ２４０は第１形態に配置され、第１流路２４２は、入口ポート２２１を内部流路２３５から流体的に隔離しながら、入口ポート２２１と第１出口ポート２３０との間に流体連通を確立する。第２部材２４５が第２位置にある時（例えば、図１０～図１３を参照）、流量コントローラ２４０は第２形態に配置され、第２流路２４４は、入口ポート２２１を第１出口ポート２３０から流体的に隔離しながら、入口ポート２２１と内部流路２３５との間に流体連通を確立する。患者と収集デバイス２００との間で流体流をさらに方向付ける／隔離するように、追加の第１部材２４１の流路及び／又は流量コントローラ２４０の形態に対応する追加の第２部材２４５の位置を含めることができる。例えば、第２部材２４５は、患者と収集デバイス２００との間の流体流を全体的に実質的に防止する、流量コントローラ２４０の第３形態に対応する第３位置を有することができる。言い換えれば、いくつかの実施形態では、すべての体液サンプルが患者から取り出された後に、収集デバイス２００内のサンプルを外部環境から実質的に封止するように、ダイヤルを第３位置に移動させることができる。

【００５１】

[1104] 動作時、収集デバイス２００を使用して、皮膚に存在する微生物及び／又は他の望ましくない外部汚染物質からの汚染を低減して、患者から体液（例えば、血液）を収集することができる。例えば、収集デバイス２００の入口ポート２２１は、アダプタ２０４を介して針又は他の内腔規定デバイス（例えば、可撓性滅菌管）に流体的に結合される。静脈穿刺（又は他の体液アクセス方法）に続いて、第２部材２４５を、図８及び図９に示すように第１位置に達するまで回転させる。別法として、第２部材２４５を第１位置に事前設定することができ、収集デバイス２００を、プリサンプルリザーバ２７０内の真空及び収集デバイス２００の無菌状態を保持するように他の方法で封止することができる。例えば、入口ポート２２１及び／又はアダプタ２０４は、収集デバイス２００が針又は他の内腔規定デバイスに結合された時に開放される弁を含むことができる。

【００５２】

[1105] 上述したように、第２部材２４５が第１位置にある時、流量コントローラ２４０は第１形態に配置され、第１部材２４１の第１流路２４２は、入口ポート２２１を内部流路２３５から流体的に隔離しながら、入口ポート２２１と第１出口ポート２３０との間に流体連通を確立する。さらに、第１サンプルリザーバ２８０及び第２サンプルリザーバ２９０は、第１形態では入口ポート２２１から流体的に隔離され、図９において矢印ＡＡによって示すように、患者の身体の一部（例えば、静脈）とプリサンプルリザーバ２７０との間に流体流路が規定される。上述したように、プリサンプルリザーバ２７０並びにサンプルリザーバ２８０及び２９０等、収集デバイス２００で使用される流体リザーバを、負圧（すなわち、収集デバイス２００が体液を抜き取るために使用されている身体の部分の流体圧力未満の圧力）を規定し、それにより、患者の身体の一部（例えば、静脈）とプリサンプルリザーバ２７０との間に流体連通が確立されると、プリサンプルリザーバ２７０内の負圧により、プリサンプルリザーバ２７０と患者の身体のその部分との間の圧力差によってプリサンプルリザーバ２７０内に体液が引き込まれるようになる。この第１形態では、流量コントローラ２４０はまた、プリサンプルリザーバ２７０を内部流路２３５から流体的に隔離する。従って、体液の第１量（所定量又は未定量）を、（例えば）静脈穿刺の直後にプリサンプルリザーバ２７０内に受け取り、後続するサンプルから隔離することができる。このように、収集デバイス２００を用いて、体表微生物及び／又は他の望ましくない外部汚染物質を含む可能性が最も高い体液の第１量が、診断又は汚染物質によって影響を受ける可能性がある他の検査のために収集され使用される体液サンプルの後続する量を汚染しないようにすることができる。

【００５３】

[1106] プリサンプルリザーバ２７０内における体液プリサンプルの体積の収集に続いて

、第２部材２４５を、図１０及び図１１に示すような第２位置に達するまで、回転させることができる。第２部材２４５が第２位置にある時、流量コントローラ２４０は第２形態に配置され、第１部材２４１の第２流路２４４は、第１出口ポート２３０（すなわち、プリサンプルリザーバ２７０）を入口ポート２２１から流体的に隔離しながら、入口ポート２２１と内部流路２３５との間に流体連通を確立する。言い換えれば、第２形態では、流量コントローラ２４０は、図１１において矢印ＢＢによって示すように第２流路２４４を介して、患者の身体の一部（例えば、静脈）と内部流路２３５との間に流体流路を確立する。

【００５４】

[1107] 流量コントローラ２４０が第２形態にある状態で、可動部材２５０及び／又は２５０’を使用者が第１位置から第２位置に作動させて（すなわち、押下して）、患者の身体の一部（例えば静脈）と第１サンプルリザーバ２８０及び／又は第２サンプルリザーバ２９０との間に流体連通を確立することができる。より具体的には、可動部材２５０は、その第１位置からその第２形態に移動して、図１２において矢印ＣＣによって示すように、穿孔部材２５５が第１サンプルリザーバ２８０の真空シール２８４に穴をあけサンプル容器２８２内部に配置されことが可能であるように、穿孔部材２５５が出口ポート２３１を通過するようにする。第２位置にある時、可動部材２５０の入口ポート２５３及び出口ポート２５４は、内部流路２３５と実質的に位置合せされかつそれに流体連通し、それにより、体液が、内部流路２３５から可動部材２５０の内部空洞２５２内に、かつ穿孔部材２５５の内腔２５６から出て第１サンプルリザーバ２８０内に流れることができる。サンプルリザーバ２８０（例えば、真空又は負圧）と内部流路２３５との圧力差により、体液がサンプルリザーバ２８０内に引き込まれる。言い換えれば、第２形態では、図１２において矢印ＤＤによって示すように、可動部材２５０は、内部流路２３５と第１サンプルリザーバ２８０との間に流体流路を確立する。第１サンプルリザーバ２８０に体液の所望の量（例えば、第２量）が収集されると、使用者は、可動部材２５０を解放して、付勢部材２５９がボタンをその第１位置に戻るように移動させるのを可能にすることができる。可動部材２５０がその第１位置に戻ると、穿孔部材２５５は第１サンプルリザーバ２８０から取り除かれ、シール２８４（例えば、自己封止膜（self sealing septum））が、第１サンプルリザーバ２８０を内部流路２３５から流体的に隔離する。

【００５５】

[1108] 同様に、流量コントローラ２４０が第２形態にある間、図１３において矢印ＥＥによって示すように、可動部材２５０’を、使用者がその第１位置から第２位置に作動させる（押下する）ことができる。このように、上述した可動部材２５０及び第１サンプルリザーバ２８０と同様の方法で、患者の身体の一部（例えば、静脈）と第２サンプルリザーバ２９０との間に（出口ポート２３２を介して）流体連通が確立される。言い換えれば、第２形態では、可動部材２５０’は、図１３において矢印ＦＦによって示すように、内部流路２３５と第２サンプルリザーバ２９０との間に流体流路を確立する。第２サンプルリザーバ２９０内に体液の所望の量（例えば、第３量）が収集されると、使用者は、可動部材２５０’を解放して、付勢部材２５９’がボタン２５０’をその第１位置に戻るように移動させるのを可能にすることができる。逐次プロセスであるものとして示しかつ記載しているが、充填の順序及び／又は順序付けは必ずしも必要ではない（すなわち、サンプルリザーバ２８０は、必ずしもサンプルリザーバ２９０より前に充填されなくてもよい、等）。言い換えれば、流量コントローラ２４０が第２形態に移動すると、第１サンプルリザーバ２８０及び第２サンプルリザーバ２９０（及び任意の追加のサンプルリザーバ）を、あらゆる順序で、同じ時点で（例えば、同時に）及び／又は一部が重なる時間間隔で充填することができる。例えば、使用者は、第１サンプルリザーバ２８０への充填を開始することができ、その後、第１サンプルリザーバ２８０が部分的に充填された後、使用者は、可動部材２５０’を押下して、第１サンプルリザーバ２８０が充填を終了している間に、第２サンプルリザーバ２９０への充填を開始するようにすることができる。さらに、サンプルリザーバ２８０及び／又は２９０内に収集された体液の体積の調整を、可動部材２

５０及び／又は２５０’を繰り返し作動させる（挿入する）ことによって可能にすることができる。上述したように、第２部材２４５は、流量コントローラ２４０の第３形態に対応する第３位置を有することができ、それにより、患者と収集デバイス２００との間の流体流を全体的に実質的に防止して、収集デバイス２００内のサンプルを外部環境から実質的に封止することができる。

【００５６】

[1109] 図２～図１３には示さないが、収集デバイス２００は、プリサンプルリザーバ２７０、第１サンプルリザーバ２８０及び／又は第２サンプルリザーバ２９０に移送される体液の体積を計量するように構成することができる流量計量デバイス等を含むことができる。例えば、いくつかの実施形態では、流量コントローラ２４０の第１部材２４１は、第１流路２４２及び第２流路２４４に流体連通している流量計量デバイスを含むことができる。他の実施形態では、流量計量デバイスを、可動部材２５０及び／又は２５０’の内部空洞２５２内に配置することができる。従って、第１サンプルリザーバ２８０及び第２サンプルリザーバ２９０に移送されかつその中に配置される体液サンプルの体積を、各サンプルリザーバ２８０及び２９０内に配置される体液サンプルの体積が例えば１０ｍＬ、２０ｍＬ、３０ｍＬ等の所定体積であるように、計量し及び／又は制御することができる。

【００５７】

[1110] 収集デバイス２００は、第１サンプルリザーバ２８０及び第２サンプルリザーバ２９０を含むものとして示されかつ記載されているが、他の実施形態では、あらゆる数のプリサンプルリザーバ及び／又はサンプルリザーバを含むことができる。例えば、図１４及び図１５は、実施形態による収集デバイス３００を示す。図示するように、収集デバイス３００のいくつかの態様は、図２～図１３を参照して上述した収集デバイス２００の対応する態様に実質的に同様であり得る。従って、同様の態様については本明細書ではそれ以上詳細には記載しない。

【００５８】

[1111] 図１４及び図１５に示すように、収集デバイス３００は、分流機構３２０、流量コントローラ３４０、プリサンプルリザーバ３７０、第１サンプルリザーバ３８０、第２サンプルリザーバ３８０’、第３サンプルリザーバ３９０及び第４サンプルリザーバ３９０’を含む。プリサンプルリザーバ３７０は、詳細に上述したプリサンプルリザーバ２７０と実質的に同様であり得る。いくつかの実施形態では、サンプルリザーバ３８０、３８０’、３９０及び３９０’は、詳細に上述したサンプルリザーバ２８０及び２９０と実質的に同様であり得る。いくつかの実施形態では、サンプルリザーバ３８０、３８０’、３９０及び３９０’は、実質的に同じ形状及びサイズを有することができ、例えば、実質的に同じ培地を含むことができる。他の実施形態では、サンプルリザーバ３８０、３８０’、３９０及び３９０’は、実質的に同じ形状及びサイズを有することができ、好気性菌用培地又は嫌気性菌用培地のうちの一方を含むことができる。例えば、いくつかの実施形態では、第１サンプルリザーバ３８０及び第３サンプルリザーバ３９０は好気性菌用培地を含むことができ、第２サンプルリザーバ３８０’及び第４サンプルリザーバ３９０’は嫌気性菌用培地を含むことができる。他の実施形態では、サンプルリザーバ３８０、３８０’、３９０及び３９０’は、各々、好気性菌用培地又は嫌気性菌用培地をあらゆる配置又は組合せで含むことができる。

【００５９】

[1112] 分流機構３２０は、ハウジング３０１と一組の可動部材３５０、３５０’、３５０’’及び３５０’’’とを含む。可動部材３５０、３５０’、３５０’’及び３５０’’’は、例えば、図５を参照して上述した可動部材２５０と実質的に同様である。従って、可動部材３５０、３５０’、３５０’’及び３５０’’’を、サンプルリザーバ３８０、３８０’、３９０及び３９０’それぞれに流体連通して配置されるように、ハウジング３０１に対して第１位置と第２位置との間で移動させることができる。ハウジング３０１は、入口ポート３２１と、プリサンプルリザーバ３７０に流体連通するように配置されるように構成された第１出口ポート３３０と、第１サンプルリザーバ３８０に流体連通する

ように配置されるように構成された第２出口ポート３３１と、第２サンプルリザーバ３８０’に流体連通するように配置されるように構成された第３出口ポート３３２と、第３サンプルリザーバ３９０’に流体連通するように配置されるように構成された第４出口ポート３３３と、第４サンプルリザーバ３９０’に流体連通するように配置されるように構成された第５出口ポート３３４とを含む。さらに、ハウジング３０１は、ハウジング２０１の内部流路２３５に関して上述したものと同様の方法で、入口ポート３２１並びに出口ポート３３１、３３２、３３３及び３３４に流体連通するように選択的に配置することができる内部流路３３５を規定している。

【００６０】

[1113] 流量コントローラ３４０は、例えば、図６～図１３を参照して上述した流量コントローラ２４０と実質的に同様である。従って、流量コントローラ３４０を、第１形態と第２形態との間で回転させて、患者とプリサンプルリザーバ３７０又はサンプルリザーバ３８０、３８０’、３９０及び３９０’との間に流体流路の一部を選択的に規定することができる。このように、使用者は、図８～図１３において収集デバイス２００に関して上述したものと同様の方法で、収集デバイス３００を操作することができる。従って、体液の第１体積をプリサンプルリザーバ３７０に移送しかつその中に配置することができ、体液の後続する体積を、サンプルリザーバ３８０、３８０’、３９０及び３９０’に移送しかつその中に配置することができる。

【００６１】

[1114] 図１６～図２２は、実施形態による収集デバイス４００を示す。収集デバイス４００は、分流機構４２０、流量コントローラ４４０並びにサンプルリザーバ４８０、４８０’、４９０及び４９０’を含む。本明細書においてさらに記載するように、収集デバイス４００を、第１形態、第２形態、第３形態、第４形態及び第５形態の間で移動させて、例えば、皮膚に存在する微生物及び／又は他の望ましくない外部汚染物質等、体外の微生物が実質的にない体液の流れを送出することができる。収集デバイス４００は、あらゆる好適な形状、サイズ又は構成であり得る。例えば、図１６～図２２において、サンプルリザーバ４８０、４８０’、４９０及び４９０’がハウジング４０１に対して垂直に向けられて示されているが、収集デバイス４００は、ハウジング４０１に対してあらゆる好適な平面において向けられ、又はハウジング４０１に対して円錐状に配置される等のサンプルリザーバ４８０、４８０’、４９０及び４９０’を有することができる。

【００６２】

[1115] サンプルリザーバ４８０、４８０’、４９０及び４９０’は、収集デバイス２００のサンプルリザーバ２８０及び／又は２９０と形態及び機能が実質的に同様であるか又は同じであり、従って、本明細書では詳細には記載しない。上述したように、サンプルリザーバ４８０、４８０’、４９０及び４９０’は、吸引を介して患者からサンプルリザーバ４８０、４８０’、４９０及び４９０’に体液を引き込むのを可能にすることができる負圧状態（真空状態）を維持する。いくつかの実施形態では、サンプルリザーバ４８０及び４８０’を好気性菌用培養ボトルとすることができ、サンプルリザーバ４９０及び４９０’を嫌気性菌用培養ボトルとすることができ、収集デバイス４００を用いて、１回の静脈穿刺から複数の好気性菌用血液培養サンプル及び複数の嫌気性菌用血液培養サンプルを収集することができる。本明細書においてさらに詳細に記載するように、サンプルリザーバ４８０、４８０’、４９０及び４９０’を、各々、体液サンプルのある体積を受け取るように分流機構４２０の少なくとも一部に流体連通するように配置することができる。体液サンプルの体積は、所定量でも未定量であり得る。さらに、サンプルリザーバ４８０、４８０’、４９０、４９０’内に体液の所望の体積が配置されると、本明細書においてさらに詳細に記載するように、各サンプルリザーバ４８０、４８０’、４９０及び４９０’を、分流機構４２０の少なくとも一部から流体的に隔離することができる。

【００６３】

[1116] 分流機構４２０は、ハウジング４０１及び分配部材４２９を含む。分流機構４２０のハウジング４０１は、分配部材４２９に物理的にかつ流体的に結合され、患者から体

液を収集する一組の流体流経路を提供し及び／又は規定している。ハウジング４０１は、凹部４６６及び一組の出口開口部４０３を規定している。凹部４６６は、本明細書においてさらに詳細に記載するように、流量コントローラ４４０に含まれるシール部材４４１を受け入れるように構成されている。出口開口部４０３の組は、各々が、分配部材４２９の異なる部分に流体連通している異なる流体流路を規定するように構成されている、第１出口開口部４０３ａ、第２出口開口部４０３ｂ、第３出口開口部４０３ｃ、第４出口開口部４０３ｄ及び第５出口開口部４０３ｅを含む。より具体的には、分配部材４２９は、第１出口開口部４０３ａに流体連通しているプリサンプルリザーバ４７０の少なくとも一部と、第２出口開口部４０３ｂに流体連通している第１流路４３５ａ、第３出口開口部４０３に流体連通している第２流路４３５ｂ、第４出口開口部４０３ｄに流体連通している第３流路４３５ｃ及び第５出口開口部４０３ｅに流体連通している第４流路４３５とを規定し及び／又は形成している。

【００６４】

[1117] 図１７及び図１８に示すように、分配部材４２９は、プリサンプルリザーバ４７０の少なくとも一部を規定するチャンバ又は空間を規定している。プリサンプルリザーバ４７０は、例えば、血液、血漿、尿等の体液を収容するように構成されている。ハウジング４０１の第１出口開口部４０３ａを、プリサンプルリザーバ４７０が患者から体液の流れを受け取るのを可能にするように、プリサンプルリザーバ４７０の開放部分と実質的に位置合せすることができる。例えば、プリサンプルリザーバ４７０は、体液の第１量又は第１体積を受け取りかつ収容することができ、ここで、体液の第１量は、所定量でも未定量でもあり得る。さらに、分流機構４２０の配置を、本明細書においてさらに詳細に記載するように、プリサンプルリザーバ４７０が流路４３５ａ、４３５ｂ、４３５ｃ及び４３５ｄ並びに／又は患者から抜き取られた体液の後続する体積から流体的に隔離して維持されるというものとすることができる。プリサンプルリザーバ２７０及び３７０を、負圧を維持するものとして上述しているが、プリサンプルリザーバ４７０は、負圧状態（真空状態）を維持せず、従って、例えば重力等の他の機構を用いて、体液をプリサンプルリザーバ４７０内に引き込むことができる。

【００６５】

[1118] 流路４３５ａ～４３５ｄは、分配部材４２９の中心から放射状に延在し、各流路４３５ａ、４３５ｂ、４３５ｃ及び４３５ｄがプリサンプルリザーバ４７０及び他の流路から流体的に隔離されるように配置されている。このように、流路４３５ａ、４３５ｂ、４３５ｃ及び４３５ｄは、出口開口部４０３ｂ、４０３ｃ、４０３ｄ及び４０３ｅそれぞれと実質的に位置合せされる第１端部と第２端部との間で流体流路を方向付け及び／又は他の方法で規定することができる。図１７及び図１８に示すように、分配部材４２９は、第１流路４３５ａの第２端部に配置された第１出口ポート４３１と、第２流路４３５ｂの第２端部に配置された第２出口ポート４３２と、第３流路４３５ｃの第２端部に配置された第３出口ポート４３３と、第４流路４３５ｄの第２端部に配置された第４出口ポート４３４とを規定している。さらに、分配部材４２９は、第１穿孔部材４５５ａ、第２穿孔部材４５５ｂ、第３穿孔部材４５５ｃ及び第４穿孔部材４５５ｄを含み、それらは、第１出口ポート４３１、第２出口ポート４３２、第３出口ポート４３３及び第４出口ポート４３４それぞれに、物理的にかつ流体的に結合されている。従って、本明細書においてさらに詳細に記載するように、穿孔部材４５５ａ～３５５ｄを用いて、サンプルリザーバ４８０、４８０’、４９０及び４９０’の真空シールに穴をあけることができ、それにより、体液の流れを開始することができる。図１７及び図１８には示さないが、サンプルリザーバ４８０、４８０’、４９０及び４９０’を、サンプルリザーバ４８０、４８０’、４９０及び４９０’が出口ポート４３１、４３２、４３３及び４３４それぞれに流体連通するように配置されるのを可能にすることができるあらゆる好適な方法で、分配部材４２９の一部に（直接、又は滅菌可撓性管等の介在構造を介して）物理的に結合することができる。

【００６６】

[1119] 流量コントローラ４４０は、ダイヤル４４５及びシール部材４４１を含む。シー

ル部材４４１は、ハウジング４０１の凹部４６６内に配置される（例えば、図２０を参照）。より詳細には、流量コントローラ４４０を、シール部材４４１が凹部４６６を規定するハウジング４０１の表面とダイヤル４４５の表面との間にかつそれらと接触して配置されるように、ハウジング４０１に結合することができる。さらに、シール部材４４１は、本明細書においてさらに詳細に記載するように、流量コントローラ４４０がハウジング４０１に結合された時、シール部材４４１が、ダイヤル４４５の表面及び凹部４６６を規定するハウジング４０１の表面と実質的流体密封シールを形成するような、サイズ及び形状を有することができる。シール部材４４１を、例えば、シリコーン、ポリ乳酸、ポリグリコール酸、ポリ乳酸－グリコール酸共重合体（ＰＬＧＡ）、ポリ酸無水物、ポリオルトエステル、ポリエーテルエステル、ポリカプロラクトン、ポリエステルアミド、ポリ（酪酸）、ポリ（吉草酸）、ポリウレタン、ナイロン、ポリエステル、ポリカーボネート、ポリアクリレート、エチレンービニルアセテート及び他のアシル置換セルロースアセテートのポリマー、ポリスチレン、ポリ塩化ビニル、ポリフッ化ビニル、ポリ（ビニルイミダゾール）、クロロスルホネートポリオレフィン、ポリエチレンオキシド並びに／又はそれらの混合物及びコポリマー等、生体適合性であるあらゆる材料から作製することができる。

【００６７】

[1120] 図１７に示すように、シール部材４４１は、静脈穿刺（又は体液にアクセスする他の方法）に続いて体液の流れを方向付けることができる一組の開口部４４４を規定している。例えば、シール部材４４１によって規定される一組の開口部４４４は、第１開口部４４４ａ、第２開口部４４４ｂ、第３開口部４４４ｃ、第４開口部４４４ｄ及び第５開口部４４４ｅを含む。シール部材４４１の配置は、シール部材４４１が凹部４４６内に配置された時、第１開口部４４４ａ、第２開口部４４４ｂ、第３開口部４４４ｃ、第４開口部４４４ｄ及び第５開口部４４４ｅが、ハウジング４０１の第１出口開口部４０３ａ、第２出口開口部４０３ｂ、第３出口開口部４０３ｃ、第４出口開口部４０３ｄ及び第５出口開口部４０３ｅそれぞれと実質的に位置合せされる、というものである。

【００６８】

[1121] 流量コントローラ４４０のダイヤル４４５は、ハウジング４０１に回転可能に結合され、かつハウジング４０１に対する第１位置、第２位置、第３位置、第４位置及び第５位置の間で移動可能である。ダイヤル４４５は、内腔４０２を規定する入口ポート４２１を含む。入口ポート４２１を、患者の体内から体液を抜き取り及び／又は収集デバイス４００に輸送するための流体流経路を規定する（図示せず）医療デバイスに流体的に結合することができる。例えば、入口ポート４２１を、針又は他の内腔規定デバイス（例えば、可撓性滅菌管）に直接又はアダプタ４０４を介して間接的に流体的に結合することができる。同様に言えば、入口ポート４２１によって規定される入口内腔４０２は、内腔規定デバイスが入口ポート４２１に結合された時、内腔規定デバイスによって規定される内腔に流体連通するように配置される。このように、入口ポート４２１を、本明細書においてさらに詳細に記載するように、プリサンプルリザーバ４７０、第１サンプルリザーバ４８０、第２サンプルリザーバ４８０’、第３サンプルリザーバ４９０及び第４サンプルリザーバ４９０’を、患者に流体連通するように選択的に配置するように構成することができる。

【００６９】

[1122] 上述したように、ダイヤル４４５は、第１位置、第２位置、第３位置、第４位置及び第５位置の間で移動可能である。ダイヤル４４５が第１位置にある時、流量コントローラ４４０は第１形態で配置され、入口ポート４２１を、シール部材４４１の第１開口部４４４ａ及びハウジング４０１の第１出口開口部４０３ａと実質的に位置合せすることができる。このように、シール部材４４１の第１開口部４４４ａは、入口ポート４２１を出口開口部４０３ｂ、４０３ｃ、４０３ｄ及び４０３ｅから流体的に隔離し、それにより入口ポート４２１を流路４３５ａ～３３５ｄから流体的に隔離しながら、入口ポート４２１と第１出口開口部４０３ａとの間に流体連通を確立する。第１出口ポート４０３ａがプリサンプルリザーバ４７０の開放部分と位置合せされると、第１開口部４４４ａ及び第１出

口開口部４０３ａは、入口ポート４２１とプリサンプルリザーバ４７０との間に流体連通を確立する。ダイヤル４４５が第２位置まで回転した（又は駆動された）時、流量コントローラ４４０は第２形態に配置され、第２出口開口部４４４ｂは、入口ポート４２１を出口開口部４０３ａ、４０３ｃ、４０３ｄ及び４０３ｅから流体的に隔離しながら、入口ポート４２１と第２出口開口部４０３ｂとの間に流体連通を確立する。第２出口開口部４０３ｂが第１流路４３５ａの第１端部と位置合せされると、第２開口部４４４ｂ及び第２出口開口部４０３ｂは、入口ポート４２１と第１流路４３５ａとの間に流体連通を確立する。

【００７０】

[1123] 収集デバイス４００は、ダイヤル４４５が第３位置、第４位置及び第５位置まで回転した時、同様に作用する。従って、入口内腔４０２が（例えば、入口ポート４２１に結合された医療デバイスを介して）患者に流体連通するように配置されると、第１出口ポート４３０、第２出口ポート４３１、第３出口ポート４３２、第４出口ポート４３３及び第５出口ポート４３４を、入口内腔４０２に流体連通するように選択的に配置して、体液のすべてがプリサンプルリザーバ４７０のうちの少なくとも１つ、又はサンプルリザーバ４８０、４８０’４９０及び４９０’のうちの１つあるいは複数に流れ込むのを可能にすることができる。いくつかの実施形態では、患者と収集デバイス４００との間で流体流をさらに方向付け／隔離するために、追加のシール出口開口部及び／又は流量コントローラ４４０の形態に対応する追加のダイヤル４４５の位置を含めることができる。例えば、ダイヤル４４５は、患者と収集デバイス４００との間の流体流を全体として実質的に防止する、流量コントローラ４４０の第６形態に対応する第６位置を有することができる。言い換えれば、いくつかの実施形態では、すべての体液サンプルが患者から取り出された後、収集デバイス４００内のサンプルを外部環境から実質的にシールするようにダイヤル４４５を第６位置に移動させることができる。

【００７１】

[1124] いくつかの実施形態では、プリサンプルリザーバ４７０内に体液の所定体積が収集される後まで、体液は、サンプルリザーバに関連する出口ポート（例えば、出口ポート４３１～４３４）に流れるのが防止される。いくつかの実施形態では、サンプルリザーバに関連する出口ポート（例えば、出口ポート４３１～４３４）を、逐次的にのみ、入口内腔４０２に流体連通するように配置することができる（例えば、出口ポート４３１は、出口ポート４３２の前に入口内腔４０２に流体連通しなければならない、等）。いくつかの実施形態では、後続するサンプルリザーバに関連する出口ポート（例えば、出口ポート４３２～４３４）を、体液の確定された体積が収集された後にのみ、入口内腔４０２に流体連通するように配置することができる。いくつかの実施形態では、サンプルリザーバに関連する出口ポート（例えば、出口ポート４３１～４３４）を、いかなる順序の優先もなくあらゆるランダムな方法で入口内腔４０２に流体連通するように配置することができる（例えば、出口ポート４３４は、出口ポート４３１の前に入口内腔４０２に流体連通することができ、出口ポート４３２は、出口ポート４３３の前に入口内腔４０２に流体連通することができる等）。

【００７２】

[1125] いくつかの実施形態では、ハウジング４０１は、ダイヤル４４５のその第１位置からその第２位置、第３位置、第４位置及び第５位置への移動を選択的に制限することができる。いくつかの実施形態では、ハウジング４０１を、第５位置まで移動したダイヤル４４５の移動を防止するように構成することができる。言い換えれば、ハウジング４０１は、ダイヤル４４５が第５位置から第１位置に戻るように移動するのを防止する係止機構を含むことができる。ダイヤル４４５及び／又はハウジング４０１は又はウジング４０１の出口開口部４０３ａ～４０３ｅに対するダイヤル４４５の正確な位置決めを確実にするように視覚的フィードバック又は触覚フィードバックを提供する、機械的戻り止め及び／又は他のインジケータを含むことも可能である。

【００７３】

[1126] 動作時、収集デバイス４００を用いて、汚染を低減して患者から体液（例えば、血液、血漿、尿等）を収集することができる。例えば、収集デバイス４００の入口ポート４２１を、針又は他の内腔規定デバイス（例えば、可撓性滅菌管）に流体的に結合することができる。静脈穿刺（又は体液にアクセスする他の方法）に続いて、図１９及び図２０に示すように、ダイヤル４４５が第１位置に達するまで駆動される（又は回される）。別法として、ダイヤル４４５を第１位置に事前設定することができ、収集デバイス４００を、収集デバイス４００の無菌状態を維持するように他の方法で封止することができる。例えば、入口ポート４２１は、収集デバイス４００が針又は他の内腔規定デバイスに結合されると開放する弁を含むことができる。

【００７４】

[1127] 上述したように、ダイヤル４４５が第１位置にある時、流量コントローラ４４０は第１形態に配置され、シール部材４４１の第１開口部４４４ａは、入口ポート４２１を４つの流路４３５ａ～３３５ｄから流体的に隔離しながら、（ハウジング４０１内に含まれる）入口ポート４２１と第１出口ポート４３０との間で流体連通を確立する。さらに、サンプルリザーバ４８０、４８０’、４９０及び４９０’は、第１形態では入口ポート４２１から流体的に隔離されており、図２０において矢印ＧＧによって示すように、患者の身体の一部（例えば、静脈）とプリサンプルリザーバ４７０との間に、流体流路が規定される。この第１形態では、体液は、患者の身体のその部分から入口ポート４２１の入口内腔４０２、シール部材４４１の第１開口部４４４ａ、第１出口ポート４３０を通り、プリサンプルリザーバ４７０内に（例えば、重力、真空等により）流れ込む。第１形態では、流量コントローラ４４０はまた、プリサンプルリザーバ４７０を流路４３５ａ～３３５ｄから流体的に隔離する。従って、体液の第１量（所定量又は未定量）を、静脈穿刺の直後にプリサンプルリザーバ４７０内に受け取り、後続するサンプルから隔離することができる。このように、収集デバイス４００を用いて、体表微生物及び／又は他の望ましくない外部汚染物質を含む可能性が最も高い体液の第１量が、診断又は汚染物質によって影響を受ける可能性がある他の試験に対して収集され使用される体液サンプルの後続する量を汚染しないようにすることができる。

【００７５】

[1128] プリサンプルリザーバ４７０内への体液プリサンプルの収集に続き、図２１及び図２２に示すように、ダイヤル４４５を、第２位置に達するまで作動させる（回転させる）ことができる。ダイヤル４４５が第２位置にある時、流量コントローラ４４０は第２形態に配置され、シール部材４４１の第２開口部４４４ｂは、プリサンプルリザーバ４７０を入口ポート４２１から流体的に隔離しながら、入口ポート４２１と流路４３５ａとの間に流体連通を確立する。言い換えれば、第２形態では、図２２において矢印ＨＨによって示すように、流量コントローラ４４０は、患者の身体の一部（例えば、静脈）と流路４３５ａとの間に流体流路を確立する。流量コントローラ４４０が第２形態にある状態で、サンプルリザーバ４８０を、使用者が、第１形態から第２形態に作動させて（例えば、穿孔部材４５５ａを押して）患者の身体の一部（例えば、静脈）と第１サンプルリザーバ４８０との間に流体連通を確立することができる。

【００７６】

[1129] 上述したように、サンプルリザーバ４８０を第２形態に移動させることにより、穿孔部材４５５ａが、サンプルリザーバ４８０の真空シールに穴をあけでサンプルリザーバ４８０の内側に配置される。この第２形態では、患者の身体の一部（例えば、静脈）が、サンプルリザーバ４８０内の負圧状態（真空）によるサンプルリザーバ４８０からの真空吸引力にさらされる。サンプルリザーバ４８０（例えば、真空又は負圧）と患者の身体のその部分との圧力差により、サンプルリザーバ４８０内に体液が引き込まれる。体液は、患者の身体のその部分から、入口ポート４２１の入口内腔４０２、シール部材４４１の第２開口部４４４ｂ、ハウジング４０１の第２出口開口部４０３ｂを通って、第１流路４３５ａ内に流れ込む。真空吸引により、体液の流れが第１流路４３５ａを通って、第２出口ポート４３１及び穿孔部材４５５ａを介してサンプルリザーバ４８０内に引き込まれる

。言い換えれば、第２形態では、流量コントローラ４４０は、入口ポート４２１とサンプルリザーバ４８０との間に流体流路を確立する。サンプルリザーバ４８０内に体液の所望の量（例えば、第２量）が収集されると、使用者は、流量コントローラ４４０を第３位置まで作動させ（回転させ）、及び／又はサンプルリザーバ４８０をその第１形態に戻るように移動させて、第１サンプルリザーバ４８０を流路４３５ａから隔離することができる。サンプルリザーバ４８０が第１形態に戻ると、穿孔部材４５５ａはサンプルリザーバ４８０から取り除かれ、サンプルリザーバ４８０のシール（例えば、自己封止膜）が、第１サンプルリザーバ４８０を流路４３５ａから隔離する。他のサンプルリザーバの充填は、流量コントローラ４４０が第３形態、第４形態及び第５形態それぞれに配置されて同様に行われる。

【００７７】

[1130] 充填の順序及び／又は順序付けは必ずしも必要ではない（すなわち、サンプルリザーバ４８０は必ずしもサンプルリザーバ４９０の前に充填されなくてもよい等）ことに留意されたい。言い換えれば、第１サンプルリザーバ４８０及び第２サンプルリザーバ４９０（及び任意の追加のサンプルリザーバ）をあらゆる順序で充填することができる。例えば、使用者は、第１サンプルリザーバ４８０の充填を開始することができ、その後、第１サンプルリザーバ４８０が部分的に充填された後、使用者は第２サンプルリザーバ４９０を充填することができる。さらに、サンプルリザーバ４８０及び／又は４９０内に収集された体液の体積の調整を、サンプルリザーバ４８０及び／又は４９０の繰り返される充填によって可能とすることができる。しかしながら、他の実施形態では、充填の順序を、体液の指定された量が第１リザーバ内に配置されたことが確認されるまで、第２サンプルリザーバにアクセスすることができない等のように、機械的に操作することができる。上述したように、ダイヤル４４５は、患者と収集デバイス４００との間の流体流を全体として実質的に防止して、収集デバイス４００内のサンプルを外部環境から実質的に封止することができる、流量コントローラ４４０の第６形態に対する第６位置を有することができる。

【００７８】

[1131] 収集デバイス４００を、４つのサンプルリザーバの組（例えば、第１サンプルリザーバ４８０、第２サンプルリザーバ４８０’、第３リザーバ４９０及び第４リザーバ４９０’）を含み及び／又はそれらに他の方法で結合しているものとして上に示し記載しているが、他の実施形態では、収集デバイスは、あらゆる好適な数のサンプルリザーバを含むことができ及び／又はそれらに結合され得る。例えば、図２３～図２５は、実施形態による収集デバイス５００を示す。図示するように、収集デバイス５００のいくつかの態様は、図１６～図２２を参照して上述した収集デバイス５００の対応する態様と実質的に同様であり得る。従って、同様の態様については本明細書ではそれ以上詳細には記載しない。

【００７９】

[1132] 収集デバイス５００は、分流機構５２０、流量コントローラ５４０、第１サンプルリザーバ５８０及び第２サンプルリザーバ５９０を含む。サンプルリザーバ５８０及び５９０は、詳細に上述したサンプルリザーバと実質的に同様であり得る。いくつかの実施形態では、サンプルリザーバ５８０及び５９０は、実質的に同じ形状及びサイズを有することができ、実質的に同じ培地を含むことができる。他の実施形態では、サンプルリザーバ５８０及び５９０は、実質的に同じ形状及びサイズを有することができ、好気性菌用培地又は嫌気性菌用培地のうちの一方を含むことができる。さらに他の実施形態では、第１サンプルリザーバ５８０は、第２サンプルリザーバ５９０のサイズより実質的に大きい第１サイズを有することができる。

【００８０】

[1133] 図２４及び図２５に示すように、分流機構５２０は、ハウジング５０１及び分配部材５２９を含む。分流機構５２０のハウジング５０１は、分配部材５２９に物理的にかつ流体的に結合されており、患者から体液を収集する一組の流体流経路を提供し及び／又

は規定している。ハウジング４０１に関して上述したように、ハウジング５０１は、凹部と、第１出口開口部５０３ａ、第２出口開口部５０３ｂ及び第３出口開口部５０３ｃとを規定することができる。凹部は、詳細に上述したように、流量コントローラ５４０に含まれるシール部材５４１を受け入れるように構成されている。第１出口開口部５０３ａ、第２出口開口部５０３ｂ及び第３出口開口部５０３ｃは、ハウジング４０１によって規定された第１出口開口部４０３ａ、第２出口開口部４０３ｂ及び第３出口開口部４０３ｃそれぞれと形態及び機能が実質的に同様であり得る。同様に、分配部材５２９は、分流部材４２９に含まれるプリサンプルリザーバ４７０、第１流路４３５ａ及び第２流路４３５ｂと実質的に同様である、プリサンプルリザーバ４７０、第１流路４３５ａ及び第２流路４３５ｂを規定している。従って、分流機構４２０に関して上述したように、プリサンプルリザーバ５７０は、第１出口開口部５０３ａに流体連通しており、第１流路５３５ａは、第２出口開口部５０３ｂに流体連通しており、第２流路５３５ｂは、第３出口開口部５０３ｃに流体連通している。図２５に示すように、分配部材５２９は、第１流路５３５ａ及び第１穿孔部材５５５ａに流体連通している第１出口ポート５３１と、第２流路５３５ｂ及び第２穿孔部材５５５ｂに流体連通している第２出口ポート５３２とを規定している。上述したように、穿孔部材５５５ａ及び５５５ｂを用いて、本明細書においてさらに詳細に記載するように、サンプルリザーバ５８０及び５９０の真空シールに穴をあけることができ、それにより、体液の流れを開始することができる。

【００８１】

[1134] 流量コントローラ５４０は、ダイヤル５４５及びシール部材５４１を含む。シール部材５４１は、上述したように、ハウジング５０１の凹部内に配置される。このように、流量コントローラ５４０がハウジング５０１に結合されると、シール部材５４１は、ダイヤル５４５の表面及び凹部を規定するハウジング５０１の表面と実質的流体密封シールを形成する。図２４及び図２５に示すように、シール部材５４１は、シール部材４４１に関して詳細に上述したように、第１出口開口部５０３ａ、第２出口開口部５０３ｂ及び第３出口開口部５０３ｃそれぞれと実質的に位置合せされる、第１開口部５４４ａ、第２開口部５４４ｂ及び第３開口部５４４ｃを規定している。

【００８２】

[1135] 流量コントローラ５４０のダイヤル５４５は、ハウジング５０１に結合されるのに好適なサイズを有していながら、ダイヤル４４５と形態及び機能が実質的に同様であり得る。従って、ダイヤル５４５を、ハウジング５０１に回転可能に結合し、ハウジング５０１に対して第１位置、第２位置及び第３位置の間で移動可能とすることができる。ダイヤル５４５は、内腔５０２を規定する入口ポート５２１を含み、入口ポート５２１を、患者から体液を抜き取り及び／又は収集デバイス５００に輸送するための流体流経路を規定する医療デバイス（図示せず）に流体的に結合することができる。このように、入口ポート５２１を、プリサンプルリザーバ５７０、第１サンプルリザーバ５８０及び第２サンプルリザーバ５９０を選択的に配置するように構成することができる。より詳細には、ダイヤル５４５が第１位置にある時、流量コントローラ５４０は第１形態に配置され、入口ポート５２１は、シール部材５４１の第１開口部５４４ａ及びハウジング５０１の第１出口開口部５０３ａと実質的に位置合せされる。このように、収集デバイス４００に関して詳細に上述したように、シール部材５４１の第１開口部５４４ａは、入口ポート５２１と第１出口開口部５０３ａとの間に流体連通を確立し、従って、入口ポート５２１を、プリサンプルリザーバ５７０に流体連通するように配置する。同様に、ダイヤル５４５が第２位置まで回される（又は駆動される）と、流量コントローラ５４０は第２形態に配置され、第２出口開口部５４４ｂは、入口ポート５２１と第２出口開口部５０３ｂ、従って第１流路５３５ａとの間に流体連通を確立し、ダイヤル５４５が第３位置まで回されると、流量コントローラ５４０は第３形態に配置され、第３出口開口部５４４ｃは、入口ポート５２１と第３出口開口部５０３ｃ、従って第２流路５３５ａとの間に流体連通を確立する。このように、収集デバイス４００に関して詳細に上述したように、収集デバイス５００を、プリサンプル５７０に体液の第１体積を移送するために使用し、その後、第１サンプルリ

ザーバ５８０及び第２サンプルリザーバ５９０それぞれに体液の第２体積及び第３体積を移送するために使用することができる。

【００８３】

[1136] 図２６～図３３は、実施形態による収集デバイス６００を示す。収集デバイス６００は、分流機構６２０、流量コントローラ６４０並びにサンプルリザーバ６８０、６８０’、６９０及び６９０’を含む。本明細書においてさらに記載するように、収集デバイス６００を、第１形態、第２形態、第３形態、第４形態及び第５形態の間で移動させて、例えば、皮膚に存在する微生物及び／又は他の望ましくない外部汚染物質等、体外の微生物が実質的ない体液の流れを送出することができる。収集デバイス６００は、あらゆる好適な形状、サイズ又は構成であり得る。例えば、収集デバイス６００の態様及び／又は部分は、上述した収集デバイス１００、２００、３００、４００及び／又は５００のいずれかの対応する態様及び／又は部分と形態及び／又は機能が同様であり得る。従って、こうした同様の態様及び／又は部分については、本明細書ではそれ以上詳細には記載しない。例として、いくつかの実施形態では、収集デバイス６００のサンプルリザーバ６８０、６８０’、６９０及び６９０’は、図１６～図２２の収集デバイス４００に含まれるサンプルリザーバ４８０、４８０’、４９０及び４９０’それぞれと形態及び／又は機能が実質的に同様であり及び／又は同じであり得る。

【００８４】

[1137] 分流機構６２０は、分配部材６２９並びに一組の結合部材６３７ａ、６３７ｂ、６３７ｃ及び６３７ｄを含む（例えば、図２７を参照）。分配部材６２９は、結合部材６３７ａ、６３７ｂ、６３７ｃ及び６３７ｄに流体連通しており、患者から体液を収集する一組の流体流経路を提供し及び／又は規定するように構成されている。図２７及び図２８に示すように、分配部材６２９は、プリサンプルリザーバ６７０に流体連通している第１出口ポート６３０と、第１結合部材６３７ａに流体連通している第２出口ポート６３１と、第２結合部分６３７ｂに流体連通している第３出口ポート６３２と、第３結合部分６３７ｃに流体連通している第４出口ポート６３３と、第４結合部分６３７ｄに流体連通している第５出口ポート６３４とを規定し及び／又は形成している。

【００８５】

[1138] 図２８に示すように、分配部材６２９は、プリサンプルリザーバ６７０の少なくとも一部を規定するチャンバ又は空間を規定している。プリサンプルリザーバ６７０は、例えば、血液、血漿、尿等の体液を収容するように構成されている。例えば、プリサンプルリザーバ６７０は、患者から体液の第１量又は第１体積を受け取りかつ収容することができ、そこでは、体液の第１量は所定量でも未定量でもあり得る。さらに、分流機構６２０及び流量コントローラ６４０の配置は、本明細書においてさらに詳細に記載するように、プリサンプルリザーバ６７０が結合部分６３７ａ、６３７ｂ、６３７ｃ及び６３７ｄ並びに／又は患者から抜き取られる体液の後続する体積から流体的に隔離されて維持されるというものであり得る。このように、出口ポート６３１、６３２、６３３及び６３４は、本明細書においてさらに詳細に記載するように、流量コントローラ６４０と結合部材６３７ａ、６３７ｂ、６３７ｃ及び６３７ｄそれぞれとの間に流体流路を方向付け及び／又は他の方法で規定することができる。いくつかの実施形態では、第１出口ポート６３０及びプリサンプルリザーバ６７０の配置は、プリサンプルリザーバ４７０及び／又は５７０と形態及び機能が実質的に同様であり得る。従って、プリサンプルリザーバ６７０について、本明細書ではそれ以上詳細には記載しない。

【００８６】

[1139] 図２９に示すように、第１結合部材６３７ａは、穿孔部材６５５ａに流体的に結合されている流路６３８ａを規定している。上述したように、結合部材６３７ａを、分配部材６２９に物理的にかつ流体的に結合することができる。例えば、流路６３８ａは、分配部材の第２出口ポート６３１の一部を受け入れて、結合部材６３７ａをそれに物理的にかつ流体的に結合することができる。いくつかの実施形態では、第２出口ポート６３１の表面は、流路６３８ａを規定する結合部分６３７ａの内面と実質的流体密封シール（例え

ば、実質的気密シールを形成することができる摩擦嵌め）を形成することができる。結合部分６３７ａの穿孔部材６５５ａは、図１６～図２２の収集デバイス４００に含まれる穿孔部材４５５ａと形態及び機能が実質的に同様であり得る。従って、穿孔部材６５５ａについては本明細書ではそれ以上記載しない。第２結合部材６３７ｂ、第３結合部材６３７ｃ及び第４結合部材６３７ｄは同様に配置される。従って、第２結合部材６３７ｂ、第３結合部材６３７ｃ及び第４結合部材６３７ｄは各々、穿孔部材６５５ｂ、６５５ｃ及び６５５ｄそれぞれを含み、各々、流路６３８ｂ、６３８ｃ及び６３８ｄそれぞれを規定している。本明細書においてさらに詳細に記載するように、第１結合部材６３７ａ、第２結合部材６３７ｂ、第３結合部材６３７ｃ及び第４結合部材６３７ｄを用いて、分流機構６２０を、第１サンプルリザーバ６８０、第２サンプルリザーバ６８０’、第３サンプルリザーバ６９０及び第４サンプルリザーバ６９０’それぞれに流体連通するように選択的に配置することができる。

【００８７】

[1140] 図３０及び図３１に示すように、流量コントローラ６４０は、ダイヤル６４５及びシール部材６４１を含む。流量コントローラ６４０のダイヤル６４５は、分配部材６２９内に回転可能に配置され（図３２及び図３３を参照）、第１位置、第２位置、第３位置及び第４位置の間で移動可能である。ダイヤル６４５は、各々が内部空間６４６に流体連通している入口ポート６２１、第１出口ポート６４７及び第２出口ポート６４８を含む（例えば、図３０を参照）。内部空間６４６は、本明細書においてさらに詳細に記載するように、シール部材６４１の一部を受け入れるように構成されている。入口ポート６２１を、患者から体液を抜き取り及び／又は収集デバイス６００に輸送するための流体流経路を規定する（図示せず）医療デバイスに流体的に結合することができる。例えば、入口ポート６２１を、針又は他の内腔規定デバイス（例えば、可撓性滅菌管）に直接又はアダプタ６０４（例えば、図２６及び図２７を参照）を介して間接的に流体的に結合することができる。第１出口ポート６４７は、プリサンプルリザーバ６７０に流体連通している。例えば、第１出口ポート６４７を、分配部材６２９の第１出口ポート６３０内に回転可能に配置することができる。ダイヤル６４５が、その第１位置、第２位置、第３位置及び第４位置にそれぞれある時、第２出口ポート６４８を、第２出口ポート６３１、第３出口ポート６３２、第４出口ポート６３３及び第５出口ポート６３４に流体連通するように選択的に配置することができる。このように、本明細書においてさらに詳細に記載するように、ダイヤル６４５の内部空間６４６を、プリサンプルリザーバ６７０、第１サンプルリザーバ６８０、第２サンプルリザーバ６８０’、第３サンプルリザーバ６９０及び第４サンプルリザーバ６９０’に流体連通するように選択的に配置することができる。

【００８８】

[1141] 流量コントローラ６４０のシール部材６４１の少なくとも一部が、ダイヤル６４５の内部空間６４６内に回転可能に配置され、第１位置と第２位置との間で移動可能である。さらに、シール部材６４１は、シール部材６４１の外面が、内部空間６４６の少なくとも一部を規定するダイヤル６４５の内面と実質的流体密封シールを形成するようなサイズ及び形状を有することができる。図３１に示すように、シール部材６４１は、第１流路６４２及び第２流路６４４を規定している。シール部材６４１が内部空間６４６内でその第１位置にある時、流路６４２は、入口ポート６２１を第２出口ポート６４８から流体的に隔離しながら、入口ポート６２１と第１出口ポート６４７との間に流体連通を確立する。同様に、シール部材６４１が内部空間６４６内でその第２位置にある時、第２流路６４４は、入口ポート６２１を第１出口ポート６４７から流体的に隔離しながら、入口ポート６２１と第２出口ポート６４８との間に流体連通を確立する。収集デバイス６００は、ダイヤル６４５が分配部材６２９内で第２位置、第３位置及び第４位置まで回転する時に同様に作用する。従って、入口ポート６２１が（例えば、入口ポート６２１及び／又はアダプタ６０４に結合された医療デバイスを介して）患者に流体連通するように配置されると、分配部材６２９の第１出口ポート６３０、第２出口ポート６３１、第３出口ポート６３２、第４出口ポート６３３及び第５出口ポート６３４を、入口ポート６２１に流体連通す

るように選択的に配置して、体液がプリサンプルリザーバ６７０、第１サンプルリザーバ６８０、第２サンプルリザーバ６８０’、第３サンプルリザーバ６９０及び第４サンプルリザーバ６９０’それぞれの中に流れ込むのを可能にすることができる。

【００８９】

[1142] 動作時、収集デバイス６００を用いて、汚染を低減して患者から体液（例えば、血液、血漿、尿等）を収集することができる。例えば、収集デバイス６００の入口ポート６２１を、針又は他の内腔規定デバイス（例えば、可撓性滅菌管）に流体的に結合することができる。静脈穿刺（又は体液にアクセスする他の方法）に続き、図３２に示すように、シール部材をその第１位置になるまで作動（又は回転）させることができる。別法として、シール部材６４１を第１位置に事前設定することができ、収集デバイス６００を、収集デバイス６００の無菌状態を維持するように他の方法で封止することができる。シール部材６４１がその第１位置にある時、流量コントローラ６４０は、入口ポート６２１を結合部材６３７ａ、６３７ｂ、６３７ｃ及び６３７ｄから流体的に隔離しながら、入口ポート６２１と分配部材６２９の第１出口ポート６３０との間に流体連通を確立する。従って、図３２において矢印ＩＩによって示すように、収集デバイス４００に関して上述したものと同様の方法で、体液を、患者から入口ポート６２１、第１流路６４２、ダイヤル６４５の第１出口ポート６４７、分配部材６２９の第１出口ポート６３０を介してプリサンプルリザーバ６７０内に移送することができる。

【００９０】

[1143] プリサンプルリザーバ６７０内における体液プリサンプルの収集に続いて、シール部材６４１をダイヤル６４５に対してその第１位置からその第２位置に作動させる（回転させる）ことができる。同様に、図３３に示すように、ダイヤル６４５を、それが分配部材６２９に対して第２位置に達するまで作動させる（又は回転させる）ことができる。シール部材６４１及びダイヤル６４５がその第２位置にある時、流量コントローラ６４０は第２形態に配置され、シール部材６４１の第２流路６４４は、プリサンプルリザーバ６７０を入口ポート６２１から流体的に隔離しながら、入口ポート６２１と第１結合部材６３７ａの流路６３８ａとの間に流体連通を確立する。流量コントローラ６４０が第２形態にある状態で、サンプルリザーバ６８０を、使用者によりその第１形態から第２形態に作動させて（例えば、穿孔部材６５５ａを押して）、患者の身体の一部（例えば、静脈）と第１サンプルリザーバ６８０との間に流体連通を確立することができる。詳細に上述したように、サンプルリザーバ６８０を第２形態に移動させることにより、穿孔部材６５５ａが、サンプルリザーバ６８０の真空シールに穴をあけてサンプルリザーバ６８０の内側に配置される。この第２形態では、患者の身体のその部分（例えば、静脈）が、サンプルリザーバ６８０内の負圧状態（真空）のためにサンプルリザーバ６８０からの真空吸引力にさらされる。従って、図３３において矢印ＪＪによって示すように、体液を、患者の身体のその部分から入口ポート６２１、第２流路６４４、第２出口ポート６３１及び流路６３８ａ並びに第１結合部材６３７ａの穿孔部材６５５ａを通って第１サンプルリザーバ６８０内に強制的に流すことができる。

【００９１】

[1144] サンプルリザーバ６８０内に体液の所望の体積（例えば、第２量）が収集されると、使用者は、流量コントローラ６４０を第３位置まで作動させ（回転させ）及び／又はサンプルリザーバ６８０をその第１形態に戻るように移動させて、第１サンプルリザーバ６８０を第２流路６４４から隔離することができる。サンプルリザーバ６８０が第１形態に戻ると、穿孔部材６５５ａは、サンプルリザーバ６８０から取り除かれ、サンプルリザーバ６８０のシール（例えば、自己封止膜）が、第１サンプルリザーバ６８０を流路６３５ａから流体的に隔離する。他のサンプルリザーバの充填は、流量コントローラ６４０が第３形態、第４形態及び第５形態それぞれに配置されている状態で同様に行われる。

【００９２】

[1145] 図３４～図４０は、実施形態による収集デバイス７００を示す。収集デバイス７００は、分流機構７２０、流量コントローラ７４０並びにサンプルリザーバ７８０及び７

９０を含む（４つのサンプルリザーバに対してホルダが存在するが、明確にするために図では２つのサンプルリザーバのみが含まれており、収集デバイス７００の一部として、追加のサンプルリザーバ（例えば、第５、第６等）を含めることができる）。本明細書においてさらに記載するように、収集デバイス７００を第１形態、第２形態、第３形態、第４形態及び第５形態の間で移動させて、例えば、皮膚に存在する微生物及び／又は他の望ましくない外部汚染物質等、体外の微生物が実質的にない体液の流れを送出することができる。収集デバイス７００は、あらゆる好適な形状、サイズ又は構成であり得る。例えば、収集デバイス７００の態様及び／又は部分は、上述した収集デバイス１００、２００、３００、４００、５００及び／又は６００のいずれかの対応する態様及び／又は部分と形態及び／又は機能が実質的に同様であり得る。従って、こうした同様の態様及び／又は部分については、本明細書ではそれ以上詳細に記載しない。例として、いくつかの実施形態では、収集デバイス７００のサンプルリザーバ７８０及び７９０は、図１６～図２２の収集デバイス４００に含まれるサンプルリザーバ４８０及び４９０それぞれと形態及び機能が実質的に同様及び／又は同じであり得る。

【００９３】

[1146] 分流機構７２０は、ハウジング７０１、分配部材７２９及びベースプレート７７１を含む。収集デバイス４００に関して上述したように、ハウジング７０１は、各々、分配部材７２９の異なる部分に流体連通しているように構成されている、第１出口開口部７０３ａ、第２で出口開口部７０３ｂ、第３出口開口部７０３ｃ、第４出口開口部７０３ｄ及び第５出口開口部７０３ｅを規定している。より具体的には、分配部材７２９は、第１出口開口部７０３ａに流体連通しているプリサンプルリザーバ７７０の少なくとも一部と、第２出口開口部７０３ｂに流体連通している第１流体チャンバ７３５ａ、第３出口開口部７０３ｂに流体連通している第２流体チャンバ７３５ｂ、第４出口開口部７０３ｄに流体連通している第３流体チャンバ７３５ｃ、第５出口開口部７０３ｅに流体連通している第４流体チャンバ７３５ｄとを規定し及び／又は形成している。さらに、本明細書においてさらに記載するように、ハウジング７０１は、流量コントローラ７４０の少なくとも一部を移動可能に受け入れるように構成された凹部７６６を規定している。

【００９４】

[1147] 図３６に示すように、分配部材７２９は、プリサンプルリザーバ７７０の少なくとも一部を形成するチャンバ又は空間を規定している。プリサンプルリザーバ７７０は、例えば、血液、血漿、尿等の体液を収容するように構成されている。ハウジング７０１の第１出口開口部７０３ａを、詳細に上述したように、プリサンプルリザーバ７７０が患者から体液の流れを受け取ることができるように、プリサンプルリザーバ７７０の開放部分と実質的に位置合せすることができる。さらに詳述すると、分配部材７２９は一組の壁７３６を含み、それらは、例えば、分配部材７２９の内部空間を互いに流体的に隔離されている部分及び／又は空間に分割することができる。例えば、図３６に示すように、一組の壁７３６は、分配部材７２９の内部空間を、プリサンプルリザーバ７７０、第１流体チャンバ７３５ａ、第２流体チャンバ７３５ｂ、第３流体チャンバ７３５ｃ及び第４流体チャンバ７３５ｄに分割することができる。いくつかの実施形態では、壁７３６は、プリサンプルリザーバ７７０及び流体チャンバ７３５ａ～７３５ｄを等しく規定し及び／又は形成することができる。他の実施形態では、プリサンプルリザーバ７７０は、流体チャンバ７３５ａ～７３５ｄによって規定される空間とは異なる空間を規定することができる。

【００９５】

[1148] 分配部材７２９は、第１流体チャンバ７３５ａ、第２流体チャンバ７３５ｂ、第３流体チャンバ７３５ｃ及び第４流体チャンバ７３５ｄそれぞれに流体連通している、第１穿孔部材７５５ａ、第２穿孔部材７５５ｂ、第３穿孔部材７５５ｃ及び第４穿孔部材７５５ｄをさらに含む。従って、穿孔部材７５５ａ～３５５ｄを用いて、本明細書においてさらに詳細に記載するように、サンプルリザーバ７８０及び７９０（並びに図３４～図４０には示さない対応するサンプルリザーバ）に穴をあけることができ、それにより、体液の流れを開始することができる。

【００９６】

[1149] 収集デバイス７００の流量コントローラ７４０は、ダイヤル７４５及びシール部材７４１を含む。シール部材７４１は、ハウジング７０１の凹部７６６内に配置される（例えば、図３８及び図４０を参照）。より詳細には、シール部材７４１が、凹部７６６を規定するハウジング７０１の表面とダイヤル７４５の表面との間にかつそれらと接触して配置されるように、流量コントローラ７４０をハウジング７０１に結合することができる。シール部材７４１を、詳細に上述したように、ダイヤル７４５の表面及び凹部７６６を規定するハウジング７０１の表面と実質的流体密封シールを形成するように構成することができる。図３５に示すように、シール部材７４１は、第１開口部７４４ａ、第２開口部７４４ｂ、第３開口部７４４ｃ、第４開口部７４４ｄ及び第５開口部７４４ｅを規定している。シール部材７４１の配置は、シール部材７４１が凹部７６６内に配置された時、第１開口部７４４ａ、第２開口部７４４ｂ、第３開口部７４４ｃ、第４開口部７４４ｄ及び第５開口部７４４ｅが、ハウジング７０１の第１出口開口部７０３ａ、第２出口開口部７０３ｂ、第３出口開口部７０３ｃ、第４出口開口部７０３ｄ及び第５出口開口部７０３ｅそれぞれと実質的に位置合せされる、というものである。

【００９７】

[1150] 流量コントローラ７４０のダイヤル７４５は、ハウジング７０１に回転可能に結合され、ハウジング７０１に対して第１位置、第２位置、第３位置、第４位置及び第５位置の間で移動可能である。ダイヤル７４５は入口ポート７２１を含み、入口ポート７２１を、患者から体液を抜き取り及び／又は収集デバイス７００に輸送するための流体流経路を規定する医療デバイスに（直接又はアダプタ７０４を介して間接的に）流体的に結合することができる。このように、入口ポート７２１を、本明細書においてさらに詳細に記載するように、プリサンプルリザーバ７７０、第１サンプルリザーバ７８０、第２サンプルリザーバ７８０’、第３サンプルリザーバ７９０及び第４サンプルリザーバ７９０’を患者に流体連通するように選択的に配置するように構成することができる。ダイヤル７４５が第１位置にある時、流量コントローラ７４０は第１形態に配置され、入口ポート７２１を、シール部材７４１の第１開口部７４４ａ及びハウジング７０１の第１出口開口部７０３ａと実質的に位置合せすることができる。このように、シール部材７４１の第１開口部７４４ａは、入口ポート７２１を出口開口部７０３ｂ、７０３ｃ、７０３ｄ及び７０３ｅから流体的に隔離し、それにより入口ポート７２１を流体チャンバ７３５ａ～３３５ｄから流体的に隔離しながら、入口ポート７２１と第１出口開口部７０３ａとの間に流体連通を確立する。ダイヤル７４５が第２位置まで回される（又は駆動される）と、流量コントローラ７４０は第２形態に配置され、第２出口開口部７４４ｂは、入口ポート７２１をプリサンプルリザーバ７７０及び流体チャンバ７３５ｂ～７３５ｄから流体的に隔離しながら、入口ポート７２１と第２出口開口部７０３ｂとの間に流体連通を確立する。収集デバイス７００は、ダイヤル７４５が第３位置、第４位置及び第５位置まで回される時、同様に作用する。従って、入口ポート７２１が（例えば、入口ポート７２１に結合された医療デビスを介して）患者に流体連通するように配置されると、体液のすべてがプリサンプルリザーバ７７０、第１サンプルリザーバ７８０又は第２サンプルリザーバ７９０（又はそれらに結合された他の任意の流体リザーバ）内に流れ込むことができるように、第１出口開口部７０３ａ、第２出口開口部７０３ｂ、第３出口開口部７０３ｃ、第４出口開口部７０３ｄ及び第５出口開口部７０３ｅを入口ポート７２１に流体連通するように選択的に配置することができる。

【００９８】

[1151] いくつかの実施形態では、ハウジング７０１は、ダイヤル７４５のその第１位置からその第２位置、第３位置、第４位置及び第５位置への移動を選択的に制限することができる。いくつかの他の実施形態では、ハウジング７０１を、第５位置まで移動したダイヤルの移動を防止するように構成することができる。言い換えれば、ハウジング７０１は、ダイヤル７４５が第５位置から第１位置に戻るように移動するのを防止する係止機構を含むことができる。この特徴により、流量チャンバ７３５ａ～７３５ｄ並びに／又はサン

プルリザーバ７８０及び７９０内に収集された体液が（表面に結合された微生物及び／又は他の望ましくない外部汚染物質を含むリスクが高い）プリサンプルリザーバ７７０内に収容された体液から汚染されるリスクを低減することができる。この係止機構により、医療従事者を、ＨＩＶ、Ｃ型肝炎等を含む可能性がある患者サンプル内の血液媒介病原体にさらされることから保護することも可能である。ダイヤル７４５及び／又はハウジング７０１は又はウジング７０１における出口ポート７０３ａ及び出口開口部７０３ａ～７０３ｄに対するダイヤル７４５の正確な位置合せを確実にするように視覚的フィードバック又は触覚フィードバックを提供する、機械的戻り止め及び／又は他のインジケータも含むことができる。

【００９９】

[1152] 図１６～図２２に示す収集デバイス４００の実施形態と同様に、収集デバイス７００は、分配部材７２９内に収容されるチャンバであるプリサンプルリザーバ７７０を含む。プリサンプルリザーバ７７０は、例えば、血液、血漿、尿等の体液を収容することができる。プリサンプルリザーバ７７０は、（ハウジング７０１内に位置する）収集デバイス７００の第１出口ポート７０３ａに流体的に結合されるように構成されている。収集デバイス７００の動作中、流量コントローラ７４０が第１位置にある時、体液は、患者の身体の一部（例えば、静脈）から、入口ポート７２１を介して、プリサンプルリザーバ７７０、シール部材７４１内に位置するプリサンプルリザーバ７４４ａ用の開口部及び第１出口ポート７０３ａ内に引き込まれる。プリサンプルリザーバ７７０は、患者から抜き取られる流体の第１量を収容するように構成され、そこでは、体液の第１量は、所定量であることも未定量であることも可能であり、それにより、体液の第１量は、患者から後に抜き取られる体液の第２量及び／又は第３量及び／又は第４量及び／又は第５量から流体的に隔離される。

【０１００】

[1153] 動作時、収集デバイス７００を用いて、汚染を低減して患者から体液（例えば、血液、血漿、尿等）を収集することができる。例えば、収集デバイス７００の入口ポート７２１を、針又は他の内腔規定デバイス（例えば、可撓性滅菌管）に流体的に結合することができる。静脈穿刺に続き、図３７及び図３８に示すように、ダイヤル７４５が第１位置に達するまで回される。別法として、上述したように、ダイヤル７４５を第１位置で事前設定することができ、収集デバイス７００の無菌状態を維持するように、収集デバイス７００を他の方法で封止することができる。ダイヤル７４５が第１位置にある状態で、流量コントローラ７４０は第１形態に配置され、シール部材７４１の第１出口開口部７４４ａは、入口ポート７２１を４つのサンプル流路７３５ａ～７３５ｄから流体的に隔離しながら、（ハウジング７０１内に含まれる）入口ポート７２１と第１出口ポート７４１との間に流体連通を確立する。この第１形態では、体液は、図３８において矢印ＫＫによって示すように、患者の身体のその部分から、入口ポート７２１、シール部材７４１の第１出口開口部７４４ａ、ハウジング７０１の第１出口ポート７０３ａを通って、分配部材７７０によって規定されたプリサンプルリザーバ７７０内に流れ込む。従って、詳細に上述したように、体液の第１量（所定量又は未定量）を、静脈穿刺の直後にプリサンプルリザーバ７７０内に受け取り、後続するサンプルから隔離することができる。

【０１０１】

[1154] プリサンプルリザーバ７７０内における体液プリサンプルの収集に続き、ダイヤル７４５を、図３９及び図４０に示すように第２位置に達するまで作動させる（又は回転させる）ことができる。ダイヤル７４５が第２位置にある時、流量コントローラ７４０は第２形態に配置され、シール部材７４１の第２出口開口部７４４ａは、プリサンプルリザーバ７７０を入口ポート７２１から流体的に隔離しながら、入口ポート７２１と第１流体チャンバ７３５ａとの間に流体連通を確立する。第１流体チャンバ７３５ａに体液が充填されると、流量コントローラ７４０を第３位置に移動させて、第１流路７３５ａを外部環境から隔離し封止することができる。さらに、サンプルリザーバ７８０を第１形態から第２形態に作動させて、体液を第１流体チャンバ７３５ａからサンプルリザーバ７８０に移

送することができる。例えば、サンプルリザーバ７８０を使用者が又は自動的に第１形態から第２形態に作動させて（穿孔部材７５５ａを押して）、患者の身体の一部（例えば、静脈）とサンプルリザーバ７８０との間に流体連通を確立することができる。上述したように、サンプルリザーバ７８０を第２形態まで移動させることにより、穿孔部材７５５ａがサンプルリザーバ７８０の真空シールに穴をあけ、サンプルリザーバ７８０の内側に配置される。第２形態では、患者の身体のその部分（例えば、静脈）は、幾つかの実施形態ではサンプルリザーバ７８０内部に存在する負圧状態（真空）によりサンプルリザーバ７８０からの真空吸引にさらされる。従って、図４０において矢印ＬＬによって示すように、体液は、患者の身体のその部分から、入口ポート７２１、シール部材７４１の第２出口開口部７４４ｂ、ハウジング７０１の第２出口開口部７０３ｂ、第２流体チャンバ７３５ｂを通って第１サンプルリザーバ７８０内に流れ込む。

【０１０２】

[1155] サンプルリザーバ７８０内に体液の所望の量（例えば、第２量）が収集されると、使用者は、流量コントローラ７４０を第３位置まで作動させ（回転させ）及び／又はサンプルリザーバ７８０をその第１形態に戻るように移動させて、第１サンプルリザーバ７８０を入口ポート７２１から隔離することができる。サンプルリザーバ７８０が第１形態に戻ると、穿孔部材７５５ａはサンプルリザーバ７８０から取り除かれ、サンプルリザーバ７８０のシール（例えば、自己封止膜）が、第１サンプルリザーバ７８０を第２流体チャンバ７３５ｂ及び外部環境から流体的に隔離する。他のサンプルリザーバの充填は、流量コントローラ７４０が第３形態、第４形態及び第５形態それぞれにある状態で同じ方法で行われる。

【０１０３】

[1156] いくつかの実施形態では、収集デバイス７００を、分配部材７２９内で異なる流体チャンバ７３５ａ～７３５ｄを分離する一組の壁７３６が存在しないように構成することができる（図１６における詳細な断面図を参照）。こうした実施形態では、分配部材７２９は、プリサンプルリザーバ７７０と結合された流体チャンバ７３５との間で分割される（すなわち、流体チャンバは、壁７３６によって４つの別個の部分に分離されない）。こうした実施形態では、使用者は、ダイヤル７４５を第２位置、第３位置、第４位置又は第５位置のいずれかに作動（回転）させることによって、一度に４つのサンプルリザーバすべてを充填することができる。

【０１０４】

[1157] 本明細書に記載する実施形態のうちのいずれも、例えば、プリサンプルリザーバ及び／又はサンプルリザーバ内への体液の流れを計量する（例えば、定量化する）ために使用することができる計量デバイスと使用することができる。場合によっては、検査標準実施により、充填体積が臨床医及び／又は瀉血専門医によって視覚的に判断され従って人的ミスを受けやすいという事実により、体液（例えば、血液試料）の正確な接種体積との一貫したコンプライアンスが確保されない。血液収集ボトルの体積インジケータは、保持されている時に読み取ることが困難であり、収集ボトルは引込み処置の間、直立して保持されないという事実が、患者から受け取られた体液サンプルの不正確な体積の要因となる可能性がある。サンプル体積が不十分である（例えば、製造業者の推奨未満である）ことにより、培養検査の感度が低下し、偽陰性結果に至る可能性がある。さらに、所定タイプの検査供給品及び装置（例えば、Franklin Lakes、NJのBecton Dickinson等の製造業者によって生成される自動微生物検出システムと使用するように設計された血液培養ボトル）に対する概要資料及び使用説明書において指示されているように、製造業者の推奨を上回る充填体積は、偽陽性をもたらす可能性がある。従って、流量計量及び体積表示機能により、検査技師及び／又は医療従事者（例えば、瀉血専門医）は、サンプルがいかに処理される必要があるかに応じて、サンプルリザーバをインキュベータに又は他の研究室検査機器内に配置する前に各個々のサンプルリザーバ内に収集される体液の体積を確認することができる。検査技師及び／又は瀉血専門医はまた、結果が受け取られる時に臨床医が評価するための正確な体積情報を（例えば、診療記録、データベース、スプレッドシート等に

）記録することも可能であり、それにより、偽陰性結果及び／又は偽陽性結果の誤った解釈の可能性を低減するのに役立つ。

【０１０５】

[1158] 例として、図４１～図４５は、１つ又は複数の計量デバイスを含むことができる収集デバイス８００を示す。収集デバイス８００は、分流機構８２０、流量コントローラ８４０、ディスプレイ８７５及びサンプルリザーバ８８０を含む。本明細書においてさらに記載するように、収集デバイス８００を第１形態、第２形態及び第３形態の間で移動させて、例えば、皮膚に存在する微生物及び／又は他の望ましくない外部汚染物質等、体外の微生物が実質的にない体液の流れを送出することができる。収集デバイス８００は、あらゆる好適な形状、サイズ又は構成であり得る。例えば、収集デバイス６００の態様及び／又は部分は、上述した収集デバイス１００、２００、３００、４００、５００、６００及び／又は７００のいずれかの対応する態様及び／又は部分と形態及び／又は機能が実質的に同様であり得る。従って、こうした同様の態様及び／又は部分については、本明細書ではそれ以上詳細に記載しない。例として、いくつかの実施形態では、収集デバイス８００のサンプルリザーバ８８０は、図１６～図２２の収集デバイス４００に含まれるサンプルリザーバ４８０と形態及び機能が実質的に同様であり及び／又は同じであり得る。

【０１０６】

[1159] 図４１～図４３に示すように、分流機構８２０は、アクチュエータ部分８２２（例えば、第１部分）、中間部分８２３（例えば、第２部分）及び結合部分８２４（例えば、第３部分）を含む。分流機構８２０のアクチュエータ部分８２２は、内部空間８０６を規定する一組のアクチュエータ壁を含む実質的に円筒状である。より具体的には、アクチュエータ部分８２２は、実質的に閉鎖されている第１端部と、内部空間８０６へのアクセスを可能にするように実質的に開放されている、第１端部と反対側の第２端部とを含む。このように、アクチュエータ部分８２２は、本明細書においてさらに詳細に記載するように、流量コントローラ８４０の少なくとも一部を移動可能に受け入れることができる。アクチュエータ部分８２２は、入口ポート８２１及び出口ポート８３１をさらに含む。入口ポート８２１を、詳細に上述したように、患者から体液を抜き取り及び／又は収集デバイス８００に輸送するための流体流経路を規定する医療デバイスに（直接又はアダプタ８０４を介して間接的に）流体的に結合することができる。

【０１０７】

[1160] アクチュエータ部分８２２の出口ポート８３１は、アクチュエータ部分８２２の内部空間８０６の一部を、中間部分８２３によって規定される内部空間８０７に流体連通するように選択的に配置することができる。図４３に示すように、中間部分８２３は、アクチュエータ部分８２２と結合部分８２４との間に配置されている。図４１～図４５には示さないが、中間部分８２３は、例えばサンプルリザーバ８８０に移送される体液の体積を計量するように構成することができる計量デバイスを含むことができる。例えば、いくつかの実施形態では、流量計量デバイスを出口ポート８３１に流体的に結合して、そこを通る体液の流れを計量することができる。図４１及び図４２に示すように、中間部分８２３はディスプレイ８７５を含み、ディスプレイ８７５は、例えば、出口ポート８３１を通って流れた体液の体積に関連する視覚的インジケータ及び／又は情報を使用者に提供することができる。他の実施形態では、流量計量デバイスを、分流機構８２０内の又はそれに沿った他のあらゆる好適な位置に配置することができる。

【０１０８】

[1161] 結合部分８２４を、中間部分８２３に物理的にかつ流体的に結合することができる。例えば、いくつかの実施形態では、結合部分８２４を、中間部分８２３の内部空間８０７内に部分的に配置し、それに、摩擦嵌め、圧入、スナップフィット、ねじ結合、接着剤等を介して少なくとも一時的に結合することができる。結合部分８２４は、詳細に上述したように、サンプルリザーバ８８０の一部を受け入れるように構成されており、サンプルリザーバ８８０の真空シールに穴をあけ、それにより体液の流れを開始することができるように使用することができる穿孔部材８５５を含む。

【０１０９】

[1162] 収集デバイス８００の流量コントローラ８４０は、アクチュエータ部分８２２によって規定された内部空間８０６内に少なくとも部分的に配置され、第１形態、第２形態及び第３形態の間で移動可能である。図４２及び図４３に示すように、流量コントローラ８４０は、第１シール部材８６１、第２シール部材８６２及び第３シール部材８６３を有する可動部材８５０と、付勢部材８５９（例えば、ばね等）とを含む。シール部材８６１、８６２及び８６３は、内部空間８０６を規定するアクチュエータ部分８２２の内面と接触している。従って、本明細書においてさらに詳細に記載するように、シール部材８６１、８６２及び８６３は各々、例えばアクチュエータ部分８２２の内部空間８０６を流体的に隔離された部分に分割することができる内面と、実質的流体密封シールを形成することができる。

【０１１０】

[1163] 可動部材８５０は、内部空間８０６内で第１位置、第２位置及び第３位置の間で移動可能である。可動部材８５０の配置は、可動部材８５０がその第１位置、第２位置及び第３位置の間で移動する際に、シール部材８６１、８６２及び８６３が内部空間８０６内で選択的に移動する、というものであり得る。より具体的には、可動部材８５０がその第１位置、第２位置及び第３位置の間で移動する際、第１シール部材８６１を可動部材８５０と同時に移動させることができる。第２シール部材８６２及び第３シール部材８６３を、互いに固定して結合し（例えば、互いに固定距離で配置し）、可動部材８５０の一部の周囲に摺動可能に配置することができ、それにより、可動部材８５０は、第２シール部材８６２及び第３シール部材８６３がアクチュエータ部分８２２に対して実質的固定位置にあり続ける間に、その第１位置（例えば、図４３を参照）からその第２位置（例えば、図４４を参照）に移動することを可能にすることができる。例えば、可動部材８５０がその第１位置と第２位置との間で移動する際、第２シール部材８６２及び第３シール部材８６３は、実質的固定位置にあり続けることができ、それにより、入口ポート８２１は第２シール部材８６２の第１側に配置され、出口ポート８３１は、第２シール部材８６２の第１側とは反対側の第２側に配置される。従って、本明細書においてさらに詳細に記載するように、可動部材８５０がその第１位置（図４３）及びその第２位置（図４４）にある時、入口ポート８２１は、第１シール部材８６１と第２シール部材８６２との間に規定された内部空間８０６の部分に流体連通しており、出口ポートは、第２シール部材８６２と第３シール部材８６３との間に規定された内部空間８０６の部分に流体連通している。

【０１１１】

[1164] 流量コントローラ８４０の配置は、可動部材８５０がその第１位置からその第２位置に移動した時に、第１シール部材８６１が第２シール部材８６２及び第３シール部材８６３に対して移動する、というものであり得る。第２シール部材８６２に対する第１シール部材８６１の移動により、それらの間に規定された空間が拡大することが可能であり、それにより、プリサンプルリザーバ８７０を形成し及び／又は他の方法で規定することができる。さらに、シール部材８６１及び８６２がアクチュエータ部分８２２の内面と実質的流体密封シールを形成していることにより、第１シール部材８６１と第２シール部材８６２との間に規定されたプリサンプルリザーバ８７０は、内部空間８０６の他の部分から流体的に隔離される。従って、可動部材８５０がその第１位置からその第２位置に移動する時、入口ポート８２１はプリサンプルリザーバ８７０に流体連通することができる。可動部材８５０がその第２位置（例えば、図４４を参照）からその第３位置（例えば、図４５を参照）まで移動する時、可動部材８５０の一部は第３シール部材８６３と接触して、内部空間８０６内で第１シール部材８６１、第２シール部材８６２及び第３シール部材８６３を実質的に同時に移動させることができる。従って、本明細書においてさらに詳細に記載するように、入口ポート８２１及び出口ポート８３１の両方が、第２シール部材８６２と第３シール部材８６３との間に規定された内部空間８０６の部分に流体連通するように、第２シール部材８６２を入口ポート８２１に対して移動させることができる。

【０１１２】

[1165] 動作時、収集デバイス８００を用いて、汚染を低減して患者から体液（例えば、血液、血漿、尿等）を収集することができる。例えば、収集デバイス８００の入口ポート８２１を、針又は他の内腔規定デバイス（例えば、可撓性滅菌管）に流体的に結合することができる。入口ポート８２１が内腔規定デバイスに結合された状態で、流量コントローラ８４０をその第１形態からその第２形態に移動させることができる。このように、使用者は、図４４において矢印ＭＭによって示すように、可動部材８５０をその第１位置からその第２位置に移動させるように力をかけることができる。上述したように、第１シール部材８６１は、可動部材８５０と同時に移動し、それによって、第１シール部材８６１と第２シール部材８６２との間に規定された空間が拡大し、それにより、プリサンプルリザーバ８７０が形成され及び／又は規定される。第１シール部材８６１及び第２シール部材８６２が、内部空間８０６を規定するアクチュエータ部分８２２の内面と実質的流体密封シールを形成していることにより、第１シール部材８６１と第２シール部材８６２との間の容積の増大によって、プリサンプリリザーバ８７０内に負圧がもたらされる。従って、患者の身体の一部（例えば、静脈）とプリサンプルリザーバ８７０との間に（例えば、図４４における入口ポート８２１を介して）流体連通が確立されると、図４４において矢印ＮＮによって示すように、プリサンプルリザーバ８７０と患者の身体のその部分との間の負圧の差により、入口ポート８２１を通してプリサンプルリザーバ８７０内に体液が引き込まれる。この第１形態では、流量コントローラ８４０はまた、プリサンプルリザーバ８７０を出口ポート８３１から流体的に隔離する。従って、体液の第１量（所定量又は未定量）を、（例えば）静脈穿刺の直後にプリサンプルリザーバ８７０内に受け取り、後続するサンプルから隔離することができる。このように、収集デバイス８００を用いて、体表微生物及び／又は他の望ましくない外部汚染物質を含む可能性が最も高い体液の第１量が、診断又は汚染物質によって影響を受ける可能性がある他の検査のために収集されかつ使用される体液サンプルの後続する量を汚染するのを防止することができる。いくつかの実施形態では、計量デバイスは、プリサンプルリザーバ８７０内に配置された体液の体積を計量し、その体積に関連する値をディスプレイ８７５に提示することができる。

【０１１３】

[1166] プリサンプルリザーバ８７０内における体液プリサンプルの体積の収集に続き、図４５において矢印ＯＯによって示すように、可動部材８５０をその第２位置からその第３位置に移動させて、流量コントローラを第３形態に配置することができる。上述したように、可動部材８５０がその第２位置からその第３位置に移動すると、可動部材８５０の部分は、第３シール部材８６３と接触するように配置される。従って、可動部材８５０は、内部空間８０６内で、第１シール部材８６１、第２シール部材８６２及び第３シール部材８６３を実質的に同時に移動させる。従って、入口ポート８２１及び出口ポート８３１両方が、第２シール部材８６２と第３シール部材８６３との間に規定された内部空間８０６の部分に流体連通するように、第２シール部材８６２を、入口ポート８２１に対して移動させることができる。さらに、体液の体積がプリサンプルリザーバ８７０内で流体的に隔離されているため、第２シール部材８６２及び第３シール部材８６３の第１シール部材８６１の方向における移動が制限される（すなわち、体液は実質的に非圧縮性流体である）。このように、体液のプリサンプル体積は、プリサンプルリザーバ８７０内で封鎖（sequester）され、第２シール部材８６２と第３シール部材８６３との間に規定された空間は、入口ポート８２１と出口ポート８３１との間に流体流路を規定する。さらに、流量コントローラ８４０の配置は、その第３形態にある時、第１シール部材８６１が付勢部材８５９と接触するように配置され、使用者により可動部材８５０にかけられる力の少なくとも一部が、付勢部材８５９を変形させ、圧縮し、屈曲させ及び／又は他の方法で再構成するように動作可能である、というものである。従って、付勢部材８５９は、本明細書においてさらに詳細に記載するように、第１シール部材８６１に対して、流量コントローラ８４０のその第２形態からその第３形態への移動に抵抗する反力を及ぼすことができる。

【０１１４】

[1167] 詳細に上述したように、穿孔部材８５５が、サンプルリザーバ８８０の真空シー

ルに穴をあけてサンプルリザーバ内部に配置されるように、サンプルリザーバ８８０を収集デバイス８００に対して配置することができる。サンプルリザーバ８８０（例えば、真空又は負圧）と身体のその部分との間の圧力差により、体液がサンプルリザーバ８８０内に引き込まれる。言い換えれば、第２形態では、流量コントローラ８４０及び分流機構８２０は、図４５において矢印ＰＰによって示すように、体液を、患者から、入口ポート８２１、第２シール部材８６２と第３シール部材８６３との間に規定された内部空間８０６の部分、及びアクチュエータ部分８２２の出口ポート８３１を通って、中間部分８２３及び結合部分８２４の穿孔部材８５５を通って、サンプルリザーバ８８０内に引き込むことができるように、流体流路を確立する。上述したように、（図示せず）計量デバイスが、例えば出口ポート８３１を通して移送される体液の体積を計量することができ、体液の体積に関連する値をディスプレイ８７５に提示することができる。

【０１１５】

[1168] サンプルリザーバ８８０内に体液の所望の体積（例えば、第２量）が収集されると、使用者は、可動部材８５０にかけられた力を取り除き及び／又は低減することができ、それにより、付勢部材８５９が、第１シール部材８６１及び可動部材８５０をそれらの第３位置からそれらの第２位置に向かって移動させることができる。さらに、プリサンプルリザーバ８７０内に配置された体液が実質的に非圧縮性であることにより、第１シール部材８６１の移動が、体液の体積を通して力を移送し、第２シール部材８６２及び第３シール部材８６３をそれらの第３位置からそれらの第２位置に向かって移動させる。いくつかの実施形態では、付勢部材８５９は、第２シール部材８６２をアクチュエータ部分８２２に対して例えば入口ポート８２１を実質的に遮断することができる第４位置に移動させるように作用可能であり得る力を、第１シール部材８６１にかけることができる。従って、入口ポート８２１を、アクチュエータ部分８２２の内部空間８０６から流体的に隔離することができる。さらに、穿孔部材８５５をサンプルリザーバ８８０から取り除くことができ、シール（例えば、自己封止膜）が、体液サンプルをサンプルリザーバ８８０の外側の空間から流体的に隔離することができる。後続するサンプルリザーバの充填を、穿孔部材８５５をサンプルリザーバ内に配置し、流量コントローラ８４０を第３形態まで移動させて体液が患者からサンプルリザーバに流れるのを可能にすることによって、同様に行うことができる。

【０１１６】

[1169] 図４６～図５３は、実施形態による収集デバイス９００を示す。収集デバイス９００は、分流機構９２０、流量コントローラ９４０及びサンプルリザーバ９８０、９８０’、９９０及び９９０’を含む。本明細書においてさらに記載するように、収集デバイス９００を、第１形態、第２形態、第３形態、第４形態及び第５形態の間で移動させて、例えば、皮膚に存在する微生物及び／又は他の望ましくない外部汚染物質等、体外の微生物が実質的にない体液の流れを送出することができる。収集デバイス９００は、あらゆる好適な形状、サイズ又は構成であり得る。例えば、収集デバイス９００の態様及び／又は部分は、上述した収集デバイス１００、２００、３００、４００、５００、６００、７００及び／又は８００のいずれかの対応する態様及び／又は部分と形態及び／又は機能が実質的に同様であり得る。従って、こうした同様の態様及び／部分については、本明細書ではそれ以上詳細に記載しない。例として、いくつかの実施形態では、収集デバイス９００のサンプルリザーバ９８０、９８０’、９９０及び９９０’は、図２６～図３３の収集デバイス６００に含まれる、サンプルリザーバ６８０、６８０’、６９０及び６９０’と形態及び機能が実質的に同様であり及び／又は同じであり得る。

【０１１７】

[1170] 分流機構９２０は、ハウジング９０１、分配部材９２９並びに可動部材９５０ａ、９５０ｂ、９５０ｃ及び９５０ｄを含む。ハウジング９０１は、分配部材９２９に物理的にかつ流体的に結合されており、患者から体液を収集する一組の流体流経路を提供し及び／又は規定している。ハウジング９０１は、本明細書においてさらに詳細に記載するように、流量計量デバイスに含め及び／又は他の方法で（例えば、電気的に及び／又は機械

的に）結合することができる一組のディスプレイ９７５’（例えば、液晶ディスプレイ（ＬＣＤ）等）を含む。ハウジング９０１は、凹部９６６、出口開口部９０３ａ、９０３ｂ、９０３ｃ、９０３ｄ、９０３ｅ及び（本明細書において「開口」とも呼ぶ）可動部材開口９５０ａ、９５０ｂ、９５０ｃ、９５０ｄを規定している。凹部９６６は、本明細書においてさらに詳細に記載するように、流量コントローラ９４０に含まれるシール部材９４１を受け入れるように構成されている。第１出口開口部９０３ａ、第２出口開口部９０３ｂ、第３出口開口部９０３ｃ、第４出口開口部９０３ｄ及び第５出口開口部９０３ｅは、各々、分配部材９２９の異なる部分に流体連通している異なる流体流路を規定するように構成されている。より具体的には、分配部材９２９は、第１出口開口部９０３ａに流体連通しているプリサンプルリザーバ９７０の少なくとも一部と、第２出口開口部９０３ｂに流体連通している第１流路９３５ａ、第３出口開口部９０３ｂに流体連通している第２流路９３５ｂ、第４出口開口部９０３ｄに流体連通している第３流路９３５ｃ、第５出口開口部９０３ｅに流体連通している第４流路９３５とを規定し及び／又は形成している。

【０１１８】

[1171] 図４７及び図４８に示すように、分配部材９２９は、プリサンプルリザーバ９７０の少なくとも一部を規定するチャンバ又は空間を規定している。プリサンプルリザーバ９７０は、例えば、血液、血漿、尿等の体液を収容するように構成されている。図１６～図２２においてプリサンプルリザーバ４７０に関して詳細に上述したように、プリサンプルリザーバ９７０が患者から体液の流れを受け取るのを可能にするように、ハウジング９０１の第１出口開口部９０３ａを、プリサンプルリザーバ９７０の開放部分と実質的に位置合せすることができる。流路９３５ａ～９３５ｄは、分配部材９２９の中心から放射状に延在し、各流路９３５ａ、９３５ｂ、９３５ｃ及び９３５ｄがプリサンプルリザーバ９７０及び他の流路から流体的に隔離されるように配置されている。このように、流路９３５ａ、９３５ｂ、９３５ｃ及び９３５ｄは、出口開口部９０３ｂ、９０３ｃ、９３０ｄ及び９０３ｅそれぞれと実質的に位置合せされた開口を規定する第１端部と、可動部材９５０ａ、９５０ｂ、９５０ｃ及び９５０ｄそれぞれを受け入れるように構成された開口又はポートを規定する第２端部との間で、流体流路を方向付け及び／又は他の方法で規定することができる。図４７及び図４８において、分配部材９２９は、実質的に閉鎖されている流路９３５ａ～９３５ｄを含むものとして示されているが、他の実施形態では、図１７及び図１８の分配部材４２９に関して上に示しかつ記載したように、流路９３５ａ～９３５ｄを実質的に開放することができる。従って、収集デバイス９００の分配部材９２９は、収集デバイス４００の分配部材４２９と実質的に同様に機能することができる。

【０１１９】

[1172] 可動部材９５０ａ、９５０ｂ、９５０ｃ及び９５０ｄは、ハウジング９０１の開口９０５ａ、９０５ｂ、９０５ｃ及び９０５ｄそれぞれと、分配部材９２９の第２端部によって規定される対応する開口とに移動可能に配置される。図４６～図５３には示さないが、いくつかの実施形態では、可動部材９５０ａ、９５０ｂ、９５０ｃ及び９５０ｄを、収集デバイス２００の可動部材２５０及び２５０’に関して詳細に上述したように、付勢部材等に動作可能に結合することができる。このように、可動部材９５０ａ、９５０ｂ、９５０ｃ及び９５０ｄを、使用者が、ハウジング９０１及び分配部材９２９に対して第１位置及び第２位置から作動させ（移動させ）て、流体流を第１サンプルリザーバ９８０、第２流体リザーバ９８０’、第３流体リザーバ９９０及び第４サンプルリザーバ９９０’それぞれの中に仕向けることができる。可動部材９５０ａ、９５０ｂ、９５０ｃ及び９５０ｄは、実質的に同じであり、従って、図４９において単一の可動部材９５０に関して記載する。さらに、可動部材９５０のいくつかの部分は、上述した可動部材２５０及び３５０と実質的に同様であり得る。従って、可動部材９５０のいくつかの部分については、本明細書においてそれ以上詳細に説明しない。可動部材９５０は、入口ポート９５３及び穿孔部材９５５に流体連通している内部空洞９５２を規定している。穿孔部材は、詳細に上述したものと実質的に同様である。入口ポート９５３は、一組の壁を通して延在し、一組の壁は、可動部材９５０の内部空間９５２を対応する流路９３５ａ、９３５ｂ、９３５ｃ

又は９３５ｄに流体連通するように選択的に配置するように内部チャンバ９５２を規定している。

【０１２０】

[1173] 図４９に示すように、可動部材９５０は、内部空間９５２内に回転可能に配置されかつ入口ポート９５３と実質的に直接流体連通している流量制御機構９６７を含む。流量計量機構９６７は、例えば、一組のスポーク又はフィンを含むことができるホイール等であり得る。このように、体液は、可動部材９５０の入口ポート９５３に入り、流量計量デバイス９６７を通過して流れることができ、それにより、流量計量デバイス９６７が可動部材９５０に対して回転することができる。従って、流量計量デバイス９６７の回転の特徴は、可動部材９５０の内部空間９５２に移送される体液の体積、体積流量等を求める際に使用可能であり得る。図４６～図５３には示さないが、可動部材９５０の流量制御機構９６７は、ハウジング９０１のディスプレイ９７５’に動作可能に結合される。従って、体液が、例えばサンプルリザーバ９８０、９８０’、９９０及び／又は９９０’に移送される際、体液の流れに関連する体積情報をディスプレイ９７５’に提示することができる。このように、使用者は、患者から体液サンプルを収集するように収集デバイス９００を操作することができ、例えばサンプルリザーバ９８０に移送される体液サンプルの正確な体積を求めるためにディスプレイ９７５’の少なくとも１つを視覚化することができる。

【０１２１】

[1174] 収集デバイス９００の流量コントローラ９４０は、ダイヤル９４５及びシール部材９４１を含む。シール部材９４１は、ハウジング９０１の凹部９６６内に配置される。より詳細には、シール部材９４１が、凹部９６６を規定するハウジング９０１の表面とダイヤル９４５の表面との間にかつそれらと接触するように配置されるように、流量コントローラ９４０をハウジング９０１に結合することができる。本明細書において詳細に記載するように、シール部材９４１を、ダイヤル９４５の表面及び凹部９６６を規定するハウジング９０１の表面と実質的流体密封シールを形成するように構成することができる。図４７に示すように、シール部材９４１は、第１開口部９４４ａ、第２開口部９４４ｂ、第３開口部９４４ｃ、第４開口部９４４ｄ及び第５開口部９４４ｅを規定している。シール部材９４１の配置は、シール部材９４１が凹部９６６内に配置されると、第１開口部９４４ａ、第２開口部９４４ｂ、第３開口部９４４ｃ、第４開口部９４４ｄ及び第５開口部９４４ｅが、ハウジング９０１の第１出口開口部９０３ａ、第２出口開口部９０３ｂ、第３出口開口部９０３ｃ、第４出口開口部９０３ｄ及び第５出口開口部９０３ｅそれぞれと実質的に位置合せされる、というものである。

【０１２２】

[1175] 流量コントローラ９４０のダイヤル９４５は、ハウジング９０１に回転可能に結合され、ハウジング９０１に対して第１位置、第２位置、第３位置、第４位置及び第５位置の間で移動可能である。ダイヤル９４５は入口ポート９２１を含み、入口ポート９２１を、患者から体液を抜き取り及び／又は収集デバイス９００に輸送するための流体流経路を規定する医療デバイスに（直接又はアダプタ９０４を介して間接的に）流体的に結合することができる。このように、入口ポート９２１を、本明細書においてさらに詳細に記載するように、プリサンプルリザーバ９７０、第１サンプルリザーバ９８０、第２サンプルリザーバ９８０’、第３サンプルリザーバ９９０及び第４サンプルリザーバ９９０’を患者に流体連通するように選択的に配置するように構成することができる。ダイヤル９４５を、収集デバイス４００のダイヤル４４５に関して上述したものと実質的に同様な方法で、第１位置、第２位置、第３位置、第４位置及び第５位置を通して回転するように構成することができ、従って、それについては本明細書においてそれ以上詳細に記載しない。

【０１２３】

[1176] 図示するように、ダイヤル９４５は、体液の流れに関連する体積情報を提示するように構成することができるディスプレイ９７５をさらに含むことができる。例えば、図４６～図５３には示さないが、ダイヤルは、可動部材９５０に含まれる流量計量デバイス

９６７等、流量計量デバイス等を含むことができる。このように、流量計量デバイスは、例えば入口ポート９２１を通る体液の流れを計量することができ、入口ポート９２１を通る体液の流れに関連する体積情報がダイヤル９４５のディスプレイ９７５に提示されるように、ディスプレイ９７５に動作可能に結合され得る。

【０１２４】

[1177] 動作時、収集デバイス９００を用いて、汚染を低減して患者から体液（例えば、血液、血漿、尿等）を収集することができる。例えば、収集デバイス９００の入口ポート９２１を、針又は他の内腔規定デバイス（例えば、可撓性滅菌管）に流体的に結合することができる。静脈穿刺（又は、体液にアクセスする他の方法）に続き、図５０及び図５１に示すように、ダイヤル９４５は、第１位置に達するまで駆動される（又は回される）。別法として、ダイヤル９４５を第１位置に事前設定することができ、収集デバイス９００の無菌状態を維持するように、収集デバイス９００を他の方法で封止することができる。

【０１２５】

[1178] 上述したように、ダイヤル９４５が第１位置にある時、流量コントローラ９４０は第１形態に配置され、シール部材９４１の第１開口部９４４ａは、入口ポート９２１を４つの流路９３５ａ～３３５ｄから流体的に隔離しながら、（ハウジング９０１内に含まれる）入口ポート９２１と第１出口ポート９３０との間に流体連通を確立する。さらに、サンプルリザーバ９８０、９８０’、９９０及び９９０’は、第１形態では入口ポート９２１から流体的に隔離されており、図５１において矢印ＱＱによって示すように、患者の身体の一部（例えば、静脈）とプリサンプルリザーバ９７０との間に、流体流路が規定される。この第１形態では、体液は、（例えば、重力、真空等により）、患者の身体のその部分から、入口ポート９２１、シール部材９４１の第１開口部９４４ａ、ハウジング９０１の第１出口ポート９０３ａを通って、プリサンプルリザーバ９７０内に流れ込む。第１形態では、流量コントローラ９４０はまた、流路９３５ａ～９３５ｄからプリサンプルリザーバ９７０を流体的に隔離する。従って、体液の第１量（所定量又は未定量）を、静脈穿刺の直後にプリサンプルリザーバ９７０内に受け取り、後続するサンプルから隔離することができる。このように、収集デバイス９００を用いて、体表微生物及び／又は他の望ましくない汚染物質を含む可能性が最も高い体液の第１量が、診断又は汚染物質によって影響を受ける可能性がある他の検査に対して収集されかつ使用される体液サンプルの後続する量を汚染しないようにすることができる。さらに、ディスプレイ９７５は、例えば、プリサンプルリザーバ９７０に移送される体液の体積に関連する、（図示せず）流量制御機構から受け取られる情報を提示することができる。従って、体液の正確な体積を、プリサンプルリザーバに移送し、かつその中で流体的に隔離することができる。

【０１２６】

[1179] プリサンプルリザーバ９７０内における体液プリサンプルの収集に続き、図５２及び図５３に示すように、ダイヤル９４５を、第２位置に達するまで作動させる（又は回転させる）ことができる。ダイヤル９４５が第２位置にある時、流量コントローラ９４０は第２形態に配置され、シール部材９４１の第２開口部９４４ｂは、プリサンプルリザーバ９７０を入口ポート９２１から流体的に隔離しながら、入口ポート９２１と流路９３５ａとの間に流体連通を確立する。流量コントローラ９４０が第２形態にある状態で、可動部材９５０ａを、使用者が第１位置から第２位置に作動させて（すなわち押下して）、患者（例えば、静脈）と第１サンプルリザーバ８８０との間に流体連通を確立することができる。より具体的には、図５３において矢印ＲＲによって示すように、可動部材９５０は、その第１位置からその第２位置に移動して、穿孔部材９５５が、第１サンプルリザーバ９８０の真空シールを通過して第１サンプルリザーバ９８０内に配置されるようにする。

【０１２７】

[1180] 第２位置にある間、可動部材９５０の入口ポート９５３は、第１流路９３５ａと実質的に位置合せされかつ流体連通し、それにより、体液が、第１流路９３５ａから稼働部材９５０の内部空洞９５２内に入り、穿孔部材９５５から出て第１サンプルリザーバ９８０に入るように流れることができる。サンプルリザーバ９８０（例えば、真空又は負圧

）と第１流路９３５ａとの圧力差により、サンプルリザーバ９８０内に体液が引き込まれる。言い換えれば、第２形態では、図５３において矢印ＳＳによって示すように、流量コントローラ９４０及び可動部材９５０ａは、ダイヤル９４５の入口ポート９２１と第１サンプルリザーバ９８０との間に流体流路を確立する。さらに、体液の可動部材９５０ａを通る流れにより、可動部材９５０に対して流量計量機構９６７が回転する。従って、流量計量機構９６７の回転は、サンプルリザーバ９８０に移送される体液サンプルの体積を求める際に使用可能であり得る。さらに、ディスプレイ９７５’は、例えば、サンプルリザーバ９８０に移送される体液の体積に関連する、流量制御機構９６７から受け取られる情報を提示することができる。従って、体液の正確な体積をサンプルリザーバ９８０に移送することができる。例えば、場合によっては、収集デバイス９００を用いて、第１サンプルリザーバ９８０、第２サンプルリザーバ９８０’及び第３サンプルリザーバ９９０の各々に２０ｍＬの３つのサンプル体積を収集する（すなわち、合計６０ｍＬのサンプル体積が収集される）ことができる。

【０１２８】

[1181] 第１サンプルリザーバ９８０内に体液の所望の体積（例えば、第２量）が収集されると、使用者は、可動部材９５０を解放して、（図示せず）付勢部材がその第１位置に戻るように移動するのを可能にすることができる。可動部材９５０がその第１位置に戻ると、穿孔部材９５５は、第１サンプルリザーバ９８０から取り除かれ、シール（例えば、自己封止膜）が、第１サンプルリザーバ９８０を内部流路９３５から流体的に隔離する。収集デバイス９００を用いて、ダイヤル９４５をその第３位置、第４位置及び第５位置までそれぞれ回転させることにより、第２サンプル体積を第２サンプルリザーバ９８０’に、第３サンプル体積を第３サンプルリザーバ９９０に、第４サンプル体積を第４サンプルリザーバ９９０’に、同様に移送することができる。

【０１２９】

[1182] 場合によっては、体液収集デバイス９００により、臨床医及び／又は瀉血専門医は、体液収集デバイス９００を収容するパッケージを開封し、（分配部材９２９を含む）ハウジング９０１のみを取り出し、ハウジング９０１を患者のベッドわきに持って行くことができる。臨床医及び／又は瀉血専門医は、あらゆる標準化技法を用いて患者の身体の一部（例えば、静脈）に対して静脈穿刺を行う（又は、患者の体液にアクセスする他のあらゆる方法を採用する）ことができる。静脈穿刺に続き、臨床医及び／又は瀉血専門医は、すべてのサンプルに対して必要な総血液体積を収集することができる。例えば、臨床医及び／又は瀉血専門医は、２．５ｍＬプリサンプル分流体積及び４つのサンプルリザーバの各々に対して１０ｍＬサンプル体積を収集することができ、それにより、収集された体液（例えば、血液）は合計４２．５ｍＬになる。体液の所望の量の収集に続き、皮下注射針を患者の身体のその部分（例えば、静脈）から取り除くことができ、臨床医及び／又は瀉血専門医は、（体液を収容している）ハウジング９０１を、膜頂部がハウジング９０１の形状に一致するカスタムトレイ内に事前に配置された状態で、４パック（又は２パック）の事前滅菌されたサンプルリザーバの上に配置することができる。サンプルリザーバのこうした事前滅菌されたパックを使用することにより、臨床医は、滅菌剤を用いてサンプルリザーバの頂部を「拭く」プロセスステップを行う必要がなく、それにより、例えば、リザーバ頂部の滅菌が不適切及び／又は不十分である場合に、汚染の可能性が低減する。そして、臨床医及び／又は瀉血専門医は、体液を含むサンプルリザーバの自動接種を正確な体積制御で起動させることができる。いくつかの実施形態では、サンプルリザーバの接種が完了した後、各個々のサンプルリザーバに対して体積情報が表示されているデバイス９００全体を、分析のために研究室に送ることができる。他の実施形態では、サンプルリザーバ９８０及び／又は９９０を個々に取り除き、分析のために研究室に送ることができる。

【０１３０】

[1183] 収集デバイス９００を、図４６～図５３を参照して、収集デバイスの一部を通して移送される体液の体積に関する体積データを提示することができる一組のディスプレイ

９７５及び９７５’を含むものとして示し記載しているが、他の実施形態では、収集デバイスは、あらゆる好適な出力インジケータを有するあらゆる好適な流量計量機構を含むことができる。例えば、図５４及び図５５は、実施形態による分流機構１０２０及び流量コントローラ１０４０を示す。分流機構１０２０及び流量コントローラ１０４０は、分流機構９２０及び流量コントローラ９４０それぞれと形態及び機能が実質的に同様であり得る。従って、同様の部分については本明細書ではそれ以上記載しない。しかしながら、分流機構１０２０及び流量コントローラ１０４０は、一組のディスプレイ１０７５の配置が異なる可能性がある。例えば、分流機構１０２０は、可動部材９５０に関して上述したよう、各々が流量計量機構を含むことができる一組の可動部材１０５０ａ、１０５０ｂ、１０５０ｃ及び１０５０ｄを移動可能に受け入れるように構成されるハウジング１００１を含む。従って、可動部材１０５０ａ、１０５０ｂ、１０５０ｃ及び１０５０ｄを用いて、それらを通して移送される体液の正確な体積を求めることができる。図５５に示すように、ハウジング１００１のディスプレイ１０７５は、小さい体積（例えば、５ｍＬ）の第１照明、中間の体積（例えば、２０ｍＬ）に関連する第２照明、及び許容可能な及び／又は大きい体積（例えば、４０ｍＬ）に関連する第３照明を含む３つの照明の組を含むことができる。このように、体液の流れが流量コントローラ１０４０及び分流機構１０２０を通して、例えば第１可動部材１０５０ａ内に移送される際、その中に含まれる流量計量機構は、信号等をディスプレイに送信することができ、ディスプレイは、可動部材１０５０を通して移送される体液の体積に従って第１照明、第２照明及び／又は第３照明を点灯するように動作可能である。

【０１３１】

[1184] 他の実施形態では、可動部材１０５０ａ、１０５０ｂ、１０５０ｃ及び１０５０ｄを、ハウジング１００１に対して第１位置から第２位置、第３位置又は第４位置に移動させることができる。こうした実施形態では、それらの位置を、例えば、サンプルリザーバに移送される体液の意図された体積に関連付けることができる。例えば、いくつかの実施形態では、使用者は、可動部材１０５０ａをその第１位置からその第２位置に作動させる（例えば、移動させる）ことができる。こうした実施形態では、第２位置を、例えば、サンプルリザーバに移送される体液の小さい体積（例えば、１０ｍＬ）に関連付けることができる。いくつかの実施形態では、ハウジング１００１及び／又は可動部材１０５０ａは、サンプルの低い体積量がサンプルリザーバに移送されるまで、可動部材１０５０ａを第２位置で一時的に保持することができる、戻り止め、ロック、留め具、突起、凹部等を含むことができる。さらに、第２位置に配置されると、ディスプレイ１０７５を、サンプルリザーバに移送される体液の事前設定された体積を使用者に示すように、小さい体積に関連する第１照明を照明するように構成することができる。体液の所望の体積がサンプルリザーバに移送されかつその中で流体的に隔離されると、分流機構１０２０を、可動部材１０５０ａをその第１位置に自動的に戻すように構成することができる。このように、分流機構１０２０及び流量コントローラ１０４０を、あらゆる数のサンプルリザーバに物理的にかつ流体的に結合し、各サンプルリザーバに体液の正確な体積を移送するように使用することができる。

【０１３２】

[1185] 図５６は、流量計量移送デバイスを用いて患者から体液の所定サンプル体積を取得する方法１１９０を示すフローチャートである。流量計量移送デバイスは、（本明細書において「収集デバイス」とも呼ぶ）本明細書に記載する移送デバイスのいずれでもあり得る。例として、いくつかの実施形態では、移送デバイスは、図４６～図５３を参照して上述した収集デバイス９００であり得る。従って、移送デバイスは、患者に流体連通するように選択的に配置されるように構成された入口ポートと、プリサンプルリザーバ及びサンプルリザーバと、患者からプリサンプルリザーバへの体液の流れ及びサンプルリザーバへの体液の流れを計量するように構成された流量計量機構とを含むことができる。方法１１９０は、１１９１において、患者と流量計量移送デバイスのポートとの間に流体連通を確立することを含む。例えば、ポートを針又は他の内腔規定デバイス（例えば、可撓性滅

菌管）に流体的に結合することができ、針又は他の内腔規定デバイスを、患者の体内に挿入することができる（例えば、静脈穿刺事象又は体液にアクセスする他の方法）。

【０１３３】

[1186] ポートが患者に流体連通している状態で、１１９２において、ポートとプリサンプルリザーバとの間の流体連通を確立する。いくつかの実施形態では、流量計量移送デバイスは流量コントローラ等（例えば、収集デバイス９００に含まれる流量コントローラ９４０等）を含むことができ、それを、ポートとプリサンプルリザーバとの間に流体連通を確立する位置（例えば、第１位置）まで作動させ及び／又は操作する（例えば、回転させる）ことができる。いくつかの実施形態では、流量コントローラの作動により、流量コントローラ及び分流機構は、ポートとプリサンプルリザーバとの間の流体流路の少なくとも一部をまとめて規定するようにすることができる。いくつかの実施形態では、プリサンプルリザーバは、患者からプリサンプルリザーバへの体液の流れを開始することができる負圧等を含むことができる。他の実施形態では、体液の流れを、他のあらゆる好適な方法（例えば、重力等）で開始することができる。

【０１３４】

[1187] １１９３において、患者からプリサンプルリザーバに移送された体液の流れを計量する。例えば、いくつかの実施形態では、ポートは、（例えば、収集デバイス９００の流量制御機構９６７に関して上述したものと同様の方法で）ポートを通過する体液の流れを計量することができる流量制御機構を含むことができる。従って、体液のプリサンプル体積がプリサンプルリザーバに移送される。方法１１９０は、１１９４において、流量計量移送デバイスの流量計量機構を介して、プリサンプルリザーバ内に配置された体液のプリサンプル体積が体液の所定プリサンプル体積であることを検証することを含む。例えば、流量計量機構は、ディスプレイ等（例えば、収集デバイス９００のディスプレイ９７５及び／又は９７５’）を含むことができ、及び／又はディスプレイ等に動作可能に結合され得る。流量計量機構を、上述したように、ディスプレイに体積情報を提示するように構成することができる。

【０１３５】

[1188] プリサンプルリザーバ内に体液のプリサンプル体積が配置されると、１１９５において、プリサンプルリザーバをポートから流体的に隔離して、プリサンプルリザーバ内で体液のプリサンプル体積を封鎖する。例えば、場合によっては、流量コントローラ及び／又は分流機構を、第１位置及び／又は第１形態から第２位置及び／又は第２形態に作動させる（又は回転させる）ことができる。流量コントローラ及び／又は分流機構が第２形態にある場合、プリサンプルリザーバは、プリサンプルリザーバの外部の空間から流体的に隔離される。いくつかの実施形態では、流量コントローラ及び／又は分流機構がその第２位置及び／又は第２形態に駆動されると、１１９６において、ポートとサンプルリザーバとの間に流体連通を確立する。例えば、いくつかの実施形態では、流量計量移送デバイスは、サンプルリザーバの一部（例えば、膜等）を穿孔するように構成された穿孔部材を含むことができる、可動部材（例えば可動部材９５０）等を含むことができる。従って、流量コントローラ及び／又は分流機構がその第２位置及び／又は第２形態にある時、サンプルリザーバのその部分の穿孔により、サンプルリザーバがポートに流体連通するように配置される。上述したように、サンプルリザーバは、例えば、患者からサンプルリザーバへの体液の流れを開始することができる負圧等を含むことができる。

【０１３６】

[1189] １１９７において、患者からプリサンプルリザーバに移送された体液の流れを計量する。例えば、上述したように、ポートは、（例えば、収集デバイス９００の流量制御機構９６７に関して上述したものと同様の方法で）ポートを通過する体液の流れを計量することができる流量制御機構を含むことができる。いくつかの実施形態では、流量制御機構を、例えば、図４９の可動部材９５０等の可動部材等に含めることができる。従って、体液のサンプル体積がサンプルリザーバに移送される。方法１１９０は、１１９８において、流量計量移送デバイスの流量計量機構を介して、サンプルリザーバ内に配置された体

液のサンプル体積が体積の所定サンプル体積であることを検証することを含む。例えば、上述したように、ディスプレイ等を、体積情報を提示するように構成することができる。

【０１３７】

[1190] このように、例えば外部に存在する微生物を含む可能性がある、体液の所定プリサンプル体積が収集される。例えば、いくつかの実施形態では、所定プリサンプル体積は、約０．１ｍＬ、約０．３ｍＬ、約０．５ｍＬ、約１．０ｍＬ、約２．０ｍＬ、約３．０ｍＬ、約４．０ｍＬ、約５．０ｍＬ、約１０ｍＬ、約２０ｍＬ、約５０ｍＬ及び／又はそれらの間のあらゆる体積あるいは体積の分数値であり得る。他の実施形態では、プリサンプル体積は、５０ｍＬを超えるか又は０．１ｍＬであり得る。他の実施形態では、所定プリサンプル体積は、約２ｍＬと約５ｍＬとの間であり得る。一実施形態では、所定プリサンプル体積は約３ｍＬであり得る。さらに、所定プリサンプル体積を収集することにより、１つ又は複数のサンプルリザーバ内に配置された所定サンプル体積に、外部に存在する微生物が実質的にないようにすることができる。いくつかの実施形態では、所定サンプル体積は、１０ｍＬと６０ｍＬとの間であり得る。他の実施形態では、所定サンプル体積は、３０ｍＬと６０ｍＬとの間であり得る。さらに他の実施形態では、所定サンプル体積は６０ｍＬであり得る。体液のサンプル体積を単一のサンプルリザーバに移送するものとして上述したが、他の実施形態では、流量計量移送デバイスを用いて、所定サンプル体積を２つ以上のサンプルリザーバに移送することができる。例えば、いくつかの実施形態では、上述したように、体液の所定プリサンプル体積を、プリサンプルリザーバに収集しかつその中で流体的に隔離することができる。プリサンプル体積が流体的に隔離されている状態で、流量計量移送デバイスを用いて、所定サンプル体積を第１サンプルリザーバに、所定サンプル体積を第２サンプルリザーバに、所定サンプル体積を第３サンプルリザーバに移送することができる。こうした場合、所定サンプル体積を例えば２０ｍＬにすることができ、それにより、第１リザーバ、第２リザーバ及び第３リザーバ内に配置される総サンプル体積は６０ｍＬとなる。

【０１３８】

[1191] 本明細書に記載した体液収集デバイスのさまざまな実施形態により、１回の静脈穿刺から２つ（又はそれより多く）の組の体液（例えば、血液）サンプルを収集するのを可能にすることができる。現標準治療では、いくつかの検査（例えば、血液培養）を、（例えば、２回の別個の静脈穿刺を介して、カテーテル＋静脈穿刺及び／又はそれらの組合せを介して）サンプルを別個の独立した体液アクセス点から獲得して行うように求められている。本明細書に記載する実施形態により、単一の体液アクセス点（例えば、静脈穿刺）から所定の診断検査（例えば、血液培養検査）のための複数のサンプルの獲得を容易にすることができ、それにより、これらのサンプルの獲得に必要な静脈穿刺の年間の数を１／２低減させることができる。これは、患者及び医療従事者両方に同様に有利である。静脈穿刺（及び／又は他の血液アクセス処置）の数が低減することにより、大幅に、医療従事者に対する針刺し損傷のリスクを低減させ、これらの処置からもたらされる患者に関連する合併症（例えば、血腫、血栓症、静脈炎、感染症等）を低減させることができる。さらに、体液アクセス処置（例えば、静脈穿刺）の数を低減させることにより、これらの処置に関連する供給品の利用、労力及び廃棄物が低減する。医療制度によって実現されるコストの削減は、重要であり、より効率的な資源の消費とともに、治療計画の展開及び実施を通知するより正確な患者診断をもたらすサンプルの完全性の改善のために患者の転帰の改善を促進する機会を示す。体液収集デバイスはまた、収集後分析からの偽陽性の発生も大幅に低減させる。本明細書に記載する体液収集デバイスはまた、体液収集プロセスを効率化し、手作業によるステップ及び「接触点」の数を低減させ、それにより外部汚染の機会を低減させることも可能である。本明細書に記載するデバイスはまた、検査技師及び／又は瀉血専門医に対する針刺し損傷及び感染のリスクを最小限にすることができる。

【０１３９】

[1192] いくつかの実施形態では、本明細書に記載した体液収集デバイス（例えば、１００、２００、３００、４００、５００、６００、７００、８００及び９００）は、消毒飽

和材料（例えば、ハウジング４０１）を含み及び／又はそれから部分的に形成され得る。現標準は、医療従事者が個々の消毒材料（例えば、イソプロピルアルコール綿棒）を個々のサンプルリザーバ（例えば、４８０、４８０’、４９０及び４９０’）の頂部に配置することに依存する。このプロトコルとのコンプライアンスを確保するために、（例えば）デバイス４００は、デバイス４００内に配置された消毒材料を含むことができ、それにより、図１６に示すように、ハウジング４０１が４パック（又は２パック）のボトルの頂部に配置された時、ハウジング４０１及びサンプルリザーバ４８０、４８０’、４９０、４９０’の頂部からの最初の接触点は、消毒材料である。このように、サンプルリザーバ４８０、４８０’、４９０、４９０’の頂部は、体液がサンプルリザーバ内に接種される前に適切な消毒が適用されることが保証される。

【０１４０】

[1193] さまざまな実施形態について特に示し記載したが、形態及び詳細のさまざまな変更を行うことができる。例えば、ダイヤル４４５（アクチュエータ）を、図１９～図２２を参照して、単一方向に回転するものとして示し記載しているが、他の実施形態では、ダイヤル４４５（アクチュエータ）を、第１方向と第１方向とは反対の第２方向とに回転させることができる。こうした実施形態では、第２方向における回転を、収集デバイスを、あらゆる数の形態を通して移動させるように構成することができる。他の実施形態では、アクチュエータの第２方向における回転を制限することができる。いくつかの実施形態では、ダイヤルは、患者から受け取られる体液の第１体積（すなわち、汚染されたサンプル）を流体的に隔離するように機械的止め具又はロックを含むことができる。言い換えれば、第１リザーバ（プリサンプルリザーバ）に体液の所定体積が充填され、使用者が、追加のサンプルの引込みを開始するようにダイヤル（アクチュエータ）を回転させると、ダイヤル（アクチュエータ）を、（プリサンプルリザーバ内に収容された）第１サンプル体積との流体連通を確立するように戻るように移動させることはできない。

【０１４１】

[1194] いくつかの実施形態について上述したが、それらは、限定としてではなく単に例として提示されていることが理解されるべきである。さまざまな実施形態を、特定の特徴及び／又は構成要素の組合せを含むものとして記載したが、本明細書に記載した実施形態のいずれかからのいずれの特徴及び／又は構成要素のいかなるコンビネーション又はサブコンビネーションを有する他の実施形態が可能である。例えば、図３４～図４０を参照して、収集デバイス７００を、第１形態、第２形態、第３形態、第４形態又は第５形態を有するものとして示し記載しているが、他の実施形態では、本明細書に記載した収集デバイスは、それより多いか又は少ない形態を有することができる。さらに、収集デバイス２００を、図２～図１３を参照して、プリサンプルリザーバ２７０として真空による収集チューブを有するものとして示し記載しているが、他の実施形態では、収集デバイス２００は、分配部材４２９内に収容されたチャンバであるプリサンプルリザーバ４７０を含む、図１６～図２２に提示した実施形態の収集デバイス４００に類似するハウジング２０１内に収容されたチャンバを有することができ、その逆も可能である。

【０１４２】

[1195] さまざまな構成要素の具体的な構成を変更することも可能である。例えば、さまざまな構成要素のサイズ及び具体的な形状は、依然として本明細書に記載するような機能を提供しながら、図示する実施形態とは異なり得る。より具体的には、さまざまな構成要素のサイズ及び形状を、体液流の流体リザーバ内への所望の流量に対して具体的に選択することができる。例えば、図４９において流量計量機構９６７を特に示すが、本明細書に記載した収集デバイスのいずれも、あらゆる好適な流量計量機構とともに使用することができる。例えば、いくつかの実施形態では、収集デバイスは、流量計量機構、及び／又は、例えば、圧力センサ、電圧センサ、光センサ、速度センサ、流量計、歪みゲージ、弁、タービン、浮き、変位分析、密度分析、重量分析、光学分析、超音波分析、熱分析、ドップラ分析、電磁場（ｅｍｆ）分析、反射分析、障害物分析、面積分析、ベンチュリ分析、コリオリ分析、視覚分析並びに／又は他のあらゆる好適なセンサ、分析及び／あるいは計

算（例えば、一例としてボイルの法則、理想気体法則、力計算（力＝質量×加速度）等を適用し及び／又は使用する）等、体液の体積特徴を測定するように構成された、他のあらゆる機構、デバイス又は方法を含むことができる。

【図１】

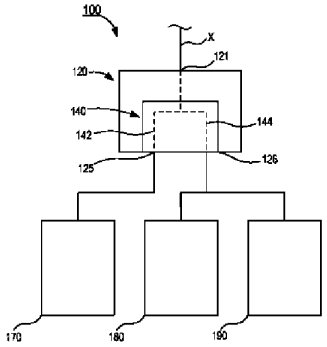


FIG. 1

【図２】

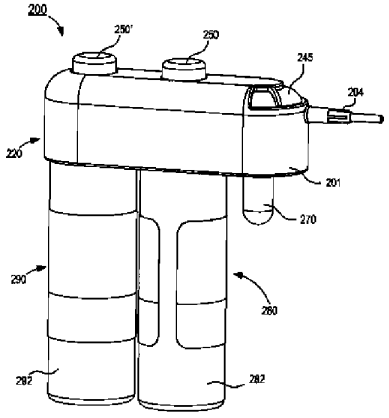


FIG. 2

【図３】

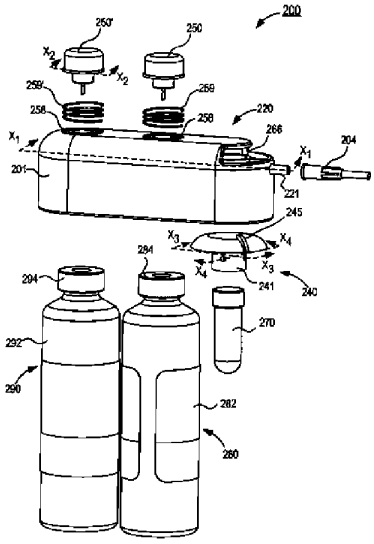


FIG. 3

【図４】

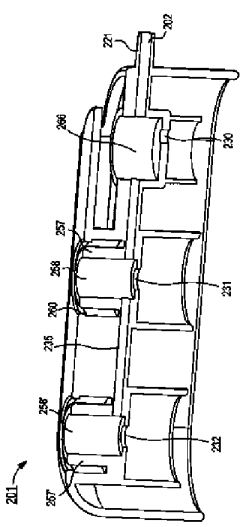


FIG. 4

【図５】

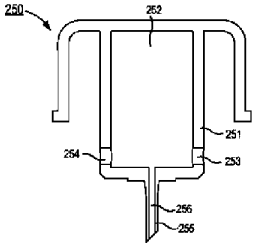


FIG. 5

【図６】

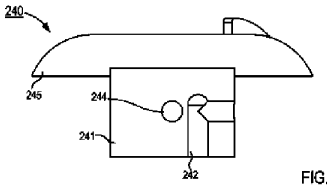


FIG. 6

【図７】

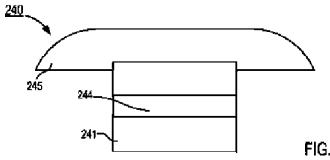


FIG. 7

【図８】

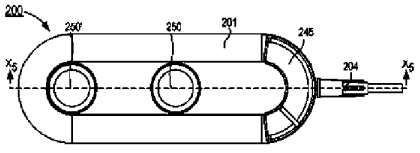


FIG. 8

【図９】

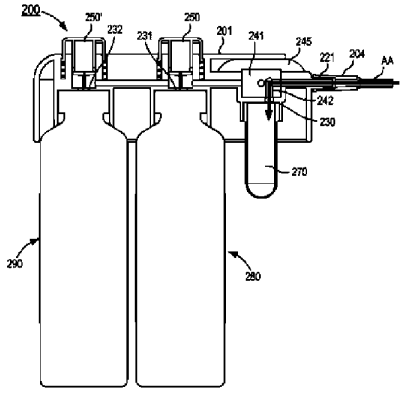


FIG. 9

【図１０】

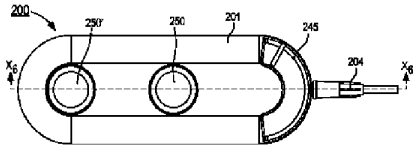


FIG. 10

【図１１】

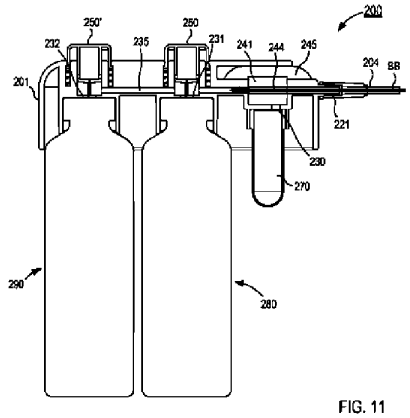


FIG. 11

【図１２】

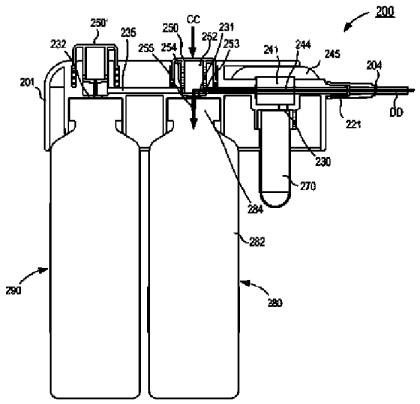


FIG. 12

【図１３】

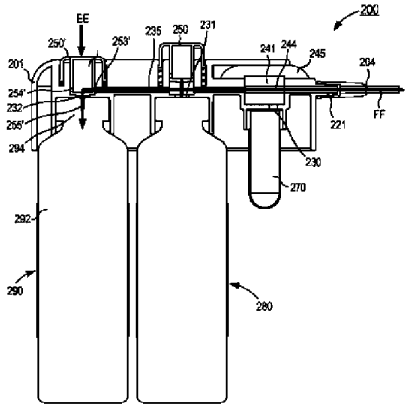


FIG. 13

【図１４】

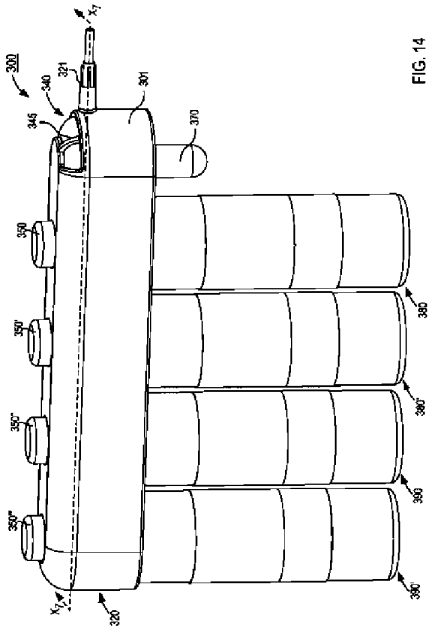


FIG. 14

【図１５】

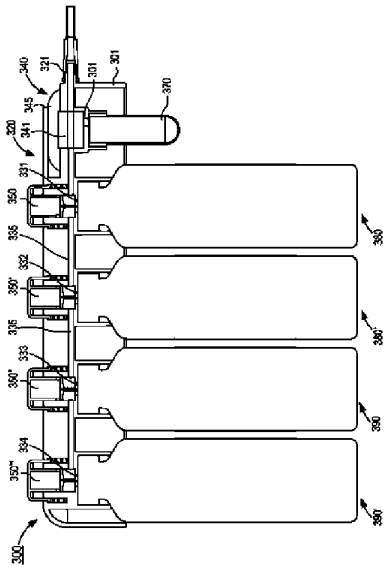


FIG. 15

【図１６】

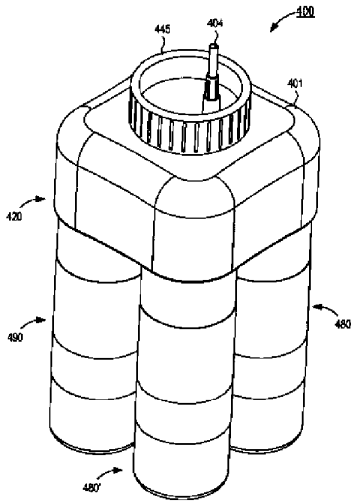


FIG. 16

【図１７】

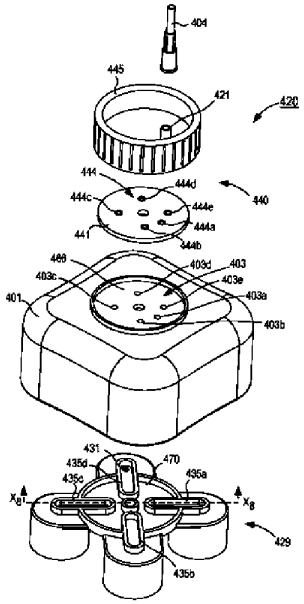


FIG. 17

【図１８】

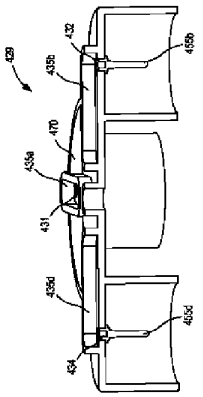


FIG. 18

【図１９】

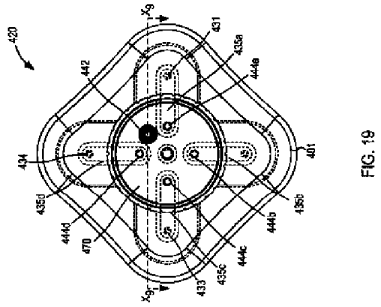


FIG. 19

【図２０】

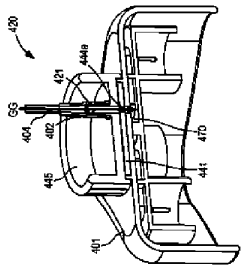


FIG. 20

【図２１】

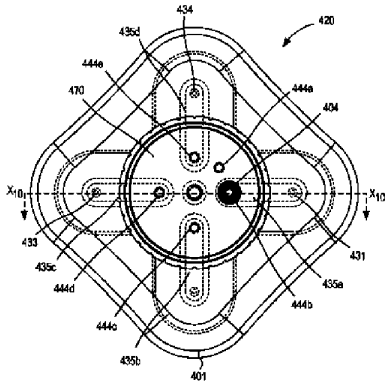


FIG. 21

【図２２】

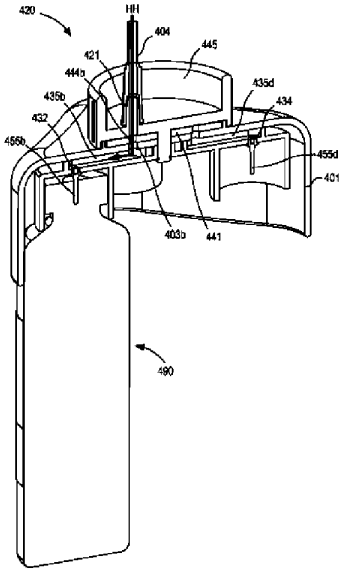


FIG. 22

【図２３】

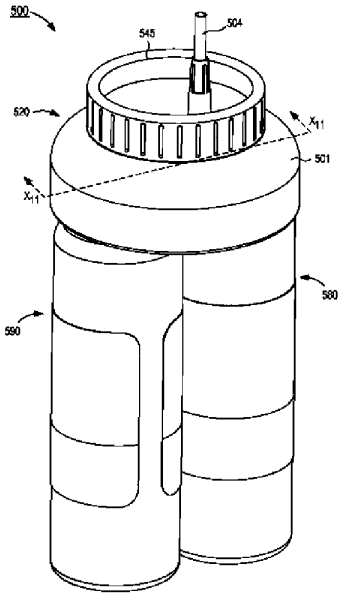


FIG. 23

【図２４】

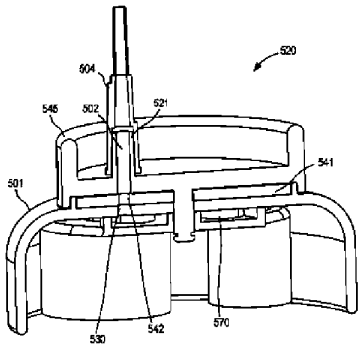


FIG. 24

【図２５】

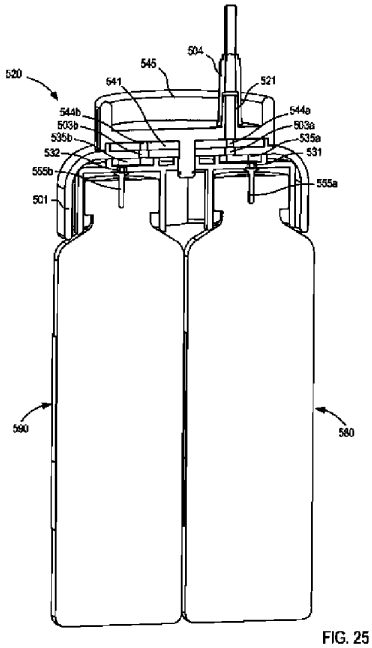


FIG. 25

【図２６】

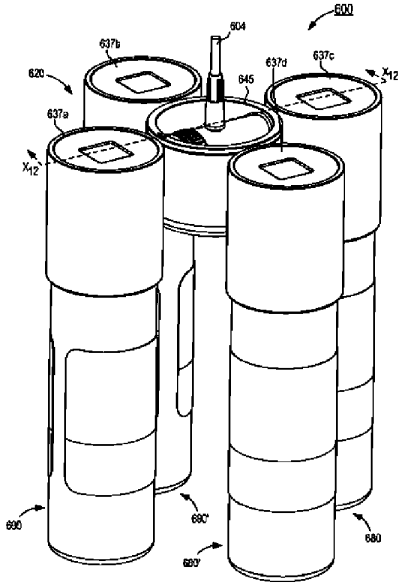


FIG. 26

【図２７】

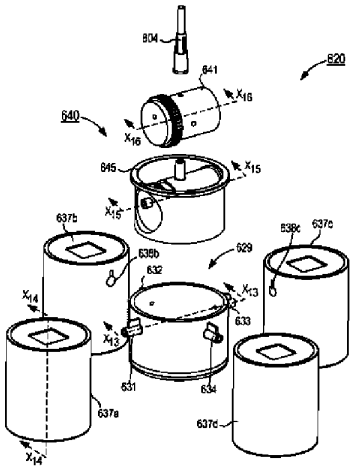


FIG. 27

【図２８】

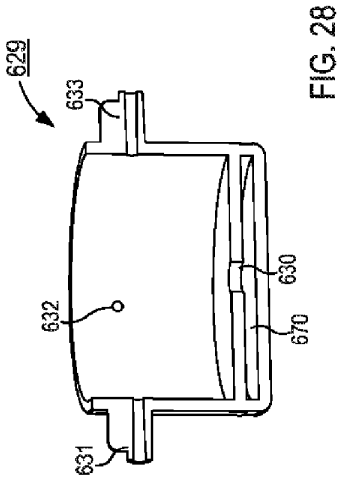


FIG. 28

【図２９】

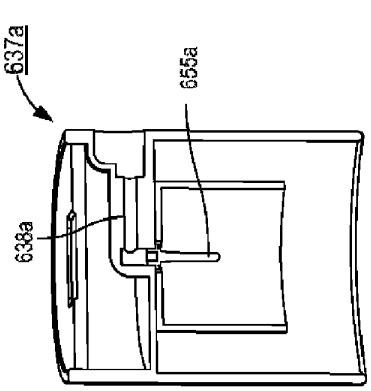


FIG. 29

【図３０】

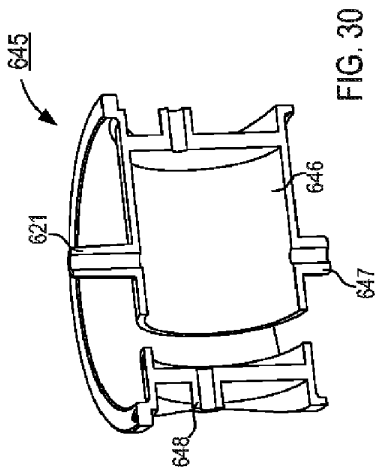


FIG. 30

【図３１】

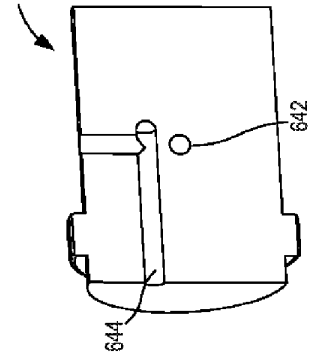


FIG. 31

【図３２】

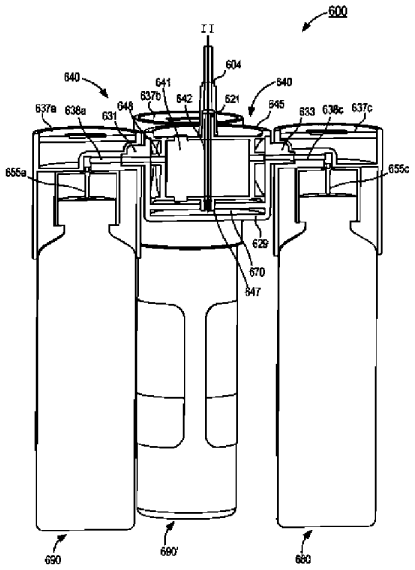


FIG. 32

【図３３】

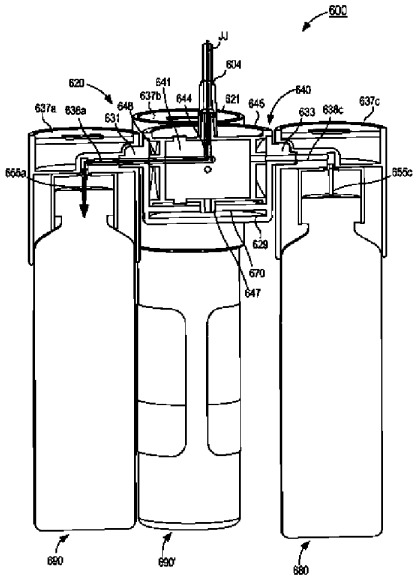


FIG. 33

【図３４】

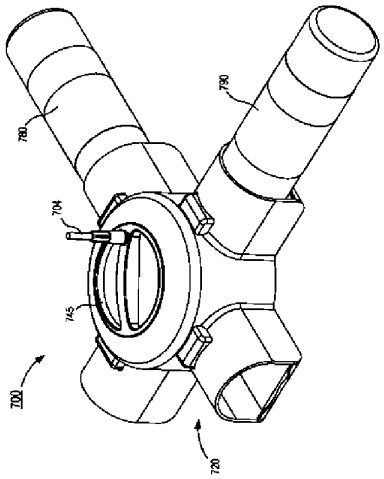


FIG. 34

【図３５】

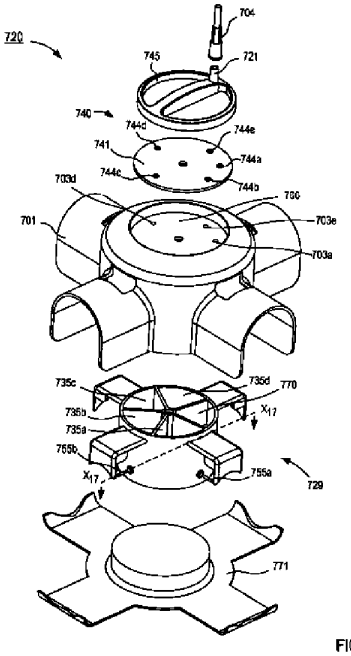


FIG. 35

【図３６】

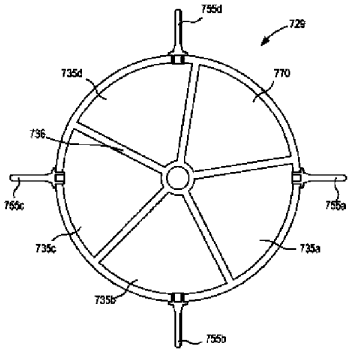


FIG. 36

【図３７】

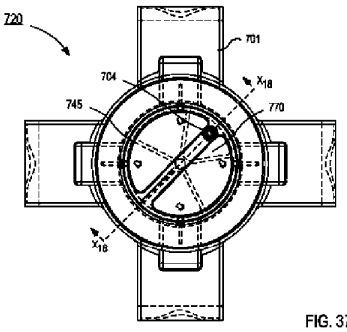


FIG. 37

【図３８】

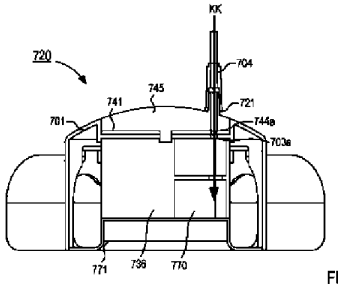


FIG. 38

【図３９】

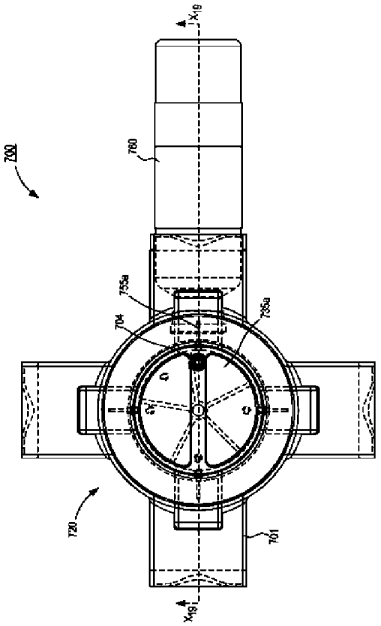


FIG. 39

【図４０】

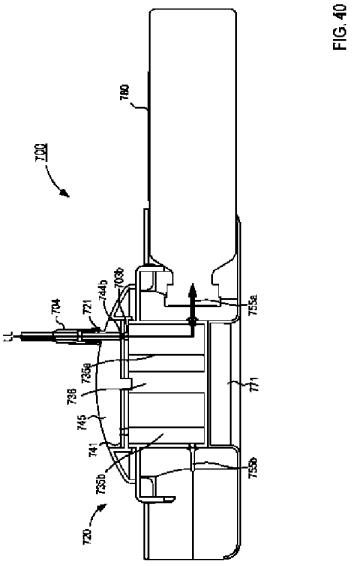


FIG. 40

【図４１】

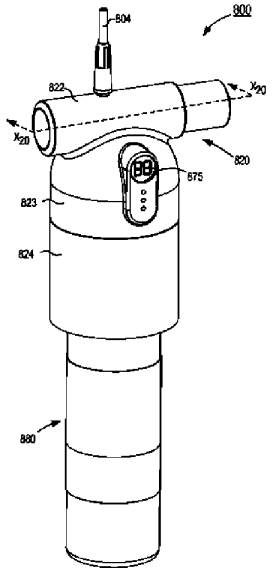


FIG. 41

【図４２】

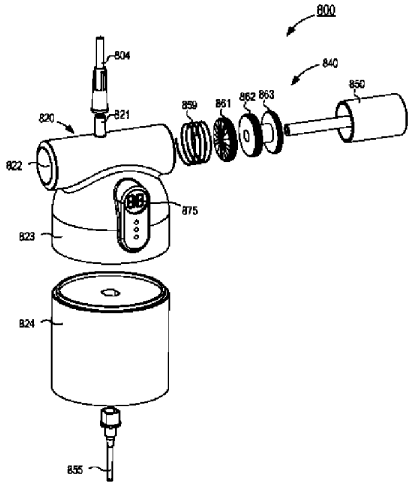


FIG. 42

【図４３】

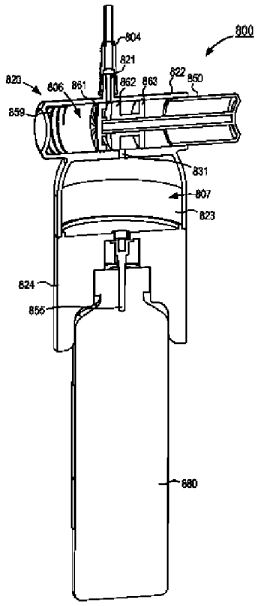


FIG. 43

【図４４】

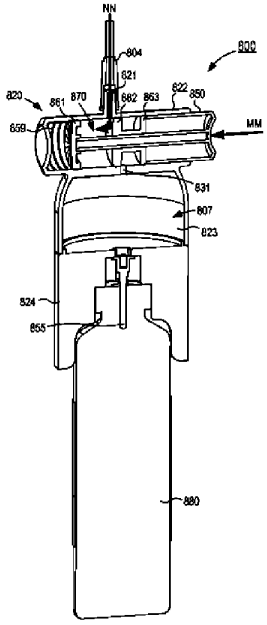


FIG. 44

【図４５】

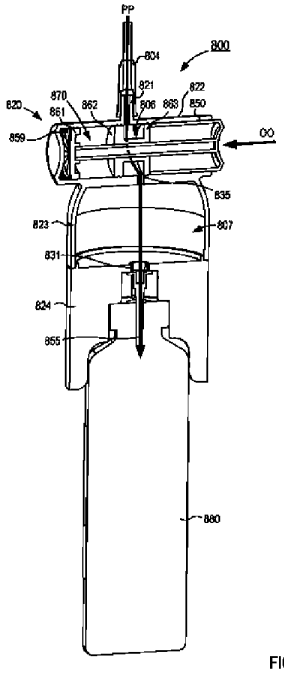


FIG. 45

【図４６】

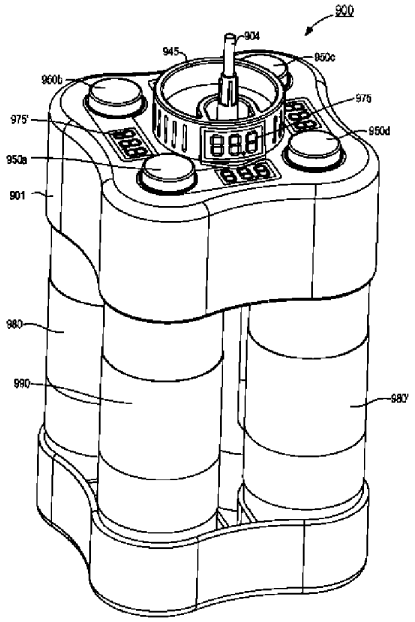


FIG. 46

【図４７】

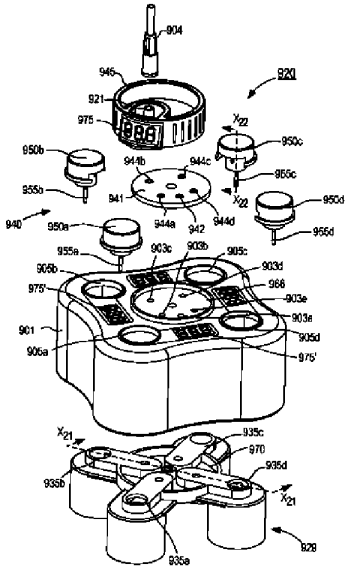


FIG. 47

【図４８】

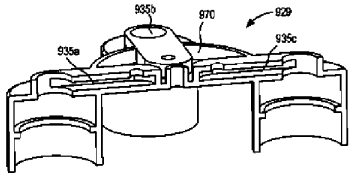


FIG. 48

【図４９】

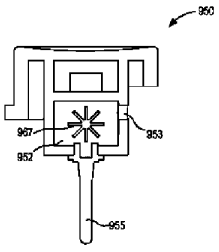


FIG. 49

【図５０】

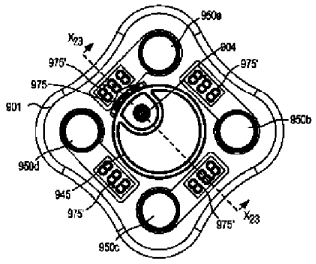


FIG. 50

【図５１】

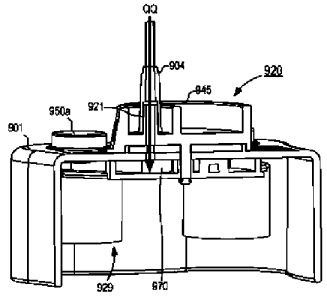


FIG. 51

【図５２】

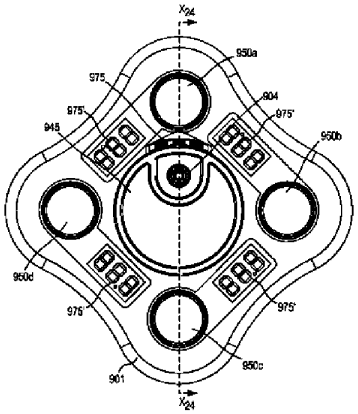


FIG. 52

【図５３】

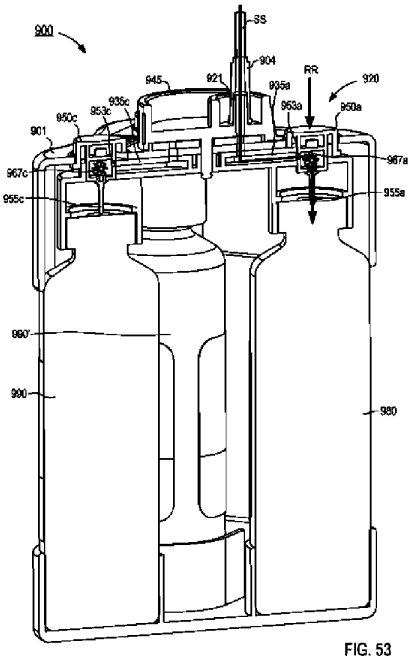
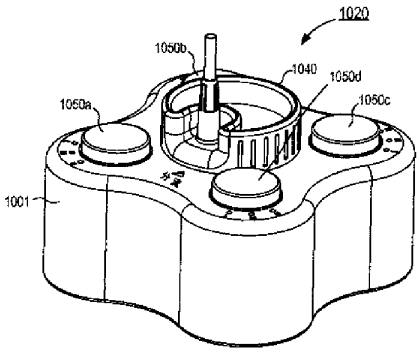
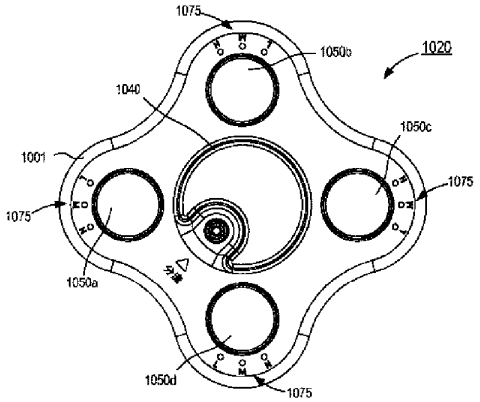


FIG. 53

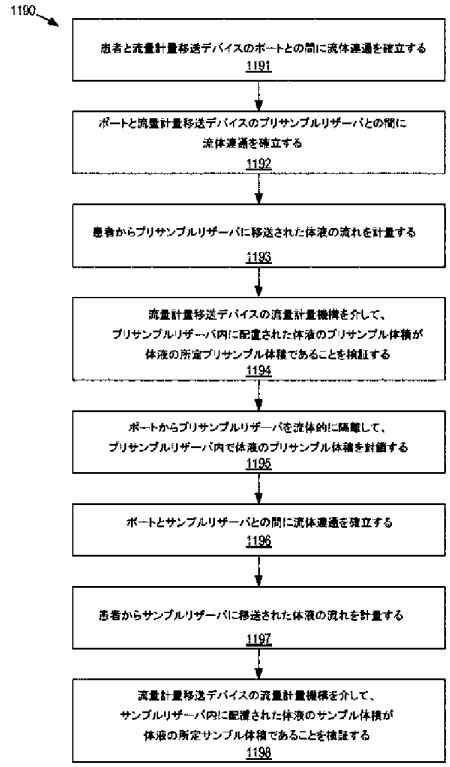
【図５４】



【図５５】



【図５６】


1190
患者と流量計量移送デバイスのポートとの間に流体連通を確立する
1191
ポートと流量計量移送デバイスのプリサンプルリザーバとの間に
流体連通を確立する
1192
患者からプリサンプルリザーバに移送された体液の流れを計量する
1193
流量計量移送デバイスの流量計量機構を介して、
プリサンプルリザーバ内に配置された体液のプリサンプル体積が
体液の所定プリサンプル体積であることを検証する
1194
ポートからプリサンプルリザーバを流体的に隔離して、
プリサンプルリザーバ内で体液のプリサンプル体積を封鎖する
1195
ポートとサンプルリザーバとの間に流体連通を確立する
1196
患者からサンプルリザーバに移送された体液の流れを計量する
1197
流量計量移送デバイスの流量計量機構を介して、
サンプルリザーバ内に配置された体液のサンプル体積が
体液の所定サンプル体積であることを検証する
1198

【国際調査報告】

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2013/073060

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - A61B 5/155 (2014.01)
USPC - 600/575
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC(8) - A61B 5/00, 5/15, 5/153, 5/155; A61M 39/22; A61J 1/05; G01N 1/10, 1/14, 1/18 (2014.01)
USPC - 422/559; 435/294.1; 600/573, 575, 576, 577, 578; 604/248, 409

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
CPC - A61B 5/1405, 5/1427, 5/1438, 5/150251; A61M 39/223 (2013.01)

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
PatBase, Google Patents, Google Scholar,

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X – Y	US 5,097,842 A (BONN) 24 March 1992 (24.03.1992) entire document	12, 15, 16, 18 – 1-11, 13, 14, 17, 19-29
X – Y	US 2008/0145933 A1 (PATTON) 19 June 2008 (19.06.2008) entire document	30-41 – 3, 13, 17, 22, 24, 25,
Y	US 2005/0148893 A1 (MATHIAS et al) 07 July 2005 (07.07.2005) entire document	1-11
Y	WO 2005/068011 A1 (MEHLHORN) 28 July 2005 (28.06.2005) entire document	14, 21-29
Y	US 3,848,581 A (CINQUALBRE et al) 19 November 1974 (19.11.1974) entire document	9, 19, 20

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"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
06 February 2014	18 FEB 2014
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201	Authorized officer: Blaine R. Copenheaver PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

Form PCT/ISA/210 (second sheet) (July 2009)

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Ｆターム(参考) 4C038 TA01 UA10 UB07

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(51) [International patent classification 6th edition]
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A61B 5/14 300 J 0277-2J
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[Preliminary examination request] Unclaimed
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(31) [Priority claim number] 08/296,207
(32) [Priority date] August 25, 1994
(33) [Country claiming priority] United States)
(81) [Designated country] EP (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, S
E), AU, CA, JP (71
)) [Applicant]
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(72) [Inventor]
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[Patent Attorney]
[Name] Michio Akaoka (1 other person))

wrap up close

(57) [Summary]
The present invention is a bifurcated capillary tube (10) including closed system blood sampli
ng devices. A second branch (32) of the bifurcated capillary tube is connected to and in fluid c
ommunication with the blood collection area. It terminates in an opening adapted to receive a
blood withdrawal device.

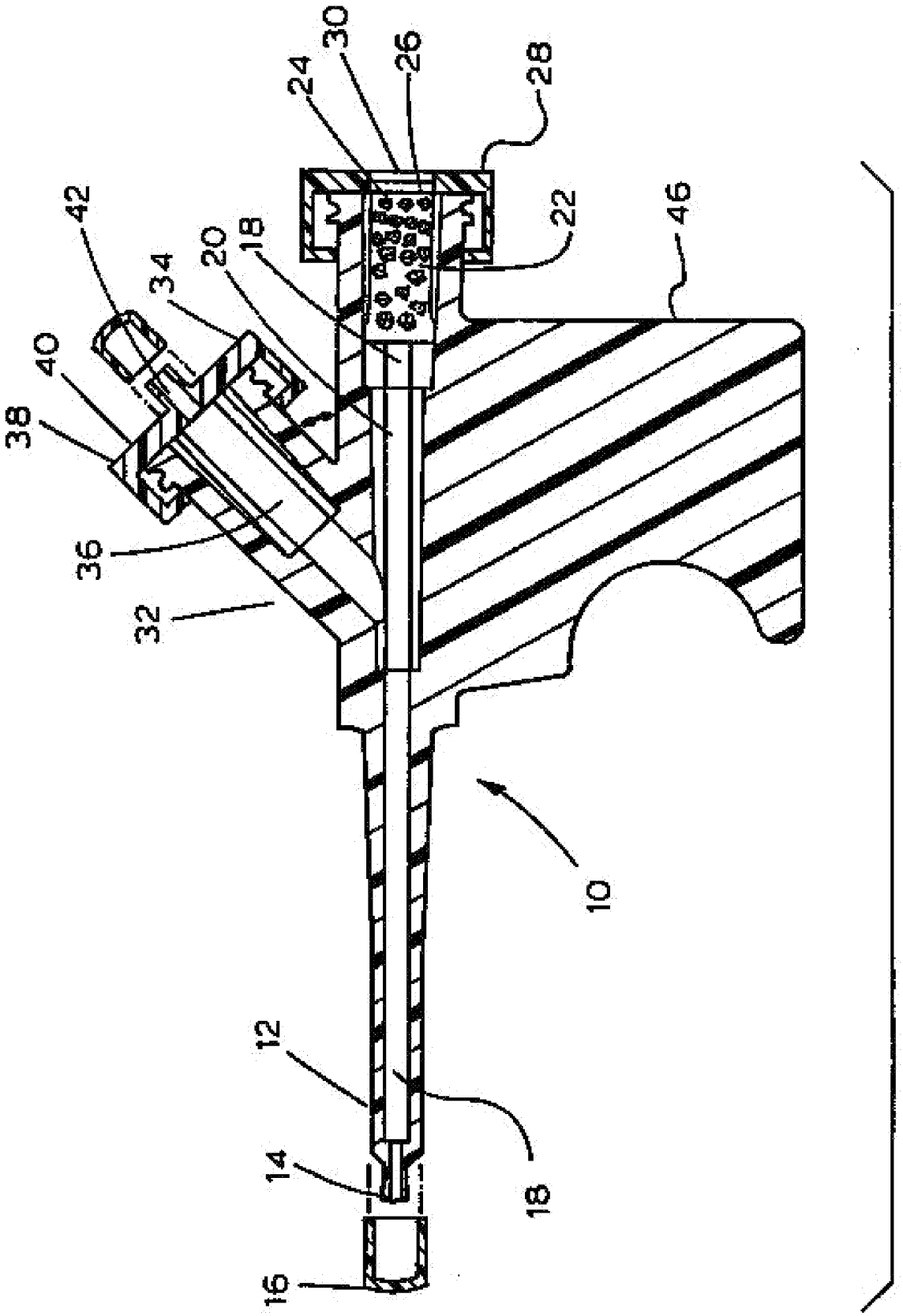


FIG. 1

The scope of the claims open ----

[Claims]

1. A closed system blood sampling device comprising a bifurcated capillary tube comprising:

a. a first branch having a cannulated

end ;

b. a blood collection area for storing an amount of withdrawn blood and supplying a first to the communicating channel;

c. a blood disposal chamber having an air permeable liquid closed end; and

d.

a second device connected to and in fluid communication with said blood collection area terminating in an opening adapted to receive a

blood extraction device.

2. 4. The cannula-shaped end is blunt, the blood waste chamber has a cap containing an air permeable hydrophobic membrane

on the end, and the blood waste chamber contains a porous blood

adsorbent 1 closed system blood sampling device.

3.

2. The closed system blood sampling device of claim 1, wherein the second branch has an internal angle of no greater than 90 degrees .

4. 4. The closed system blood sampling device of Claim 3, wherein the second branch has an angle of about 60 degrees

.

5. 3. The closed system blood

sampling .

6. 3. The closed system blood sampling device of Claim 2 , wherein said blunt cannulated distal end is

adapted to be received by an injection site including a resilient resealing means. 7. 7. The closed . 8. 3. The closed system blood sampling device of claim 2, wherein said blood collection area has a volume greater than the volume of said blood waste chamber . 9. A method of sampling blood from a patient having an artery connected to a venipuncture device attached to an injection site comprising the closed system blood sampling device of claim 1.

A law comprising:

a.

drawing blood through the cannulated end of the closed system blood sampling device , there by subsequently

filling the blood waste chamber and then the blood collection area;

b. withdrawing the blood contained within the blood collection area

through the opening in the second branch for subsequent processing; and then

c. and discarding the closed system blood sampling device

.

10. 10. The method of claim 9, wherein said cannula is blunt, said blood disposal chamber is c apped at its end with an air permeable hydrophobic

membrane and comprises a porous blood adsorbent. 11. 10. The method of claim 9, wherein t he second branch has an internal angle of no greater than 90 degrees . 12. Claim 1, wherein t he second branch has an angle of about 60 degrees.

1 method.

13. 11. The method of claim 10, wherein the cannulated end is tapered.

14.

11. The method of claim 10, wherein the blunt cannula-shaped distal end is adapted to be rec eived by an injection site including a resilient resealing means

.

15. 15. The method of claim 14, wherein the injection site is a pre-slit injection site

.

16.

11. The method of Claim 10, wherein the blood collection area has a volume greater than the volume of the blood waste chamber .

detailed description open —

Description:

CLOSED SYSTEM BLOOD SAMPLING APPARATUS

FIELD OF THE INVENTION The

present invention relates to closed system blood sampling apparatus.

BACKGROUND OF THE INVENTION

Arterial blood gas sampling is a standard procedure often used to . In some cases, samples . For a typical neonatal patient weighing 1000 grams and having a total blood volume , blood sample volume becomes a critical factor. A technique called the "three drops method" is gaining substantial clinical acceptance in neonatal units throughout the country . This method requires inserting a blunt hypodermic needle as far as possible into a standard sleeved T-connector . Three drops of blood, estimated at about 0.06 cc , are drawn onto the gauge pad, thereby removing heparinized or non-circulating blood from the cannula while providing a fresh arterial blood sample on its surface. Three more drops are then collected in the microcontainer after which the cannula is withdrawn. The blood cannula contents within the cannula lumen and the immediately prior collected microcontainer sample are then blood tested for testing.

Aspirated into a tuberculin-type syringe for transport to the chamber. A wash of the T-connector is then subsequently performed to remove residual blood. This procedure uses a controlled blood volume (0.06 cc as required to discard, and actual It provides the ability to draw 0.12 cc to possibly 0.20 cc) for blood gas testing on-the-fly.

There are several opportunities for procedure refinement. One problem is that the collection method is an open environment, which could facilitate the spread of blood contamination and/or communicable diseases . Second, the acquisition process is difficult to control with respect to volumetric accuracy and is highly sensitive to variations in physician technique, catheter placement and arterial pressure. In the treatment of neonatal patients where blood volume levels are critical, if a device could be designed for closed system collection that would also ensure sample volume consistency every time.

, improved accuracy could be of great clinical benefit.

BRIEF

DESCRIPTION OF THE DRAWING FIG. 1 is a horizontal cut-away side .

FIG. 2 is an upright, partial schematic showing a closed system blood sampling device conne

cted to an injection site, which is then connected
into a venipuncture device used to draw arterial blood;
is a diagram.

In the drawings, similar parts have similar numbers.

The Invention The present invention is a closed system blood sampling device that includes a bifurcated capillary tube having a first branch

with a
cannulated .
A blood collection area is
for .
It also supplies the first fraction of blood withdrawn to a communicating blood waste chamber having an air permeable liquid closed end.

A second branch of the bifurcated capillary is connected to and communicates with the blood collection area.
liquid communication. It
terminates .

In a preferred embodiment, the cannulated
end blunt, the blood waste chamber
is capped at its end with an air permeable hydrophobic membrane, and the blood waste chamber is porous. of blood adsorbents. The second branch
has an interior angle no greater than 90 degrees, and preferably the interior angle is 60 degrees.
It is also desirable that the cannulated end be tapered
so that fully below .

Preferably, the closed system blood sampling device
is
withdrawn from the injection site before the blood sample is withdrawn therefrom by such means as by direct aspiration into a tuberculin syringe or blood gas analyzer.

Although closed system blood sampling devices are particularly well suited for obtaining neonatal blood samples
, the devices are readily adaptable for obtaining samples from a variety of patient types.
be done.

Detailed Description of the Invention

In FIG
.
It is preferably formed of a transparent, chemically inert, non-toxic plastic such as polycarbonate or the like . It includes a blood withdrawal
cannula shaped end 12 . The cannula tip 14 is blunt and
narrowed to prevent backflow of blood at the injection site during arterial blood sampling.

A blood sampling device is used at the cannula tip to maintain sterility
It is fitted with a removable cap 16, which is removed just before.

FIG. 1 shows a cannulated distal end 12 that is tapered.
This particular configuration was chosen so that the cannula could engage and
generally later . The internal bore 18 at the cannulated distal end is sized
by capillary action driven by normal positive arterial blood pressure . The internal capillary 1 8 connects with and leads into a larger diameter lumen 20 . The continuous bore 18 and lume n 20 of the cannula 12 constitute the blood collection area. Hole 18 where it exits lumen 20 tr ansitions into blood waste chamber 22 . In a preferred embodiment of the invention , blood di sposal chamber 22 includes blood retention means such as absorbent material 24, which may be rayon or cellulose wadding or the like. The open end 26 of the blood waste chamber 22 has a cap 28 fitted on top of it with a liquid impervious, air permeable hydrophobic membrane 30 that allows air to escape from the blood sampling device 10 of the present invention. is closed by A suitable thin film material is sheet polytetrafluoroethylene . Connected to the lumen 20 and in fluid communication therewith is a second branch or port 32 . It is arranged to have an internal angle 34 not exceeding 90 degrees. The interior angle is

Preferably it is about 60 degrees. Hole 36 connects with hole 18 and matches it in dimensions . The port 32 is terminated at its distal end with an adapter cap 38 (at its top 40 a capillary lu er
Joint 42 is connected
is sealed by The capillary luer is protected from contamination
by a protective cap 44 that is removed just before blood is drawn from the closed blood sampl ing device.
Port 32 and its hole 36 form
part . For convenience of use, the closed blood sampling device is coupled with
a pistol grip handle 46.

The blood collection area has a liquid volume greater than the liquid volume of the blood dis posal chamber. If
the closed blood sampling device described is to be used
in , the fluid volume of the blood collection area
may be 0.12 cc, and the fluid volume of the blood waste chamber 22 may be It would be abo ut 0.06cc.

The use of the closed blood
sampling is illustrated in FIG
. A communicating artery 48 is shown. Neck 54 of venipuncture device 50
is adapted to receive injection site 56 . Although a conventional injection site may
be used as such or adapted for use in the practice of the present invention, the injection site i s preferably pre-slit with a resilient reseal. It is desirable to be of a type having a possible par tition. This type of injection site is available from Baxter Healthcare Corporation and is availab le from Baxter Healthca.

Neonatal Tee Connector Luer Fitting sold under the trademark InterLink, a registered tradema rk of re Corporation .

Such pre-slit, resilient, resealable injection
sites and methods of their manufacture are described in US Pat. No. 5,188,620.
, the disclosure of which is incorporated herein by reference.
The pre-slit, resilient, resealable injection site described in this patent
is designed to accept a blunt cannula.
Another injection site related to the injection site detailed in US Pat. No. 5,188,620
is described in US Pat. No. 5,300,034. This patent is also a preferred embodiment used in the practice of this invention.
The plethora of publications and references describing various injection sites are elaborated
. This patent and publications cited therein are also
incorporated .

Injection site 56 is connected to a T-connector 58 which in turn is connected to
microbore tubing which is connected through female luer fitting 62 to intravenous line 64
. The distal end of injection site 56 is connected to neck 54 of venipuncture device 50 . A prox imal end 66 of injection site 56 is a pre-slit, resilient member adapted to receive blood withdr awal cannula 12 sized to fit snugly into
the injection site. , is connected with the resealing septum 68 . Inserted into the second branc h or port 32 is a conventional syringe 70 such as a tuberculin blood aspiration syringe or an ar terial blood gas loss resistant syringe. The cannula 12 of the device is inserted through the s

eptum 68 of the injection site 56 and positioned so that the tip 14 of the cannula 12 is fully in serted into the injection site adjacent the venipuncture device. be. Doing so would remove the residual from the blood draw volume as a measurable factor. Arterial pressure causes blood to enter and flow up the device through capillary action.

will let As blood rises to the hydrophobic membrane 30 of the device, air
will escape through the upstream hydrophobic membrane 30 . Original blood originally presen t in the catheter will be forced up past
the luer fitting branch for retention and eventual disposal in the device . The device will be wit hdrawn from the T-connector as soon as visual confirmation
of a blood-filled lumen is formed.
The vent
removal cap 44 will be removed from the bifurcated luer fitting 42 and replaced by a syringe 7 0 that will be aspirated to remove the arterial blood
sample
. The residual blood volume upstream of the bifurcation will remain in the device for subseque nt disposal
.

drawing open —

[Fig. 1]

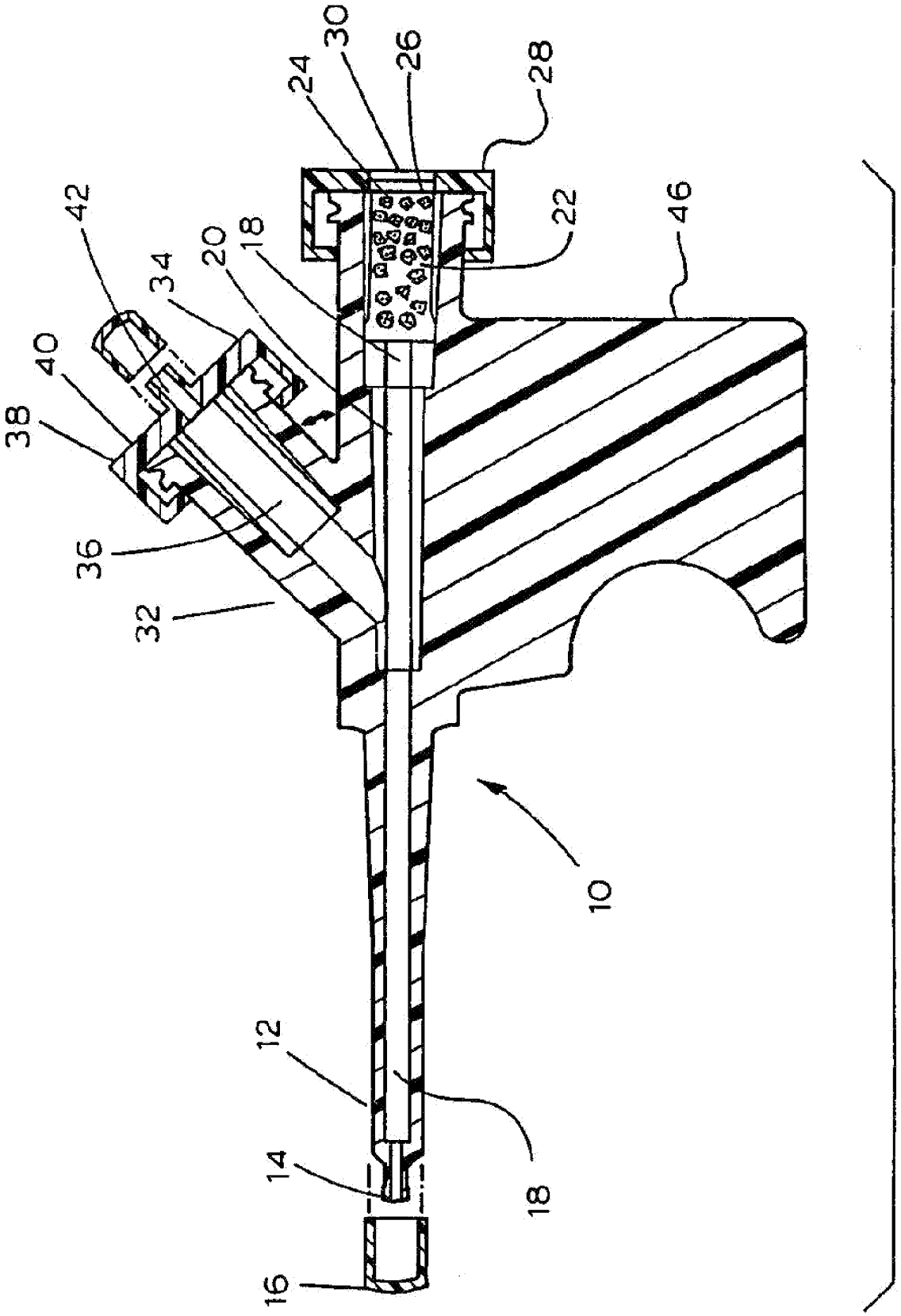


FIG. 1

[Figure 2]

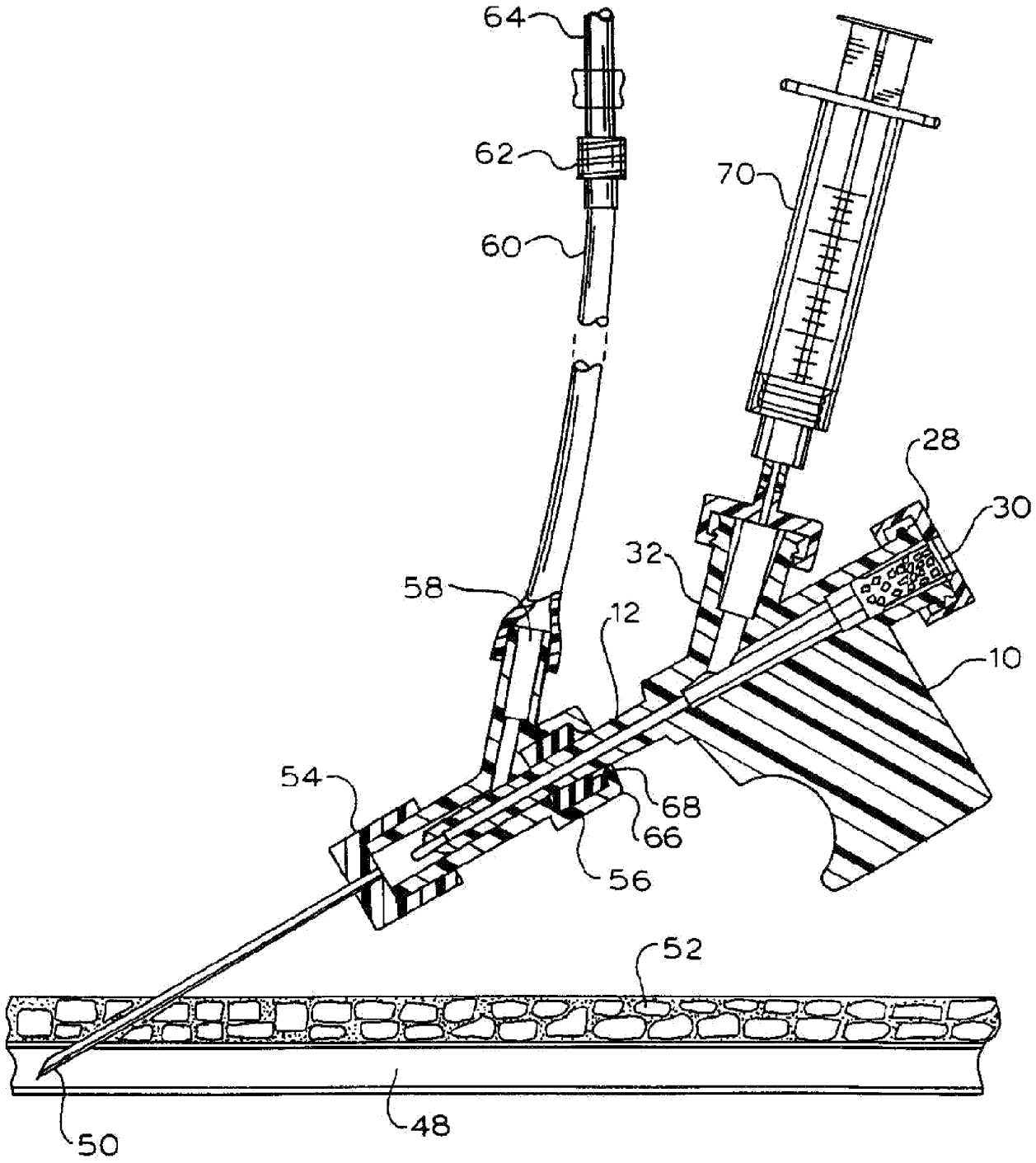


FIG. 2

search report open +

drawing open

Representative drawing 1 2

Magnify and Rotate

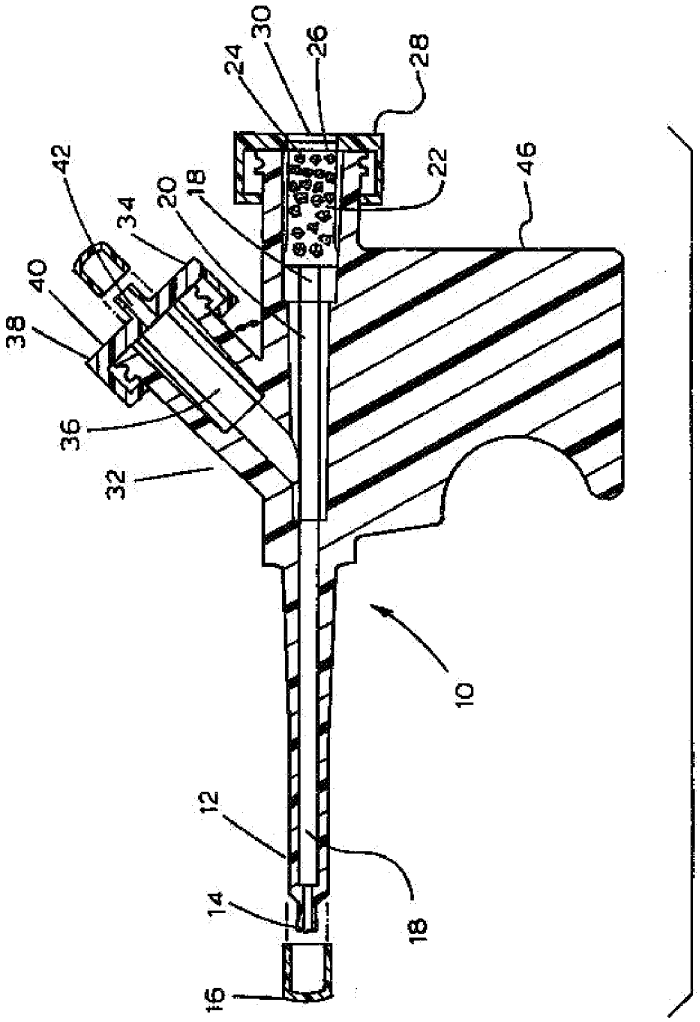


FIG. 1

Representative drawing

1 / 1 display

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(54)【発明の名称】　閉鎖系血液サンプリング装置

(57)【要約】
本発明は、血液を抜き取りそして連通した血液収集区域へ血液を移送するための、カニューレ形の末端(14)を有する第一の枝(12)を有する、分岐した毛細管(10)を含む閉鎖系血液サンプリング装置を含む。該分岐した毛細管の第二の枝(32)は、該血液収集区域へと連結され、そしてそれと液体連通している。それは、血液抜き取り装置を受け入れるのに適合させた開口に終わっている。

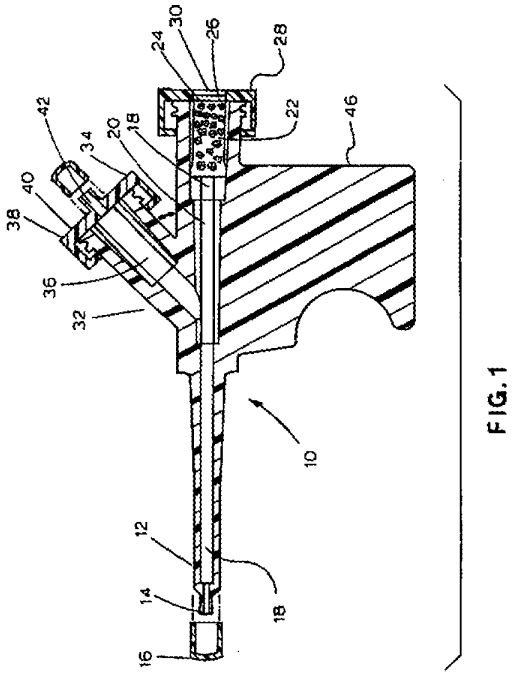


FIG. 1

【特許請求の範囲】

１．　分岐した毛細管を含む閉鎖系血液サンプリング装置であって、

ａ．血液を抜取って連通路へと血液を移送するためのカニューレ形の末端を有する第一の枝と、

ｂ．ある量の抜き取られた血液を貯蔵し、そして抜き取られた血液の最初の画分を連通路へと供給するための血液収集区域と、

ｃ．空気透過性の液体閉鎖性の末端を有する血液廃棄室と、そして、

ｄ．血液抜き取り装置を受け入れるのに適合させた開口に終わる該血液収集区域に連結されそしてこれと液体連通している第二の技と、

を含む閉鎖系血液サンプリング装置。

２．　該カニューレ形の末端が鈍く、該血液廃棄室が空気透過性の疎水性薄膜を含むキャップをその末端に嵌めてあり、そして該血液廃棄室が多孔性の血液吸着剤を含むものである、請求項１の閉鎖系血液サンプリング装置。

３．　第二の枝が９０度よりも大きくない内角を有するものである、請求項１の閉鎖系血液サンプリング装置。

４．　第二の枝が約６０度の角度を有するものである、請求項３の閉鎖系血液サンプリング装置。

５．　該カニューレ形の末端が先細っている、請求項２の閉鎖系血液サンプリング装置。

６．　該鈍いカニューレ形の末端が、弾力のある再シールする手段を含む注射部位によって受け入れられるのに適合させてあるものである、請求項２の閉鎖系血液サンプリング装置。

７．　該注射部位が予めスリットを入れてある注射部位である、請求項６の閉鎖系血液サンプリング装置。

８．　該血液収集区域が、該血液廃棄室の体積よりも大きな体積を有するものである、請求項２の閉鎖系血液サンプリング装置。

９．　請求項１の該閉鎖系血液サンプリング装置を含む注射部位に取付けられた静脈穿刺装置と連結された動脈を有する患者から、血液をサンプリングする方

法であって、

ａ．該閉鎖系血液サンプリング装置の該カニューレ形の末端を通して血液を抜き取り、それによってその後該血液廃棄室そして次いで該血液収集区域を満たすステップと、

ｂ．その後の処理のために、該血液収集区域内に含まれた該血液を該第二の枝にある該開口を通して抜き取るステップと、そして、次いで、

ｃ．該閉鎖系血液サンプリング装置を捨てるステップと、

を含む方法。

１０．　該カニューレが鈍く、該血液廃棄室がその末端に空気透過性の疎水性薄膜を含むキャップを嵌めてあり、そして多孔性の血液吸着剤を含むものである、請求項９の方法。

１１．　第二の枝が９０度よりも大きくない内角を有するものである、請求項９の方法。

１２．　第二の枝が約６０度の角度を有するものである、請求項１

１の方法。

１３．　該カニューレ形の末端が先細っている、請求項１０の方法。

１４．　該鈍いカニューレ形の末端が、弾力のある再シールする手段を含む注射部位によって受け入れられるのに適合させてあるものである、請求項１０の方法。

１５．　該注射部位が予めスリットを入れてある注射部位である、請求項１４の方法。

１６．　該血液収集区域が、該血液廃棄室の体積よりも大きな体積を有するものである、請求項１０の方法。

【発明の詳細な説明】

閉鎖系血液サンプリング装置

本発明の分野

本発明は、閉鎖系血液サンプリング装置に関する。

本発明の背景

動脈血のガスサンプリングは、重態の疾病において呼吸機能の評価を助けるためにしばしば使用される標準的な手順である。場合により、一日に20回ものサンプルが抜き取られることができる。1000グラムの体重でそして約85ccの全血液体積を有する典型的な新生児患者にとって、血液サンプルの体積は重大な要素になる。

「３滴法」と呼ばれる技術が、国中の新生児ユニットにおいて実質的に臨床上受入れられつつある。この方法は標準のスリーブで止められたＴ字形コネクターの中へとできる限り遠く、鈍い皮下針を挿入することを要求する。約0.06ccと推定される三滴の血液が、ゲージパッド上へとたらされ、それによってその表面に新鮮な動脈血サンプルを提供する間にヘパリン加血液又は非循環血をカニューレから取り除く。次いで、更なる三滴がマイクロコンテナー中に集められ、その後にカニューレが引き抜かれる。カニューレ管腔内の血液カニューレ内容物へ及び直前に収集されたマイクロコンテナーサンプルは、次いで検査のために血液試験室へと輸送するためにツベルクリンタイプの注射器中へと吸引される。次いで残りの血液を除去するためにＴコネクターの洗浄がその後行われる。この手順は制御された血液体積（捨てるのに必要なものとして0.06cc、及び実

際の血液ガス検査のために0.12cc乃至多分0.20cc）を抜き取る能力を提供する。

手順の改良のための幾つかの機会が存在する。一つの問題は、血液汚染及び／又は伝染病の拡散を促進し得るであろうその収集方法が開放した環境であることである。第二には、体積の正確さに関しては収集過程が制御しにくく、そして医者の技術、カテーテル配置及び動脈圧の変化に対して非常に影響されやすい。もし、毎回サンプル体積の一貫性も保証することができるであろう閉鎖系の収集のための装置が設計できれば、血液体積レベルが重大である新生児患者の治療では

、正確さの改善は大きな臨床上の利益になりうる。

図面

図１は、本発明の閉鎖系血液サンプリング装置を示す水平方向の切り取った側面図である。

図２は、注射部位に連結され、次いで、該注射部位が動脈血を抜き取るために使用される静脈穿刺装置中へと連結されている閉鎖系血液サンプリング装置を示す直立の部分的に概要的な図である。

該図面中では、類似の部品は類似の番号を有する。

本発明

本発明は、血液を抜き取って連通した血液収集区域へ移送するためのカニューレ形の末端を有する第一の枝を有する分岐した毛細管を含む閉鎖系血液サンプリング装置である。血液収集区域はある量の抜き取られた血液を貯蔵するためのものである。それは、抜き取られた血液の最初の画分を空気透過性の液体閉鎖性の末端を有する連通した血液廃棄室へ供給をもする。

分岐した毛細管の第二の分岐は血液収集区域に連結されてこれと

液体連通している。それは血液抜取り装置を受け入れるのに適合させた開口に終わっている。

好ましい具体例においては、閉鎖系血液サンプリング装置のカニューレ形の末端は鈍く、血液廃棄室はその末端に空気透過性の疎水性薄膜を含むキャップがはめてあり、そして血液廃棄室は多孔性の血液吸着剤を含む。第二の枝は90度より大きくない内角を有し、そして好ましくは該内角は60度である。後に一層完全に記述される好ましい注射部位中へと、カニューレ形の末端がぴったり嵌合するように、カニューレ形の末端が先細りであることも同様に望ましい。

好ましくは、閉鎖系血液サンプリング装置は、血液サンプルがツベルクリン注射器又は血液ガス分析器中へと直接的に吸引される等のような手段によってそこから抜き取られる前に、注射部位から抜き取られる。

閉鎖系血液サンプリング装置は、新生児の血液サンプルを得るのに特に適しているが、該装置はさまざまな患者のタイプからサンプルを得るために直ちに適合

される。

本発明の詳細な記述

図１において、閉鎖系血液サンプリング装置は全体として数字10によって指示されている。それは、ポリカーボネート等のような透明で化学的に不活性な毒性のないプラスチックによって好ましくは形成される。それは血液抜取りカニューレ形の末端12を含む。カニューレ先端14は鈍く、そして動脈血サンプリングの間注射部位の血液逆流を防止するようにくびれて細まっている。無菌性を維持するために、カニューレ先端には、血液サンプリング装置が使用される

直前に取り外される、取外し可能なキャップ16が嵌められている。

図１は、先細りにされるカニューレ形の末端12を示している。その詳細は後に一層完全に記述されるであろうが、カニューレが特有の注射部位と係合そして一般的に嵌合することができるように、この特有の構成が選ばれた。カニューレ形の末端の内部穴18は、正常な正の動脈血圧によって駆動される毛管作用によって、抜き取られた血液が該穴に沿って移動することを許容するように寸法が与えられている。

内部毛細穴18は、一層大きな直径の管腔20と連結しその中へと続いている。該カニューレ12の連続した穴18及び管腔20は血液収集区域を構成する。それが管腔20を出るところの穴18は、血液廃棄室22内へと移行している。本発明の好ましい具体例では、血液廃棄室22は、レーヨン又はセルロース詰め綿等であってよい吸着材料24のような血液保持手段を含む。血液廃棄室22の開口末端26は、本発明の血液サンプリング装置10から空気が排出されることを許容する、液体を通さない、空気透過性の疎水性薄膜30をその頂部に嵌めてあるキャップ28によって閉じられている。適した薄膜材料は、約0.8ミクロンの厚さを有するシート状のポリテトラフルオロエチレンである。

該管腔20に連結されてそれと液体連通しているのは第二の分岐又はポート32である。それは、90度を越えない内角34を有するように配置されている。該内角は好ましくは約60度である。穴36は穴18と連結し、そして寸法においてそれと一致する。ポート32は末端においてアダプターキャップ38（その頂部40に毛管ルアー

継手42が連結

されている）によってシールされている。毛管ルアーは、血液が閉鎖された血液サンプリング装置から抜き取られる直前に取り外される保護キャップ44によって、汚染から保護される。ポート32とその穴36は前に記述された血液収集区域の一部を形成する。使用の便宜のために、閉鎖された血液サンプリング装置はピストル握り把手46と連結される。

血液収集区域は、血液廃棄室の液体容積よりも大きな液体容積を有する。もし、記述された閉鎖された血液サンプリング装置が新生児の血液サンプリングにおいて用いられるためであれば、血液収集区域の液体容積は0.12ccであるかもしれず、そして血液廃棄室22の液体容積は約0.06ccであろう。

血液を抜き取ってサンプリングするための本発明の閉鎖された血液サンプリング装置の使用が図２中に図解されており、該図には皮下組織52を突き通して挿入された静脈穿刺装置50と連通した動脈48を示している。静脈穿刺装置50の首54は注射部位56を受け入れるよう適合させてある。慣用の注射部位がそのようなものとして使用されてよく、又は本発明の実施において用いられるのに適合させてよいが、該注射部位は好ましくは予めスリットを入れてある弾力性のある再シール可能な隔壁を有するタイプであることが望ましい。このタイプの注射部位はBaxter Healthcare Corporationから入手可能であり、そしてこれはBaxter Healthcare Corporationの登録商標であるInterLinkという商標の下に販売される新生児T字形コネクタールアー継手である。

そのような予めスリットを入れてある、弾力性のある、再シール可能な注射部位及びそれらの製造の方法が米国特許5,188,620中に

記述されており、その開示が参照によってここに導入される。この特許中に記述されている予めスリットを入れてある、弾力性のある、再シール可能な注射部位は鈍いカニューレを受け入れるように設計されている。米国特許5,188,620中に詳しく述べられた注射部位に関係した他の一つの注射部位が米国特許5,300,034中に記述されている。この特許も同じく、この発明の実施中で使用される好まし

い注射部位を記述するおびただしい数の刊行物及び参照文献を詳しく述べている。この特許及びその中に挙げられた刊行物も同じく参照によってここに導入される。

注射部位56はＴ字形コネクター58と連結され、Ｔ字形コネクター58が今度は、雌のルアー継手62を通じて静脈内ライン64へと連結される微細穴チューブと連結される。注射部位56の先端側末端は静脈穿刺装置50の首54へと連結されている。注射部位56の根元側末端66は、該注射部位中へぴったり嵌合するように寸法が与えられた、血液抜取りカニューレ12を受け入れるよう適合させた、予めスリットを入れてある、弾力性のある、再シールする隔壁68と連結されている。第二の枝又はポート32中へと挿入されているのは、ツベルクリン血液吸引注射器のような慣用の注射器70又は動脈血ガス損失抵抗性注射器である。

装置のカニューレ12は、注射部位56の隔壁68を貫通して挿入され、そしてカニューレ12の先端14が静脈穿刺装置に隣接した注射部位中へと完全に挿入されるように配置されるであろう。そのように実施すると、実際のＴ字形ハウジングの残余の体積が血液吸引体積中から、測定可能な要素としては除かれるであろう。動脈圧が、血液をして毛細管作用を通じて該装置へと入りそして該装置を流れ登らせるであろう。血液が該装置の疎水性薄膜30へと上昇するにつれて、空気が上流の疎水性の薄膜30を通して散逸するであろう。該カテーテル中に最初に存在した元々の血液は、該装置中における保持及び最終的な廃棄のためにルアー継手分岐を通り越して押し上げられるであろう。該装置は、血液が満たされた管腔の視覚的確認が形成されるとすぐにＴ字形コネクターから引き抜かれるであろう。ガス抜き除去キャップ44が分岐したルアー継手42から除去され、そして動脈血サンプルを取り除くために吸引されるであろう注射器70によって置き換えられるであろう。分岐の上流の残余血液体積が、その後の廃棄のために該装置中に残るであろう。

【図１】

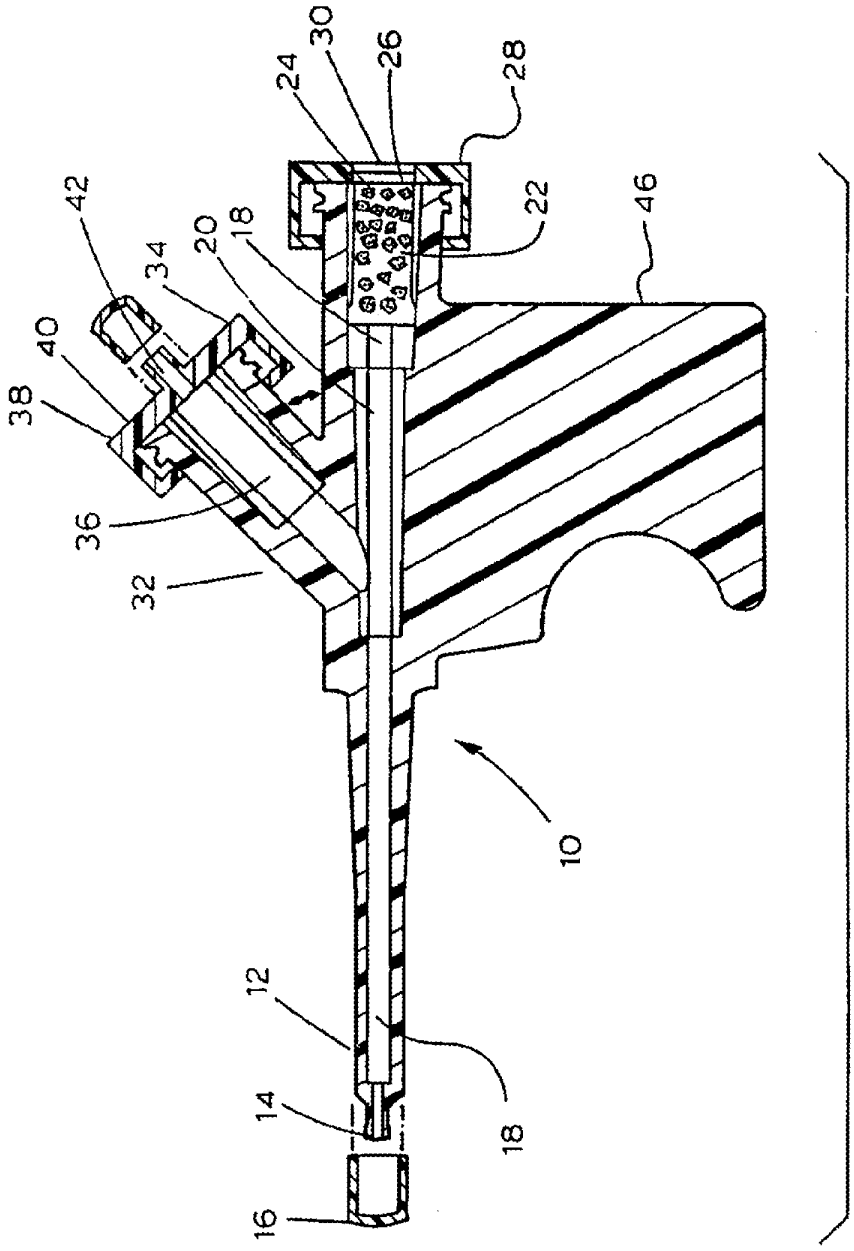


FIG. 1

【図２】

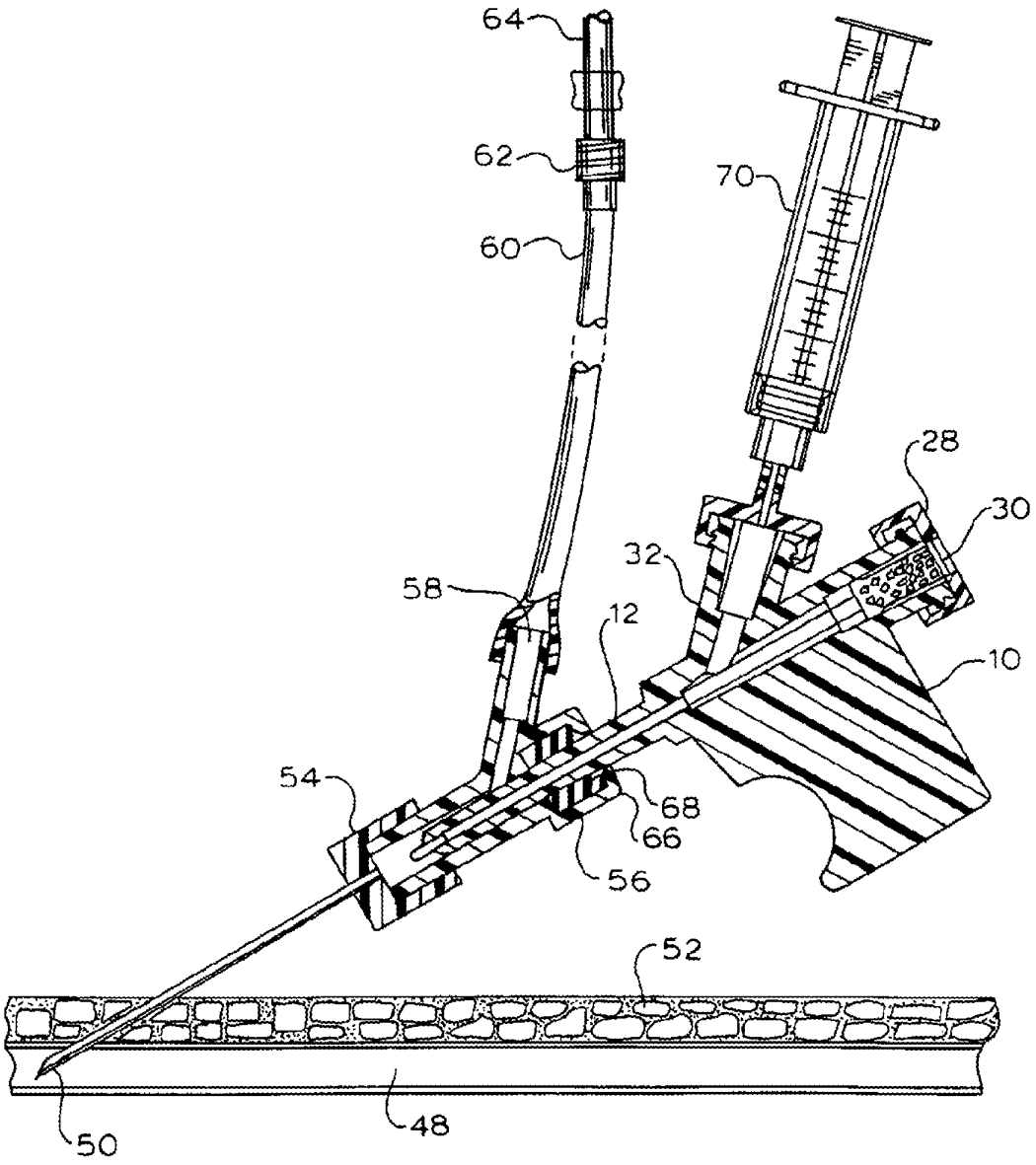


FIG. 2

【国際調査報告】

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US95/10702

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) :A 61M 5/00
US CL : 604/122

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 604/122, 35, 125, 126, 128, 256, 258, 283, 284
128/ 760, 762, 767, 768

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X -- Y	US, A, 4,531,937 (Yates) 30 July 1985, See Entire Reference	1-7,9-15 --- 8,16

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be part of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E"	earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search 08 DECEMBER 1995	Date of mailing of the international search report 04 JAN 1996
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No.	Authorized officer SAM RIMELL Telephone No. (703) 308-0858

Form PCT/ISA/210 (second sheet)(July 1992)*

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Literature display help

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Patent 5825146

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(54) [Title of the invention] Control device and control method for an operation target device in a vehicle
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B60R 16/02 630J
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[Number of Claims] 14
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(22) [Application date] February 29, 2012 (2012.2.29)

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[Patent Attorney]
[Name] Shunichi Takahashi
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[Name] Manabu
Karasawa [Examiner] Nobuhide Kato
(56) [References]
[Reference] JP-A-2000-228126 (JP, A) [Reference] JP-A-2007-076491 (JP, A) [Reference] Japanese Utility Model Laid-Open No. 61-161852 (JP, U) [Reference] JP-A-06-156114 (JP, A) (58) [Field investigated] (Int.Cl., DB name) B60R 16/02 B60R 16/027

The scope of the claims open —

(57) [Scope of Claims]

[Claim 1] A sensor

having a plurality of detection areas and is mounted in a predetermined range of a grip portion of a steering wheel of a vehicle so as to cover the grip portion gripped by the driver. a sensor data generation unit that generates sensor data including position data indicating which detection area is being touched based on a contact detection signal obtained from the touch sensor

; A detection unit that detects whether or not the grip is gripped and an input operation to the touch sensor, and the detection unit

detects that the driver is gripping the grip, and the touch sensor detects a control unit that controls an operation target device to be operated by the touch sensor in response to the specific input operation when it is detected that a specific input operation has been performed on

the

control A control device for an operation target device in a vehicle, characterized in that, when a direction indicator is operated, the vehicle is in a specific state , and the section invalidates the control of the operation target device. 2. A contact detection signal obtained from a touch sensor which has a plurality of detection areas and which is mounted in a predetermined range of a handle gripped by a driver on a steering wheel of a vehicle so as to cover said handle. a sensor data generator that generates sensor data including position data indicating which detection area is being touched, based on

a detection unit that detects whether or not the driver is gripping the grip based on the sensor data and an input operation to the touch sensor

; and when it is detected that a specific input operation has been performed on the touch sensor, the operation target device to be operated by the touch sensor in response to the specific input operation. and a control unit for controlling the operation target device,

wherein

the control unit invalidates the control of the operation target device by determining that the vehicle is in a specific state when the shift position of the shift lever is reversed. A control device for an operation target device in a vehicle. 3. The touch sensor includes a part of the plurality of detection areas and includes a grip detection area for detecting contact of a driver's palm and another part of the plurality of detection areas, and includes a grip detection area for detecting contact with the driver's palm. and an operation detection area for detecting the specific input operation caused by the contact of the grip detection area, and the detection unit detects when the driver grips the grip based on sensor data based on the contact detection signal obtained from the grip detection area. 3. The specific input operation is detected by sensor data based on a contact detection signal obtained from the operation detection area . Con

trol device. [Claim 4]

Based on a contact detection signal obtained from a touch sensor that has a plurality of dete ction areas and is attached to a predetermined range of a grip portion gripped by a driver on a steering wheel of a vehicle so as to cover the grip portion. a sensor data generation unit tha t generates sensor data including position data indicating whether a detection area is being to uched; and based on the sensor data, whether or not the driver is gripping the grip and the to uch

sensor a detection unit that detects an input operation to the touch sensor, and the

detection unit detects that the driver is gripping the grip, and detects that a specific input op eration has been performed on the touch sensor and a control unit

that controls an operation target device to be operated by the touch sensor in response to th e specific input operation, wherein the touch sensor includes a part of the plurality of detectio n areas

. , a grip detection area for detecting the contact of the driver's palm, and an operation dete ction area for detecting the specific input operation by finger contact, including other parts of the plurality of detection areas, are set,

The detection unit detects whether or not the driver is gripping the grip by sensor data base d on the contact detection signal obtained from the grip detection area, and the sensor based on the contact detection signal obtained from the operation detection area. A control device fo r an operation target device in a vehicle, wherein the specific input operation is detected by d ata, and the

control unit disables control of the operation target device when the vehicle is in a specific st ate.

5.

The controller controls, as the specific input operation, two points spaced apart in the circum ferential direction in a cross section of the steering wheel when the grip is cut in the radial dir ection with respect to the operation detection area. is operated with two fingers, the operation target device is controlled according to the pattern5. The control device for an operation targe t device in a vehicle according to claim 3 or 4, characterized in that :

6.

The controller determines that the vehicle is in a specific state when the rotation angle of th e steering wheel exceeds a predetermined angle, and invalidates the control of the device to b e operated . A control device for an operation target device in a vehicle according to any one of claims 1 to 4 .

7.

The touch sensor includes a first touch sensor mounted in a predetermined range of the grip portion gripped with the left hand of the driver and a second touch sensor mounted in a prede termined range of the grip portion gripped with the right hand of the driver. a touch sensor;

The control unit controls, as the specific input operation, the operation target device accordi ng to a pattern of a combination of a first input operation on the first touch sensor and a seco nd input operation on the second touch sensor. The control

device for an operation target device in a vehicle according to any one of claims 1 to 6, char acterized in that it controls the

8.

A driver grips a touch sensor which has a plurality of detection areas and is mounted within a predetermined range of a grip of a steering wheel of a vehicle so as to cover said grip. detec ting whether or not

a specific input operation has been performed on the touch sensor; detecting whether or not a direction indicator has been operated; When it is detected that the driver is not in a specifi c state, it is detected that the driver is gripping the touch sensor, and it is detected that the s pecific input operation is performed, the touch sensor detects An operation target device to be operated is controlled , and control of the operation target device is disabled when it is detec ted that the vehicle is in a specific state in which a direction indicator is operated. A control m ethod for an operation target device in a vehicle. 9. A driver grips a touch sensor which has a plurality of detection areas and is mounted within a predetermined range of a grip portion of a steering wheel of a vehicle so as to cover said grip portion to be gripped by the driver. It is detected whether or not a specific input operation has been performed on the touch sensor, and the shift position of the shift lever is reversed.

It is detected that

the vehicle is not in a specific state in which the shift position of the shift lever is in reverse , it is detected that the driver is gripping the touch sensor, and the specific When it is detected that the input operation is performed, the touch sensor controls the operation target device to be operated, and the vehicle is in a specific state in which the shift position of the shift lever is in reverse.

A control method for an operation target device in a vehicle, comprising: invalidating control of the operation target device when the operation target device is detected .

10.

The touch sensor includes a part of the plurality of detection areas, a grip detection area for

detecting a contact of the driver's palm, and another part of the plurality of detection areas, w herein and an operation detection area for detecting the specific operation due to contact with the

grip detection area, and detecting that the driver is gripping the touch sensor by contact of t he palm with the

grip detection area. 10. The method of controlling an operation target device in a vehicle acc ording to

claim 8, wherein the execution of the specific input operation is detected by finger contact . 11.

A driver grips a touch sensor which has a plurality of detection areas and is mounted within a predetermined range of a grip portion of a steering wheel of a vehicle so as to cover said gri p portion. detecting whether or not there is,

detecting whether or not a specific input operation has been performed on the touch sensor,

detecting whether the vehicle is in a specific state,

detecting that the vehicle is not in a specific state, detecting that the driver is gripping the to uch sensor, and performing the specific input operation When the operation is detected, the o peration target device to be operated is controlled by the touch sensor, and the touch sensor

includes a part of the plurality of detection areas and detects the contact of the driver's pal m. A grip detection area for detection and an operation detection area for detecting the specifi c operation by finger contact, which includes another part of the plurality of detection areas, a re set,

The palm contact with the grip detection area detects that the driver is gripping the touch se nsor, and the finger contact with the operation detection area detects

that the specific input operation has been performed.

A control method for an operation target device in a vehicle characterized by:

12.

As said specific input operation, two points spaced apart in a circumferential direction in a cr oss section of said steering wheel when said grip is cut in said operation detection area by two fingers. 12. The method of controlling an operation target device in a vehicle according to clai m 10, wherein the operation target device is controlled according to an operation pattern . 13.

When the rotation angle of the steering wheel exceeds a predetermined angle, it is determin ed that the vehicle is in a specific state, and the control of the device to be operated is disable d . The method for controlling an operation target device in a vehicle according to any one of Claims 1 to 1 .

14.

The touch sensor comprises a first touch sensor mounted in a predetermined range of the gr ip portion gripped by the left hand of the driver and a second touch sensor mounted in a pred etermined range of the grip portion gripped by the right hand of the driver. and a touch senso

r, and

according to a pattern of a combination of a first input operation on the first touch sensor an d a second input operation on the second touch sensor as the specific input operation, the ope ration target.

14. The method for controlling an operation target device in a vehicle according to any one o f claims 8 to 13, characterized in that the device is controlled .

detailed description open —

Description: BACKGROUND OF THE INVENTION 1.

Field of the Invention The present invention relates to a vehicle operation control system for controlling the operation of a vehicle, such as an on-vehicle device such as a navigation syste m installed in a vehicle, or a transmission, a direction indicator, or the like. The present invent ion relates to a control device and a control method for controlling an operation target device, which is an operation target device. 2. Description of the Related Art Vehicles in which opera tion switches for operating vehicle-mounted equipment such as a navigation system are arran ged on a steering wheel have become widespread (see Patent Document 1). By arranging the operation switch on the steering wheel, the driver does not have to reach for the in-vehicle eq uipment when operating the in-vehicle equipment, thereby improving operability. As described in Japanese Patent Application Laid-Open No. 2002-200015, the operation switch is actually n ot the annular portion of the steering wheel, which is the grip portion that the driver grips, bu t the central portion where the airbag is accommodated and the circular portion. It is usually arranged in the connecting part connecting between the annular parts. Therefore, in order to operate the operation switch, the driver needs to release his/her hand from the gripped annul ar portion or move the hand largely. Patent Literature 2 describes that operation switches are arranged on the back surface and the inner side surface of the annular portion. [Prior Art Doc uments] [Patent Documents] [Patent Document 1] Japanese Patent Laid- Open Publication N o. 2007-106353 [Patent Document 2] Japanese Patent Laid-Open Publication No. 2005-34812 3 [Patent Document 3] Japanese Patent Laid- Open Publication No. 2008-195220 [Invention] Overview] [Problems to be solved by the invention]

According to the invention disclosed in Patent Document 2, since the operation switches are arranged on the annular portion, the operation switches can be operated without releasing the hand from the annular portion or moving the hand largely . child
can be done. However, the operation switch described in Patent Literature 2 is a push-button key or a key with projections and depressions, and such keys may interfere with the driver's o peration of the steering wheel. It is not preferable to provide large irregularities in the annular portion gripped by the driver. In addition, when an operation unit such as an operation switch is arranged in the annular portion, the driver does not have the intention to operate the opera tion target device, unlike the case where the driver grips the annular portion for normal drivin g. In such cases, it is required to prevent the operation target device from being operated car elessly. Furthermore, depending on the state of the vehicle, erroneous operations may be cau sed, and it is required to reduce erroneous operations as much as possible.
[0005]

In order to meet such a demand, the present invention enables a device to be operated to b e operated without removing the hand from the grip or moving the hand largely, and the drive r can operate the steering wheel. It is an object of the present invention to provide a control d evice and a control method for an operation target device in a vehicle, which can greatly redu ce the possibility of hindrance during operation. Another object of the present invention is to p rovide a control device and a control method for an operation target device in a vehicle that c an significantly reduce erroneous operations.
SUMMARY OF THE INVENTION In order to solve the above-described problems of the prior ar t, the present invention provides a grip portion of a steering wheel
detection areas . A sensor that generates sensor data including position data indicating which detection area is being touched based on a contact detection signal obtained from a touch sen sor attached to cover the grip portion in a predetermined range of data generator and
a detection unit for detecting whether or not a driver is gripping the grip based on the sensor data and an input operation to the touch sensor; an operation target to be operated by the to uch sensor in response to the specific input operation when it is detected that a specific input operation is performed on the touch sensor. a controller for controlling a device , wherein the controller determines that the vehicle is in a specific state when the direction indicator is oper ated , and invalidates the control of the device to be operated. A controller for a target device

is provided. [0007] In order to solve the above-described problems of the prior art, the present invention has a plurality of detection areas, and a steering wheel of a vehicle is provided with a grip portion within a predetermined range of the grip portion to be gripped by the driver. A sensor data generation unit that generates sensor data including position data indicating which detection area is being touched based on a contact detection signal obtained from a touch sensor that is mounted so as to cover it; and based on the sensor data, a detection unit that detects whether or not a driver is gripping the grip portion and an input operation to the touch sensor; the detection unit detects that the driver is gripping the grip portion; and a control unit that controls an operation target device to be operated by the touch sensor in response to the specific input operation when it is detected that a specific input operation has been performed on the touch sensor. A control device for an operation target device in a vehicle, wherein the control unit invalidates control of the operation target device by determining that the vehicle is in a specific state when the shift position of the shift lever is in reverse. I will provide a.

[0008]

In the above-described control device for an operation target device in a vehicle, the touch sensor includes a grip detection area ; An operation detection area set, and the detection unit is based on a contact detection signal obtained from the grip detection area. Preferably, sensor data is used to detect whether or not a driver is gripping the grip portion, and sensor data based on a contact detection signal obtained from the operation detection area is used to detect the specific input operation.

[0009]

In order to solve the above-described problems of the prior art, the present invention has a plurality of detection areas,

A position indicating which detection area is being touched based on a contact detection signal obtained from a touch sensor attached to a predetermined range of a grip portion of a steering wheel gripped by a driver so as to cover the grip portion. a sensor data generation unit that generates sensor data including data; a detection unit that detects whether or not a driver is gripping the grip based on the sensor data and an input operation to the touch sensor; When the detection unit detects that the driver is gripping the grip and also detects that a specific input operation has been performed on the touch sensor, the specific input operation is performed. Accordingly, a control unit for controlling an operation target device to be operated by the touch sensor, wherein the touch sensor includes part of the plurality of detection areas and detects contact of the driver's palm. A detection area and an operation detection area that includes other parts of the plurality of detection areas and detects the specific input operation by finger contact are set, and the detection unit obtains information from the grip detection area. Detecting whether or not the driver is gripping the grip by sensor data based on the contact d

etection signal obtained from the operation detection area, detecting the specific input operation by sensor data based on the contact detection signal obtained from the operation detection area, The control unit disables control of the operation target device when the vehicle is in a specific state.

[0010]

In the above-described control device for an operation target device in a vehicle, the control unit is configured to, as the specific input operation, cut the grip portion in the radial direction of the steering wheel with respect to the operation detection area. It is preferable that the operation target device is controlled in accordance with a pattern in which two locations spaced apart in the circumferential direction on the cross section of are operated with two fingers.

In the above control device for an operation target device in a vehicle, the control unit further disables control of the operation target device by determining that the vehicle is in a specific state when the rotation angle of the steering wheel exceeds a predetermined angle. It is preferable to

In the above-described control device for an operation target device in a vehicle, the touch sensors include a first touch sensor of a grip portion gripped by a driver's right hand. and a second touch sensor attached to the controller, and the control unit performs a first input operation on the first touch sensor and a second input operation on the second touch sensor as the specific input operation. It is preferable that the operation target device is controlled according to a combination pattern of and.

[0011] In order to solve the above-described problems of the prior art, the present invention has a plurality of detection areas, and a grip portion of a steering wheel

gripped by a driver , has a grip portion within a predetermined range. It detects whether or not the driver is gripping a touch sensor mounted so as to cover the part , detects whether or not a specific input operation has been performed on the touch sensor, and detects whether or not the direction indicator has been operated. detects whether the vehicle is not in a specific state in which the direction indicator is operated, detects that the driver is gripping the touch sensor, and detects whether the specific input operation is detected to be performed, control the operation target device to be operated by the touch sensorand, when it is detected that the vehicle is in a specific state in which the direction indicator is operated, the control of the operation target device is invalidated . offer.

[0012]

In order to solve the above-described problems of the prior art, the present invention has a plurality of detection areas, and a steering wheel of a vehicle is provided with a grip portion within a predetermined range of the grip portion to be gripped by the driver. It detects whether or not the driver is gripping a touch sensor mounted so as to cover it, detects whether or not a specific input operation has been performed on the touch sensor, and shifts the shift position of the shift lever to reverse. It is detected that the vehicle is not in a specific state in which the shift position of the shift lever is in reverse, it is detected that the driver is gripping the to

uch sensor, and the specific When it is detected that the input operation is performed, the touch sensor controls the operation target device to be operated, and the vehicle is in a specific state in which the shift position of the shift lever is in reverse. If it is detected, the control of the operation target device is invalidated.

A control method for an operation target device in a vehicle is provided.

[0013]

In the above-described control method for a device to be operated in a vehicle, the touch sensor includes a grip detection area ; An operation detection area set, and the driver grips the touch sensor by contact of the palm with the grip detection area. It is preferable to detect that the specific input operation has been performed by a finger touching the operation detection area.

[0014]

In order to solve the above-described problems of the prior art, the present invention has a plurality of detection areas, and a steering wheel of a vehicle is provided with a grip portion in a predetermined range so as to cover the grip portion to be gripped by the driver. Detects whether the driver is gripping the attached touch sensor, detects whether a specific input operation has been performed on the touch sensor, and detects whether the vehicle is in a specific state. and when it is detected that the vehicle is not in a specific state, it is detected that the driver is gripping the touch sensor, and it is detected that the specific input operation is performed, A touch sensor controls an operation target device to be operated, and the touch sensor includes a grip detection area that includes a part of the plurality of detection areas and detects contact with the driver's palm, and the plurality of detection areas. and an operation detection area for detecting the specific operation by finger contact is set, and the driver is gripping the touch sensor by palm contact with the grip detection area and detecting that the specific input operation has been performed by touching the operation detection area with a finger.

[0015]

In the method for controlling an operation target device in a vehicle described above, the specific input operation is a circumferential direction in a cross section of the steering wheel when the grip portion is cut in the radial direction of the steering wheel with respect to the operation detection area. It is preferable that the device to be operated is controlled according to a pattern in which two locations spaced apart from each other are operated with two fingers.

In the above method for controlling an operation target device in a vehicle, it is preferable that control of the operation target device is invalidated on the assumption that the vehicle is in a specific state when the rotation angle of the steering wheel exceeds a predetermined angle.

.

In the control method for the operation target device in the vehicle,The touch sensor includes a first touch sensor and a second touch sensor and controlling the operation target device according to a pattern of a combination of a first input operation on the first touch sensor and a second input operation on the second touch sensor as the specific input operation. is preferre

d.

EFFECTS OF THE INVENTION According to the control device and control method for the devi ce to be operated in the vehicle of the present invention, the device to be operated can be op erated without releasing the hand from the grip portion or moving the hand largely

.

It is possible to greatly reduce the possibility of hindrance when the driver operates the steeri ng wheel. In addition, erroneous operations can be greatly reduced.

BRIEF DESCRIPTION OF THE DRAWINGS

[0017]

FIG. 1 is a block diagram showing an embodiment of a control device for an operation target device in a vehicle according to the present invention;

FIG. 2 is a partial plan view showing an example of a vehicle provided with a control device fo r an operation-targeted device according to one embodiment;

3A and 3B are diagrams showing examples of positions and ranges in which a touch sensor is mounted on a steering wheel according to one embodiment; FIG.

4A and 4B are diagrams showing other examples of the positions and ranges where the touch sensor is mounted on the steering wheel according to the embodiment; FIG.

FIG. 5 is a diagram showing an example of attaching a touch sensor to a modified steering wh eel;

FIG. 6 is a partial perspective view showing an example of a portion of the steering wheel fro m which sensor data can be obtained while the touch sensor portion is being gripped;

FIG. 7 is a cross-sectional view showing coordinates in the circumferential direction of the cro ss-section of the touch sensor;

8 is a plan view showing a state in which the touch sensor shown in FIG. 6 is unfolded; FIG.

9 is a schematic diagram showing a state in which each area shown in FIG. 8 is converted into uniform sizes; FIG.

FIG. 10 is a diagram showing an example of requirements for determining that the touch sens or portion of the steering wheel is being gripped;

FIG. 11 is a schematic diagram showing an example of a specific input operation on the touch sensor;

FIG. 12 is a schematic diagram showing another example of a specific input operation on the t ouch sensor;

13A and 13B are schematic diagrams showing still another example of a specific input operati on on the touch sensor; FIG.

FIG. 14 is a flowchart for explaining the operation of one embodiment;

FIG. 15 is a diagram for explaining the rotation angle of the steering wheel;

16 is a flow chart showing a specific example of processing in step S4 of FIG. 14; FIG.

FIG. 17 is a schematic perspective view showing a configuration example for changing colors when a touch sensor is operated;

FIG. 18 is a schematic perspective view showing a configuration example for changing the tac tile sensation when the touch sensor is operated;

19 is a plan view showing a configuration example of a steering wheel; FIG.

BEST MODE FOR CARRYING OUT THE INVENTION An embodiment of a control device and con trol method

for

an operation target device in a vehicle according to the present invention will be described b elow with reference to the accompanying drawings. 1 and 2, the in-vehicle device 100 is mou nted inside the dashboard of the vehicle. In the example shown in FIG. 1, the in-vehicle devic e 100 includes a control unit 10, a navigation processing unit 11, an audio reproduction unit 1 2, a television (TV) tuner 13, a video signal processing unit 14, a video display unit 15, an au dio signal processing unit 16. , a display element 17 and a storage unit 18 . The control unit 1 0 includes a detection unit 10a. The navigation processing unit 11 has a storage unit for hold ing map data, a GPS antenna, etc. The control unit 10 and the navigation processing unit 11 work together to provide route guidance

.

The audio reproducing unit 12 reproduces an audio signal recorded on an optical disk such as a compact disk or a semiconductor memory under the control of the control unit 10 . The TV t uner 13 receives TV broadcast wave signals from a predetermined broadcasting station under the control of the control unit 10 . A video signal output from the navigation processing unit 1 1 or the TV tuner 13 is input to the video signal processing unit 14 via the control unit 10, pro cessed, and displayed on a video display unit 15 such as a liquid crystal panel.

[0020]

Audio signals output from the navigation processing unit 11 , the audio reproduction unit 12 , and the TV tuner 13 are input to the audio signal processing unit 16 via the control unit 10 , processed, and produced by the external speaker 20 . The audio signal processor 16 includes an amplifier. The speaker 20 is installed inside the door of the vehicle or the like. The display element 17 is, for example, a light-emitting diode (LED), and is turned on or off according to t he contact state of the touch sensor 21 described later under the control of the control unit 10 . The display element 17 is arranged, for example, on the housing of the in-vehicle device 100 so that it can be visually recognized by the driver. The display element 17 may be separated f rom the in-vehicle device 100 and arranged near the steering wheel 200 of the vehicle. The st orage unit 18 is a non-volatile memory. As shown in FIG. 2, the touch sensor 21, which is an operation unit, is attached to an annular portion 200r of the steering wheel 200. As shown in FIG

.

The annular portion 200r is a grip portion that is gripped by the driver during driving. In the e xample shown in FIG. 2, the touch sensor 21 is located at the annular portion 200r.

It is mounted in a predetermined angle range on each of the left and right sides. The touch se

nsor 21 is a so-called multi-point detection (multi-touch) touch sensor capable of detecting co ntact at multiple points. The touch sensor 21 is preferably mounted on the circumference of t he cross section in the radial direction of the annular portion 200r within a range of 360°. Eve n if the range is less than 360°, it is sufficient that it covers substantially the entire circumfere nce of the cross section of the annular portion 200r.

The driver grips the portion of the annular portion 200r on which the touch sensor 21 is mounted. In FIG. 1 , the output of the touch sensor 21 is input to the sensor data generator 22 . When the touch sensor 21 is touched with a hand, a contact detection signal is input to t he sensor data generator 22 . Based on the input contact detection signal, the sensor data ge neration unit 22 generates sensor data including position data indicating from which position o n the touch sensor 21 the contact detection signal was obtained, and supplies the sensor data to the control unit 10 . The touch sensor 21 and the sensor data generator 22 may be integrat ed, or the sensor data generator 22 may be provided within the controller 10 .

As the touch sensor 21, for example, a projective capacitance (mutual capacitance) type touch sensor can be use d. As the touch sensor 21 attached to the annular portion 200r, for example, a flexible touch p anel developed by Micro Technology Laboratory can be adopted. This flexible touch panel has a structure in which an ultra-thin glass plate having a thickness of 0.02 to 0.05 mm is used as a sensor portion, and an ultra-thin glass plate and a PET (polyethylene terephthalate) film are bonded together. Even if the touch sensor 21 is attached to the annular portion 200r, the touc h sensor 21 does not have unevenness that can be sensed by the hand or fingers, so that it h ardly interferes with the operation of the steering wheel 200 by the driver. do not have.

[0024]

As shown by the dashed line in FIG. 2, it is preferable to wire the electric wire connecting th e touch sensor 21 and the in-vehicle device 100 through the inside of the steering wheel 200 and the dashboard. 1 and 2, a steering angle sensor 31 detects the rotation angle of a steeri ng wheel 200. As shown in FIG .

The direction indicator sensor 32 detects operation of the direction indicator 320 . The shift le ver sensor 33 detects where the shift position by the shift lever 330 is. Detection signals from the steering angle sensor 31 , direction indicator sensor 32 , and shift lever sensor 33 are sup plied to the control section 10 via the in-vehicle communication section 34 . An example of t he position and range of mounting the touch sensor 21 on the annular portion 200r of the ste ering wheel 200 will be described with reference to FIG .

Note that up, down, right, and left refer to up, down, right, and left when the steering wheel 2 00 is viewed from the driver's position when the steering wheel 200 is not rotated (the vehicle is traveling straight ahead). Suppose that FIG. 3A shows an example in which the touch senso r 21 is attached to the entire circumference of the annular portion 200r. FIG. 3B is the same a

s FIG. 2, and shows an example in which the touch sensors 21 are mounted separately from e ach other within predetermined angular ranges on the left and right above the annular portion 200r. FIG. 3C shows an example in which the touch sensor 21 is mounted in a predetermined angular range only on the upper right side of the annular portion 200r.

FIG.

3(D) shows an example in which the touch sensors 21 are spaced apart from each other wit hin predetermined angular ranges on the left and right sides below the annular portion 200r. F IG. 3(E) is an example in which the touch sensor 21 is mounted over a relatively wide angular range above the top of the annular portion 200r. FIG. 3(E) corresponds to connecting the left and right touch sensors 21 in FIG. 3(B).

FIG.

4 shows an example in which the left and right touch sensors 21 in FIG. 3B are divided into an upper touch sensor 21a and a lower touch sensor 21b. In the example of FIG. 4, the upper touch sensor 21a detects contact with the index finger and thumb of the hand, and the lower touch sensor 21b mainly detects contact with the palm, middle finger, and ring finger. Figure 5 shows a modified steering wheel that is not circular.

This is an example in which a touch sensor 21 is attached to a rule 201. FIG. The touch senso r 21 is attached to the left and right straight portions 201 s of the modified steering wheel 20 1 . The driver grips the linear portion 201s, which is the grip portion, while driving, and the to uch sensor 21 detects contact with the palm or fingers. Here, as shown in FIG. 2, the touch sensors 21 are mounted on the left and right sides above the annular portion 200r

.

Describe how palm and finger contact is detected. FIG. 6 shows an example of a range in whic h the palm and fingers are in contact when the driver grips the touch sensor 21 on the right si de of FIG. The manner in which the driver grips the annular portion 200r and the size of the h and are not uniform, and FIG. 6 is merely an example. In the example shown in FIG. 6, a pl urality of detection areas R indicated by hatched Tp are portions where the contact of the pal m is detected, and a plurality of detection areas R indicated by hatched Tt are those of the th umb

.

This is the part that detects contact. Hereinafter, they are referred to as a palm contact detect ion section Tp and a thumb contact detection section Tt. The back side of the touch sensor 2 1, which is not visible in FIG. 6, is in contact with the forefinger.

As shown in FIG .

6, the touch sensor 21 has a plurality of detection regions R as detection portions for detecti ng contact of palms and fingers. Coordinates are set in each detection area R of the touch sen sor 21 . As shown in FIG. 6, in the circumferential direction of the annular portion 200r, the de tection region R located at the lower end of the touch sensor 21 is set to 0, and the detection region R located at the upper end is 1, 2, 1, 2, 2, . . . , 30, 31 and the coordinates in the circu

mferential direction are set. Let the circumferential coordinate of the annular portion 200r in t he touch sensor 21 be the Y coordinate.

[0032]

FIG. 7 is a cross-sectional view of the annular portion 200r cut in the radial direction of the a nnular portion 200r at the portion where the touch sensor 21 is mounted. As shown in FIG. 7, in the cross-section of the annular portion 200r, a detection region R positioned, for example, on the inner diameter side of the annular portion 200r is assumed to be coordinate 0. As sho wn in FIG. 7 from the inner diameter side to the front side, from the front side to the outer di ameter side, from the outer diameter side to the back side, and from the back side to the inne r diameter side in the counterclockwise direction of FIG. are set to 1, 2, . . . , 21, 22. Let the c oordinate in the circumferential direction of the cross section of the touch sensor 21 be the X coordinate. The sensor data generator 22 can obtain position data indicating where on the tou ch sensor 21 the driver is touching from the X and Y coordinates of the detection area R from which the contact detection signal is obtained.

FIG.

8 shows the development of the touch sensor 21 shown in FIG. FIG. 9 schematically shows a state in which each area of the touch sensor 21 shown in FIG. 8 is converted into uniform size s. 8 and 9, in addition to the palm contact detection portion Tp and the thumb contact detecti on portion Tt, the index finger contact detection portion Ti, which is a plurality of detection re gions R in contact with the index finger, is also shown. If the touch sensor 21 is touched by th e middle finger, the ring finger, or the little finger, the touch sensor 21 also detects the contact of those fingers. In this embodiment, the driver uses the thumb or forefinger suitable for perf orming a specific input operation on the touch sensor 21 as a finger for operation.

[0034]

The details of the input operation with the thumb or index finger will be described later. Base d on the sensor data output from the sensor data generator 22, the detector 10a of the contro ller 10 detects that an input operation has been performed on the touch sensor 21 with the th umb or forefinger. Based on the sensor data output from the sensor data generation unit 22, t he detection unit 10a also detects that the annular portion 200r (touch sensor 21) is gripped. The control unit 10 controls the operation target device according to a specific input operation performed on the touch sensor 21 .

[0035]

An example of the device to be operated is the vehicle-mounted device 100 . Specifically, th e control unit 10

In accordance with the input operation, the navigation processing unit 11 can perform control related to route guidance, the audio reproduction unit 12 can reproduce or stop audio signals, and the track (music) to be reproduced can be advanced or reversed. In addition, the control unit 10 can switch the receiving channel in the TV tuner 13 or control the amplification unit of the audio signal processing unit 16 to decrease or increase the sound volume according to a s

pecific input operation.

Another

example of the device to be operated is a vehicle motion control device for controlling the m otion of a vehicle. Specifically, the control unit 10 may control the transmission, the direction i ndicator, the on/off of the air conditioner, the set temperature of the air conditioner, and the li ke, through the in-vehicle communication unit 34 . When the operation target device is a vehi cle motion control device, it is preferable to input the sensor data output from the sensor data generator 22 to a control portion of the vehicle to control the vehicle motion control device. T he control unit that controls the operation target device may be the control unit 10 in the vehi cle-mounted device 100 or may be a control unit outside the vehicle-mounted device 100 pro vided in the vehicle. According to this embodiment, the extremely thin touch sensor 21 is att ached to the annular portion 200r gripped by the driver, and the device to be operated is oper ated by operating the touch sensor 21

.

The device to be operated can be operated without releasing the hand or moving the hand lar gely. In addition, since the touch sensor 21 has no irregularities on the surface of the annular portion 200r, there is almost no possibility that it will interfere with the operation of the steeri ng wheel 200 by the driver.

[0038]

By the way, when the driver does not intend to operate the operation target device, such as when the driver grips the annular portion 200r for normal driving, the operation target device should be prevented from being inadvertently operated. is required. Therefore, in this embodi ment, the following measures are taken to avoid erroneous operations not intended by the dri ver. As shown in FIGS. 8 and 9, a plurality of detection areas R on the touch sensor 21 are p rovided with a grip detection area Arg for detecting contact of the palm and an operation inpu t by the thumb or forefinger

.

An operation detection area Arv for detecting an input and an operation invalid area Ariv whic h is an intermediate area between the grip detection area Arg and the operation detection are a Arv and invalidates an operation input are set. The palm contact detection portion Tp is loca ted within the grip detection area Arg, and the thumb contact detection portion Tt and the for efinger contact detection portion Ti are located within the operation detection area Arv. Like the grip detection area Arg and the operation detection area Arv, the operation invalid area Ar iv has a detection area R for detecting the contact of the palm or fingers, but the control secti on 10 (detection section 10a) or the sensor data generation

section

22 can be made an operation invalid area by processing to invalidate the input operation from the operation invalid area Ariv. Further, by configuring the touch sensor 21 so that the detecti on area R is not provided in the range of the operation invalid area Ariv, the operation invalid

area may be set. This case is substantially equivalent to the example shown in FIG.

[0041]

When the driver grips the annular portion 200r for normal driving, the palm contact detectio n portion Tp, the thumb contact detection portion Tt, and the index finger contact detection p ortion Ti are relatively close to each other. Therefore, in order to accurately distinguish betwee n the case where the driver simply grips the annular portion 200r and the case where the driv er touches the touch sensor 21 to operate the operation target device, the operation invalid ar ea Ariv is provided. When the driver intends to operate the device to be operated, the driver i ntentionally extends his or her thumb or forefinger to touch the touch sensor 21 to perform a specific input operation, which will be described later. The control unit 10 controls the operatio n target device according to the input operation when a specific input operation, which will be described later, is performed within the operation detection area Arv.

[0042]

It is also necessary to avoid erroneous operation of the operation target device when the dri ver carelessly touches the operation detection area Arv without gripping the annular portion 2 00r for driving. Therefore, in the present embodiment, the detection unit 10a determines that the annular portion 200r is gripped when a palm contact detection portion Tp having a predet ermined area or more is obtained in the grip detection area Arg. The control unit 10 is configu red to control the operation target device when the annular portion 200r is gripped and a spec ific operation is performed within the operation detection area Arv. The area of the palm conta ct detection portion Tp for determining that the annular portion 200r is being gripped may be appropriately set by statistically examining the area when a plurality of drivers grip the steeri ng wheel 200 in a normal gripping manner. Just do it.

The area of the palm contact detection portion Tp in the grip detection area Arg is an example of requirements for determining that the driver is gripping the annular portion 200r ,

and the requirements for determination are limited to this. isn't it. FIG. 10 shows a cross sec tion of the annular portion 200r cut at the portion of the grip detection area Arg of the touch s ensor 21. As shown in FIG. The detection unit 10a can determine that the annular portion 200 r is being gripped when the angle θ in the circumferential direction of the cross-section of the palm contact detection portion Tp is equal to or greater than a predetermined angle. The pred etermined angle is, for example, 180°.

[0044]

As described above, in the present embodiment, it is determined whether or not the driver is gripping the annular portion 200r (touch sensor 21), and operation input to the touch sensor 21 is performed only when the driver is gripping the annular portion 200r. is accepted, it is po ssible to avoid an erroneous operation when the operation detection area Arv is carelessly tou ched. In this embodiment, as a preferred configuration, the operation detection area Arv is pr ovided at a position separated from the grip detection area Arg by a predetermined distance, so that the driver intentionally performs a specific input operation on the touch sensor 21. You

can detect exactly what you are doing. Therefore, erroneous operations can be greatly reduce d. In this embodiment, the area of the palm contact detection portion Tp in the grip detectio n area Arg and the angle θ in the circumferential direction of the cross section are used as req uirements for determining whether or not the driver is gripping the annular portion 200r

.

Therefore, it can be accurately determined whether or not the user is gripping the annular por tion 200r. Therefore, it is possible to avoid an erroneous operation when the driver carelessly t ouches the operation detection area Arv without gripping the annular portion 200r. When the detection unit 10a detects that the driver is gripping the annular portion 200r (touch sensor 2 1) based on the sensor data based on the contact detection signal from the grip detection are a Arg, the control unit

10

The display element 17 is turned on in order to inform the driver that the operation input by t he operation detection area Arv is possible. The driver can determine whether or not the oper ation target device can be operated by the touch sensor 21 by turning on/off the display elem ent 17 . It is preferable to arrange the display element 17 near the steering wheel 200 .

[0047]

By the way, when the touch sensor 21 is attached to the entire circumference of the annular portion 200r as shown in FIG. , the position where the driver grips the touch sensor 21 is not fixed. Therefore, the positions of the grip detection area Arg and the operation detection area Arv described with reference to FIGS. 8 and 9 and the operation invalid area Ariv provided as necessary are dynamically changed according to the position at which the driver grips the tou ch sensor 21. Must be set.

Therefore ,

when the touch sensor 21 is gripped while the grip detection area Arg and the like are not se t, the control section 10 sets the area including the palm contact detection portion Tp as the g rip detection area Arg. A predetermined range of Y coordinates including the palm contact det ection part Tp is defined as a grip detection area A

rg. As described above, since the palm contact detection portion Tp has a predetermined area or more, a portion of the plurality of detection regions R on the touch sensor 21 that is detect ed to be touched with a predetermined area or more is the palm contact detection portion Tp. becomes. Alternatively, as described with reference to FIG. 10, in the circumferential direction of the cross section obtained by cutting the annular portion 200r at the portion of the touch s ensor 21, the portion detected to be touched at a predetermined angle or more becomes the palm contact detection portion Tp. . After setting the grip detection area Arg, the control unit 10 sets a predetermined range of Y coordinates above the grip detection area Arg as the oper ation detection area Arv

.

In this case, if necessary, a predetermined range of Y coordinates adjacent to the grip detecti

on area Arg is set as the operation invalid area Ariv, and the grip detection area Arg is positio ned away from the grip detection area Arg. 11 to 13, examples of specific input operations p erformed by the driver on the touch sensor 21 using his thumb or forefinger will now be descr ibed

.

11A to 11E schematically show half of the touch sensor 21, which is the front side or the back side facing the driver, in a plane view. The operations shown in FIGS. 11A to 11E are perform ed with the thumb on the front side and with the index finger on the back side. In FIG. 11A, D R is a rightward drag by sliding the thumb or forefinger on the touch sensor 21 (operation detection area Arv), and DL is a leftward dragging by sliding the thumb or forefinger to the right. It is a directional drag. D U is an upward drag that slides the thumb or forefinger upward; is a downward drag that slides in t he direction the thumb or index finger is pointing.

In FIG . 11(A), instead of the

rightward drag D R , leftward drag D L , upward drag D U , and downward drag D D , the tou ch sensor 21 is flicked with the thumb or forefinger in the respective directions. It may be a fli ck.

FIG.

11(B) shows a tap T of tapping the touch sensor 21 with the thumb or index finger. FIG. 11 (C) shows an arc drag DC in which the thumb or forefinger is dragged on the touch sensor 21 so as to draw an arc. F IG. 11(D) shows a zigzag drag DZ in which the thumb or forefinger is dragged on the touch sensor 21 in a zigzag p attern. FIG. 11(E) shows a symbol input drag DS that is dragged as if writing a symbol with the thumb or forefinger . FIG. 11E shows a state in which the number 3 is drawn as a symbol. As symbols, it is preferable to use numbers and alphabets that are relatively easy to recognize.

[0053]

FIGS. 12A to 12D show a schematic plan view of a front portion 21f, which is the front half o f the touch sensor 21, and a rear portion 21r, which is the rear half of the touch sensor 21, wh en the touch sensor 21 is opened. . The front portion 21f is the portion of X coordinates 0 to 1 1 shown in FIGS. 8 and 9, and the rear portion 21r is the portion of X coordinates 12 to 22. A s shown in FIG. Strictly speaking, in the examples shown in FIGS. 8 and 9, the front portion 2 1f and the back portion 21r do not have the same area, but in FIGS. Shown in area. 12A to 1 2D, for ease of understanding, the rear surface portion 21r is not viewed from the rear surfac e side of the annular portion 200r, but is seen through the rear surface portion 21r from the fr ont surface portion 21f. state. As shown in FIGS. 12A to 12D, a combination of an input oper ation with the thumb on the front portion 21f and an input operation with the index finger on t he back portion 21r can be used as a specific input operation on the touch sensor 21

.

good. FIG. 12A shows an example of performing both a rightward drag DTR in which the thum b slides rightward on the front portion 21f and a rightward drag DIR in which the index finger slides righ tward on the back portion 21r. FIG. 12A is realized by dragging both the thumb and index finger from

the inner circumference side to the outer circumference side of the annular portion 200r. A pat tern in which both the thumb and the forefinger are dragged in the direction opposite to that i n FIG. 12A may be employed.

FIG. 12B shows an example of performing both a leftward drag DTL

in which the thumb slides leftward on the front portion 21f and a rightward drag DIR in which the index finger slides rightward on the back portion 21r. is. FIG. 12B is realized by dragging t he thumb from the outer peripheral side to the inner peripheral side of the annular portion 20 0r and dragging the index finger from the inner peripheral side to the outer peripheral side of the annular portion 200r. FIG. 12C shows an example of performing both a rightward drag DTR in which the thumb slides rightward on the front portion 21f and a leftward drag DIL in which the i ndex finger slides leftward on the back portion 21r. FIG. 12C is realized by dragging the thumb from the in ner circumference side to the outer circumference side of the annular portion 200r and draggi ng the index finger from the outer circumference side to the inner circumference side of the a nnular portion 200r. FIG . 12(D) shows an example of performing both an upward drag D TU

in which the thumb slides upward on the front portion 21f and a downward drag D ID in whic h the index finger slides downward on the back portion 21r. is. A pattern in which the thumb i s dragged downward and the index finger is dragged upward may be adopted, or a pattern in which both the thumb and the index finger are dragged upward or downward may be adopte d. Here, various patterns are shown in which the input operation with the thumb on the front portion 21f and the input operation with the index finger on the back portion 21r are combine d. [0057]

As shown in FIGS. 12A to 12D, if a pattern combining an input operation with the thumb and an input operation with the index finger is used as a specific input operation for controlling the device to be operated, erroneous operations are greatly reduced. can be reduced. Furthermo re, as shown in FIGS. 3(A), (B), (D), (E) and FIGS. 4 and 5, when the touch sensors 21 (21a, 21b) can be operated with the left and right hands

,

, a combination of left and right hand operations can be used as a specific input operation for controlling the operation target device. FIGS. 13A to 13D show operations by the left and righ t hands when the left touch sensor 21 in FIG. 3B is the left touch sensor 21L and the right tou ch sensor 21 is the right touch sensor 21R. Examples of combined patterns are shown. Here, a plane corresponding to the front portion 21f of FIG. 12 operated by the thumb is shown as a schematic plane.

FIG. 13A

shows a leftward drag DTL caused by sliding the thumb leftward on the left touch sensor 21L and a rightward drag DTR caused by sliding the thumb rightward on the right touch sensor 21R

. This pattern is a combination of FIG. 13B shows a combination of a rightward drag DTR in wh ich the thumb is slid rightward on the left touch sensor 21L and a leftward drag DTL in which t he thumb is slid leftward on the right touch sensor 21R . pattern.

FIG. 13C

shows an upward drag D in which the thumb is slid upward on both the left touch sensor 21L and the right touch sensor 21R. This pattern is a combination of TUs . FIG. 13(D) shows a pattern in wh ich a downward drag DTD of sliding the thumb downward is combined for both the left touch sensor 21L and the right touch sensor 21R. If a combination of input operations with left and right h ands is used as a specific input operation for controlling the device to be operated, the driver grasps the annular portion 200r with both hands, which contributes to safe driving

.

It is possible to contribute. In particular, the example of FIG. 3B is most preferable in that it c ontributes to safe driving because the touch sensor 21 is mounted at the most appropriate po sition for gripping the annular portion 200r with both hands. An input operation may be accep ted when the left and right touch sensors 21 are gripped with both hands. A state may be ado pted in which input operations are not accepted when one hand is removed from the touch se nsor 21 . When one hand leaves the touch sensor 21, the state of accepting the input operatio n may be continued. Even when a specific input operation with only one hand is used, if the in put operation is accepted when the left and right touch sensors 21 are gripped with both hand s, it contributes to safe driving.

. When the driver grips the annular portion 200r for normal driving and does not intend to o perate the device to be operated, he accidentally combines the input operation with the thum b and the input operation with the index finger

.

It is considered that the possibility of becoming a specific pattern combining input operations with left and right hands is relatively low. Therefore, when using only a specific pattern in whi ch an input operation with the thumb and an input operation with the index finger are combin ed, or a specific pattern in which an input operation with the left and right hands is combined, one of the devices for avoiding the above-described erroneous operation. Some or all may be omitted. Of course, even when only a specific pattern combining input operations with the left and right hands is used, it is preferable to employ a device for avoiding the above-described e rroneous operation. The storage unit 18 stores a table that associates the above-described s pecific input operations or patterns of combinations of specific input operations with types of c ontrol for the device to be operated

.

The control unit 10 controls the operation target device according to the operation input to th e touch sensor 21 according to the table stored in the storage unit 18 . The storage unit 18 m ay be provided within the control unit 10 .

[0064]

The processing executed by the control unit 10 in this embodiment will be described again u sing the flowchart of FIG. 14 . In FIG. 13, the control unit 10 acquires sensor data output fro m the sensor data generation unit 22 in step S1. In step S2, the control unit 10 determines w hether or not the annular portion 200r is being gripped based on the detection output from th e detection unit 10a. If it is determined that the annular portion 200r is gripped (YES), the co ntrol unit 10 shifts the process to step S3, and if it is not determined that the annular portion 200r is gripped (NO), the control unit 10 returns the process to step S1. At step S3, the cont rol section 10 determines whether or not there is an input operation based on the detection o utput from the detection section 10a

.

If it is determined that an input operation has been performed (YES), the control unit 10 mov es the process to step S4, and if it is not determined that an operation input has been perfor med (NO), the control unit 10 returns the process to step S1. In step S4, the control unit 10 d etermines whether or not to permit the operation of the operation target device by the input o peration in step S3. If it is determined that the operation is permitted (YES), the control secti on 10 moves the process to step S5, and if it is not determined that the operation is permitte d (NO), the control section 10 returns the process to step S1. As described above, the contr ol unit 10 permits the operation of the operation target device when a specific input operation is performed within the operation detection area Arv, and permits the operation of the operati on target device when a specific input operation is performed within the operation invalid area Ariv

.

, the operation to the operation target device is not permitted. Further, even if some input ope ration is performed within the operation detection area Arv, the control unit 10 does not permi t the operation to the operation target device unless the above-described specific input operat ion is performed, and only when the specific input operation is performed. Permission to opera te the operation target device.

[0067]

The control unit 10 confirms an operation based on the input operation in step S5, executes control according to the confirmed operation on the operation target device in step S6, and re turns the process to step S1. .

[0068]

Further, in step S4, when the vehicle is in a specific state, it is preferable to disallow (that is, disable) the control of the device to be operated. The rotation angle of the steering wheel 200 is set in the control unit 10 for determining whether or not to permit control of the device to b e operated. As shown in FIG. 15, a state in which the steering wheel 200 is not rotated is ass umed to be a rotation angle of 0°. Touch sensor 21 within a range of 30°

input operation to the touch sensor 21 is enabled and permitted, and if the rotation angle exc eeds ±30°, the input operation to the touch sensor 21 is disabled and not permitted.

When the turning angle exceeds ±30°, the vehicle is in a specific state such as turning right or left, or cornering. If an attempt is made to control the device to be operated in such a specific state, there is a high possibility that an erroneous operation will occur. In other words, there is a high possibility that an operation input in such a specific state is an operation input unintended by the user. Moreover, it is not preferable in terms of safety. Therefore, in this embodiment, when the vehicle is in a specific state, control of the operation target device is disabled. As described above, the rotation angle of the steering wheel 200 detected by the steering angle sensor 31 is input to the controller 10

.

The control unit 10 switches between enabling and disabling the input operation to the touch sensor 21 according to the rotation angle of the steering wheel 200 detected by the steering angle sensor 31 . A detection signal from the direction indicator sensor 32 is also input to the control unit 10 . Therefore, the control unit 10 may invalidate the input operation to the touch sensor 21 when the direction indicator 320 is operated by the detection signal from the direction indicator sensor 32 . When the direction indicator 320 is operated, it can be considered to be in a specific state in which the steering wheel 200 is rotated over a predetermined rotation angle. In some cases, the direction indicator 320 is also used for operations other than signaling a right turn or left turn, but the operation of the direction indicator 320 here is an operation for signaling a right turn or a left turn.

[0071]

Furthermore, it is not preferable to perform a specific input operation on the touch sensor 21 to control the operation target device while the vehicle is being reversed. There is a high possibility that an erroneous operation will occur, and this is not preferable in terms of safety. Therefore, it is preferable that the control unit 10 invalidates the input operation to the touch sensor 21 even when the shift position of the shift lever 330 is reversed by the detection signal from the shift lever sensor 33 . When the rotation angle of the steering wheel 200 exceeds a predetermined angle of ±30°, for example, or when the direction indicator 320 is operated, and when the shift position of the shift lever 330 is reversed, the operation target device Although it is preferable to disable the control for , only one of them may be disabled. It should be noted that disabling the control of the operation target device means disabling the control of the operation target device by disabling the specific input operation even if the above-described specific input operation is performed

.

Even if some sensor data is input from the sensor data generation unit 22 to the control unit 10, the control unit 10 may invalidate the sensor data. As a result, it is sufficient to invalidate the control on the operation target device.

[0073]

A specific example of the processing of step S4 in FIG. 14 will be described with reference to the flowchart in FIG. In FIG. 16, in step S41, the control unit 10 determines whether or not th

e shift position of the shift lever 330 is reverse. If the shift position is reverse (YES), in step S 45, the control unit 10 disallows the input operation in step S3, and proceeds to step S1 in FI G. If the shift position is not reverse (NO), control unit 10 determines in step S42 whether dir ection indicator 320 has been operated. If the direction indicator 320 is operated (YES), the c ontroller 10 disallows the input operation in step S3 in step S45, and proceeds to step S1 in F IG. If the direction indicator 320 has not been operated (NO), the controller 10 determines i n step S43 whether or not the rotation angle of the steering wheel 200 has exceeded a predet ermined angle

.

If the rotation angle of the steering wheel 200 exceeds the predetermined angle (YES), in ste p S45, the control unit 10 disallows the input operation in step S3, and proceeds to step S1 in FIG.

Let If the rotation angle of steering wheel 200 does not exceed the predetermined angle (N O), control unit 10 determines in step S44 whether or not a specific input operation has been performed within operation detection area Arv. If a specific input operation has not been perfo rmed (NO), in step S45, the control unit 10 disallows the input operation in step S3, and proc eeds to step S1 in FIG. If the input operation is disallowed in step S45, control of the operatio n target device is invalidated. If a specific input operation is performed (YES), the control unit 10 permits the input operation in step S3 in step S46, and proceeds to step S5 in FIG. Altho ugh all steps S41, S42 and S43 are provided in the example shown in FIG. 16, only one or tw o of these steps may be provided

.

Moreover, when providing all of steps S41, S42, and S43 or two of these steps, the order is ar bitrary. Although referred to as a shift lever 330 here, the shape of the operating portion for s witching between straight forward and backward movement of the vehicle and for changing th e gear ratio of the transmission is arbitrary, and may be any of floor shift, column shift, paddl e shift, and the like. All of these are included in the shift lever.

As described

above, when the vehicle is in a specific state such as right turn, left turn, cornering, or rever se, if the control of the device to be operated is disabled, the driver can No input operation is performed on the touch sensor 21 . Therefore, it contributes to the improvement of safety.

[0077]

The operation according to this embodiment is summarized as follows. The detection unit 10 a (first detection unit) detects a first area of the touch sensor 21 attached to the grip portion (annular portion 200r or straight portion 201s) of the steering wheels 200 and 201 held by th e driver. Detects that the An example of the first area is the grip detection area Arg. The dete ction unit 10a (second detection unit) performs a specific input operation on a second area of the touch sensor 21 located above the first area while the first area is being touched. Detect what has been done. An example of the second area is the operation detection area Arv. Since

the thumb or forefinger is positioned higher than the palm during driving, the upper side of th e first area may be the second area. When the first area is touched and a specific input operat ion is performed, the touch sensor 21 controls the operation target device to be operated acco rding to the specific input operation. The upper area is an area above the first area when the steering wheel 200 is not rotated and the driver grips the grip

.

It is preferable to determine that the first area is being touched when it is detected that the fir st area is being touched over a predetermined area.

[0079]

Moreover, from another viewpoint, it is as follows. The detection unit 10a (first detection uni t) is mounted in a predetermined range of the grip portion (annular portion 200r or linear port ion 201s) of the steering wheels 200 and 201 that the driver grips so as to cover the grip port ion. The touch sensor 21 touches the first area on the touch sensor 21 at a predetermined an gle or more in the circumferential direction of the cross section of the steering wheels 200 and 201 when the grip portion is cut in the radial direction. to detect The detection unit 10a (seco nd detection unit) detects that a specific input operation is performed on a second area of the touch sensor 21 that is different from the first area while the first area is being touched at a p redetermined angle or more. Detect what has been done. When the first area is touched at th e predetermined angle or more and a specific input operation is performed, the operation targ et device to be operated by the touch sensor 21 is controlled according to the specific input op eration.

The second

area is preferably an area located above the first area. The area located above is an area loc ated above the first area when the driver grips the grip portion while the steering wheel 200 i s not rotated.

FIGS.

17 and 18 show examples of construction for effectively informing the driver that the touch s ensor 21 has been operated. 17 and 18 are schematic diagrams in which the touch sensor 21 is expanded and converted into a rectangular shape, similar to FIG. FIG. 17 shows an exampl e in which a color changing sheet 41 containing a coloring substance is provided on the lower surface side of the touch sensor 21 . By using a transparent conductive film for the touch sens or 21 , the driver can see the color of the color change sheet 41 arranged on the lower surfac e of the touch sensor 21 through the touch sensor 21 . The driver can recognize that the touc h sensor 21 has been operated by changing the color of the color change sheet 41 at the porti on where the touch sensor 21 is touched under the control of the control unit 10 .

FIG.

18 shows an example in which a tactile feedback sheet 42 for changing the tactile sense (ha nd feeling) is provided on the upper surface side of the touch sensor 21 . As the tactile feedba ck sheet 42, for example, a sheet called "E-Sense" developed by Senseg of Finland can be ad

opted. This sheet provides tactile feedback by charging the film. Even if the tactile feedback s heet 42 is provided on the upper surface side of the touch sensor 21, the touch sensor 21 can detect the contact of a finger or the like. When the touch sensor 21 is operated via the tactile feedback sheet 42 , the driver can recognize that the touch sensor 21 has been operated by c hanging the tactile sensation of the tactile feedback sheet 42 under the control of the control unit 10 . can.

[0083]

Next, a configuration example of the steering wheel will be described with reference to FIG. 19 . A steering wheel 210 shown in FIG. 19 is configured to output a control signal to an oper ation target device from the steering wheel 210 . In FIG. 19, the same parts as those in FIGS. 1 and 2 are denoted by the same reference numerals, and the description thereof will be omit ted as appropriate. As shown in FIG. 19, the steering wheel 210 includes, for example, a sens or data generation unit 23 similar to the sensor data generation unit 22 in FIG. I have. The co ntroller 24 has a detector 24a similar to the detector 10a and a control signal generator 24b.

When the steering wheel 210 is mounted on the vehicle, the control signal generator 24b ge nerates a control signal for controlling the device to be operated in accordance with a specific input operation to the touch sensor 21. FIG

.

The control signal output from the control signal generator 24b is output to the output termin al 26 via the cable 25. FIG. By connecting the output terminal 26 to the device to be operate d, the device to be operated can be controlled by the control signal. Examples of specific input operations are similar to FIGS. 11-13. The requirements for the control signal generator 24b t o generate the control signal are the same as those described above. The present invention i s not limited to the embodiments described above, and various modifications can be made wit hout departing from the gist of the present invention

.

The touch sensor 21 may be detachably attached to the annular portion 200r using a hook-an d-loop fastener. Although the annular portion 200r is used as the grip portion, the grip portion does not necessarily have to be annular.

[0086]

The touch sensor 21 need not be composed of one sheet, and may be composed of a pluralit y of touch sensor pieces. If the touch sensor 21 is composed of a plurality of touch sensor pie ces, the shape of each touch sensor piece can be simplified, which is advantageous in manufa cturing touch sensors. Note that when the touch sensor 21 is composed of a plurality of touch sensor pieces, the touch sensor pieces do not necessarily have to be arranged without gaps. T he touch panel 21 of the present embodiment is mounted so as to cover the grip portion. It al so includes that the sensor 21 is mounted over the grip portion with a gap between the pieces of the touch sensor.

[0087]

Furthermore, the range in which the touch sensor 21 is provided is not limited to the grippin g portion (annular portion 200r or straight portion 201s) that the driver grips during driving. Y ou may extend to the surface of the connection part which connects between. In FIG. 2, the c onnection part is the part located between the left and right hands in the state shown in FIG. 2, and in FIG. In this way, the touch sensor 21 may be extended to the surface of the connect ing portion, and the operation detection area Arv may be set at a position near the grip portio n of the connecting portion. If the position is close to the grip portion, the driver can operate t he operation target device without releasing the hand from the grip portion or moving the han d largely during driving. Therefore, even if the touch sensor 21 is extended to the surface of t he connecting portion, there is almost no possibility that the driver's operation of the steering wheels 200, 201, 210 will be hindered. 10

, 24 control units 10a, 24a detection unit 11 navigation processing unit 12 audio reprodu ction unit 13 television tuner 14 video signal processing unit 15 video display unit 16 au dio signal processing unit 17 display element 18 storage unit 20 speaker 21 touch senso rs 22, 23 sensor data generator 24b control signal generator 25 cable

26 output terminal

31 steering angle sensor

32 direction indicator sensor

33 shift lever sensor

34 in-vehicle communication section

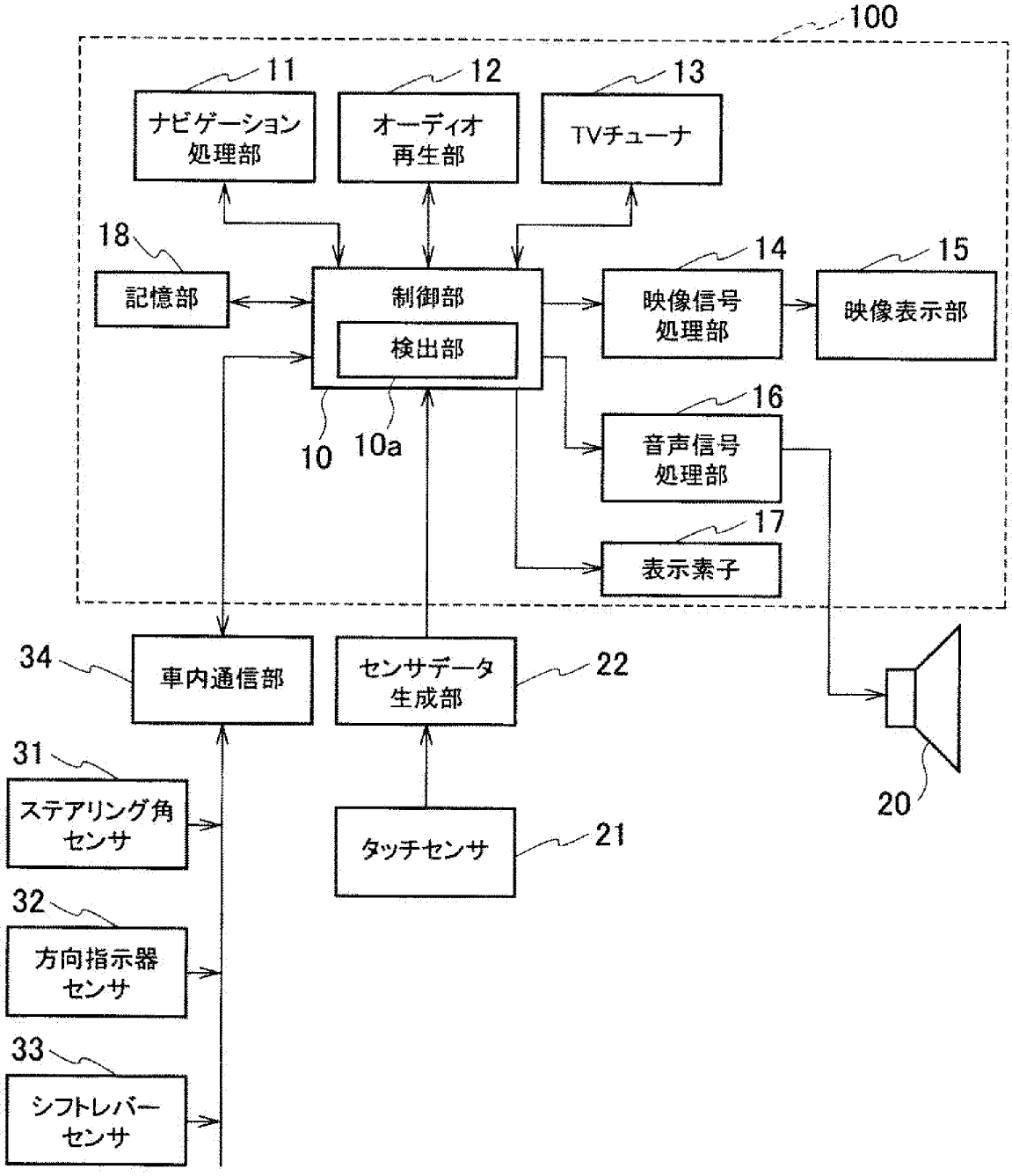
200, 201, 210 steering wheel

200r annular section (grip section)

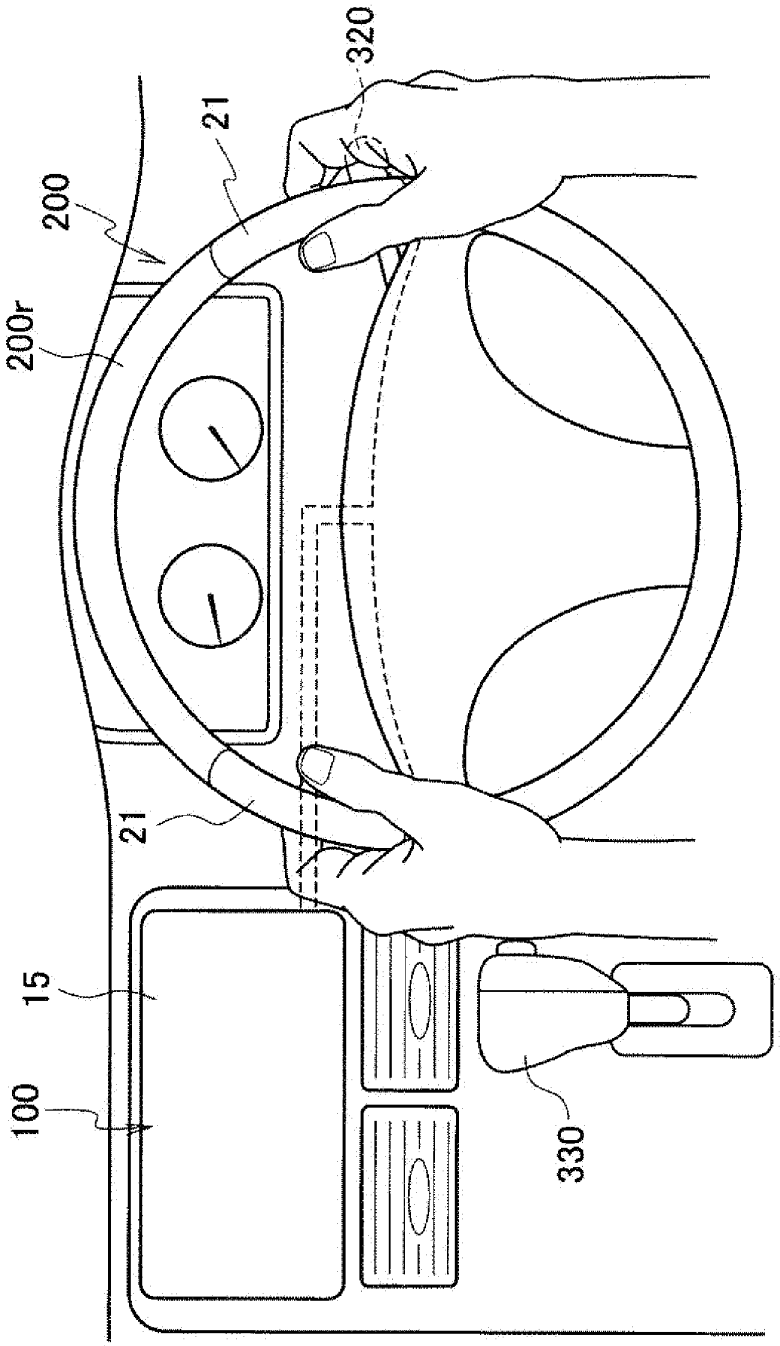
201s linear section (grip section)

drawing	open —

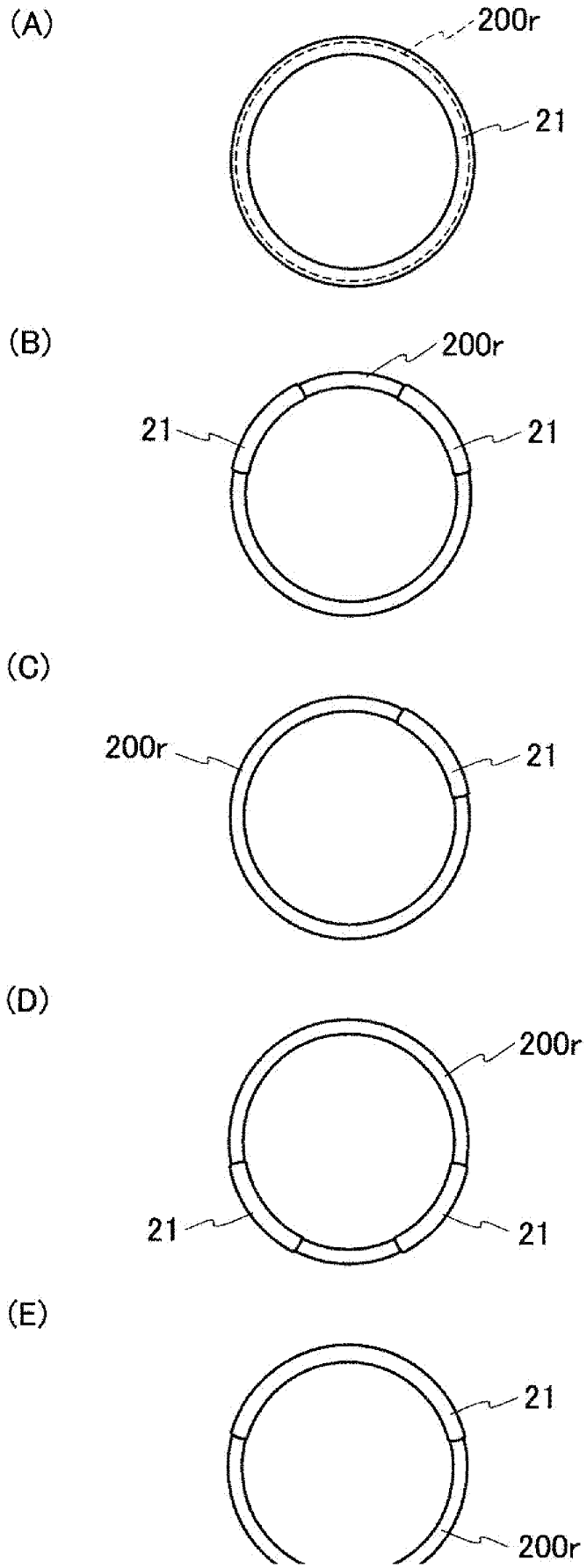
[Fig. 1]


100
11
ナビゲーション処理部
12
オーディオ再生部
13
TVチューナ
18
記憶部
制御部
検出部
14
映像信号処理部
15
映像表示部
10
10a
16
音声信号処理部
17
表示素子
34
車内通信部
センサデータ生成部
22
20
31
ステアリング角センサ
タッチセンサ
21
32
方向指示器センサ
33
シフトレバーセンサ

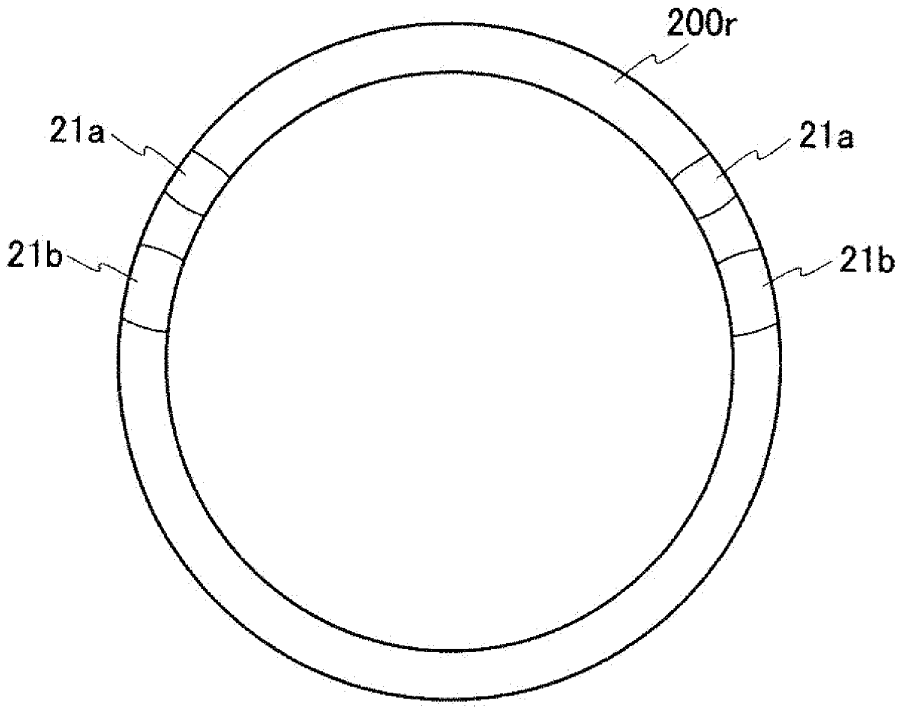
[Figure 2]


320
21
200
200r
21
15
100
330

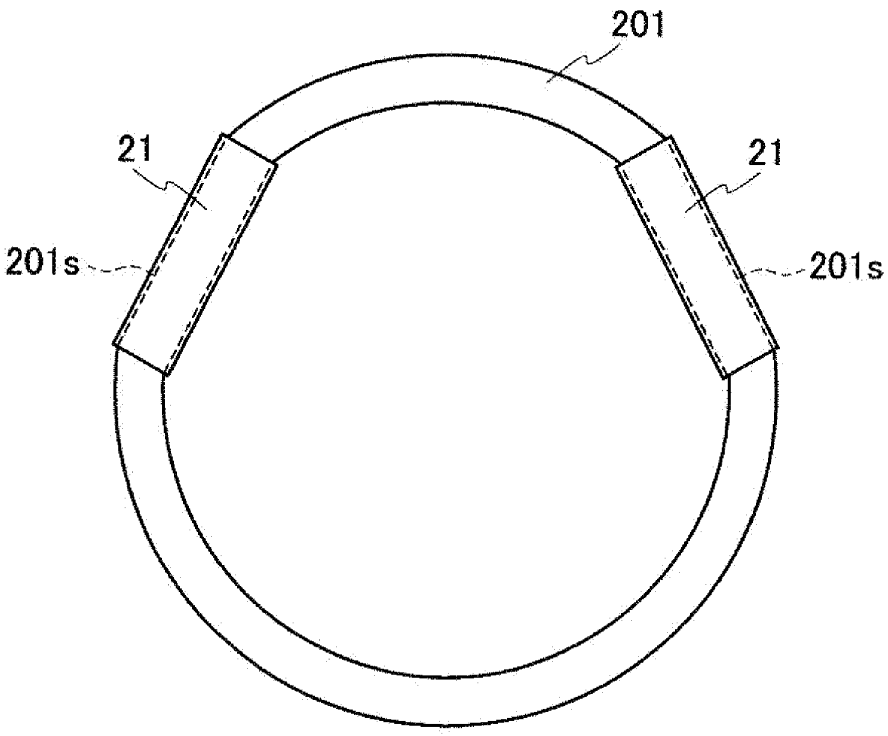
[Figure 3]


(A)
200r
21
(B)
200r
21
21
(C)
200r
21
(D)
200r
21
21
(E)
21
200r

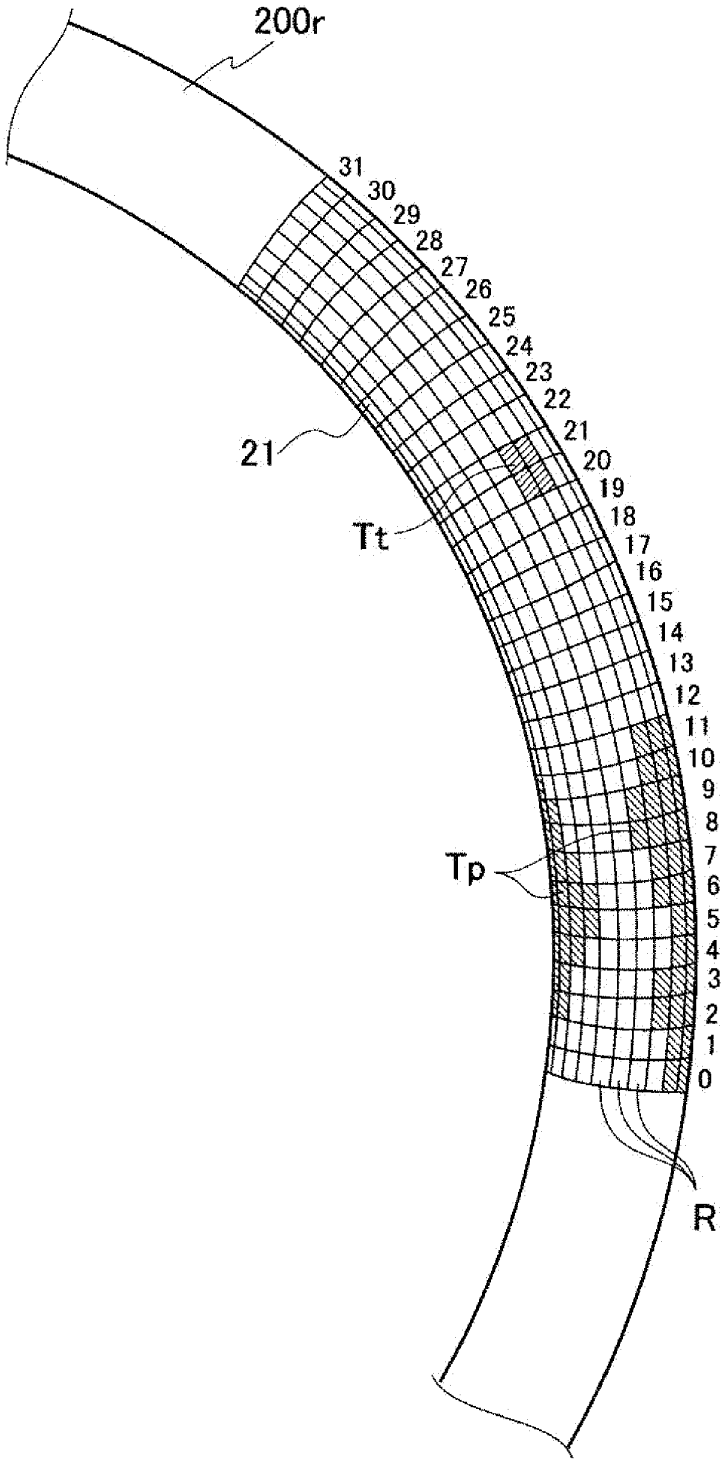
[Figure 4]



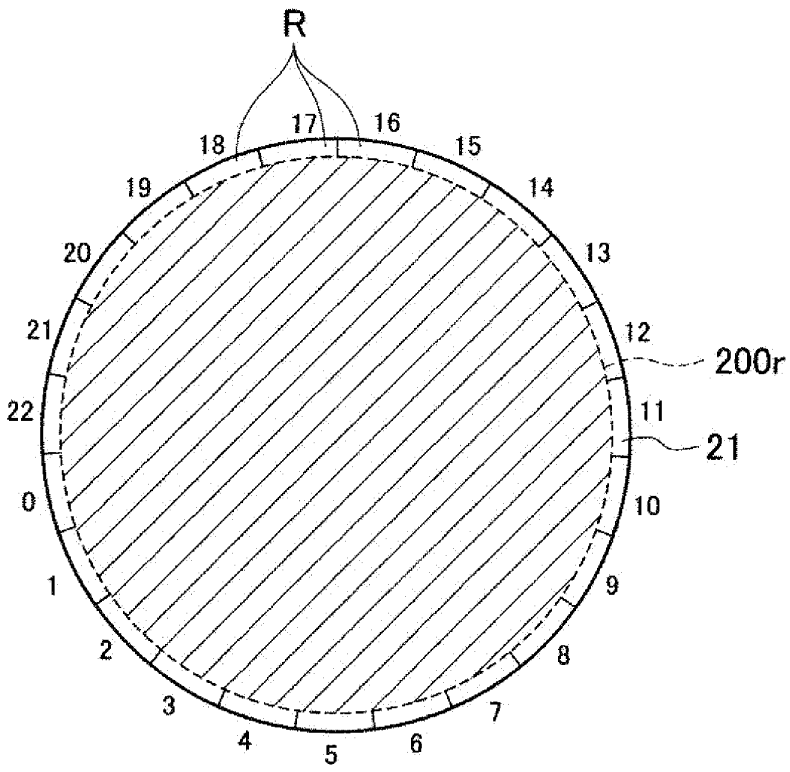
[Figure 5]



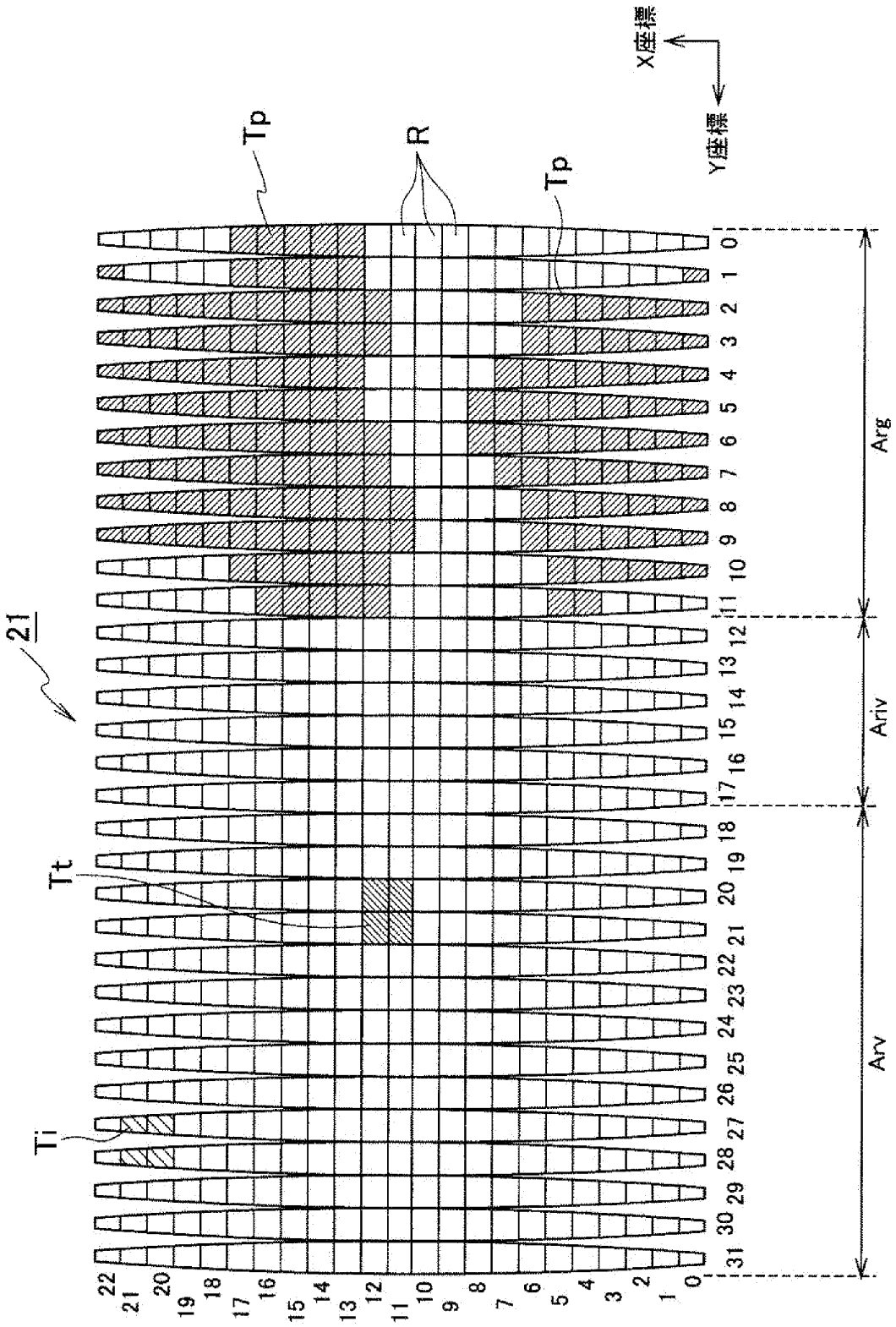
[Fig. 6]


200r
31
30
29
28
27
26
25
24
23
22
21
21
20
19
18
17
16
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
Tt
Tp
R

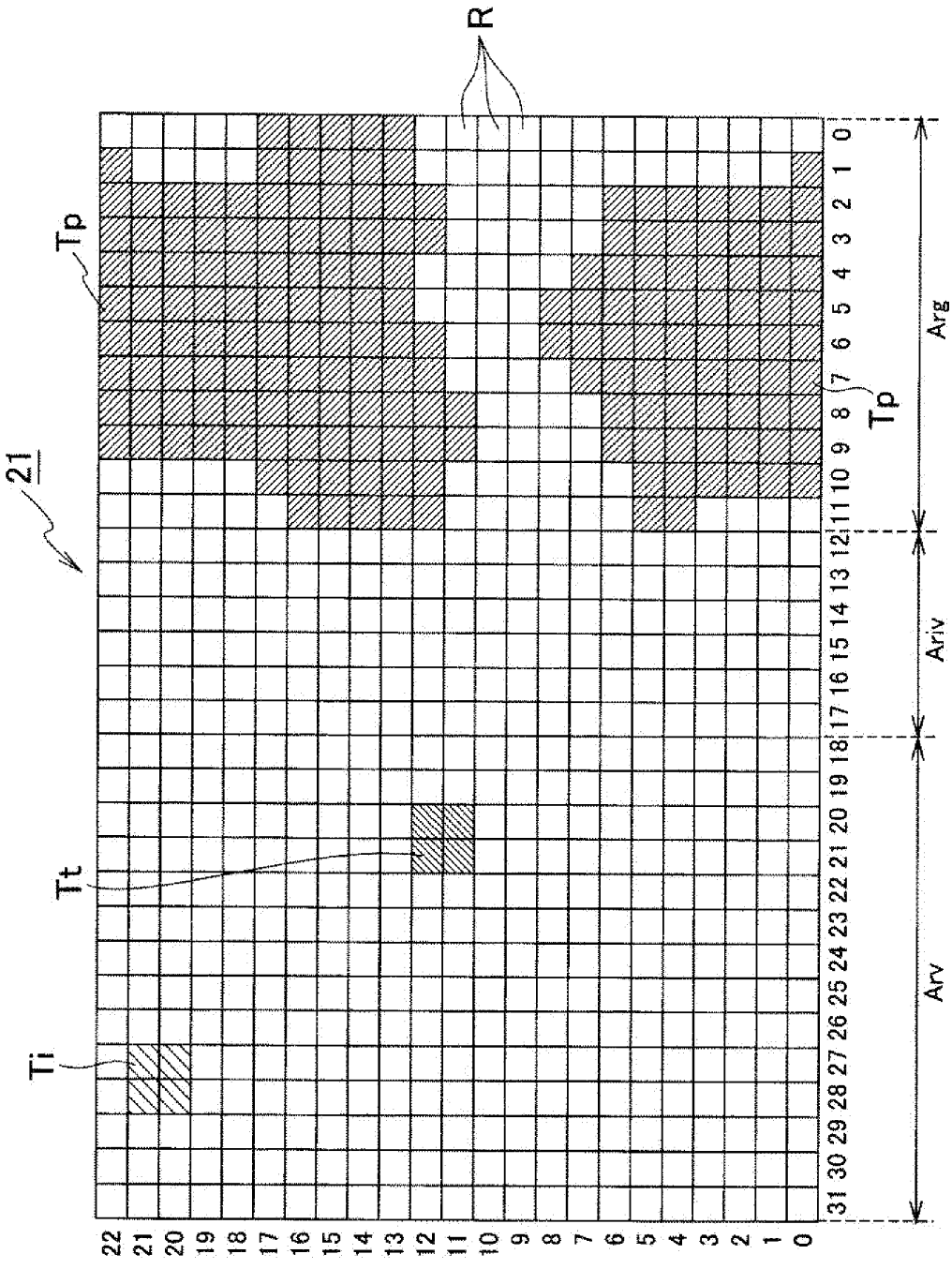
[Fig. 7]


R
17
16
18
15
19
14
20
13
21
12
200r
22
11
21
0
10
1
9
2
8
3
7
4
6
5

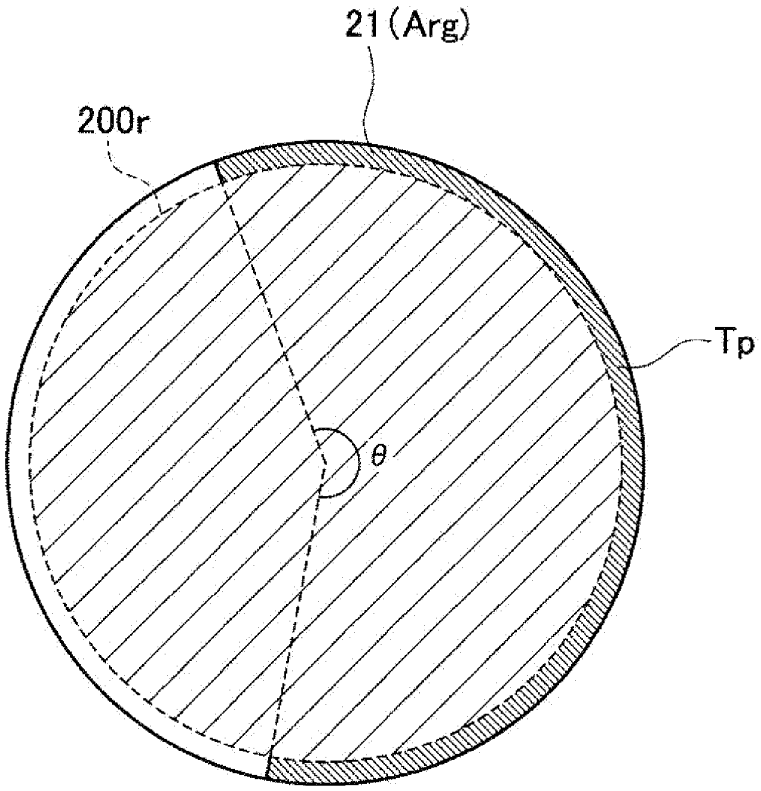
[Fig. 8]


X座標
Y座標
Tp
R
Tp
21
Tt
Ti
Arg
Ariv
Arv

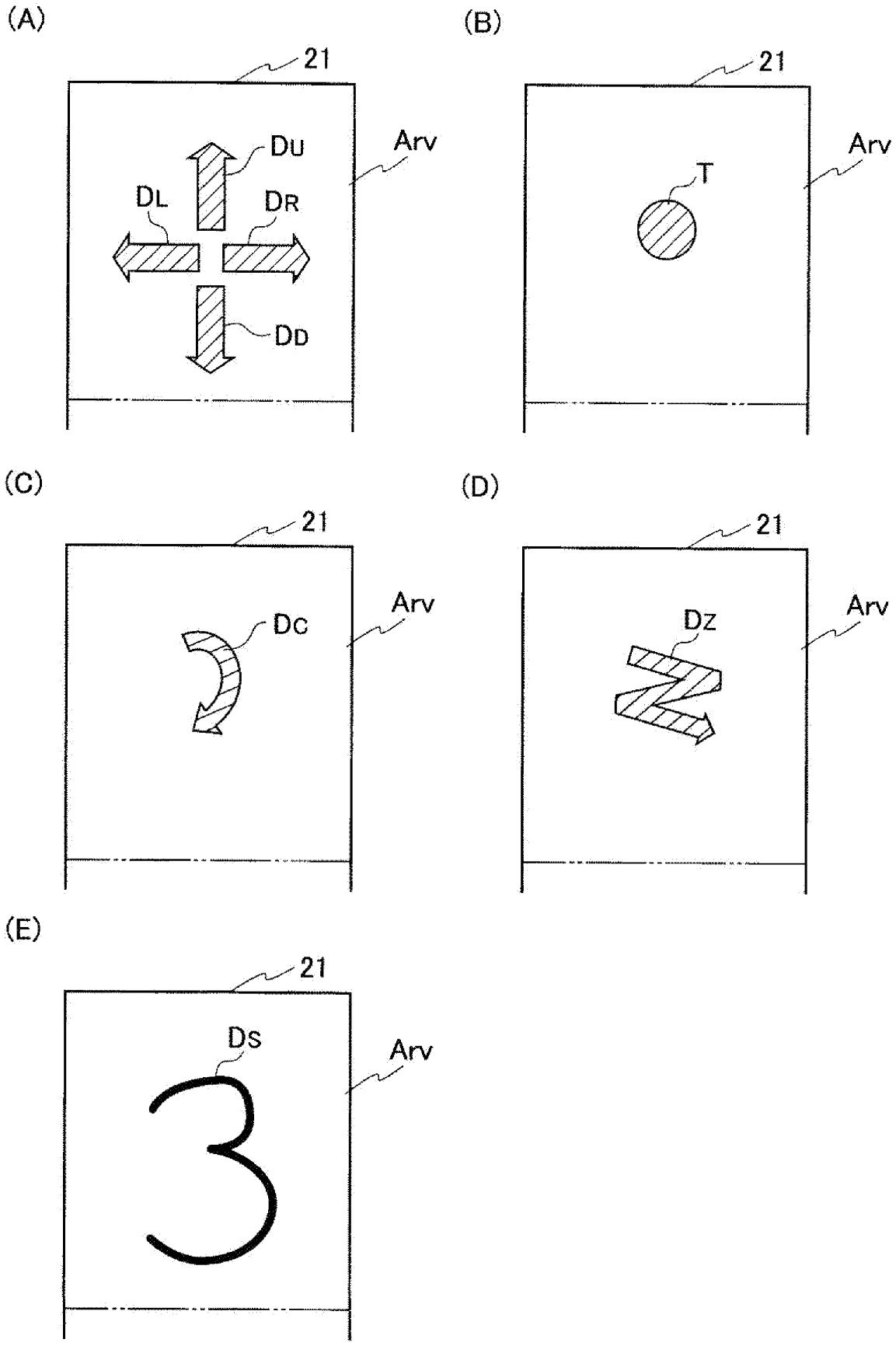
[Fig. 9]


R
Tp
21
Tt
Ti
Tp
Arg
Ariv
Arv
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31
22 21 20 19 18 17 16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0

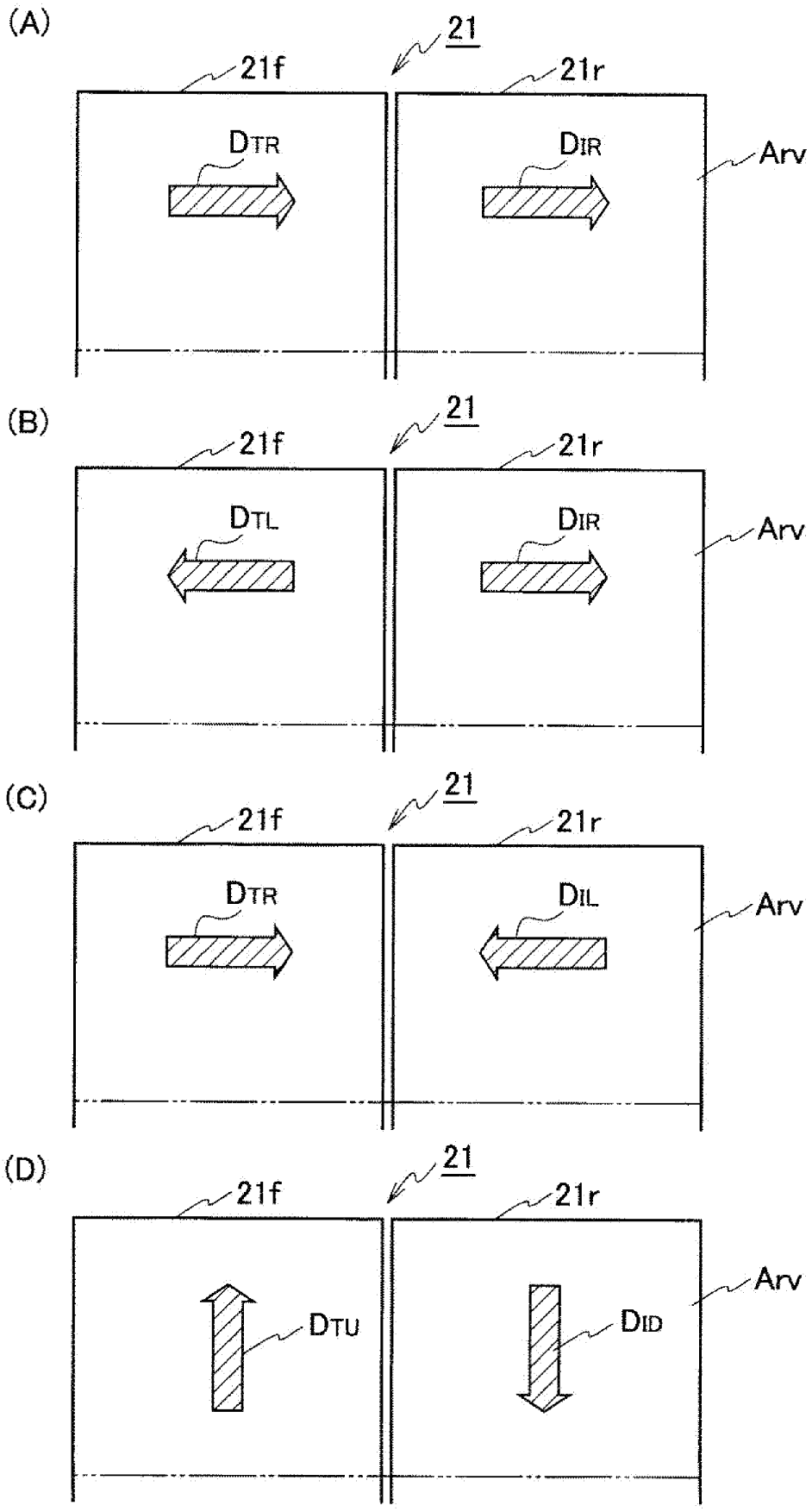
[Fig. 10]


21 (Arg)
200r
Tp
θ

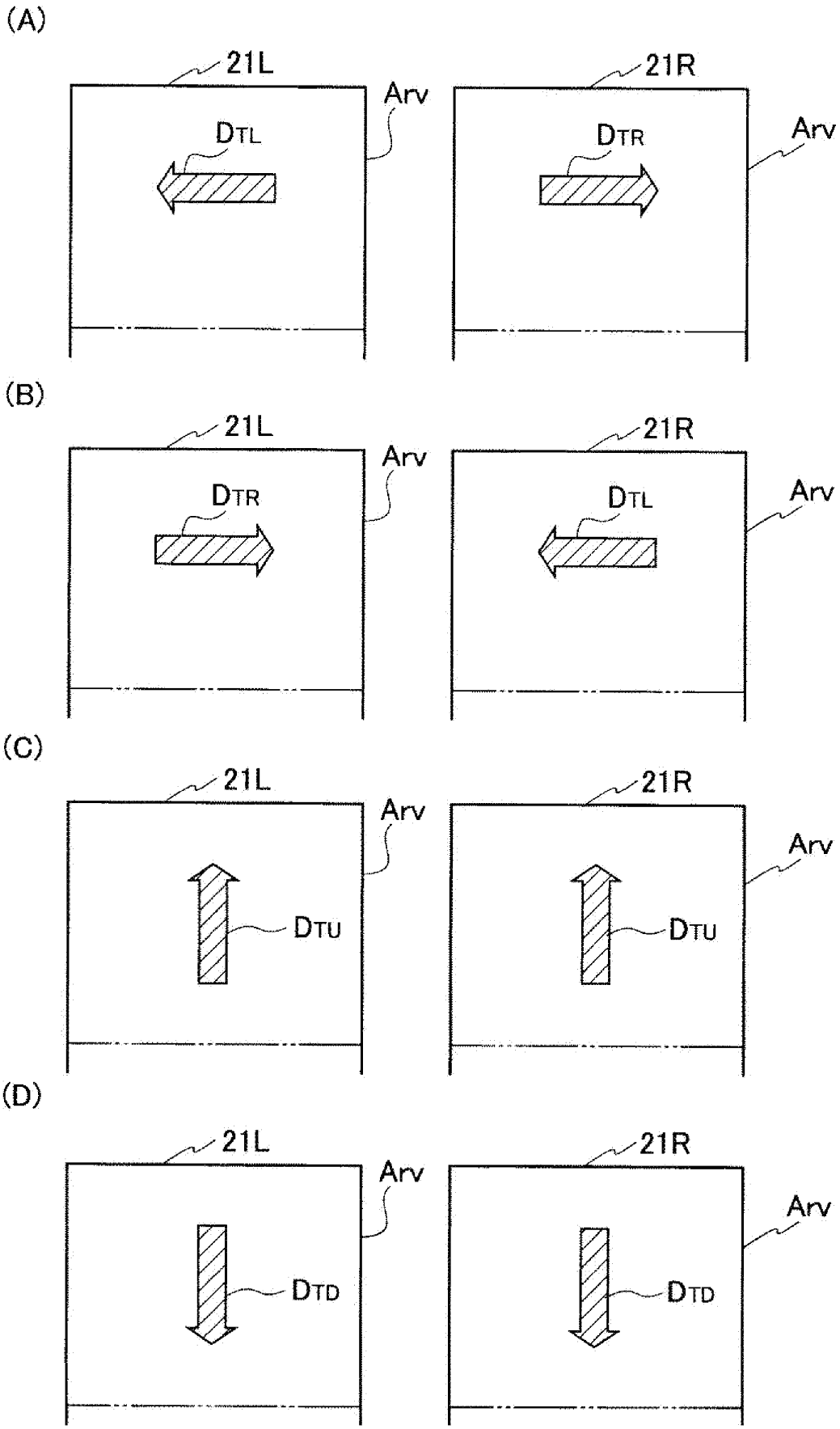
[Fig. 11]


(A)
21
Arv
DU
DL
DR
DD
(B)
21
Arv
T
(C)
21
Arv
DC
(D)
21
Arv
DZ
(E)
21
Arv
DS
3

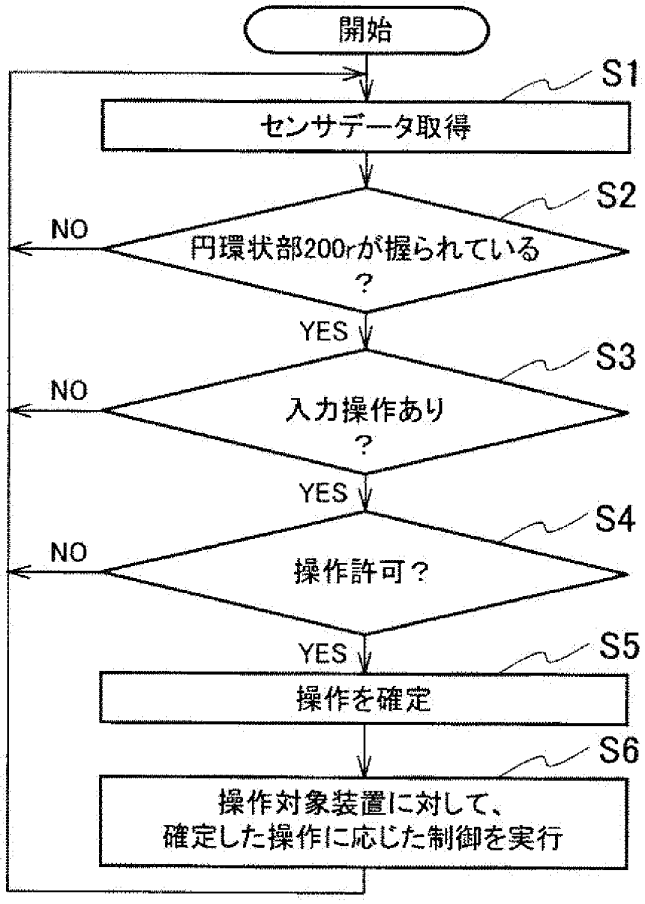
[Fig. 12]


(A)
21
21f
21r
DTR
DIR
Arv
(B)
21
21f
21r
DTL
DIR
Arv
(C)
21
21f
21r
DTR
DIL
Arv
(D)
21
21f
21r
DTU
DID
Arv

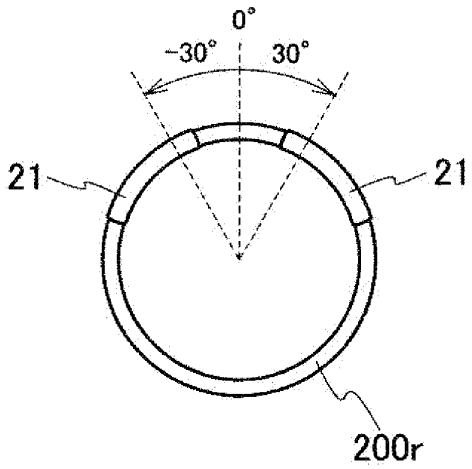
[Fig. 13]


(A)
21L
Arv
DTL
21R
Arv
DTR
(B)
21L
Arv
DTR
21R
Arv
DTL
(C)
21L
Arv
DTU
21R
Arv
DTU
(D)
21L
Arv
DTD
21R
Arv
DTD

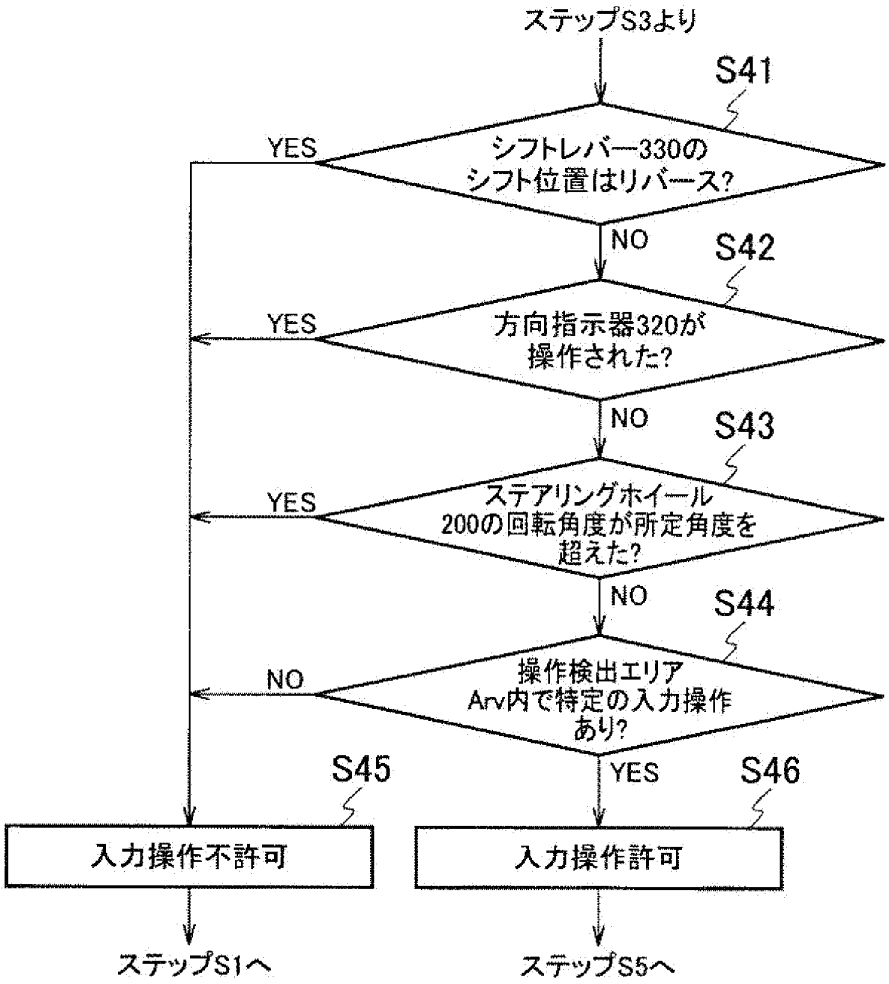
[Fig. 14]


開始
S1
センサデータ取得
S2
円環状部200rが握られている？
NO
YES
S3
入力操作あり？
NO
YES
S4
操作許可？
NO
YES
S5
操作を確定
S6
操作対象装置に対して、
確定した操作に応じた制御を実行

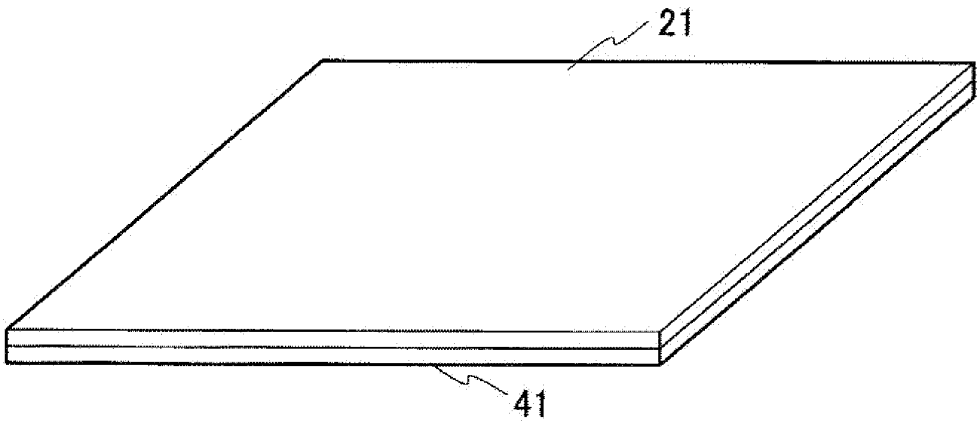
[Fig. 15]



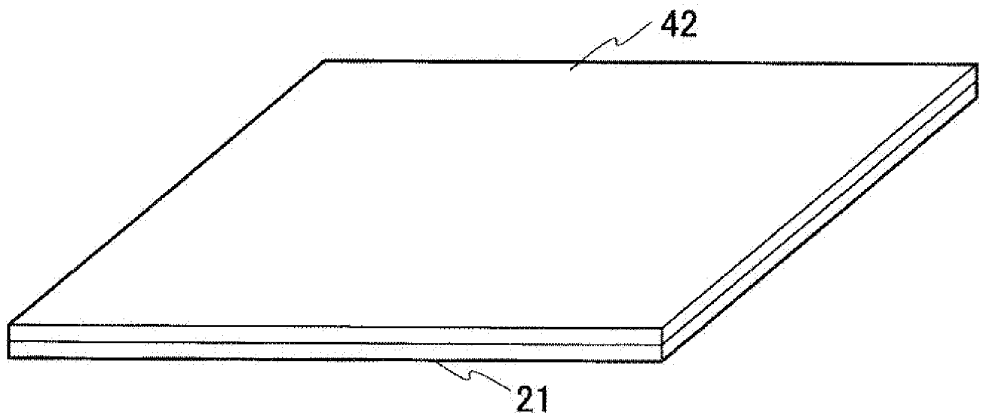
[Fig. 16]


ステップS3より
S41
シフトレバー330の
シフト位置はリバース?
YES
NO
S42
方向指示器320が
操作された?
YES
NO
S43
ステアリングホイール
200の回転角度が所定角度を
超えた?
YES
NO
S44
操作検出エリア
Arv内で特定の入力操作
あり?
NO
YES
S45
S46
入力操作不許可
入力操作許可
ステップS1へ
ステップS5へ

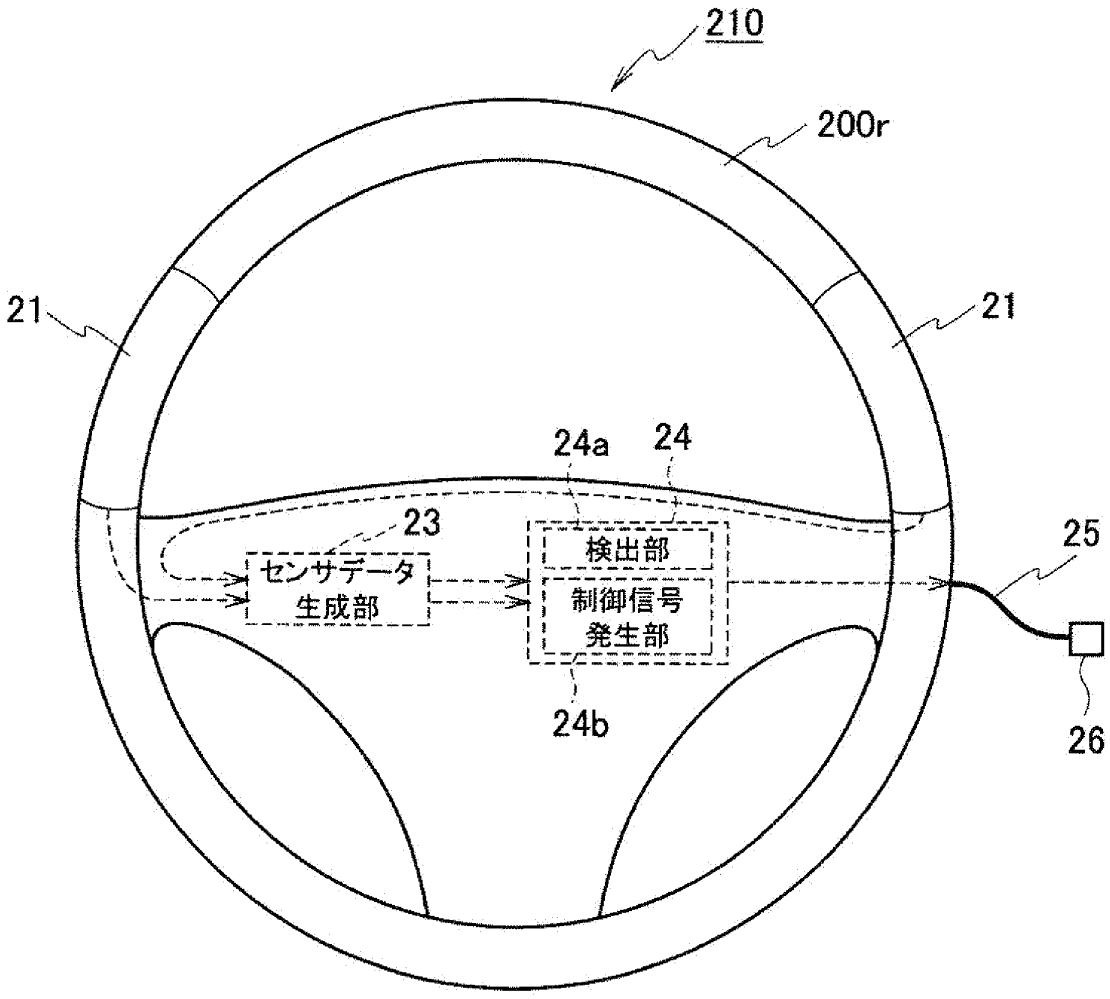
[Fig. 17]


21
41

[Fig. 18]



[Fig. 19]



drawing open —

1 2 3 Four Five 6 7 8 9 Ten ...

Magnify and Rotate

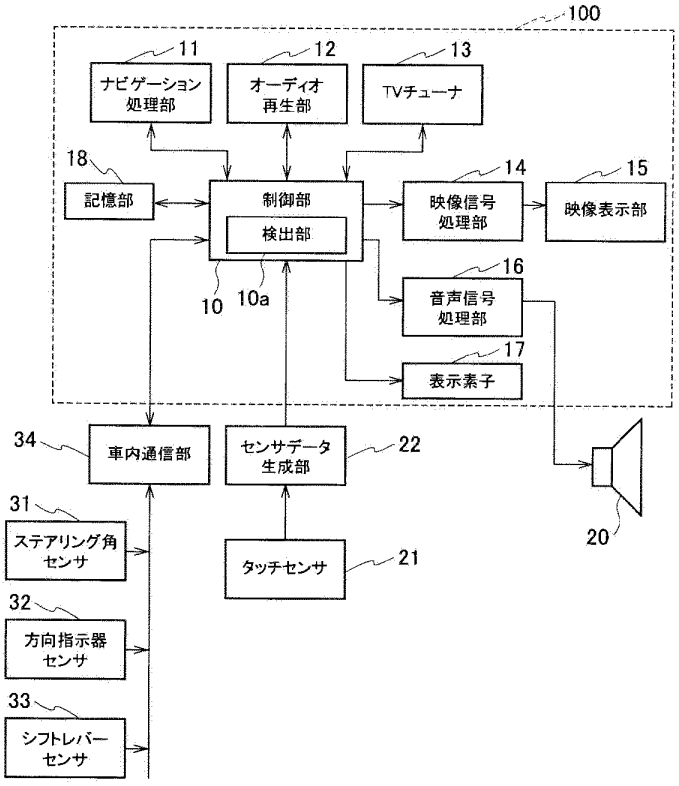


Figure 1

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Espacenet

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DEVICE AND METHOD FOR CONTROLLING OPERATION TARGET DEVICE IN VEHICLE

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Classification: **- international:** ***B60R16/02; B60R16/027***
- cooperative:

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Abstract of JP2013075652 (A)

PROBLEM TO BE SOLVED: To provide a control device for controlling an operation target device in a vehicle, which can operate the operation target device without detaching or largely shifting a hand from a gripping part.SOLUTION: A sensor data generation part 22 generates sensor data based on a contact detection signal obtained from a touch sensor 21 mounted to cover the gripping part of a steering wheel. A detection part 10a detects whether the driver grips the gripping part or not and an input operation to the touch sensor 21. When it is detected by the detection part 10a that the driver grips the holding part and it is detected that a specific input operation has been performed to the touch sensor 21, a control part 10 controls the operation target device according to the specific input operation. The control part 10 invalidates the control of the operation target device when the vehicle is in a specific condition.

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最終頁に続く

(54)【発明の名称】車両における操作対象装置の制御装置及び制御方法

(57)【特許請求の範囲】
【請求項１】
複数の検出領域を有し、車両のステアリングホイールにおける運転者が握る握持部の所定の範囲に、前記握持部を覆うように装着されたタッチセンサから得られる接触検出信号に基づいて、どの検出領域が触られているかを示す位置データを含むセンサデータを生成するセンサデータ生成部と、
前記センサデータに基づいて、運転者が前記握持部を握っているか否か、及び、前記タッチセンサに対する入力操作を検出する検出部と、
前記検出部によって運転者が前記握持部を握っていることが検出され、かつ、前記タッチセンサに対して特定の入力操作が行われたことが検出された場合に、前記特定の入力操作に応じて、前記タッチセンサによって操作する対象の操作対象装置を制御する制御部と、
を備え、
前記制御部は、方向指示器が操作されたとき車両が特定の状態にあるとして、前記操作対象装置の制御を無効とすることを特徴とする車両における操作対象装置の制御装置。
【請求項２】
複数の検出領域を有し、車両のステアリングホイールにおける運転者が握る握持部の所定の範囲に、前記握持部を覆うように装着されたタッチセンサから得られる接触検出信号に基づいて、どの検出領域が触られているかを示す位置データを含むセンサデータを生成するセンサデータ生成部と、

前記センサデータに基づいて、運転者が前記握持部を握っているか否か、及び、前記タッチセンサに対する入力操作を検出する検出部と、
前記検出部によって運転者が前記握持部を握っていることが検出され、かつ、前記タッチセンサに対して特定の入力操作が行われたことが検出された場合に、前記特定の入力操作に応じて、前記タッチセンサによって操作する対象の操作対象装置を制御する制御部と、
を備え、
前記制御部は、シフトレバーのシフト位置がリバースとなったとき車両が特定の状態にあるとして、前記操作対象装置の制御を無効とすることを特徴とする車両における操作対象装置の制御装置。

【請求項３】
前記タッチセンサには、前記複数の検出領域の一部を含み、運転者の手のひらの接触を検出するグリップ検出エリアと、前記複数の検出領域の他の一部を含み、指の接触による前記特定の入力操作を検出する操作検出エリアとが設定されており、
前記検出部は、前記グリップ検出エリアから得られる接触検出信号に基づくセンサデータによって運転者が前記握持部を握っているか否かを検出し、前記操作検出エリアから得られる接触検出信号に基づくセンサデータによって前記特定の入力操作を検出する
ことを特徴とする請求項１または２に記載の車両における操作対象装置の制御装置。

【請求項４】
複数の検出領域を有し、車両のステアリングホイールにおける運転者が握る握持部の所定の範囲に、前記握持部を覆うように装着されたタッチセンサから得られる接触検出信号に基づいて、どの検出領域が触られているかを示す位置データを含むセンサデータを生成するセンサデータ生成部と、
前記センサデータに基づいて、運転者が前記握持部を握っているか否か、及び、前記タッチセンサに対する入力操作を検出する検出部と、
前記検出部によって運転者が前記握持部を握っていることが検出され、かつ、前記タッチセンサに対して特定の入力操作が行われたことが検出された場合に、前記特定の入力操作に応じて、前記タッチセンサによって操作する対象の操作対象装置を制御する制御部と、
を備え、
前記タッチセンサには、前記複数の検出領域の一部を含み、運転者の手のひらの接触を検出するグリップ検出エリアと、前記複数の検出領域の他の一部を含み、指の接触による前記特定の入力操作を検出する操作検出エリアとが設定されており、
前記検出部は、前記グリップ検出エリアから得られる接触検出信号に基づくセンサデータによって運転者が前記握持部を握っているか否かを検出し、前記操作検出エリアから得られる接触検出信号に基づくセンサデータによって前記特定の入力操作を検出し、
前記制御部は、車両が特定の状態にあるときに、前記操作対象装置の制御を無効とすることを特徴とする車両における操作対象装置の制御装置。

【請求項５】
前記制御部は、前記特定の入力操作として、前記操作検出エリアに対して、前記握持部を前記ステアリングホイールの径方向に切断したときの断面における周方向に離間した２箇所を２つの指によって操作したパターンに応じて、前記操作対象装置を制御することを特徴とする請求項３または４に記載の車両における操作対象装置の制御装置。

【請求項６】
前記制御部は、さらに、前記ステアリングホイールの回転角度が所定の角度を超えたとき車両が特定の状態にあるとして、前記操作対象装置の制御を無効とすることを特徴とする請求項１～４のいずれか１項に記載の車両における操作対象装置の制御装置。

【請求項７】
前記タッチセンサは、運転者が左手で握る握持部の所定の範囲に装着された第１のタッチセンサと右手で握る握持部の所定の範囲に装着された第２のタッチセンサとを含み、

前記制御部は、前記特定の入力操作として、前記第１のタッチセンサに対する第１の入力操作と前記第２のタッチセンサに対する第２の入力操作との組み合わせによるパターンに応じて、前記操作対象装置を制御する

ことを特徴とする請求項１～６のいずれか１項に記載の車両における操作対象装置の制御装置。

【請求項８】

複数の検出領域を有し、車両のステアリングホイールにおける運転者が握る握持部の所定の範囲に、前記握持部を覆うように装着されたタッチセンサを運転者が握っているか否かを検出し、

前記タッチセンサに対して特定の入力操作が行われたか否かを検出し、

方向指示器が操作されたか否かを検出し、

車両が、方向指示器が操作された特定の状態にはないことが検出され、運転者が前記タッチセンサを握っていることが検出され、かつ、前記特定の入力操作が行われたことが検出された場合に、前記タッチセンサによって操作する対象の操作対象装置を制御し、車両が、方向指示器が操作された特定の状態にあることが検出された場合には、前記操作対象装置を制御を無効とする

ことを特徴とする車両における操作対象装置の制御方法。

【請求項９】

複数の検出領域を有し、車両のステアリングホイールにおける運転者が握る握持部の所定の範囲に、前記握持部を覆うように装着されたタッチセンサを運転者が握っているか否かを検出し、

前記タッチセンサに対して特定の入力操作が行われたか否かを検出し、

シフトレバーのシフト位置がリバースとなったか否かを検出し、

車両が、シフトレバーのシフト位置がリバースとなった特定の状態にはないことが検出され、運転者が前記タッチセンサを握っていることが検出され、かつ、前記特定の入力操作が行われたことが検出された場合に、前記タッチセンサによって操作する対象の操作対象装置を制御し、車両が、シフトレバーのシフト位置がリバースとなった特定の状態にあることが検出された場合には、前記操作対象装置を制御を無効とする

ことを特徴とする車両における操作対象装置の制御方法。

【請求項１０】

前記タッチセンサには、前記複数の検出領域の一部を含み、運転者の手のひらの接触を検出するグリップ検出エリアと、前記複数の検出領域の他の一部を含み、指の接触による前記特定の操作を検出する操作検出エリアとが設定されており、

前記グリップ検出エリアに対する手のひらの接触によって、運転者が前記タッチセンサを握っていることを検出し、

前記操作検出エリアに対する指の接触によって、前記特定の入力操作が行われたことを検出する

ことを特徴とする請求項８または９に記載の車両における操作対象装置の制御方法。

【請求項１１】

複数の検出領域を有し、車両のステアリングホイールにおける運転者が握る握持部の所定の範囲に、前記握持部を覆うように装着されたタッチセンサを運転者が握っているか否かを検出し、

前記タッチセンサに対して特定の入力操作が行われたか否かを検出し、

車両が特定の状態にあるか否かを検出し、

車両が特定の状態にはないことが検出され、運転者が前記タッチセンサを握っていることが検出され、かつ、前記特定の入力操作が行われたことが検出された場合に、前記タッチセンサによって操作する対象の操作対象装置を制御し、

前記タッチセンサには、前記複数の検出領域の一部を含み、運転者の手のひらの接触を検出するグリップ検出エリアと、前記複数の検出領域の他の一部を含み、指の接触による前記特定の操作を検出する操作検出エリアとが設定されており、

前記グリップ検出エリアに対する手のひらの接触によって、運転者が前記タッチセンサを握っていることを検出し、
前記操作検出エリアに対する指の接触によって、前記特定の入力操作が行われたことを検出する
ことを特徴とする車両における操作対象装置の制御方法。
【請求項１２】
前記特定の入力操作として、前記操作検出エリアに対して、前記握持部を前記ステアリングホイールの径方向に切断したときの断面における周方向に離間した２箇所を２つの指によって操作したパターンに応じて、前記操作対象装置を制御することを特徴とする請求項１０または１１に記載の車両における操作対象装置の制御方法。
【請求項１３】
前記ステアリングホイールの回転角度が所定の角度を超えたとき車両が特定の状態にあるにあるとして、前記操作対象装置の制御を無効とすることを特徴とする請求項８～１１のいずれか１項に記載の車両における操作対象装置の制御方法。
【請求項１４】
前記タッチセンサは、運転者が左手で握る握持部の所定の範囲に装着された第１のタッチセンサと右手で握る握持部の所定の範囲に装着された第２のタッチセンサとを含み、
前記特定の入力操作として、前記第１のタッチセンサに対する第１の入力操作と前記第２のタッチセンサに対する第２の入力操作との組み合わせによるパターンに応じて、前記操作対象装置を制御する
ことを特徴とする請求項８～１３のいずれか１項に記載の車両における操作対象装置の制御方法。
【発明の詳細な説明】
【技術分野】
【０００１】
本発明は、車両に搭載されているナビゲーション装置等の車載機器、または、変速機や方向指示器等の車両の動作を制御する車両動作制御装置を操作対象装置とし、操作対象装置を制御する制御装置及び制御方法に関する。
【背景技術】
【０００２】
車両に搭載されているナビゲーション装置等の車載機器を操作するための操作スイッチをステアリングホイールに配置した車両が普及している（特許文献１参照）。操作スイッチをステアリングホイールに配置すれば、運転者は車載機器を操作する際に車載機器まで手を伸ばす必要がないので、操作性が向上する。特許文献１に記載されているように、操作スイッチは、実際には、運転者が手で握る握持部であるステアリングホイールの円環状部ではなく、エアバッグが収納されているセンター部と円環状部との間を連結する連結部に配置されるのが通常である。従って、運転者は、操作スイッチを操作するために、握っている円環状部から手を離したり、手を大きくずらしたりする必要がある。特許文献２には、円環状部の背面や内側側面に操作スイッチを配置することが記載されている。
【先行技術文献】
【特許文献】
【０００３】
【特許文献１】特開２００７－１０６３５３号公報
【特許文献２】特開２００５－３４８１２３号公報
【特許文献３】特開２００８－１９５２２０号公報
【発明の概要】
【発明が解決しようとする課題】
【０００４】
特許文献２に記載の発明によれば、円環状部に操作スイッチを配置しているので、円環状部から手を離したり、手を大きくずらしたりすることなく、操作スイッチを操作するこ

とができる。しかしながら、特許文献２に記載されている操作スイッチは押しボタンによるキーや凹凸を設けたキーであり、この種のキーは運転者がステアリングホイールを操作する際の支障となる可能性がある。運転者が握る円環状部に大きな凹凸を設けることは好ましくない。また、円環状部に操作スイッチのような操作部を配置した場合、運転者が通常の運転のために円環状部を握っている場合のように、操作対象装置を操作しようとする意思がない場合に、不用意に操作対象装置が操作されないようにすることが求められる。さらに、車両の状態によっては誤操作を招く場合があり、誤操作を極力少なくすることが求められる。

【０００５】

本発明はこのような要望に対応するため、握持部から手を離したり、手を大きくずらしたりすることなく操作対象装置を操作することができ、運転者がステアリングホイールを操作する際に支障となる可能性を大幅に低減させることができる車両における操作対象装置の制御装置及び制御方法を提供することを目的とする。また、誤操作を大幅に低減させることができる車両における操作対象装置の制御装置及び制御方法を提供することを目的とする。

【課題を解決するための手段】

【０００６】

本発明は、上述した従来の技術の課題を解決するため、複数の検出領域を有し、車両のステアリングホイールにおける運転者が握る握持部の所定の範囲に、前記握持部を覆うように装着されたタッチセンサから得られる接触検出信号に基づいて、どの検出領域が触られているかを示す位置データを含むセンサデータを生成するセンサデータ生成部と、前記センサデータに基づいて、運転者が前記握持部を握っているか否か、及び、前記タッチセンサに対する入力操作を検出する検出部と、前記検出部によって運転者が前記握持部を握っていることが検出され、かつ、前記タッチセンサに対して特定の入力操作が行われたことが検出された場合に、前記特定の入力操作に応じて、前記タッチセンサによって操作する対象の操作対象装置を制御する制御部とを備え、前記制御部は、方向指示器が操作されたとき車両が特定の状態にあるとして、前記操作対象装置の制御を無効とすることを特徴とする車両における操作対象装置の制御装置を提供する。

【０００７】

本発明は、上述した従来の技術の課題を解決するため、複数の検出領域を有し、車両のステアリングホイールにおける運転者が握る握持部の所定の範囲に、前記握持部を覆うように装着されたタッチセンサから得られる接触検出信号に基づいて、どの検出領域が触られているかを示す位置データを含むセンサデータを生成するセンサデータ生成部と、前記センサデータに基づいて、運転者が前記握持部を握っているか否か、及び、前記タッチセンサに対する入力操作を検出する検出部と、前記検出部によって運転者が前記握持部を握っていることが検出され、かつ、前記タッチセンサに対して特定の入力操作が行われたことが検出された場合に、前記特定の入力操作に応じて、前記タッチセンサによって操作する対象の操作対象装置を制御する制御部とを備え、前記制御部は、シフトレバーのシフト位置がリバースとなったとき車両が特定の状態にあるとして、前記操作対象装置の制御を無効とすることを特徴とする車両における操作対象装置の制御装置を提供する。

【０００８】

上記の車両における操作対象装置の制御装置において、前記タッチセンサには、前記複数の検出領域の一部を含み、運転者の手のひらの接触を検出するグリップ検出エリアと、前記複数の検出領域の他の一部を含み、指の接触による前記特定の入力操作を検出する操作検出エリアとが設定されており、前記検出部は、前記グリップ検出エリアから得られる接触検出信号に基づくセンサデータによって運転者が前記握持部を握っているか否かを検出し、前記操作検出エリアから得られる接触検出信号に基づくセンサデータによって前記特定の入力操作を検出することが好ましい。

【０００９】

本発明は、上述した従来の技術の課題を解決するため、複数の検出領域を有し、車両の

ステアリングホイールにおける運転者が握る握持部の所定の範囲に、前記握持部を覆うように装着されたタッチセンサから得られる接触検出信号に基づいて、どの検出領域が触られているかを示す位置データを含むセンサデータを生成するセンサデータ生成部と、前記センサデータに基づいて、運転者が前記握持部を握っているか否か、及び、前記タッチセンサに対する入力操作を検出する検出部と、前記検出部によって運転者が前記握持部を握っていることが検出され、かつ、前記タッチセンサに対して特定の入力操作が行われたことが検出された場合に、前記特定の入力操作に応じて、前記タッチセンサによって操作する対象の操作対象装置を制御する制御部とを備え、前記タッチセンサには、前記複数の検出領域の一部を含み、運転者の手のひらの接触を検出するグリップ検出エリアと、前記複数の検出領域の他の一部を含み、指の接触による前記特定の入力操作を検出する操作検出エリアとが設定されており、前記検出部は、前記グリップ検出エリアから得られる接触検出信号に基づくセンサデータによって運転者が前記握持部を握っているか否かを検出し、前記操作検出エリアから得られる接触検出信号に基づくセンサデータによって前記特定の入力操作を検出し、前記制御部は、車両が特定の状態にあるときに、前記操作対象装置の制御を無効とすることを特徴とする車両における操作対象装置の制御装置を提供する。

【００１０】

上記の車両における操作対象装置の制御装置において、前記制御部は、前記特定の入力操作として、前記操作検出エリアに対して、前記握持部を前記ステアリングホイールの径方向に切断したときの断面における周方向に離間した２箇所を２つの指によって操作したパターンに応じて、前記操作対象装置を制御することが好ましい。

上記の車両における操作対象装置の制御装置において、前記制御部は、さらに、前記ステアリングホイールの回転角度が所定の角度を超えたとき車両が特定の状態にあるとして、前記操作対象装置の制御を無効とすることが好ましい。

上記の車両における操作対象装置の制御装置において、前記タッチセンサは、運転者が左手で握る握持部の所定の範囲に装着された第１のタッチセンサと右手で握る握持部の所定の範囲に装着された第２のタッチセンサとを含み、前記制御部は、前記特定の入力操作として、前記第１のタッチセンサに対する第１の入力操作と前記第２のタッチセンサに対する第２の入力操作との組み合わせによるパターンに応じて、前記操作対象装置を制御することが好ましい。

【００１１】

本発明は、上述した従来の技術の課題を解決するため、複数の検出領域を有し、車両のステアリングホイールにおける運転者が握る握持部の所定の範囲に、前記握持部を覆うように装着されたタッチセンサを運転者が握っているか否かを検出し、前記タッチセンサに対して特定の入力操作が行われたか否かを検出し、方向指示器が操作されたか否かを検出し、車両が、方向指示器が操作された特定の状態にはないことが検出され、運転者が前記タッチセンサを握っていることが検出され、かつ、前記特定の入力操作が行われたことが検出された場合に、前記タッチセンサによって操作する対象の操作対象装置を制御し、車両が、方向指示器が操作された特定の状態にあることが検出された場合には、前記操作対象装置を制御を無効とすることを特徴とする車両における操作対象装置の制御方法を提供する。

【００１２】

本発明は、上述した従来の技術の課題を解決するため、複数の検出領域を有し、車両のステアリングホイールにおける運転者が握る握持部の所定の範囲に、前記握持部を覆うように装着されたタッチセンサを運転者が握っているか否かを検出し、前記タッチセンサに対して特定の入力操作が行われたか否かを検出し、シフトレバーのシフト位置がリバースとなったか否かを検出し、車両が、シフトレバーのシフト位置がリバースとなった特定の状態にはないことが検出され、運転者が前記タッチセンサを握っていることが検出され、かつ、前記特定の入力操作が行われたことが検出された場合に、前記タッチセンサによって操作する対象の操作対象装置を制御し、車両が、シフトレバーのシフト位置がリバースとなった特定の状態にあることが検出された場合には、前記操作対象装置を制御を無効と

することを特徴とする車両における操作対象装置の制御方法を提供する。

【００１３】

上記の車両における操作対象装置の制御方法において、前記タッチセンサには、前記複数の検出領域の一部を含み、運転者の手のひらの接触を検出するグリップ検出エリアと、前記複数の検出領域の他の一部を含み、指の接触による前記特定の操作を検出する操作検出エリアとが設定されており、前記グリップ検出エリアに対する手のひらの接触によって、運転者が前記タッチセンサを握っていることを検出し、前記操作検出エリアに対する指の接触によって、前記特定の入力操作が行われたことを検出することが好ましい。

【００１４】

本発明は、上述した従来の技術の課題を解決するため、複数の検出領域を有し、車両のステアリングホイールにおける運転者が握る握持部の所定の範囲に、前記握持部を覆うように装着されたタッチセンサを運転者が握っているか否かを検出し、前記タッチセンサに対して特定の入力操作が行われたか否かを検出し、車両が特定の状態にあるか否かを検出し、車両が特定の状態にはないことが検出され、運転者が前記タッチセンサを握っていることが検出され、かつ、前記特定の入力操作が行われたことが検出された場合に、前記タッチセンサによって操作する対象の操作対象装置を制御し、前記タッチセンサには、前記複数の検出領域の一部を含み、運転者の手のひらの接触を検出するグリップ検出エリアと、前記複数の検出領域の他の一部を含み、指の接触による前記特定の操作を検出する操作検出エリアとが設定されており、前記グリップ検出エリアに対する手のひらの接触によって、運転者が前記タッチセンサを握っていることを検出し、前記操作検出エリアに対する指の接触によって、前記特定の入力操作が行われたことを検出することを特徴とする車両における操作対象装置の制御方法を提供する。

【００１５】

上記の車両における操作対象装置の制御方法において、前記特定の入力操作として、前記操作検出エリアに対して、前記握持部を前記ステアリングホイールの径方向に切断したときの断面における周方向に離間した２箇所を２つの指によって操作したパターンに応じて、前記操作対象装置を制御することが好ましい。

上記の車両における操作対象装置の制御方法において、前記ステアリングホイールの回転角度が所定の角度を超えたとき車両が特定の状態にあるにあるとして、前記操作対象装置の制御を無効とすることが好ましい。

上記の車両における操作対象装置の制御方法において、前記タッチセンサは、運転者が左手で握る握持部の所定の範囲に装着された第１のタッチセンサと右手で握る握持部の所定の範囲に装着された第２のタッチセンサとを含み、前記特定の入力操作として、前記第１のタッチセンサに対する第１の入力操作と前記第２のタッチセンサに対する第２の入力操作との組み合わせによるパターンに応じて、前記操作対象装置を制御することが好ましい。

【発明の効果】

【００１６】

本発明の車両における操作対象装置の制御装置及び制御方法によれば、握持部から手を離したり、手を大きくずらしたりすることなく操作対象装置を操作することができ、運転者がステアリングホイールを操作する際に支障となる可能性を大幅に低減させることができる。また、誤操作を大幅に低減させることができる。

【図面の簡単な説明】

【００１７】

【図１】本発明の車両における操作対象装置の制御装置の一実施形態を示すブロック図である。

【図２】一実施形態の操作対象装置の制御装置を備える車両の例を示す部分平面図である。

【図３】一実施形態におけるタッチセンサをステアリングホイールに装着する位置及び範囲の例を示す図である。

【図４】一実施形態におけるタッチセンサをステアリングホイールに装着する位置及び範囲の他の例を示す図である。
【図５】タッチセンサを変形ステアリングホイールに装着する例を示す図である。
【図６】ステアリングホイールにおけるタッチセンサの部分を握っている状態でセンサデータが得られる部分の例を示す部分斜視図である。
【図７】タッチセンサにおける断面周方向の座標を示す断面図である。
【図８】図６に示すタッチセンサを展開した状態を示す平面図である。
【図９】図８に示す各領域を均等の大きさに変換した状態を示す模式図である。
【図１０】ステアリングホイールにおけるタッチセンサの部分を握っていると判定するための要件の例を示す図である。
【図１１】タッチセンサに対する特定の入力操作の例を示す模式図である。
【図１２】タッチセンサに対する特定の入力操作の他の例を示す模式図である。
【図１３】タッチセンサに対する特定の入力操作のさらに他の例を示す模式図である。
【図１４】一実施形態の動作を説明するためのフローチャートである。
【図１５】ステアリングホイールの回転角度を説明するための図である。
【図１６】図１４のステップＳ４の具体的な処理の例を示すフローチャートである。
【図１７】タッチセンサを操作した際に色を変化させるための構成例を示す模式的な斜視図である。
【図１８】タッチセンサを操作した際に触覚を変化させるための構成例を示す模式的な斜視図である。
【図１９】ステアリングホイールの構成例を示す平面図である。
【発明を実施するための形態】
【００１８】
以下、本発明の車両における操作対象装置の制御装置及び制御方法の一実施形態について、添付図面を参照して説明する。図１，図２において、車載機器１００は、車両のダッシュボード内に装着されている。図１に示す例では、車載機器１００は、制御部１０，ナビゲーション処理部１１，オーディオ再生部１２，テレビジョン（ＴＶ）チューナ１３，映像信号処理部１４，映像表示部１５，音声信号処理部１６，表示素子１７，記憶部１８を備えている。制御部１０は検出部１０ａを含む。
【００１９】
ナビゲーション処理部１１は地図データを保持する記憶部とＧＰＳアンテナ等を有しており、制御部１０とナビゲーション処理部１１とが協同して経路案内を行う。オーディオ再生部１２は、制御部１０による制御に従って、例えばコンパクトディスク等の光ディスクや半導体メモリに記録されているオーディオ信号を再生する。ＴＶチューナ１３は、制御部１０による制御に従って、所定の放送局のＴＶ放送波信号を受信する。ナビゲーション処理部１１またはＴＶチューナ１３より出力された映像信号は、制御部１０を介して映像信号処理部１４に入力されて処理され、液晶パネル等の映像表示部１５に表示される。
【００２０】
ナビゲーション処理部１１，オーディオ再生部１２，ＴＶチューナ１３より出力された音声信号は、制御部１０を介して音声信号処理部１６に入力されて処理され、外部のスピーカ２０にて発音される。音声信号処理部１６は増幅部を含む。スピーカ２０は、車両のドアの内部等に設置されている。表示素子１７は例えば発光ダイオード（ＬＥＤ）であり、制御部１０による制御に従って、後述するタッチセンサ２１の接触状態に応じて点灯または消灯する。表示素子１７は、運転者から視認できるように、例えば車載機器１００の筐体に配置する。表示素子１７を車載機器１００から離して、車両のステアリングホイール２００の近傍に配置してもよい。記憶部１８は不揮発性のメモリである。
【００２１】
図２に示すように、操作部であるタッチセンサ２１は、ステアリングホイール２００の円環状部２００ｒに装着されている。円環状部２００ｒは、運転者が運転の際に握る部分である握持部である。図２に示す例では、タッチセンサ２１は、円環状部２００ｒにおけ

る左右それぞれの所定の角度範囲に装着されている。タッチセンサ２１は、複数箇所の接触を検出することができる、いわゆる多点検出（マルチタッチ）のタッチセンサである。タッチセンサ２１は、円環状部２００ｒの径方向の断面の周上に、３６０°の範囲で装着することが好ましい。３６０°未満の範囲であっても、実質的に円環状部２００ｒの断面の周のほぼ全体を覆っていればよい。

【００２２】

運転者は、円環状部２００ｒのタッチセンサ２１が装着された部分を握っている。図１において、タッチセンサ２１の出力はセンサデータ生成部２２に入力される。タッチセンサ２１を手で触ると、接触検出信号がセンサデータ生成部２２へと入力される。センサデータ生成部２２は、入力された接触検出信号に基づいて、タッチセンサ２１のどの位置から接触検出信号が得られたかを示す位置データを含むセンサデータを生成して制御部１０に供給する。タッチセンサ２１とセンサデータ生成部２２とを一体化してもよいし、センサデータ生成部２２を制御部１０内に設けてもよい。

【００２３】

タッチセンサ２１としては、例えば投影式静電容量（相互キャパシタンス）方式のタッチセンサを用いることができる。円環状部２００ｒに装着するタッチセンサ２１としては、一例として、ミクロ技術研究所が開発した可撓性を有するタッチパネルを採用することができる。この可撓性を有するタッチパネルは、センサ部を０．０２～０．０５ｍｍの板厚を有する超薄板ガラスとし、超薄板ガラスとＰＥＴ（ポリエチレンテレフタレート）フィルムとを貼り合わせた構造になっている。円環状部２００ｒにタッチセンサ２１を装着しても、タッチセンサ２１は手や指で知覚できるほどの凹凸を有さないので、運転者がステアリングホイール２００を操作する際に支障となることはほとんどない。

【００２４】

図２に破線にて示すように、タッチセンサ２１と車載機器１００とを結ぶ電線を、ステアリングホイール２００及びダッシュボードの内部を通して配線することが好ましい。

【００２５】

図１，図２において、ステアリング角センサ３１は、ステアリングホイール２００の回転角度を検出する。方向指示器センサ３２は、方向指示器３２０の操作を検出する。シフトレバーセンサ３３は、シフトレバー３３０によるシフト位置がどこにあるかを検出する。ステアリング角センサ３１，方向指示器センサ３２，シフトレバーセンサ３３の各検出信号は、車内通信部３４を介して制御部１０へと供給される。

【００２６】

図３を用いて、タッチセンサ２１をステアリングホイール２００の円環状部２００ｒに装着する位置及び範囲の例について説明する。なお、上、下、右、左とは、ステアリングホイール２００を回転させていない状態（車両が直進する状態）において、運転者の位置からステアリングホイール２００を見たときの上、下、右、左であるとする。図３（Ａ）は、円環状部２００ｒの全周にタッチセンサ２１を装着した例である。図３（Ｂ）は、図２と同様であり、円環状部２００ｒにおける上方で左右それぞれの所定の角度範囲にタッチセンサ２１を互いに離間させて装着した例である。図３（Ｃ）は、円環状部２００ｒにおける上方で右側のみの所定の角度範囲にタッチセンサ２１を装着した例である。

【００２７】

図３（Ｄ）は、円環状部２００ｒにおける下方で左右それぞれの所定の角度範囲にタッチセンサ２１を互いに離間させて装着した例である。図３（Ｅ）は、円環状部２００ｒにおける頂部を含む上方の比較的広い角度範囲にタッチセンサ２１を装着した例である。図３（Ｅ）は図３（Ｂ）における左右のタッチセンサ２１を連結したものに相当する。

【００２８】

図４は、図３（Ｂ）における左右のタッチセンサ２１を、上側のタッチセンサ２１ａと下側のタッチセンサ２１ｂとに分割した例である。図４の例では、上側のタッチセンサ２１ａは手の人差し指と親指による接触を検出し、下側のタッチセンサ２１ｂは主として手のひら，中指，薬指による接触を検出する。図５は、円形ではない変形ステアリングホイ

ール２０１にタッチセンサ２１を装着した例である。タッチセンサ２１は、変形ステアリングホイール２０１の左右の直線部２０１ｓに装着されている。運転者は握持部である直線部２０１ｓを握って運転し、タッチセンサ２１が手のひらや指による接触を検出する。

【００２９】

ここで、図２に示すように、タッチセンサ２１が円環状部２００ｒにおける上方で左右に装着されており、運転者がタッチセンサ２１の部分を握っている場合に、タッチセンサ２１によって手のひらや指の接触がどのように検出されるかについて説明する。図６は、図２の右側のタッチセンサ２１を運転者が握った場合に、手のひらと指が接触している範囲の例を示している。運転者が円環状部２００ｒを手で握る握り方、手の大きさは一様ではなく、図６は単なる例である。

【００３０】

図６に示す例では、ハッチングを付したＴｐで示す複数の検出領域Ｒが手のひらの接触を検出している部分であり、ハッチングを付したＴｔで示す複数の検出領域Ｒが親指の接触を検出している部分である。以下、手のひら接触検出部Ｔｐ、親指接触検出部Ｔｔと称することとする。図６では見えていない車両の進行方向側であるタッチセンサ２１の裏面側には、人差し指が接触する。

【００３１】

図６に示すように、タッチセンサ２１は手のひらや指の接触を検出する検出部分として複数の検出領域Ｒを有している。タッチセンサ２１の各検出領域Ｒには座標が設定されている。図６に示すように、円環状部２００ｒの周方向において、タッチセンサ２１の下端部に位置している検出領域Ｒを座標０とし、上端部に位置している検出領域Ｒまで１，２，…，３０，３１と周方向の座標を設定している。タッチセンサ２１における円環状部２００ｒの周方向の座標をＹ座標とする。

【００３２】

図７は、タッチセンサ２１を装着している部分で円環状部２００ｒの径方向に円環状部２００ｒを切断した断面図である。図７に示すように、円環状部２００ｒの断面において、例えば円環状部２００ｒの内径側に位置している検出領域Ｒを座標０とする。断面における周方向のそれぞれの検出領域Ｒに、円環状部２００ｒの内径側から正面側、正面側から外径側、外径側から裏面側、裏面側から内径側へと図７の反時計方向に１，２，…，２１，２２と座標を設定している。タッチセンサ２１における断面の周方向の座標をＸ座標とする。センサデータ生成部２２は、接触検出信号が得られた検出領域ＲのＸ座標，Ｙ座標によって運転者がタッチセンサ２１のどこを触っているかを示す位置データを得ることができる。

【００３３】

図６に示すタッチセンサ２１を展開すると、図８のようになる。図８に示すタッチセンサ２１の各領域を均等の大きさに変換した状態を模式的に示すと、図９のようになる。図８，図９においては、手のひら接触検出部Ｔｐと親指接触検出部Ｔｔに加えて、人差し指が接触している複数の検出領域Ｒである人差し指接触検出部Ｔｉも示している。なお、タッチセンサ２１に中指や薬指または小指が接触すれば、タッチセンサ２１はそれらの指の接触も検出する。本実施形態においては、運転者が、タッチセンサ２１上で特定の入力操作を行うのに好適な親指または人差し指を操作のための指として用いることとする。

【００３４】

親指または人差し指による入力操作の詳細については後に詳述することとする。制御部１０の検出部１０ａは、センサデータ生成部２２から出力されるセンサデータに基づいて、親指または人差し指によってタッチセンサ２１上で入力操作が行われたことを検出する。検出部１０ａは、センサデータ生成部２２から出力されるセンサデータに基づいて、円環状部２００ｒ（タッチセンサ２１）を握っていることも検出する。制御部１０は、タッチセンサ２１に対して行った特定の入力操作に応じて操作対象装置を制御する。

【００３５】

操作対象装置は一例として車載機器１００である。具体的には、制御部１０は、特定の

入力操作に応じて、ナビゲーション処理部１１における経路案内に関する制御を実行させたり、オーディオ再生部１２におけるオーディオ信号を再生または停止させたり、再生するトラック（楽曲）を進めたり戻したりすることができる。また、制御部１０は、特定の入力操作に応じて、ＴＶチューナ１３における受信チャンネルを切り換えたり、音声信号処理部１６の増幅部を制御して音量を減少または増加させたりすることができる。

【００３６】

操作対象装置の他の例は、車両の動作を制御する車両動作制御装置である。具体的には、制御部１０は、車内通信部３４を介して、変速機、方向指示器、エアーコンディショナのオン・オフ、エアーコンディショナの設定温度等を制御してもよい。なお、操作対象装置を車両動作制御装置とする場合には、センサデータ生成部２２から出力されるセンサデータを車両が有する制御部に入力して、車両動作制御装置を制御することが好ましい。操作対象装置を制御する制御部は、車載機器１００内の制御部１０であってもよいし、車両に備えられている車載機器１００外部の制御部であってもよい。

【００３７】

本実施形態によれば、運転者が握る円環状部２００ｒに極めて薄いタッチセンサ２１を装着して、タッチセンサ２１を操作することによって操作対象装置を操作するので、円環状部２００ｒから手を離したり、手を大きくずらしたりすることなく操作対象装置を操作することができる。また、タッチセンサ２１は円環状部２００ｒの表面上で凹凸がないため、運転者がステアリングホイール２００を操作する際に支障となる可能性はほとんどない。

【００３８】

ところで、運転者が通常の運転のために円環状部２００ｒを握っている場合のように、操作対象装置を操作しようとする意思がない場合に、不用意に操作対象装置が操作されないようにすることが必要となる。そこで、本実施形態においては、運転者が意図しない誤操作を回避するために、次のようにしている。

【００３９】

図８，図９に示すように、タッチセンサ２１上の複数の検出領域Ｒに、手のひらの接触を検出するためのグリップ検出エリアＡｒｇと、親指または人差し指による操作入力を有効として、操作入力を検出するための操作検出エリアＡｒｖと、グリップ検出エリアＡｒｇと操作検出エリアＡｒｖとの間の中間領域であり、操作入力を無効とする操作無効エリアＡｒivとを設定している。手のひら接触検出部Ｔｐはグリップ検出エリアＡｒｇ内に位置し、親指接触検出部Ｔｔ及び人差し指接触検出部Ｔｉは操作検出エリアＡｒｖ内に位置する。

【００４０】

操作無効エリアＡｒivは、グリップ検出エリアＡｒｇと操作検出エリアＡｒｖと同様に、手のひらまたは指の接触を検出する検出領域Ｒを有するものの、制御部１０（検出部１０ａ）またはセンサデータ生成部２２が操作無効エリアＡｒivからの入力操作を無効とするように処理することによって、操作無効エリアとすることができる。また、操作無効エリアＡｒivの範囲に検出領域Ｒを設けないようにタッチセンサ２１を構成することにより、操作無効エリアとしてもよい。この場合、図４に示す例と実質的に等価である。

【００４１】

運転者が通常の運転のために円環状部２００ｒを握っている場合には、手のひら接触検出部Ｔｐと親指接触検出部Ｔｔ及び人差し指接触検出部Ｔｉとは比較的近い位置となる。そこで、運転者が単に円環状部２００ｒを握っている場合と、操作対象装置を操作しようとしてタッチセンサ２１を触った場合とを的確に区別するために、本実施形態においては、操作無効エリアＡｒivを設けている。運転者は、操作対象装置を操作しようとする場合には、親指や人差し指を意図的に伸ばしてタッチセンサ２１を触って、後述する特定の入力操作を行うようにする。制御部１０は、操作検出エリアＡｒｖ内で後述する特定の入力操作が行われた場合に、入力操作に応じて操作対象装置を制御する。

【００４２】

運転者が運転のために円環状部２００ｒを握っていない状態で、操作検出エリアＡｒｖに不用意に触った場合に、操作対象装置が誤操作されることを回避することも必要である。そこで、本実施形態においては、検出部１０ａは、グリップ検出エリアＡｒｇで所定の面積以上の手のひら接触検出部Ｔｐが得られた場合に、円環状部２００ｒを握っていると判断する。制御部１０は、円環状部２００ｒを握っており、かつ、操作検出エリアＡｒｖ内で特定の操作が行われた場合に操作対象装置を制御するように構成している。円環状部２００ｒを握っていると判断する手のひら接触検出部Ｔｐの面積は、複数の運転者がステアリングホイール２００を通常の握り方で握った場合の面積を統計的に調べて、適宜に設定すればよい。

【００４３】

グリップ検出エリアＡｒｇにおける手のひら接触検出部Ｔｐの面積は、運転者が円環状部２００ｒを握っていると判定するための要件の一例であり、判定するための要件これに限定されるものではない。図１０は、タッチセンサ２１のグリップ検出エリアＡｒｇの部分で円環状部２００ｒを切断した断面を示している。検出部１０ａは、手のひら接触検出部Ｔｐの断面周方向の角度θが所定の角度以上のときに円環状部２００ｒを握っていると判断することができる。所定の角度は例えば１８０°である。

【００４４】

以上のように、本実施形態においては、運転者が円環状部２００ｒ（タッチセンサ２１）を握っているか否かを判定して、円環状部２００ｒを握っている場合のみタッチセンサ２１に対する操作入力を受け付けるようにしているので、操作検出エリアＡｒｖに不用意に触った場合の誤操作を回避することができる。本実施形態においては、好ましい構成として、操作検出エリアＡｒｖをグリップ検出エリアＡｒｇから所定の距離離間させた位置に設けているので、運転者が意図的にタッチセンサ２１に対して特定の入力操作を行っていることを的確に検出することができる。従って、誤操作を大幅に低減させることができる。

【００４５】

また、本実施形態においては、グリップ検出エリアＡｒｇにおける手のひら接触検出部Ｔｐの面積や断面周方向の角度θを、運転者が円環状部２００ｒを握っているか否かを判定する要件としているので、円環状部２００ｒを握っているか否かを的確に判定することができる。従って、運転者が円環状部２００ｒを握っていない状態で、操作検出エリアＡｒｖに不用意に触った場合の誤操作も回避することができる。

【００４６】

制御部１０は、検出部１０ａが、グリップ検出エリアＡｒｇからの接触検出信号に基づくセンサデータによって運転者が円環状部２００ｒ（タッチセンサ２１）を握っていることを検出した場合に、運転者に、操作検出エリアＡｒｖによる操作入力が可能であることを知らせるために、表示素子１７を点灯させる。運転者は、表示素子１７の点灯・消灯によって、タッチセンサ２１によって操作対象装置を操作することができるか否かを判断することができる。表示素子１７をステアリングホイール２００の近傍に配置する方が好ましい。

【００４７】

ところで、図３（Ａ）のように円環状部２００ｒの全周にタッチセンサ２１を装着したり、図３（Ｅ）のように比較的広い範囲にタッチセンサ２１を装着したりした場合には、運転者がタッチセンサ２１を握る位置は固定されない。そこで、図８及び図９で説明したグリップ検出エリアＡｒｇと操作検出エリアＡｒｖや、必要に応じて設ける操作無効エリアＡｒivの位置は、運転者がタッチセンサ２１を握った位置に応じて動的に設定する必要がある。

【００４８】

そこで、制御部１０は、グリップ検出エリアＡｒｇ等が未設定の状態でタッチセンサ２１が握られた場合には、手のひら接触検出部Ｔｐを含む領域をグリップ検出エリアＡｒｇに設定する。手のひら接触検出部Ｔｐを含むＹ座標の所定の範囲をグリップ検出エリアＡ

ｒｇとすればよい。前述のように、手のひら接触検出部Ｔｐは所定の面積以上となるので、タッチセンサ２１上の複数の検出領域Ｒにおいて所定の面積以上触られていることが検出された部分が手のひら接触検出部Ｔｐとなる。または、図１０で説明したように、タッチセンサ２１の部分で円環状部２００ｒを切断した断面周方向で、所定の角度以上触られていることが検出された部分が手のひら接触検出部Ｔｐとなる。

【００４９】

制御部１０は、グリップ検出エリアＡｒｇを設定したら、グリップ検出エリアＡｒｇよりも上側のＹ座標の所定の範囲を操作検出エリアＡｒｖと設定する。この場合、必要に応じて、グリップ検出エリアＡｒｇと隣接するＹ座標の所定の範囲を操作無効エリアＡｒivとして設定し、グリップ検出エリアＡｒｇをグリップ検出エリアＡｒｇから離間させた位置とする。

【００５０】

次に、図１１～図１３を用いて、運転者が親指または人差し指を用いてタッチセンサ２１に対して行う特定の入力操作の例を説明する。図１１（Ａ）～（Ｅ）は、タッチセンサ２１の運転者と対向する正面側または裏面側である半分を模式的な平面で示している。図１１（Ａ）～（Ｅ）に示す操作は、正面側であれ親指で、裏面側であれば人差し指で行われることになる。図１１（Ａ）において、D_Rは、親指または人差し指をタッチセンサ２１（操作検出エリアＡｒｖ）上で右方向に滑らせる右方向ドラッグであり、D_Lは親指または人差し指を右方向に滑らせる左方向ドラッグである。D_Uは親指または人差し指を上方向に滑らせる上方向ドラッグであり、D_Dは親指または人差し指をした方向に滑らせる下方向ドラッグである。

【００５１】

図１１（Ａ）において、右方向ドラッグD_R，左方向ドラッグD_L，上方向ドラッグD_U，下方向ドラッグD_Dの代わりに、親指または人差し指でそれぞれの方向にタッチセンサ２１をはじくフリックとしてもよい。

【００５２】

図１１（Ｂ）は、親指または人差し指でタッチセンサ２１をたたくタップＴを示している。図１１（Ｃ）は、親指または人差し指でタッチセンサ２１上に円弧を描くようにドラッグする円弧ドラッグD_Cを示している。図１１（Ｄ）は、親指または人差し指でタッチセンサ２１上にジグザグ状にドラッグするジグザグドラッグD_Zを示している。図１１（Ｅ）は、親指または人差し指で記号を書くようにドラッグする記号入力ドラッグD_Sを示している。図１１（Ｅ）は記号として数字の３を描いた状態を示している。記号としては、認識が比較的容易な数字やアルファベットを用いることが好ましい。

【００５３】

図１２（Ａ）～（Ｄ）は、タッチセンサ２１を開いてタッチセンサ２１の正面側の半分である正面部２１ｆと裏面側の半分である裏面部２１ｒとを模式的な平面で示している。正面部２１ｆは、図８，図９に示すＸ座標の０～１１の部分であり、裏面部２１ｒは、Ｘ座標の１２～２２の部分である。図８，図９に示す例では、厳密には正面部２１ｆと裏面部２１ｒとは均等の面積にはならないが、図１２（Ａ）～（Ｄ）では正面部２１ｆと裏面部２１ｒとを同じ面積で示している。図１２（Ａ）～（Ｄ）は理解を容易にするため、裏面部２１ｒは、裏面部２１ｒを円環状部２００ｒの裏面側から見た状態ではなく、正面部２１ｆから裏面部２１ｒを透視した状態を示している。

【００５４】

図１２（Ａ）～（Ｄ）に示すように、正面部２１ｆに対する親指による入力操作と裏面部２１ｒに対する人差し指による入力操作とを組み合わせたパターンをタッチセンサ２１に対する特定の入力操作としてもよい。図１２（Ａ）は、正面部２１ｆで親指を右方向に滑らせる右方向ドラッグD_{TR}と、裏面部２１ｒで人差し指を右方向に滑らせる右方向ドラッグD_{IR}との双方を行う例である。親指及び人差し指の双方を円環状部２００ｒの内周側から外周側へとドラッグすることにより、図１２（Ａ）が実現される。親指と人差し指の双方を、図１２（Ａ）とは逆方向にドラッグするパターンとしてもよい。

【００５５】
図１２（Ｂ）は、正面部２１ｆで親指を左方向に滑らせる左方向ドラッグD_{TL}と、裏面部２１ｒで人差し指を右方向に滑らせる右方向ドラッグD_{IR}との双方を行う例である。親指を円環状部２００ｒの外周側から内周側へとドラッグし、人差し指を円環状部２００ｒの内周側から外周側へとドラッグすることにより、図１２（Ｂ）が実現される。図１２（Ｃ）は、正面部２１ｆで親指を右方向に滑らせる右方向ドラッグD_{TR}と、裏面部２１ｒで人差し指を左方向に滑らせる左方向ドラッグD_{IL}との双方を行う例である。親指を円環状部２００ｒの内周側から外周側へとドラッグし、人差し指を円環状部２００ｒの外周側から内周側へとドラッグすることにより、図１２（Ｃ）が実現される。
【００５６】
図１２（Ｄ）は、正面部２１ｆで親指を上方向に滑らせる上方向ドラッグD_{TU}と、裏面部２１ｒで人差し指を下方向に滑らせる下方向ドラッグD_{ID}との双方を行う例である。親指を下方向、人差し指を上方向にドラッグとするパターンとしてもよく、親指と人差し指の双方を上方向または下方向にドラッグするパターンとしてもよい。ここでは、正面部２１ｆに対する親指による入力操作と裏面部２１ｒに対する人差し指による入力操作とを組み合わせた種々のパターンを示したが、入力操作のしやすさを考慮して適宜選択すればよい。
【００５７】
図１２（Ａ）～（Ｄ）に示すように、親指による入力操作と人差し指による入力操作とを組み合わせたパターンを、操作対象装置を制御するための特定の入力操作とすれば、さらに大幅に誤操作を低減させることが可能となる。
【００５８】
さらには、図３（Ａ），（Ｂ），（Ｄ），（Ｅ）や図４，図５のように、左右の手でタッチセンサ２１（２１ａ，２１ｂ）を操作できる場合に、左右の手による操作を組み合わせたパターンを、操作対象装置を制御するための特定の入力操作とすることも可能である。図１３（Ａ）～（Ｄ）は、図３（Ｂ）における左側のタッチセンサ２１を左側タッチセンサ２１Ｌとし、右側のタッチセンサ２１を右側タッチセンサ２１Ｒとした場合の、左右の手による操作を組み合わせたパターンの例を示している。ここでは、親指によって操作する図１２の正面部２１ｆに相当する面を模式的な平面で示している。
【００５９】
図１３（Ａ）は、左側タッチセンサ２１Ｌに対して親指を左方向に滑らせる左方向ドラッグD_{TL}と、右側タッチセンサ２１Ｒに対して親指を右方向に滑らせる右方向ドラッグD_{TR}とを組み合わせたパターンである。図１３（Ｂ）は、左側タッチセンサ２１Ｌに対して親指を右方向に滑らせる右方向ドラッグD_{TR}と、右側タッチセンサ２１Ｒに対して親指を左方向に滑らせる左方向ドラッグD_{TL}とを組み合わせたパターンである。
【００６０】
図１３（Ｃ）は、左側タッチセンサ２１Ｌと右側タッチセンサ２１Ｒの双方に対して、親指を上方向に滑らせる上方向ドラッグD_{TU}を組み合わせたパターンである。図１３（Ｄ）は、左側タッチセンサ２１Ｌと右側タッチセンサ２１Ｒの双方に対して、親指を下方向に滑らせる下方向ドラッグD_{TD}を組み合わせたパターンである。
【００６１】
左右の手による入力操作を組み合わせたパターンを、操作対象装置を制御するための特定の入力操作とすれば、運転者は円環状部２００ｒを両手で握ることになるので、安全運転に寄与することが可能である。特に、図３（Ｂ）の例は、円環状部２００ｒを両手で握る最も適切な位置にタッチセンサ２１を装着しているので、安全運転に寄与する点で最も好ましい。両手で左右のタッチセンサ２１を握っている場合に入力操作を受け付けるようにしてもよい。片手がタッチセンサ２１から離れた場合に入力操作を受け付けない状態としてもよい。片手がタッチセンサ２１から離れた場合には入力操作を受け付ける状態を継続してもよい。片手のみの特定の入力操作を用いる場合であっても、両手で左右のタッチセンサ２１を握っている場合に入力操作を受け付けるようにすれば、安全運転に寄与する

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【００６２】

運転者が通常の運転のために円環状部２００ｒを握っていて、操作対象装置を操作しようとする意思がない場合に、偶然に、親指による入力操作と人差し指による入力操作とを組み合わせた特定のパターンや、左右の手による入力操作を組み合わせた特定のパターンになってしまう可能性は比較的低いと考えられる。そこで、親指による入力操作と人差し指による入力操作とを組み合わせた特定のパターンや、左右の手による入力操作を組み合わせた特定のパターンのみを用いる場合には、上述した誤操作を回避するための工夫の一部または全てを省略してもよい。勿論、左右の手による入力操作を組み合わせた特定のパターンのみを用いる場合であっても、上述した誤操作を回避するための工夫を併せて採用することが好ましい。

【００６３】

記憶部１８は、以上説明した特定の入力操作または特定の入力操作を組み合わせたパターンと、操作対象装置に対する制御の種別とを対応させたテーブルを記憶している。制御部１０は、記憶部１８に記憶されたテーブルに従って、タッチセンサ２１に入力された操作に応じて操作対象装置を制御する。記憶部１８を制御部１０内に設けてもよい。

【００６４】

図１４のフローチャートを用いて、本実施形態において制御部１０で実行される処理について改めて説明する。図１３において、制御部１０は、ステップＳ１にて、センサデータ生成部２２から出力されるセンサデータを取得する。制御部１０は、ステップＳ２にて、検出部１０ａによる検出出力に基づいて、円環状部２００ｒが握られているか否かを判定する。円環状部２００ｒが握られていると判定されれば（YES）、制御部１０は、ステップＳ３に処理を移し、円環状部２００ｒが握られていると判定されなければ（NO）、制御部１０は、ステップＳ１に処理を戻す。

【００６５】

制御部１０は、ステップＳ３にて、検出部１０ａによる検出出力に基づいて、入力操作があったか否かを判定する。入力操作があったと判定されれば（YES）、制御部１０は、ステップＳ４に処理を移し、操作入力があったと判定されなければ（NO）、制御部１０は、ステップＳ１に処理を戻す。制御部１０は、ステップＳ４にて、ステップＳ３における入力操作によって操作対象装置に対する操作を許可するか否かを判定する。操作を許可すると判定されれば（YES）、制御部１０は、ステップＳ５に処理を移し、操作を許可すると判定されなければ（NO）、制御部１０は、ステップＳ１に処理を戻す。

【００６６】

上述のように、制御部１０は、操作検出エリアＡｒｖ内で特定の入力操作がなされた場合に操作対象装置に対する操作を許可し、操作無効エリアＡｒiv内で特定の入力操作がなされたとしても操作対象装置に対する操作を許可しない。また、制御部１０は、操作検出エリアＡｒｖ内で何らかの入力操作がなされたとしても、上述した特定の入力操作でない場合は操作対象装置に対する操作を許可せず、特定の入力操作がなされた場合のみ操作対象装置に対する操作を許可する。

【００６７】

制御部１０は、ステップＳ５にて、入力操作に基づいた操作を確定し、ステップＳ６にて、操作対象装置に対して、確定した操作に応じた制御を実行して、ステップＳ１に処理を戻す。

【００６８】

また、ステップＳ４では、車両が特定の状態にあるときに、操作対象装置に対する制御を許可しないようにする（即ち、無効にする）ことが好ましい。制御部１０には、操作対象装置に対する制御を許可するか否かを判断するためのステアリングホイール２００の回転角度が設定されている。図１５に示すように、ステアリングホイール２００を回転させていない状態を回転角度０°とし、例えば右方向に回転させたときをプラス、左方向に回転させたときをマイナスとして、一例として回転角度±３０°の範囲でタッチセンサ２１

に対する入力操作を有効として許可し、回転角度が±３０°を超えたらタッチセンサ２１に対する入力操作を無効として不許可とする。

【００６９】

回転角度が±３０°を超えた場合には、車両は右折または左折をしていたり、コーナリング走行していたりする特定の状態である。このような特定の状態で操作対象装置を制御しようとすれば誤操作が発生する可能性が高い。言い換えれば、このような特定の状態における操作入力は、ユーザの意図していない操作入力である可能性が高い。また安全性の上でも好ましくない。そこで、本実施形態では、車両が特定の状態にあるときには、操作対象装置に対する制御を無効とする。

【００７０】

前述のように、制御部１０にはステアリング角センサ３１によって検出されたステアリングホイール２００の回転角度が入力される。制御部１０は、ステアリング角センサ３１によって検出されたステアリングホイール２００の回転角度に応じて、タッチセンサ２１に対する入力操作を有効とする状態と無効とする状態とを切り換える。制御部１０には方向指示器センサ３２からの検出信号も入力される。そこで、制御部１０は、方向指示器センサ３２からの検出信号によって方向指示器３２０が操作された場合に、タッチセンサ２１に対する入力操作を無効としてもよい。方向指示器３２０が操作された場合は、ステアリングホイール２００が所定の回転角度を超えて回転される特定の状態になるとみなすことができる。なお、方向指示器３２０が右折または左折の合図以外の操作を兼用している場合があるが、ここでの方向指示器３２０の操作とは右折または左折の合図を行う操作である。

【００７１】

さらに、車両を後退させている最中にタッチセンサ２１に対して特定の入力操作を行って操作対象装置を制御することは好ましくない。誤操作が発生する可能性が高く、安全性の上でも好ましくない。そこで、制御部１０は、シフトレバーセンサ３３からの検出信号によって、シフトレバー３３０のシフト位置がリバースとなった場合にも、タッチセンサ２１に対する入力操作を無効とすることが好ましい。ステアリングホイール２００の回転角度が例えば±３０°の所定角度を超えた場合、または、方向指示器３２０が操作された場合に加えて、シフトレバー３３０のシフト位置がリバースとなった場合に操作対象装置に対する制御を無効とすることが好ましいが、一方のみとしてもよい。

【００７２】

なお、操作対象装置に対する制御を無効にするとは、仮に上述した特定の入力操作がなされたとしても特定の入力操作を無効として操作対象装置に対する制御を不許可とすることであってもよく、制御部１０に対してセンサデータ生成部２２から何らかのセンサデータが入力されても、制御部１０がセンサデータを無効することであってもよい。結果として、操作対象装置に対する制御を無効とすればよい。

【００７３】

図１６のフローチャートを用いて、図１４のステップＳ４の具体的な処理の例を説明する。図１６において、制御部１０は、ステップＳ４１にて、シフトレバー３３０のシフト位置がリバースであるか否かを判定する。シフト位置がリバースであれば（YES）、制御部１０は、ステップＳ４５にて、ステップＳ３での入力操作を不許可として、図１４のステップＳ１に移行させる。シフト位置がリバースでなければ（NO）、制御部１０は、ステップＳ４２にて、方向指示器３２０が操作されたか否かを判定する。方向指示器３２０が操作されたら（YES）、制御部１０は、ステップＳ４５にて、ステップＳ３での入力操作を不許可として、図１４のステップＳ１に移行させる。

【００７４】

方向指示器３２０が操作されなかったら（NO）、制御部１０は、ステップＳ４３にて、ステアリングホイール２００の回転角度が所定角度を超えたか否かを判定する。ステアリングホイール２００の回転角度が所定角度を超えたら（YES）、制御部１０は、ステップＳ４５にて、ステップＳ３での入力操作を不許可として、図１４のステップＳ１に移行さ

せる。ステアリングホイール２００の回転角度が所定角度を超えていなかったら（NO）、制御部１０は、ステップＳ４４にて、操作検出エリアＡｒｖ内で特定の入力操作がなされたか否かを判定する。特定の入力操作がなされなかったら（NO）、制御部１０は、ステップＳ４５にて、ステップＳ３での入力操作を不許可として、図１４のステップＳ１に移行させる。ステップＳ４５にて、入力操作を不許可とすれば、操作対象装置に対する制御が無効となる。特定の入力操作がなされたら（YES）、制御部１０は、ステップＳ４６にて、ステップＳ３での入力操作を許可して、図１４のステップＳ５に移行させる。

【００７５】

図１６に示す例では、ステップＳ４１，Ｓ４２，Ｓ４３の全てを設けたが、これらのステップの内の１つまたは２つのみとしてもよい。また、ステップＳ４１，Ｓ４２，Ｓ４３の全てまたはこれらのステップの内の２つを設ける場合、順番は任意である。なお、ここではシフトレバー３３０と称したが、車両の直進と後退の切り換え、変速機の変速比を変える操作部の形状は任意であり、フロアシフト，コラムシフト，パドルシフト等のいずれでもよい。これらは全てシフトレバーに含まれる。

【００７６】

以上のように、車両が右折，左折，コーナリング走行，後退等の特定の状態にあるときに、操作対象装置に対する制御を無効とすれば、運転者はこれらの特定の状態のときにタッチセンサ２１に対する入力操作を行わない。従って、安全性の向上に寄与する。

【００７７】

本実施形態による動作をまとめると、次の通りである。検出部１０ａ（第１の検出部）は、ステアリングホイール２００，２０１における運転者が握る握持部（円環状部２００ｒまたは直線部２０１ｓ）に装着されたタッチセンサ２１における第１のエリアが触られている状態であることを検出する。第１のエリアの例は、グリップ検出エリアＡｒｇである。検出部１０ａ（第２の検出部）は、第１のエリアが触られている状態で、タッチセンサ２１における第１のエリアよりも上側に位置する第２のエリアに対して特定の入力操作がなされたことを検出する。第２のエリアの例は、操作検出エリアＡｒｖである。運転時、親指または人差し指は手のひらよりも上方に位置するので、第１のエリアよりも上側を第２のエリアとすればよい。そして、第１のエリアが触られている状態であり、特定の入力操作がなされたら、タッチセンサ２１によって操作する対象の操作対象装置を特定の入力操作に応じて制御する。

【００７８】

上側に位置するエリアとは、ステアリングホイール２００を回転させていない状態で運転者が握持部を握った状態で、第１のエリアよりも上側に位置するエリアである。第１のエリアが所定の面積以上触られていることを検出した場合に、第１のエリアが触られている状態であるとすることが好ましい。

【００７９】

また、別の観点では、次の通りである。検出部１０ａ（第１の検出部）は、ステアリングホイール２００，２０１における運転者が握る握持部（円環状部２００ｒまたは直線部２０１ｓ）の所定の範囲に、握持部を覆うように装着されたタッチセンサ２１が、タッチセンサ２１上の第１のエリアにおいて、握持部をステアリングホイール２００，２０１の径方向に切断したときの断面における周方向の所定角度以上触られている状態であることを検出する。検出部１０ａ（第２の検出部）は、第１のエリアが所定角度以上触られている状態で、タッチセンサ２１における第１のエリアとは異なる第２のエリアに対して特定の入力操作がなされたことを検出する。第１のエリアが前記所定角度以上触られている状態であり、特定の入力操作がなされたら、タッチセンサ２１によって操作する対象の操作対象装置を特定の入力操作に応じて制御する。

【００８０】

第２のエリアは、第１のエリアよりも上側に位置するエリアであることが好ましい。上側に位置するエリアとは、ステアリングホイール２００を回転させていない状態で運転者が握持部を握った状態で、第１のエリアよりも上側に位置するエリアである。

【００８１】
図１７及び図１８は、タッチセンサ２１を操作したことを運転者に効果的に知らせるための構成例を示している。図１７及び図１８は、図９と同様、タッチセンサ２１を展開して矩形状に変換した模式図である。図１７は、タッチセンサ２１の下面側に発色物質を含む色変化シート４１を設けた例である。タッチセンサ２１に透明導電膜を用いることにより、運転者は、タッチセンサ２１を介して、タッチセンサ２１の下面に配置されている色変化シート４１の色を見ることができる。制御部１０による制御によって、タッチセンサ２１を触った部分の色変化シート４１の色を変化させることにより、運転者はタッチセンサ２１を操作したことを認識することができる。
【００８２】
図１８は、タッチセンサ２１の上面側に触覚（手触り）を変化させる触覚フィードバックシート４２を設けた例である。触覚フィードバックシート４２としては、例えば、フィンランドのSenseg社が開発した“E-Sense”と称されるシートを採用することができる。このシートは、フィルムを帯電させることで触覚のフィードバックを実現するものである。タッチセンサ２１の上面側に触覚フィードバックシート４２を設けても、タッチセンサ２１は指等の接触を検出することが可能である。触覚フィードバックシート４２を介してタッチセンサ２１を操作した場合に、制御部１０による制御によって、触覚フィードバックシート４２の触覚を変化させることにより、運転者はタッチセンサ２１を操作したことを認識することができる。
【００８３】
次に、図１９を用いてステアリングホイールの構成例について説明する。図１９に示すステアリングホイール２１０は、操作対象装置に対する制御信号をステアリングホイール２１０から出力させるように構成したものである。図１９において、図１，図２と同一部分には同一符号を付し、その説明を適宜省略する。図１９に示すように、ステアリングホイール２１０は、例えば円環状部２００ｒ以外の部分に、図１のセンサデータ生成部２２と同様のセンダデータ生成部２３と、制御部１０と同様の制御部２４を備えている。制御部２４は、検出部１０ａと同様の検出部２４ａと、制御信号発生部２４ｂを有する。
【００８４】
ステアリングホイール２１０を車両に装着した場合、制御信号発生部２４ｂは、タッチセンサ２１に対する特定の入力操作に応じて、操作対象装置を制御するための制御信号を発生する。制御信号発生部２４ｂより出力された制御信号はケーブル２５を介して出力端子２６へと出力される。出力端子２６を操作対象装置に接続すれば、制御信号によって操作対象装置を制御することが可能となる。特定の入力操作の例は図１１～図１３と同様である。制御信号発生部２４ｂが制御信号を発生する要件も上述と同様である。
【００８５】
本発明は以上説明した本実施形態に限定されるものではなく、本発明の要旨を逸脱しない範囲において種々変更可能である。タッチセンサ２１を、面ファスナを用いて円環状部２００ｒに着脱自在に装着するようにしてもよい。円環状部２００ｒを握持部としたが、握持部は必ずしも円環状でなくてもよい。
【００８６】
タッチセンサ２１は１枚のシートによって構成する必要はなく、複数のタッチセンサの片によってタッチセンサ２１を構成してもよい。複数のタッチセンサの片によってタッチセンサ２１を構成すれば、一つ一つのタッチセンサの片の形状を簡単な形にすることができるため、タッチセンサを生産する際に有利である。なお、複数のタッチセンサの片によってタッチセンサ２１を構成する場合、必ずしもタッチセンサの片を隙間なく配置しなくてもよい。本実施形態のタッチパネル２１は、握持部を覆うように装着されているが、本実施形態における、握持部を覆うように装着されているということは、複数のタッチセンサの片からなるタッチセンサ２１が、タッチセンサの片と片との間に隙間がある状態で、握持部を覆うように装着されていることも含むものとする。
【００８７】

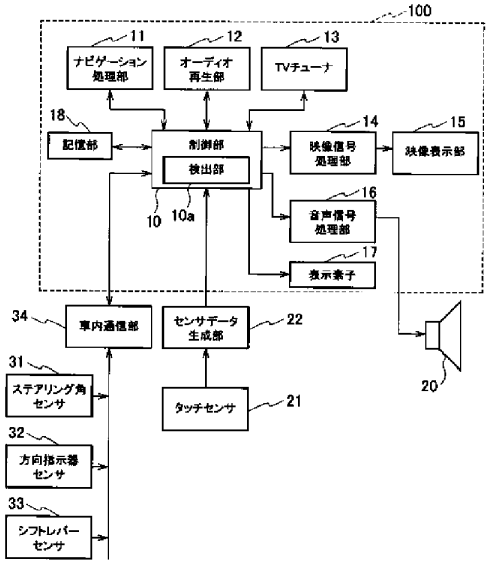
さらには、タッチセンサ２１を設ける範囲を、運転者が運転時に握る握持部（円環状部２００ｒまたは直線部２０１ｓ）に限定せず、例えばエアバッグ等が収納されるセンター部と円環状部２００ｒとの間を連結する連結部の表面まで広げてもよい。連結部は、図２においては、図2に示す状態で左右の手の間に位置する部分であり、図１９においては、センサデータ生成部２３及び制御部２４が設けられている部分である。このようにタッチセンサ２１を連結部の表面まで広げて、連結部における握持部に近い位置に操作検出エリアＡｒｖを設定してもよい。握持部に近い位置であれば、運転者が運転時に握持部から手を離したり、手を大きくずらしたりすることなく操作対象装置を操作することができる。よって、タッチセンサ２１を連結部の表面まで広げた構成としても、運転者がステアリングホイール２００，２０１，２１０を操作する際に支障となる可能性はほとんどない。

【符号の説明】

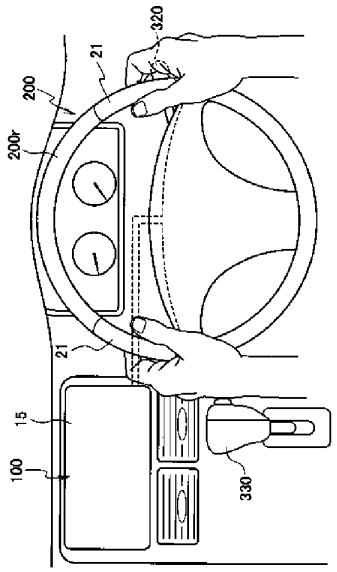
【００８８】

１０，２４　制御部
１０ａ，２４ａ　検出部
１１　ナビゲーション処理部
１２　オーディオ再生部
１３　テレビジョンチューナ
１４　映像信号処理部
１５　映像表示部
１６　音声信号処理部
１７　表示素子
１８　記憶部
２０　スピーカ
２１　タッチセンサ
２２，２３　センサデータ生成部
２４ｂ　制御信号発生部
２５　ケーブル
２６　出力端子
３１　ステアリング角センサ
３２　方向指示器センサ
３３　シフトレバーセンサ
３４　車内通信部
２００，２０１，２１０　ステアリングホイール
２００ｒ　円環状部（握持部）
２０１ｓ　直線部（握持部）

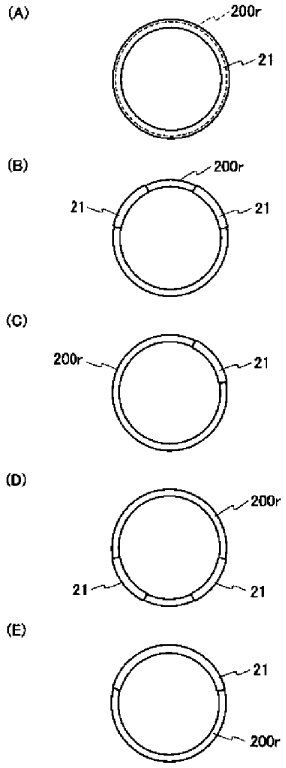
【図１】


100
11
ナビゲーション処理部
12
オーディオ再生部
13
TVチューナ
18
記憶部
制御部
検出部
14
映像信号処理部
15
映像表示部
10
10a
16
音声信号処理部
17
表示素子
20
34
車内通信部
センサデータ生成部
22
31
ステアリング角センサ
タッチセンサ
21
32
方向指示器センサ
33
シフトレバーセンサ

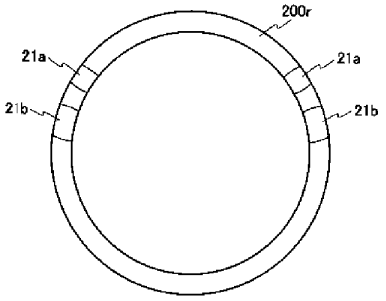
【図２】


320
21
200
200r
21
15
100
330

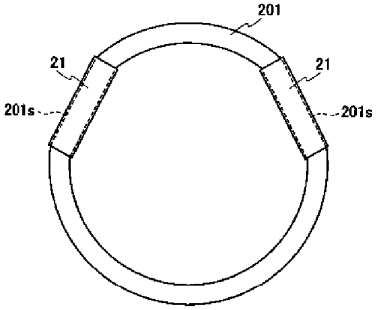
【図３】


(A)
200r
21
(B)
200r
21
21
(C)
200r
21
(D)
200r
21
21
(E)
21
200r

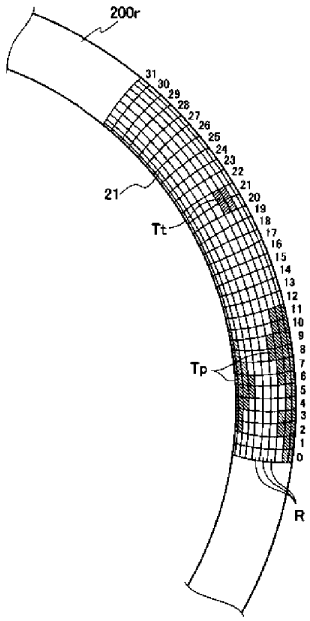
【図４】


200r
21a
21a
21b
21b

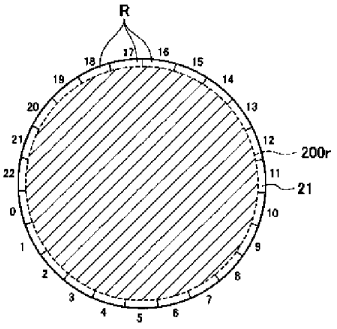
【図５】


201
21
21
201s
201s

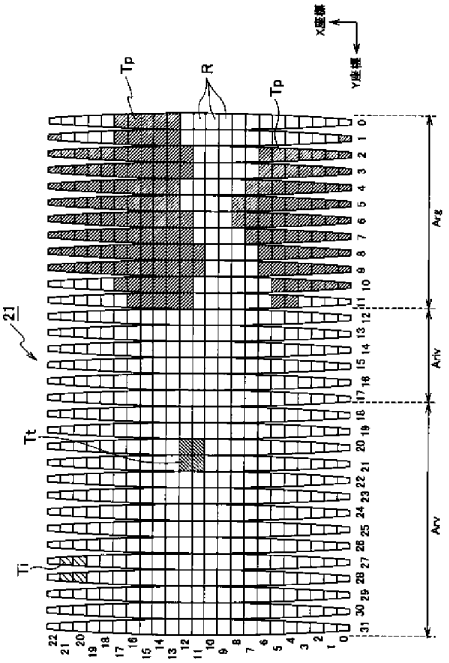
【図６】


200r
21
Tt
Tp
R

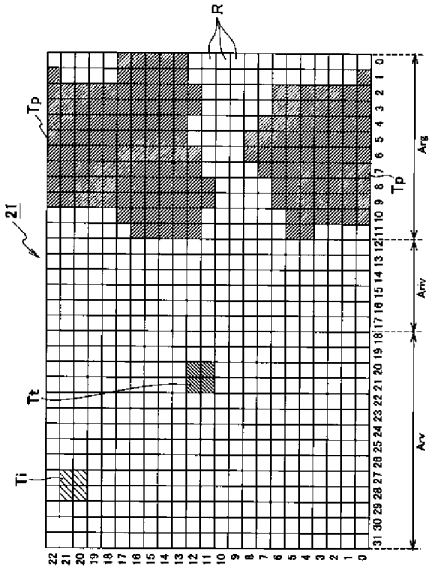
【図７】


R
200r
21

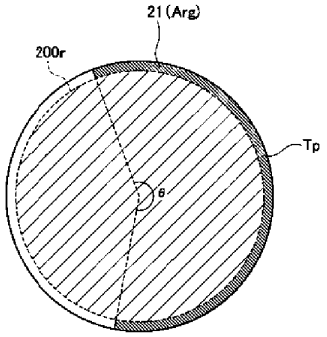
【図８】


X座標
Y座標
Tp
R
Tp
21
Tt
Ti
Arg
Arv
Arv

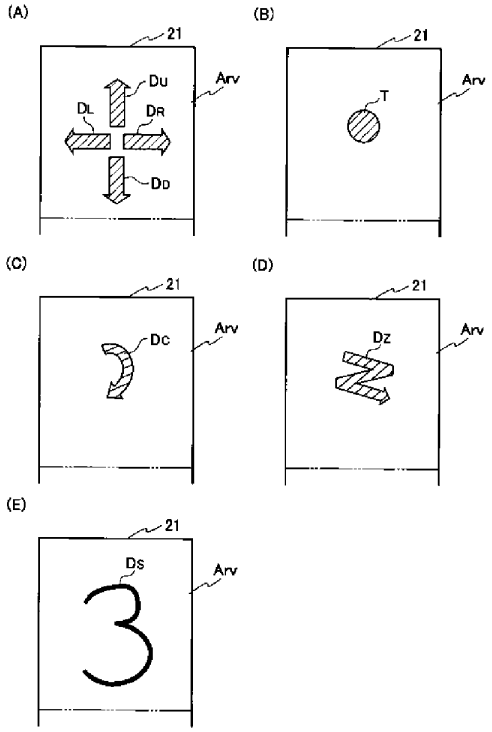
【図９】


R
Tp
21
Tt
Ti
Tp
Arg
Arv
Arv

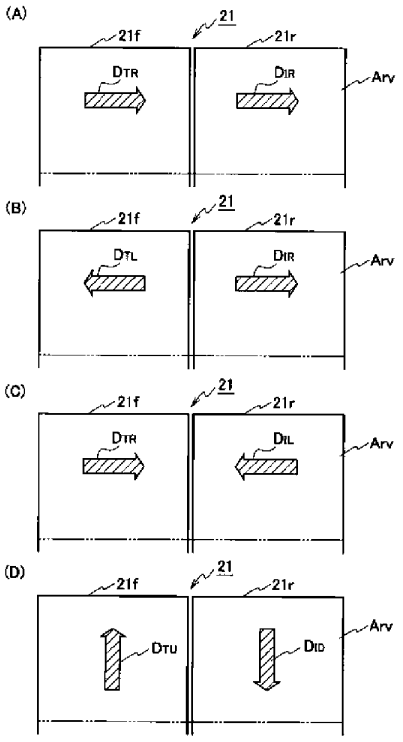
【図１０】



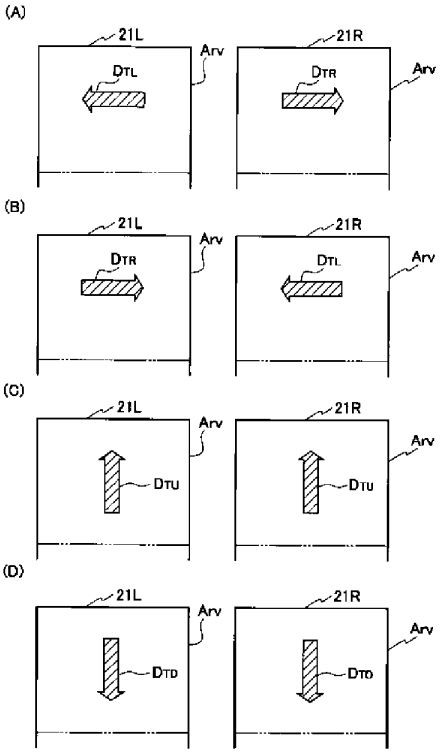
【図１１】



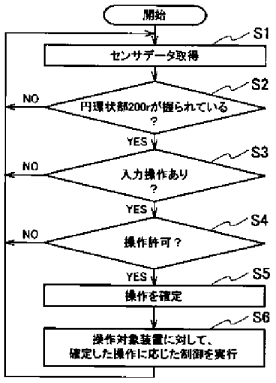
【図１２】



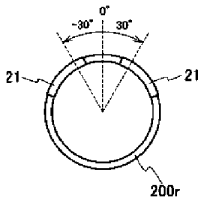
【図１３】



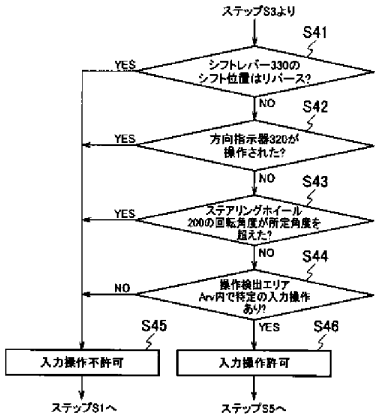
【図１４】



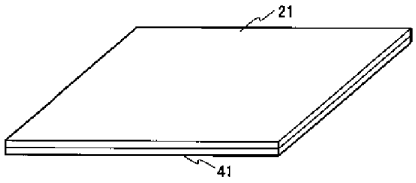
【図１５】



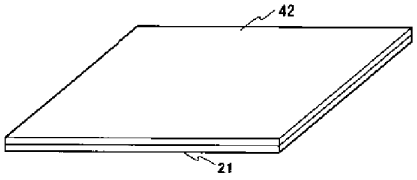
【図１６】



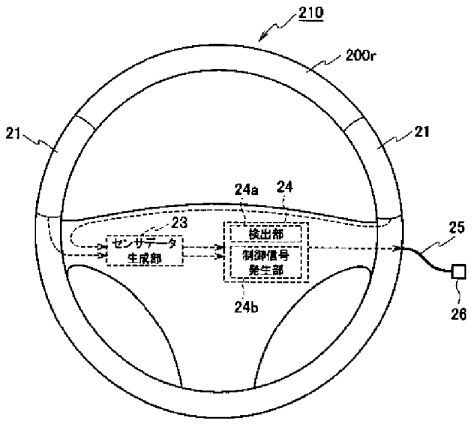
【図１７】



【図１８】



【図１９】



フロントページの続き

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特開２００７－０７６４９１（ＪＰ，Ａ）
実開昭６１－１６１８５２（ＪＰ，Ｕ）
特開平０６－１５６１１４（ＪＰ，Ａ）

(58)調査した分野(Int.Cl.，ＤＢ名)
Ｂ６０Ｒ　１６／０２
Ｂ６０Ｒ　１６／０２７

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(51) [International Patent Classification]

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A61B 5/153 (2006.01)

[FI]

A61B 5/14 300E

A61B 5/14 300F

[Request for examination] Yes

[Number of claims] 12

[Application form] OL

[Application in foreign language]

[Total number of pages] 14

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(22) [Filing date] July 16, 2013 (2013.7.16)

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[Name] Eugene E. Weilbacher
(72) [Inventor]
[Name] Anthony Jay. Satchetti
(72) [Inventor]
[Name] Michael Jay. Noble
[Theme code (reference)]
4C038
[F term (reference)]
4C038TA01
4C038TA03
4C038UJ02

wrap up close

(57) [Summary] (Modified)
[Problem] To provide a cheaper and simpler phlebotomy needle that facilitates visualization of flashbacks.
A central portion (106) of the needle (100) includes a hole or opening (110) that communicates with a flow path defined by the needle (100), and a transparent housing (112) covers the opening (110). Positioned around to facilitate visualization of blood flow through needle 100 . A material that allows passage of air and provides an indication of blood flow through needle 10

0 is positioned over opening 110 . The material is in the form of plugs or alternatively in the f orm of patches or collars. The phlebotomy needle includes a needle 100, a housing 112 with a passive vent, and an observation area for visualizing blood flow in the housing 112. FIG. [Selection] Figure 2-1

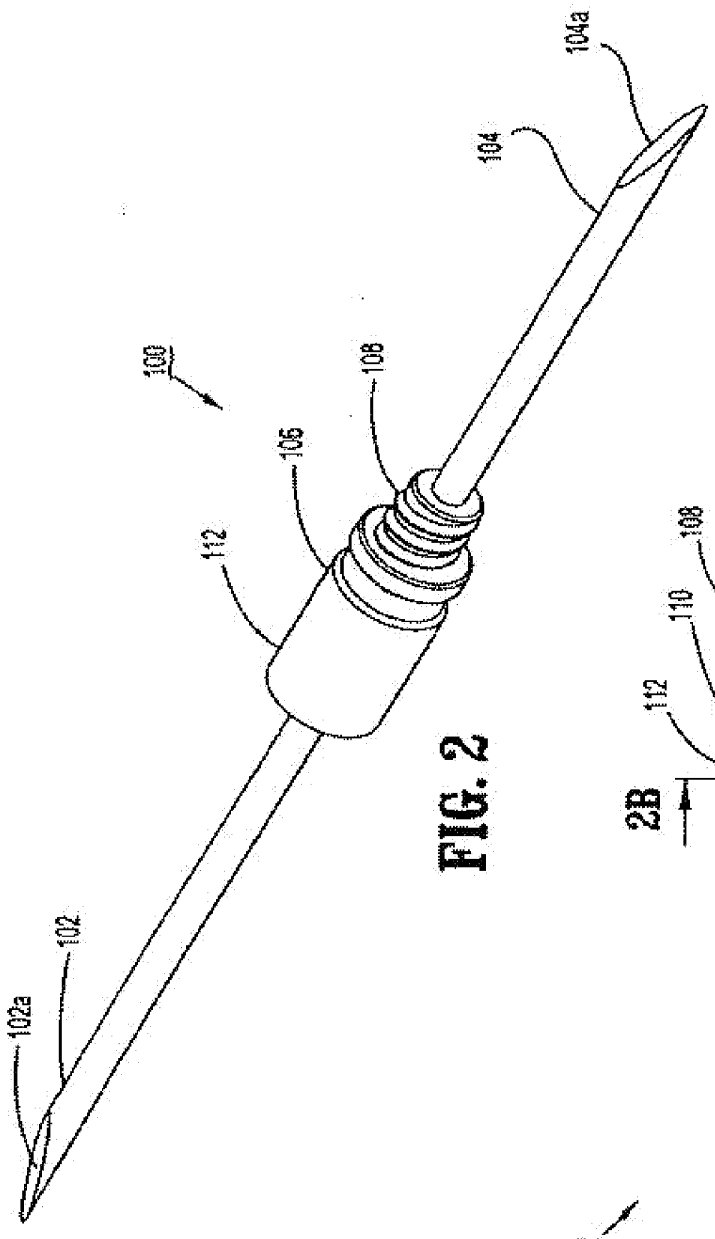


FIG. 2

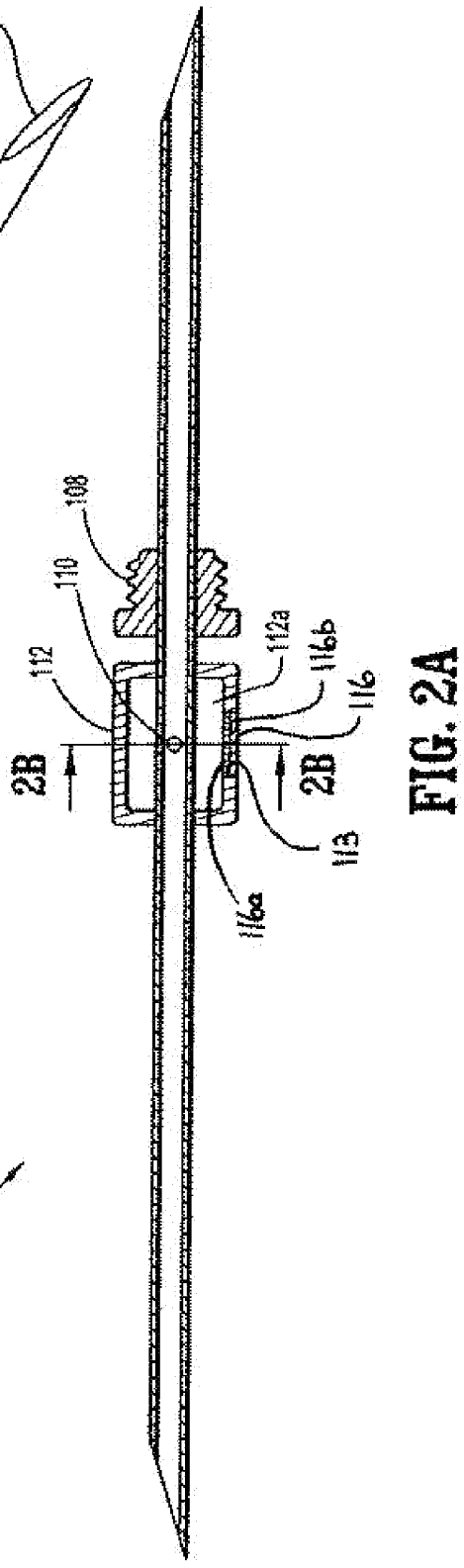


FIG. 2A

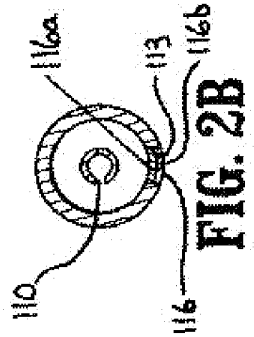


FIG. 2B

The scope of the claims open ----

Claims:

1. A

_phlebotomy needle: a distal needle portion

_having a sharpened distal end configured to pierce tissue; and a distal needle portion configured to pierce a stopper of a blood collection tube. a proximal needle portion having a sharpened proximal end, the distal needle portion and the proximal needle portion defining a fluid channel; a housing supported over the needle

_; a housing, comprising a passive vent, the housing defining a viewing area for viewing blood in the housing; and an elastomeric shield positioned about the proximal needle portion

_, A phlebotomy needle comprising an elastomeric shield and an elastomeric shield wherein the proximal needle portion defines a fluid flow path into the housing.

2. The phlebotomy needle of claim 1

, further comprising a fluted member positioned within said housing, said fluted member defining a plurality of fluid channels.

3.

The phlebotomy needle of claim 2, wherein said fluted member extends distally beyond said elastomeric shield.

4.

The phlebotomy needle of claim 2, wherein the fluid channel of the fluted member is configured to allow the passage of blood.

5.

The phlebotomy needle of claim 2, further comprising a hydrophilic material supported within said housing. 6. The phlebotomy of claim 5, wherein said flow path directs blood from the proximal end of said needle into the fluid channel of said fluted member and into contact with said hydrophilic material

.

needle.

[Claim 7]

6. The phlebotomy needle of claim 5, wherein a portion of said fluted member is surrounded by said hydrophilic material.

8. The method of claim

5, wherein the proximal end of said fluted member is surrounded by said elastomeric shield and the distal end of said fluted member is surrounded by said hydrophilic material. Phlebotomy needle.

9.
The phlebotomy needle of claim 5, wherein the proximal portion of the housing includes an inwardly extending annular rib.
10.
The elastomeric shield has an open distal end including an annular flange, and an annular rib of the housing engages the flange to extend the distal end of the elastomeric shield into the housing. 10. The phlebotomy needle according to claim 9, held in the
11.
The phlebotomy needle of claim 10, wherein the elastomeric shield flange is positioned adjacent to the hydrophilic material.
12.
The phlebotomy needle of claim 1, wherein the distal end of said elastomeric shield is received in said housing and the proximal end of said elastomeric shield extends proximally from said housing.

detailed description open ----

Description: BACKGROUND 1.
Technical Field The present disclosure relates to medical needles having structures that facilitate visualization of flashback. More particularly, the present disclosure provides vented phlebotomy needles that include structures that facilitate visualization of flashback.

Regarding. 2. Background of Related Art
Medical devices for drawing blood from a patient are well known. These devices include standard needle-syringes, butterfly needle sets, and phlebotomy needles. A butterfly needle set typically includes a hollow needle having a sharpened distal end and a proximal end secured to a needle hub. A proximal portion of the needle hub is connected to flexible tubing. The needle hub defines a fluid conduit in communication with the tubing and includes a pair of flexible, radially extending wings that facilitate grasping of the butterfly needle set by a medical practitioner. Generally, the flexible tubing is formed of a transparent material that allows medical personnel to visualize blood flow, or flashback, through the tubing proximate to the needle hub. Flashback visualization allows medical personnel to confirm that the needle has been correctly inserted into the patient. [0003] Some clinicians utilize a hypodermic needle-syringe with a clear needle hub to take blood samples. During insertion, these clinicians usually observe flashb

acks in the needle hub. Phlebotomy needles generally do not include structures for visualizin g flashback. The lack of a flashback visualization feature on the phlebotomy needle is not a m ajor drawback for more experienced HCWs, but for HCWs with little experience of drawing blo od with a phlebotomy needle, the needle may be a problem. Not having any means of confirm ing proper positioning in the patient can increase the time required to draw blood and can incr ease patient discomfort. [0005]

In an attempt to overcome the above disadvantages, US Pat. No. 6,200,300 to Norris et al. discloses a phlebotomy needle, which is attachable to a blood collection tube, comprises an ou ter needle, an inner needle, and a valve (bulb). The valve is transparent, allowing medical pe rsonnel to visualize the blood when the outer needle is correctly positioned within the patien t's vein. The valve also includes a button that can be depressed by a medical practitioner to v ent air from within the needle. Air in the needle prevents blood from flowing through the need le and must be vented.
[0006]
[
0006] US
Pat . No. 5,450,856 . SUMMARY OF THE INVENTION [0007] The Norris phlebotomy needle i s a However, a cheaper and simpler phlebotomy needle that facilitates flashback visualization i s desired. SUMMARY OF THE INVENTION The present disclosure relates to a phlebotomy nee dle having a sharpened distal end configured to penetrate tissue.

a proximal needle portion having a sharpened proximal end configured to penetrate a blood c ollection tube stopper; and a central needle portion defining an opening. The distal needle por tion, the proximal needle portion and the central needle portion define a fluid channel in com munication with the opening. A material is positioned adjacent to the opening. The material is

of a type that allows air to exit the fluid channel through the openings while preventing the pa ssage of blood. In one embodiment, the material provides a visual indication of blood flow, or flashback, adjacent the opening.

[0009]

In one embodiment, the material comprises a hydrophobic material. In alternative embodim ents, the material comprises a hydrophilic capillary action material. In yet another embodime nt, the material includes hydrophobic plugs. Alternatively, the material may define a collar pos itioned around the opening.

[0010]

In one embodiment, the opening is circular. Alternatively, the openings are envisioned to be of various configurations, such as rectangular or slot-shaped.

[0011]

In one embodiment, a transparent housing is positioned around the opening to facilitate visu alization of the flashback. A housing may also be positioned to contain the material and may i nclude a vent for venting air from the needle.

[0012]

In one embodiment, the phlebotomy needle includes engagement structure configured to en gage the needle holder.

In one

embodiment, a check valve is provided to prevent air from entering the fluid channel throug h the opening. In yet another embodiment, the phlebotomy needle includes a needle holder. For example, the present invention provides the following items.

(Item 1)

A phlebotomy needle,

a distal needle portion having a sharpened distal end configured to penetrate tissue and a sh arpened

proximal end configured to pierce a stopper of a blood collection tube. and a central needle p ortion

defining an opening, wherein the distal needle portion, the proximal needle portion and the c entral needle portion are in fluid communication with the opening a central needle portion defi ning a channel;

A material positioned adjacent to the opening of a type that allows air to exit the fluid chann el through the opening while preventing the passage of blood to reduce blood flow.

A phlebotomy needle comprising a material that further enables visual indication .

(Item 2)

The phlebotomy needle of item 1, wherein the material comprises a hydrophobic material.

3.

The phlebotomy needle of claim 1, wherein said material comprises a hydrophilic capillary ac tion material.

4.

The phlebotomy needle of claim 1, wherein said material comprises an inner layer of hydrophilic material facing towards said opening and an outer layer of hydrophobic material.

(Item 5)

The phlebotomy needle according to item 1, wherein the opening is circular.

6.

The phlebotomy needle of claim 1, wherein the opening defines an elongated slot.

7.

The phlebotomy needle of claim 1, further comprising a transparent housing positioned around the opening. Clause 8.

The phlebotomy needle of clause 1, further comprising an engagement structure supported by the phlebotomy needle, the

engagement structure configured to engage a needle holder.

9.

The phlebotomy needle of claim 1, wherein the material defines a collar covering the opening and positioned about the needle.

10.

The phlebotomy needle of claim 9, further comprising a transparent housing positioned around the collar material.

11.

The phlebotomy needle of claim 1, further comprising a check valve for preventing air from entering the fluid channel through the opening.

12.

The phlebotomy needle of claim 1, further comprising a needle holder.

13.

The phlebotomy needle of claim 1, wherein the material provides a visual indication of blood flow through the opening.

(Item 14)

A phlebotomy needle,

a distal needle portion having a sharpened distal end configured to penetrate tissue and a

sharpened proximal end configured to pierce a stopper of a blood collection tube. and a central needle portion

defining an opening, wherein the distal needle portion, the proximal needle portion and the central needle portion are in fluid communication with the opening A central needle portion defining a channel and

a hydrophobic material positioned adjacent the opening to permit air to exit the fluid channel through the opening while allowing blood to exit the fluid channel. A hydrophobic material of a type that prevents passage and further permits visual indication of blood flow, a

transparent housing positioned around the opening, and

an engagement supported by the phlebotomy needle. A

phlebotomy needle comprising: a structure, and an engagement structure configured to eng age the needle holder .

(Item 15)

The phlebotomy needle of item 14, further comprising the needle holder.

(Item 16)

A phlebotomy needle,

a distal needle portion having a sharp distal tip configured to penetrate tissue;

a proximal needle portion having a sharpened proximal end configured to penetrate a blood collection tube stopper; and a central needle portion

defining an opening, the distal needle portion, the proximal The needle portion and the centr al needle portion define a fluid channel in communication with the opening, a hydrophilic

capillary action material positioned adjacent the central needle portion and the opening, whe rein air flows into the a hydrophilic capillary active material of a type that allows exiting the fl uid channel through the opening while preventing the passage of blood, further permitting a v isual indication of blood flow; and the opening

. and an engagement structure supported by the phlebotomy needle

, the engagement structure configured to engage a needle holder

.

(Item 17)

The phlebotomy needle of item 16, further comprising the needle holder.

(Item 18)

A phlebotomy needle, the phlebotomy needle

penetrating a distal needle portion having a sharpened distal end configured to penetrate tis sue and a stopper of a blood collection tube. a proximal needle portion having a pointed proxi mal end configured to define a fluid channel

; a housing that includes a passive vent and

defines an observation area for visualizing blood in the housing

.

(Item 19)

19, further comprising an elastomeric shield positioned about the proximal needle portion, th e elastomeric shield and the proximal needle portion defining a fluid flow path into the housin g; Phlebotomy needle as described.

(Item 20)

20. The phlebotomy needle of any one of items 18 and 19, further comprising a fluted memb er positioned within the housing, the fluted member defining a plurality of fluid channels.

(Item 21)

The phlebotomy needle according to any one of items 18 to 20, further including a hydrophili c material supported within the housing.

22.

The phlebotomy needle of any one of items 18-21, wherein the needle has a central portion defining an opening into the housing.

BRIEF DESCRIPTION OF THE DRAWINGS

[0014]

An embodiment of the presently disclosed vented phlebotomy needle with a flashback chamber is disclosed herein with reference to the drawings.

1 is a perspective view, with parts separated, of a "prior art" phlebotomy needle with a needle holder, a protective needle cover and a blood collection tube shown in phantom; FIG.

1A is a side cross-sectional view of an assembled "prior art" phlebotomy needle, needle holder, and blood collection tube shown in phantom, with the distal portion of the phlebotomy needle positioned within a vein; It is

2-1 is a side perspective view of one embodiment of the presently disclosed phlebotomy needle; FIG . 2A is a cross-sectional view of the phlebotomy needle shown in FIG. 2; FIG . 2B is a cross-sectional view along section line 2B-2B of FIG. 2A.

2-2C is a side cross-sectional view of another embodiment of a phlebotomy needle of the present disclosure; FIG.

3 is a side cross-sectional view of an alternate embodiment of the phlebotomy needle of the present disclosure; FIG . FIG. 3A is a cross-sectional view taken along section line 3A--3A of FIG.

FIG. 4 is a side perspective cutaway view of another embodiment of the phlebotomy needle of the present disclosure; FIG . FIG. 4A is a cross-sectional view along section line 4A--4A of FIG.

FIG. 5 is a side perspective cutaway view of another embodiment of the phlebotomy needle of the present disclosure; FIG.

6 is a side cross-sectional view of another embodiment of the phlebotomy needle of the present disclosure; FIG.

7 is a cross-sectional view along section line 7-7 of FIG. 6; FIG.

DETAILED DESCRIPTION OF EMBODIMENTS Embodiments of vented phlebotomy needles of the present disclosure with flashback chambers will now be described in detail with reference to the drawings

, In the drawings, like reference numbers indicate identical or corresponding elements in each of the several drawings. FIG . 1 shows a known phlebotomy needle 10, needle holder 12, and needle covers 14 and 16. As shown in FIG. A blood collection tube 17 is shown in phantom. Phlebotomy needle 10 includes a distal needle portion 20 , a proximal needle portion 22 and an intermediate needle hub 23 with an engaging portion 24 . Engaging portion 24 is provided to facilitate connecting phlebotomy needle 10 to needle holder 12 . In one embodiment, the engaging portion includes a male fitting 24 a configured to engage a female fitting or engaging member 26 , which engages the distal end of needle holder 12 . provided to Alternatively, oth

er engagement structures may be used, including screws, snap-type connectors, and the like. An elastomeric shield 28 is positioned over the proximal needle portion 22 to seal the proxima l needle portion 22, as described in further detail below . [0017]

Needle holder 12 includes a substantially cylindrical body 30 having a distal end including en gagement member 26 and a proximal end including a pair of flange members 32 . Flange me mber 32 facilitates grasping and insertion of blood collection tube 17 by medical personnel. Cy lindrical body 30 defines cavity 34 (FIG. 1A) for receiving blood collection tube 17 . Blood coll ection tube, usually
17 is sealed by a penetrable stopper 17a to define a low pressure cavity 17b (FIG. 1A). The di stal end of holder 12 defines an opening 36 through engagement member 26 , opening 36 siz ed to receive proximal needle portion 22 . In use, needle 10 is secured to the distal end of n eedle holder 12 via engagement portion 24 and engagement member 26, as shown in FIG. 1A .
When needle 10 is secured to needle holder 12 , proximal needle portion 22 is positioned with in cavity 34 of body 30 of needle holder 12 and elastomeric shield 28 is positioned over proxi mal needle portion 22 . be. A blood collection tube 17 (shown in phantom) containing a penet rable stopper 17a is then positioned within cavity 34 . When blood collection tube 17 is inserte d into cavity 34 , proximal needle portion 22 engages stopper 17 a and penetrates shield 28 . Shield 28 is compressed downward (FIG. 1A) so that proximal needle portion 22 penetrates st opper 40 and enters cavity 17b of blood collection tube 17 . Once the distal needle portion 20 is properly positioned in the patient's vein 38 and the blood collection tube 17 is positioned wi thin the cavity 34, blood is typically flowed through the needle 10 and into the blood collection tube 17. The blood collection tube 17 is maintained under vacuum. When the blood collection tube 17 is removed from the needle holder 12 , the resilient elastomeric shield 28 returns to it s original configuration, covering and sealing the proximal needle portion 22 .
[0019]
FIGS. 2 and 2A illustrate one embodiment of the phlebotomy needle of the present disclosur e with a flashback chamber, generally indicated as 100. FIG. Needle 100 includes distal end 1 02 , proximal end 104 and central portion 106 . Distal end 102 has a pointed end 102a config ured to penetrate patient tissue, and proximal end 104 is configured to pierce stopper 17a of blood collection tube 17 (see FIG. 1A). It has a sharp edge 104a. Central portion 106 includes an engagement member 108, as discussed above, which is configured to engage a needle hol der (FIG. 1). Central portion 106 also includes an opening or hole 110 and a translucent or tra

nsparent housing 112 positioned around central portion 106 of the portion defining opening 1 10 . Although opening 110 is shown as circular, other configurations are envisioned, such as r ectangular, square, oval, elongated slot 39 (FIG. 5), and the like. A transparent housing 112 d efines a blood reservoir 112a. Vent openings 113 are preferably formed in transparent housin g 112 . Vent opening 113 facilitates venting needle 100 and allows blood flow through needle 100 . As discussed below, the vent opening 113 of the housing 112 may be covered with a ma terial that allows passage of air but not liquid, such as blood, for example. Referring to FIGS . 2A and 2B, vent opening 113 may be covered with filter 116 .

Filter 116 preferably includes an inner layer 116a of hydrophilic material and an outer layer 1 16b of hydrophobic material. Preferably, at least one of layers 116a and 116b has a pore size of less than 0.45 microns. Such a pore size allows air to pass through but prevents bacteria fr om entering the housing 112 .

[0021]

Referring to FIG. 2C, in an alternative embodiment, filter 116 may be replaced by a hydroph obic check valve, such as flap valve 150, for example. As shown, flap valve 150 is configured t o flex outward from housing 112 to expose vent opening 113 and vent housing 112 when bloo d begins to flow into housing 112 . be.

A hydrophobic sheet 152 is positioned over opening 113 to prevent blood from exiting vent op ening 113 when the check valve is open . Prior to blood beginning to flow into housing 112 , fl ap valve 150 seals opening 113 to prevent material from entering housing 112 . Alternatively, flap valve 150 may be formed from a hydrophilic material if the pore size of the hydrophilic m aterial is sized to block the passage of blood components. When the distal end 102 of needle 100 is properly positioned within the patient's vein, ie,

blood

The transparent housing 112 allows the medical practitioner to visualize blood flow through th e needle 100 as air flows through the needle 100 and air is vented and blood enters the reser voir 112a through the opening 110. make it possible. This allows the medical practitioner to c onfirm that the distal end 102 of the needle 100 has been properly positioned within the patie nt's vein for drawing blood. This provides a significant benefit to medical practitioners attempt ing to draw blood from patients, especially those who have limited experience with drawing bl ood from patients with phlebotomy needles.

[0023]

FIG. 3 illustrates an alternative embodiment of the vented phlebotomy needle of the present disclosure with a flashback chamber generally indicated as 200. As shown in FIG. Needle 200 i s substantially similar to needle 100, except as described below. Needle 200 includes distal en d 202 , proximal end 204 and central portion 206 . Distal end 202 has a sharpened end 202a configured to pierce patient tissue, and proximal end 204 has a sharpened end 202a configure d to pierce a stopper of a blood collection tube (see FIG. 1A). It has a tapered end 204a. Cent

ral portion 206 includes an opening or hole 210 and an engagement member 212a. Material 2 14 is positioned over hole 210 . Material 214 may be a hydrophilic material that wicks blood in to the material so that blood flow through needle 200 can be readily discerned by medical per sonnel. To facilitate venting of needle 200, material 214 may be a hydrophilic material that is permeable to air but impermeable to liquids, such as blood. In one embodiment, the hydrophil ic material can be of the type that changes color when in contact with blood. The material ma y be in the form of collar 250 (Fig. 3) or plug 252 (Fig. 4). Additionally, the material may be p ositioned within a transparent housing or hub 212, or alternatively positioned adjacent openin g 210 without any housing. In an alternative embodiment, the material is a hydrophobic mate rial that is air permeable but blood impermeable. It is noted that ventilation openings 226 ma y be provided in housing 212 to facilitate ventilation of the housing. A vent can be in the form of an opening in housing 212 that allows air to flow out of housing 212 as blood enters.

[0024]

In an alternative embodiment, further illustrated in FIGS. 3 and 3A, material 214 may be for med of an expandable material that allows air to pass through vent openings 226 before cont acting the expandable material with blood. enable Material 214 may expand upon contact with blood, closing vent opening 226 . Although only hydrophilic and hydrophobic materials have been disclosed herein, other materials that facilitate the passage of air while preventing the p assage of blood and provide an indication of blood flow are disclosed in the present disclosure .

phlebotomy needles. The material may have other configurations not disclosed herein. For exa mple, the material may define a pad that covers the opening.

FIGS.

6 and 7 illustrate another embodiment of the phlebotomy needle of the present disclosure wi th a flashback chamber, generally indicated as device 398. FIG. Phlebotomy needle 398 includ es needle 400 and stepped housing 408 . Needle 400 includes distal end 402 , proximal end 4 04 and central portion 406 . Distal end 402 has a pointed end 402a configured to penetrate ti ssue of a patient, and proximal end 404 is adapted to pierce a stopper (not shown) of a blood collection tube (not shown). It has a configured pointed end 404a.

The

stepped housing 408 has a distal portion 408a and a larger diameter proximal portion 408b. A stepped housing 408 is supported at the central portion 406 . Distal portion 408a defines a t hroughbore 412 sized to receive central portion 406 of the needle. Distal portion 408a is seale d and secured to needle 400 using adhesive 410, for example. Alternatively, other known tech niques such as crimping, clamping, screws, welding, etc. may be used to secure needle 400 to housing 408 . Proximal portion 408b is a transparent or translucent material.

formed to facilitate visualization within proximal portion 408 b of housing 408 . Proximal porti on 408 b also defines a through hole 414 that communicates with through hole 412 but has a larger diameter than through hole 412 . Proximal portion 408 b defines an annular recess 416

between portion 408 b and proximal end 404 of needle 400 . Recess 416 is sized to receive hy drophilic material 418 and inner fluted member 420 . An inner fluted member 420 is positione d around proximal end 404 of needle 400 and defines a plurality of channels 422 in communic ation with hydrophilic material 418 . A ventilation opening 409 is provided through housing 40 8 .

[0028]

An elastomeric shield 428 is positioned over the proximal end 404 of the needle 400 . As dis cussed above, elastomeric shield 428 may be resilient, sealing proximal end 404 of needle 40 0 when proximal end 404 of needle 400 is not connected to a blood collection tube (not show n). function to Elastomeric shield 428 includes a closed proximal end 428a and an open distal end 428b. Open distal end 428 b includes an annular flange 430 positioned adjacent material 418 within recess 416 of housing 408 . A proximal portion 408b of the housing 408 includes a n inwardly extending annular rib 432 that engages a flange 430 of an elastomeric shield 428 a nd a distal end 428b of the shield 428. within recess 416 of housing 408 . A channel 436 is de fined between elastomeric shield 428 and proximal end 404 of needle 400 , as indicated by ar row 434 . Channel 436 directs blood from proximal end 404 of needle 400 into fluted channel 422 of fluted member 420 and into contact with hydrophilic material 418 . In use, when blood contacts material 418 , material 418 provides a visual indication of blood flow that is visible th rough proximal portion 408 b of housing 408 .

[0029]

defined with filter 116 (FIGS. 2A-2B), defined with filter 252 (FIGS. 4-4A), or defined with fil ter 39 (FIG. 5), or defined with check valve 150 (FIG. 5). FIG. 2C) Vent opening 113, as well as openings 226 (FIGS. 3-3A) and opening 409 (FIG. 6) can all be described as passive vent o penings, which are positioned within the needle cannula. Allows gases with pressures greater than atmospheric pressure to automatically leak into the atmosphere. These passive ventilatio n openings do not require any action by the user of the device according to the invention.

[0030]

It is understood that various modifications may be made to the embodiments disclosed herei n. Therefore, the above should not be construed as limiting, but merely as exemplifications of preferred embodiments. Those skilled in the art will envision other modifications within the sc ope and spirit of the claims appended hereto.

drawing open —

[Fig. 1-1]

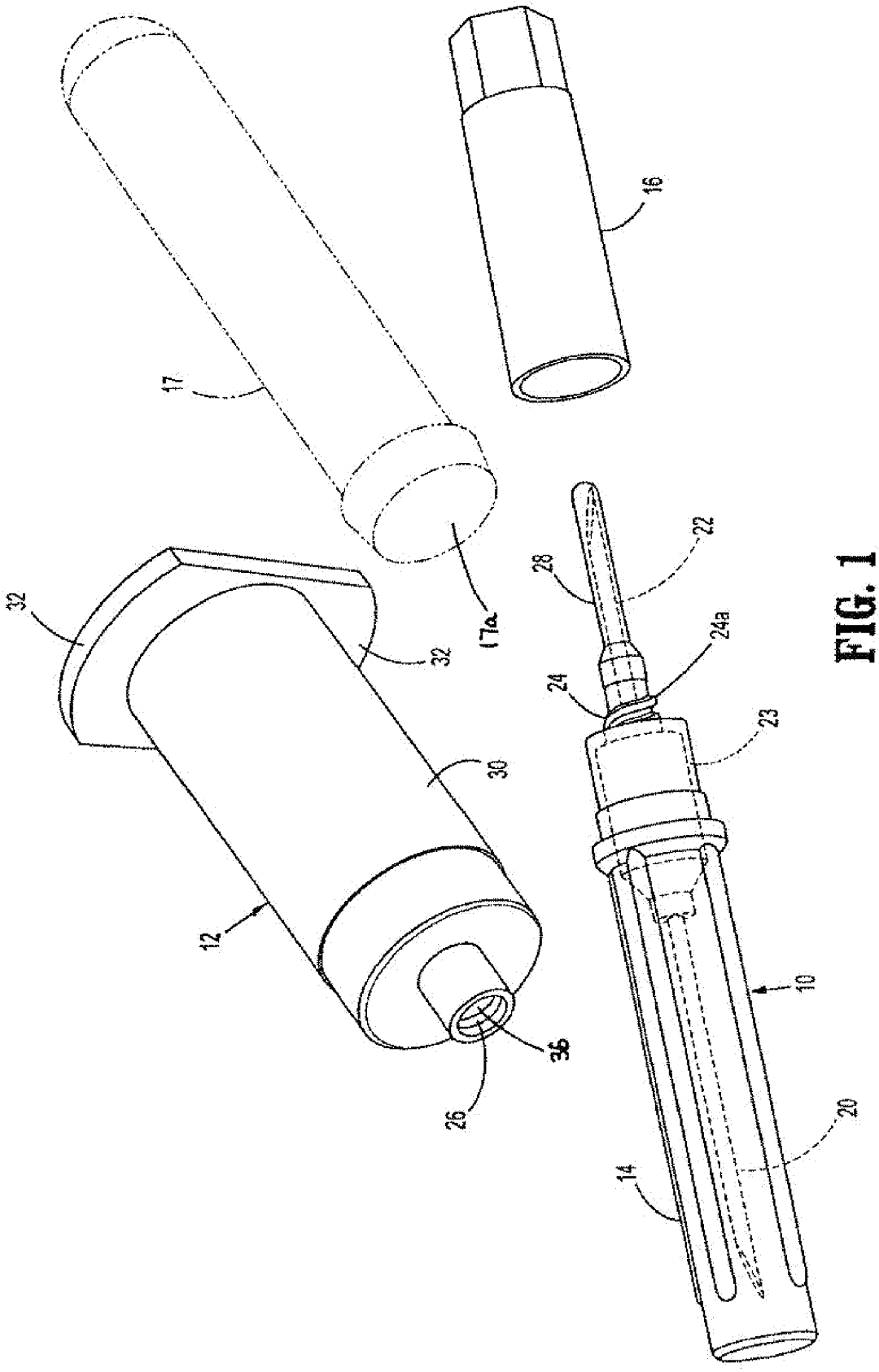


FIG. 1

[Figure 1-2]

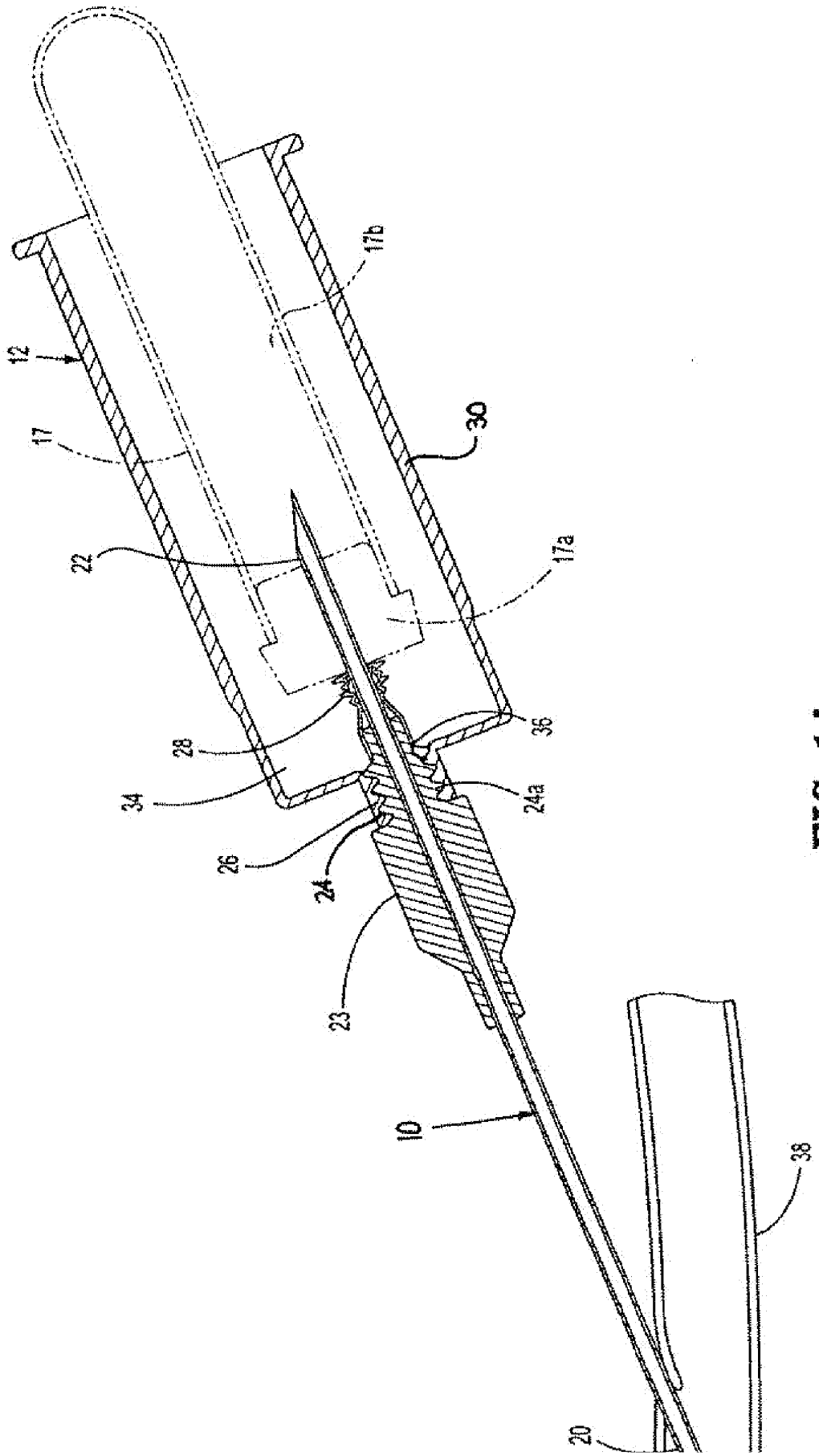
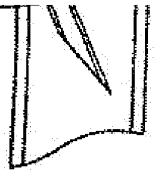


FIG. 1A

[Figure 2-1]



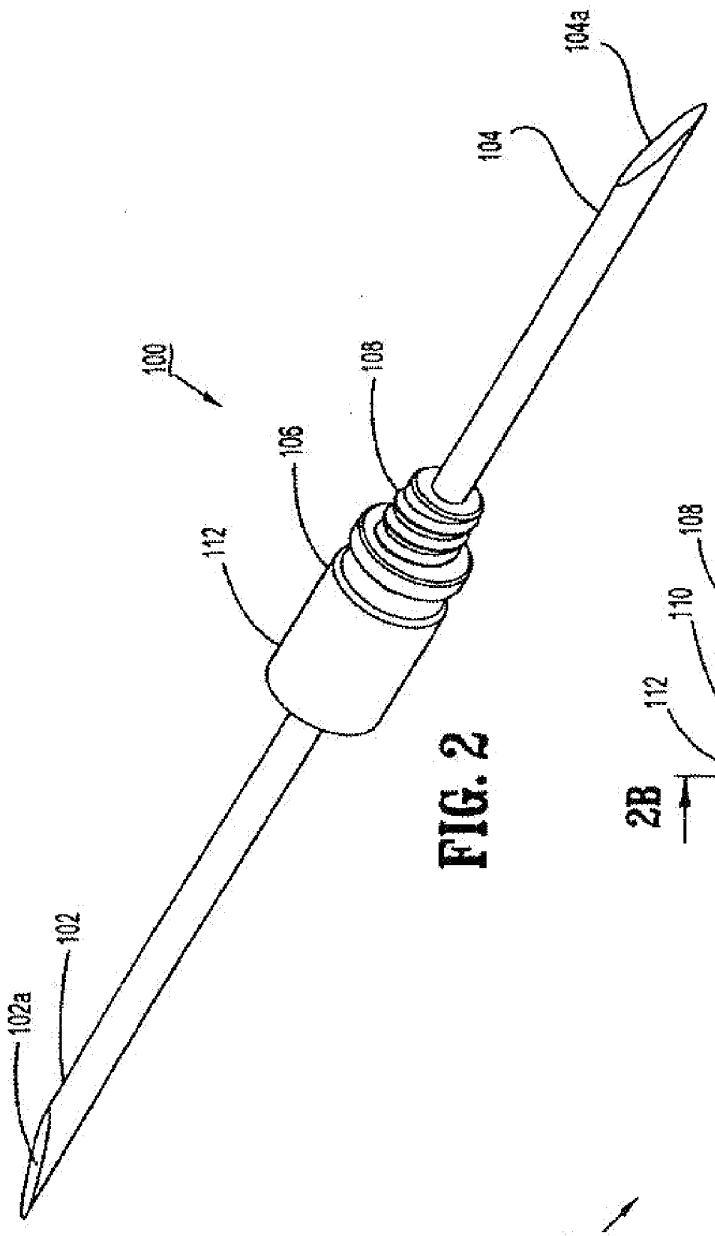


FIG. 2

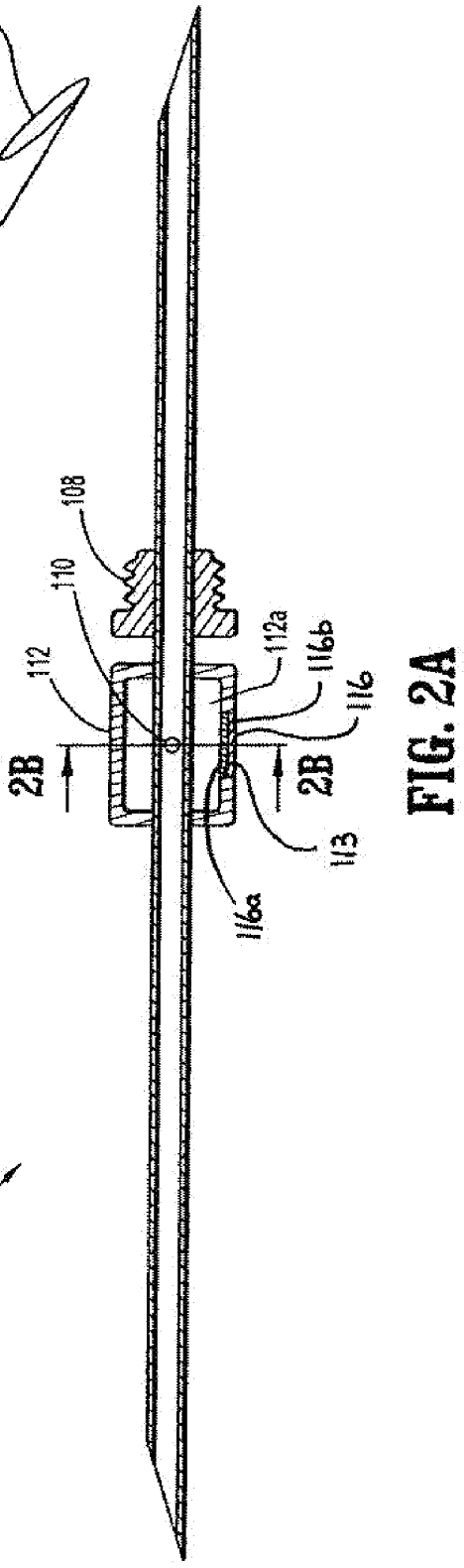


FIG. 2A

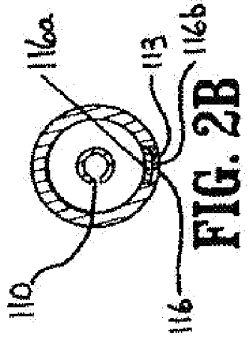


FIG. 2B

[Figure 2-2]

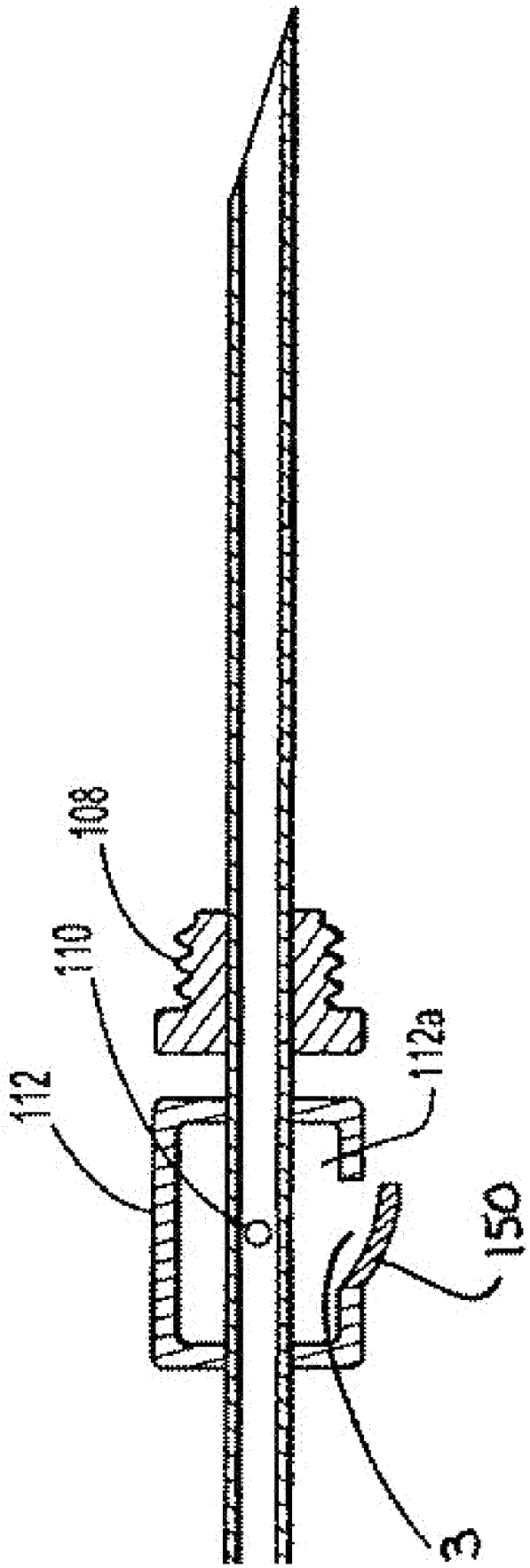
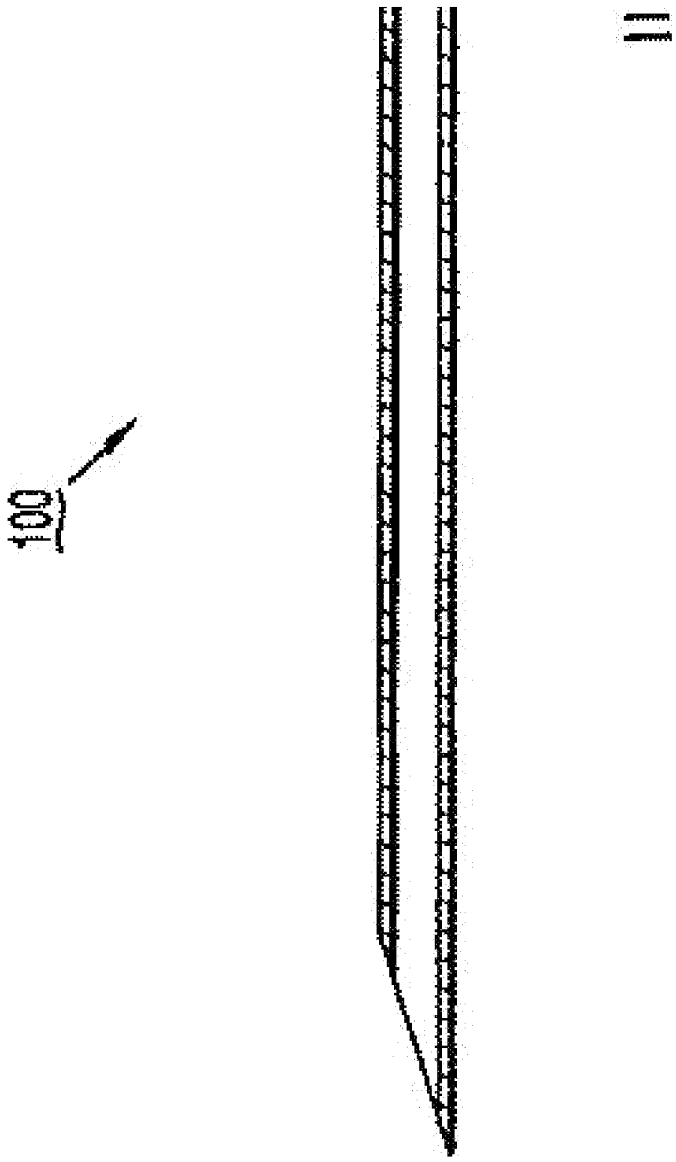


FIG. 2C

[Figure 3]



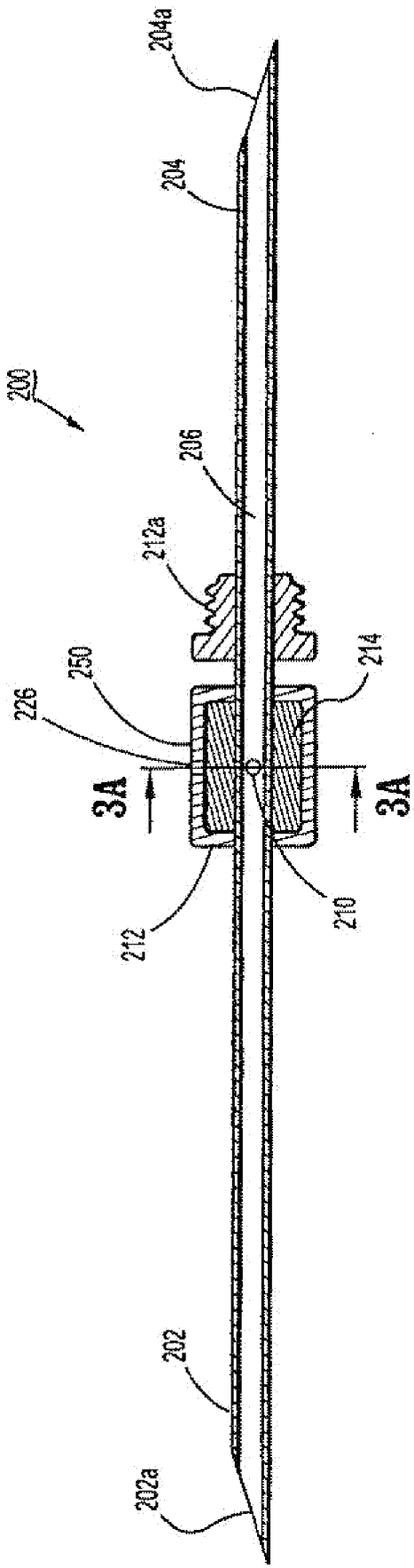

200
204a
204
206
212a
214
250
226
3A
3A
212
210
202
202a

FIG. 3

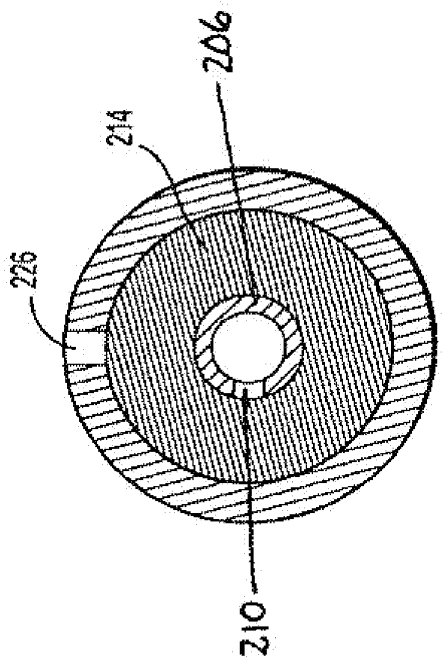

206
214
226
210

FIG. 3A

[Figure 4]

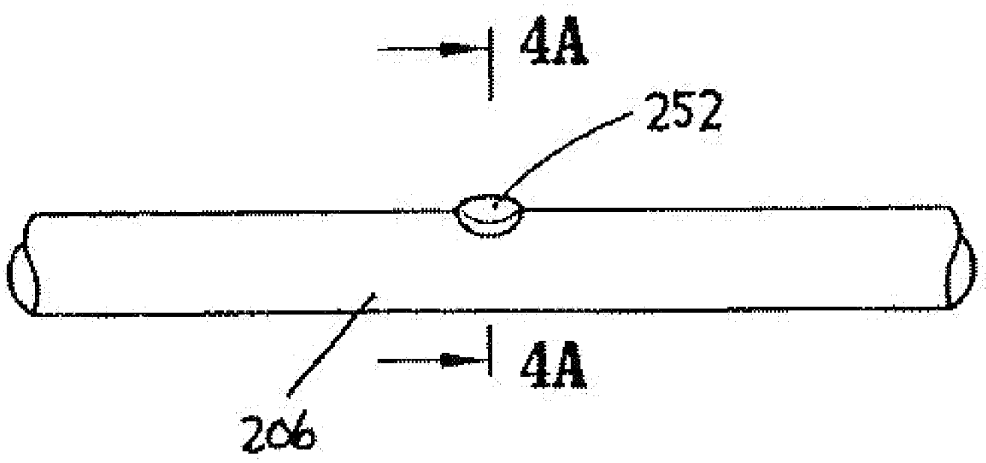


FIG. 4

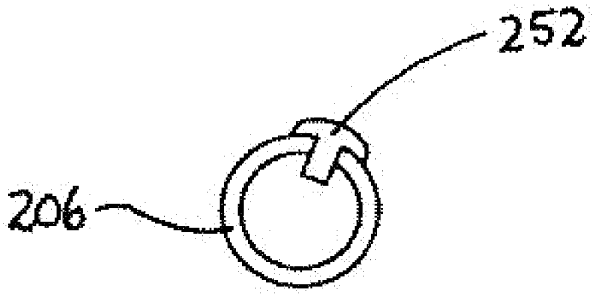


FIG. 4A

[Figure 5]

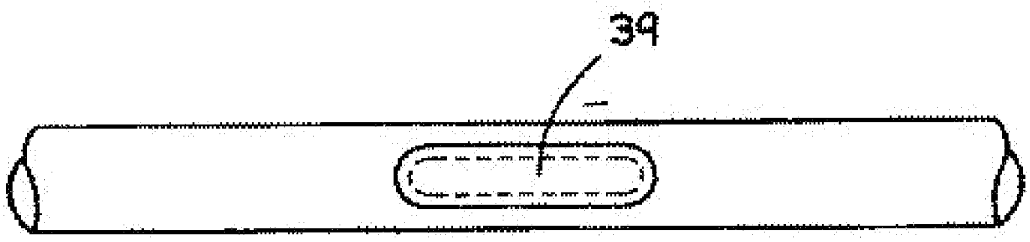


FIG. 5

[Fig. 6]

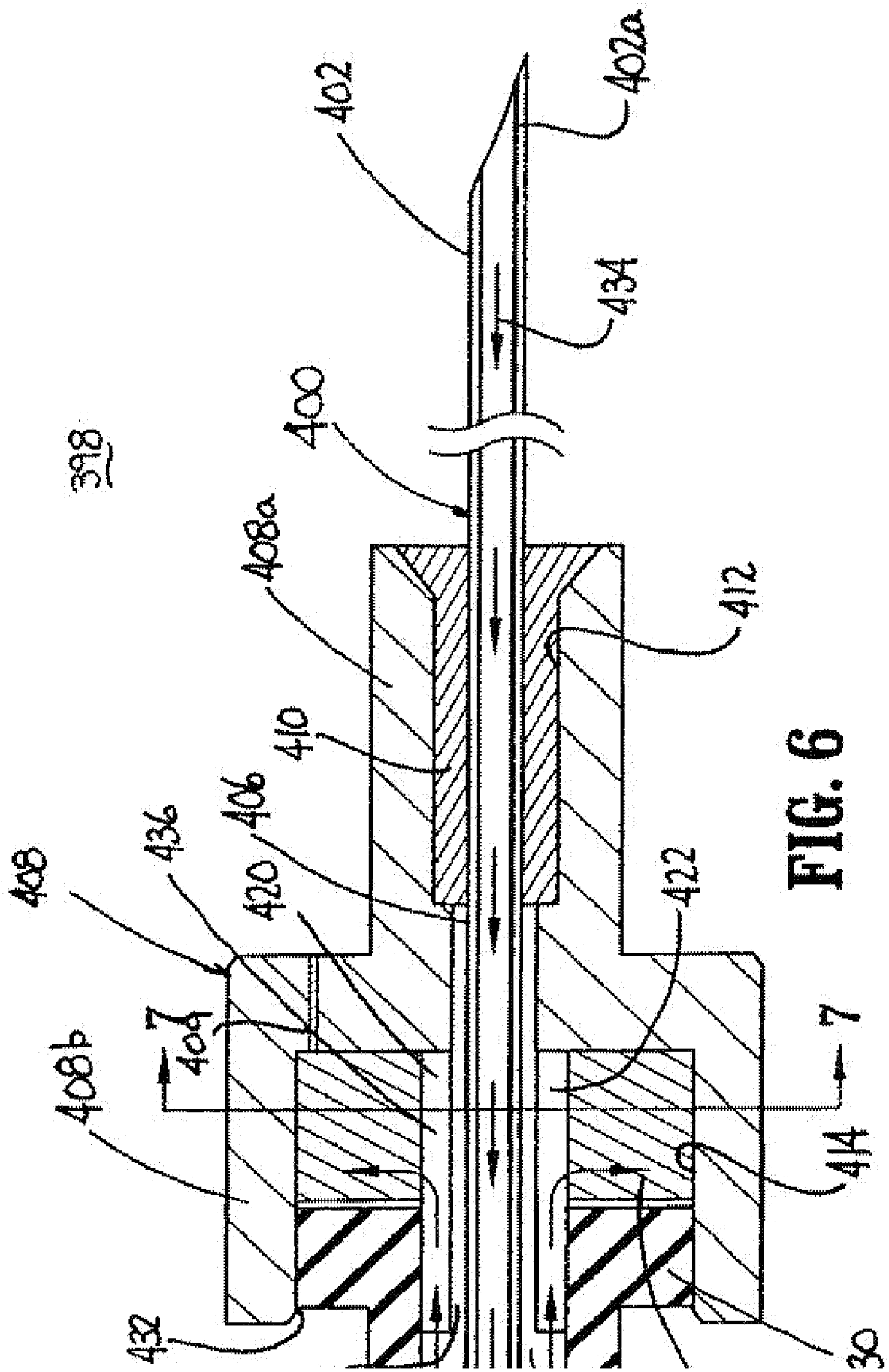

402
402a
434
400
398
408a
412
410
406
436
408
420
422
7
409
7
408b
414
432
30

FIG. 6

[Fig. 7]

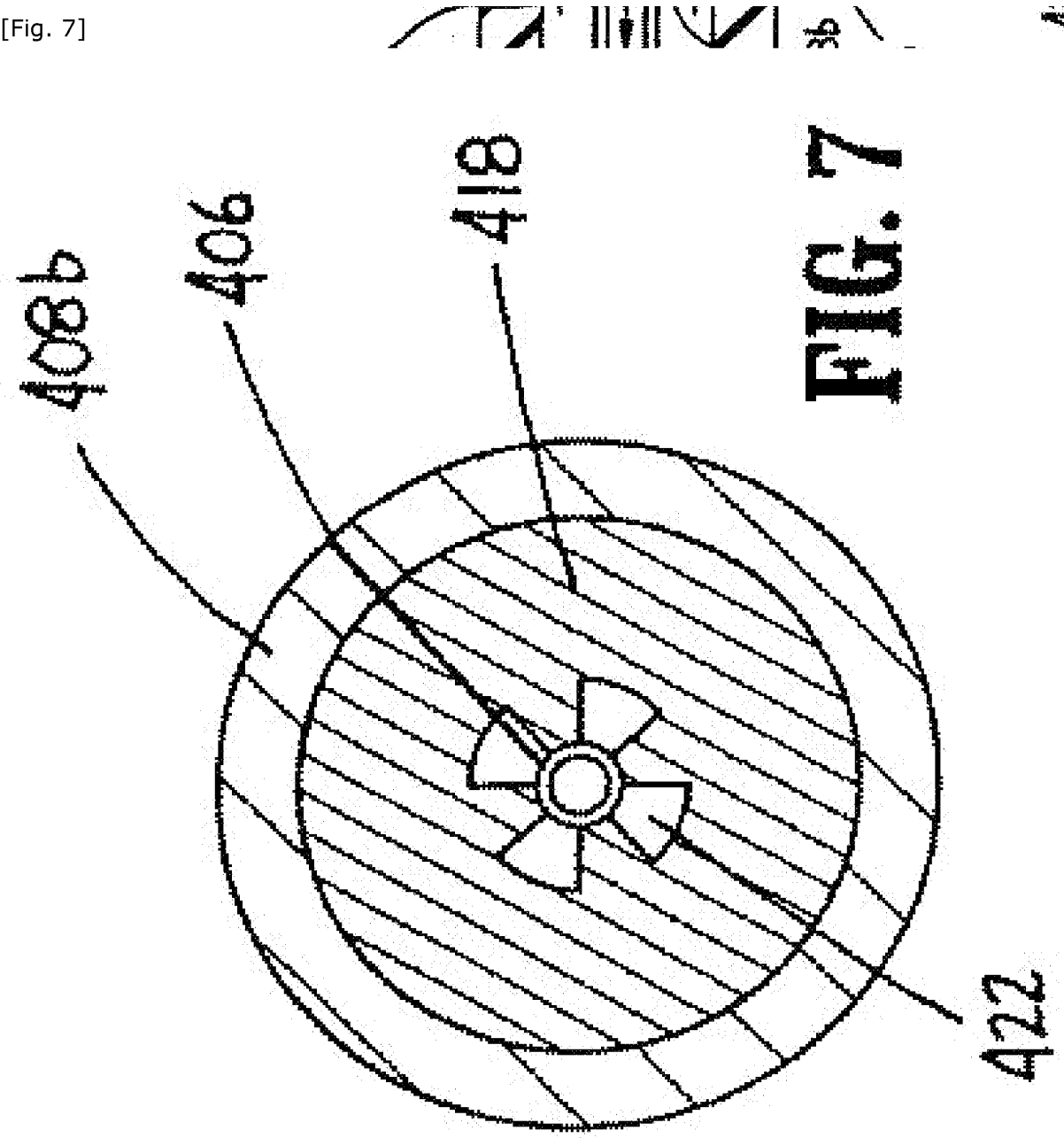


FIG. 7

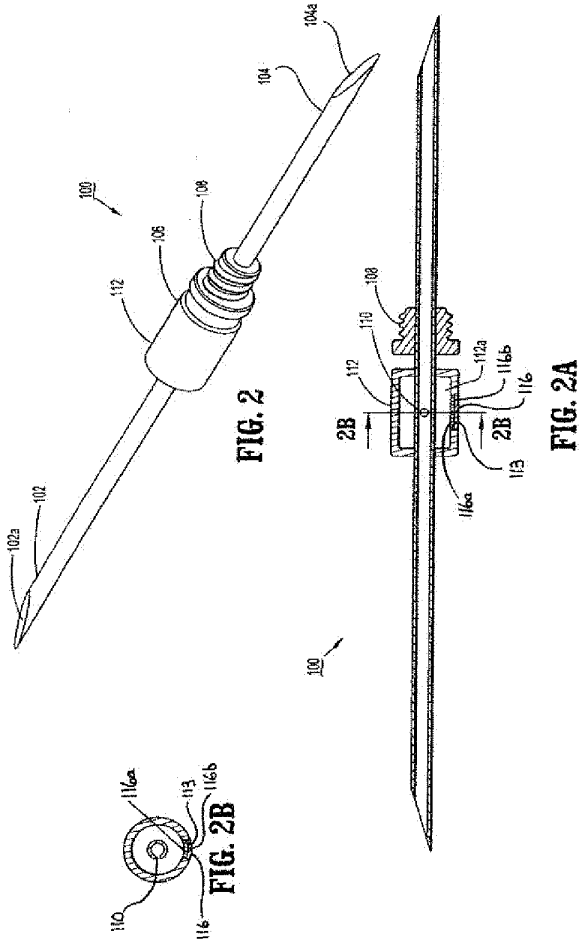
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Representative drawing

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VENTED PHLEBOTOMY NEEDLE WITH FLASHBACK CHAMBER

Inventor(s): WEILBACHER EUGENE E; SACCHETTI ANTHONY J; NOBLE MICHAEL J ± (WEILBACHER EUGENE E, ; SACCHETTI ANTHONY J, ; NOBLE MICHAEL J)

Applicant(s): COVIDIEN LP ± (COVIDIEN LP)

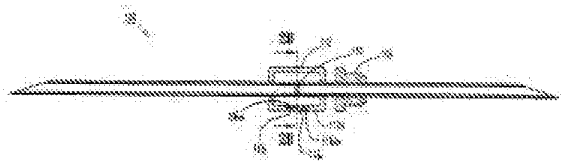
Classification: **- international:** ***A61B5/153; A61B5/154***
- cooperative: **A61B5/15003 (EP, US); A61B5/150213 (EP, US); A61B5/150389 (EP, US); A61B5/150473 (EP, US); A61B5/150572 (EP, US); A61B5/150732 (EP, US); A61B5/1545 (EP, US)**

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Abstract of JP2013240628 (A)



PROBLEM TO BE SOLVED: To provide a less expensive, less complex phlebotomy needle which facilitates visualization of flashback.SOLUTION: A central portion 106 of a needle 100 includes a hole or opening 110 which communicates with a flow channel defined by the needle 100 and a transparent housing 112 is positioned about the opening 110 to facilitate visualization of blood flow through the needle 100. A material which allows passage of air and provides an indication of blood flow through the needle 100 is positioned over the opening 110. The material is in the form of a plug or, alternately, in the form of a patch or collar. The phlebotomy needle includes the needle 100 and the housing 112 having a passive vent and a viewing region for visualizing blood flow in the housing 112.

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A61B	5/153	(2006.01)	A61B	5/14	300F	

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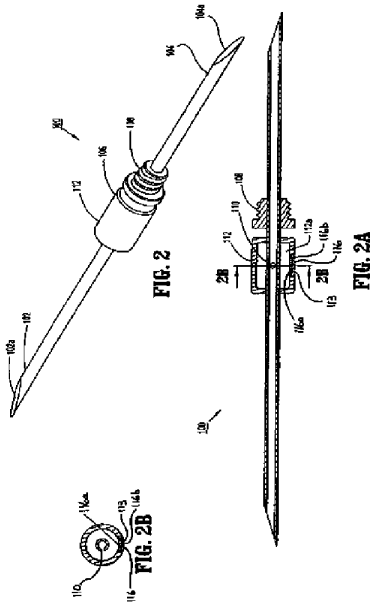
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(54)【発明の名称】フラッシュバックチャンバを備えた通気型瀉血針

(57)【要約】　（修正有）
【課題】フラッシュバックの可視化を容易にするより安価な、より簡単な瀉血針の提供。
【解決手段】針１００の中央部分１０６は穴または開口部１１０を含み、該穴または開口部１１０は、針１００によって画定された流路と連通し、透明の筐体１１２が、開口部１１０の周りに位置決めされ、針１００を通る血流の可視化を容易にする。空気の通過を可能にし、針１００を通る血流の表示を提供する材料が、開口部１１０を覆い位置決めされる。材料は、プラグの形であるか、または代替として、パッチまたはカラーの形である。瀉血針は、針１００と、受動通気孔を有する筐体１１２と、筐体１１２の血流を可視化するための観察領域とを含む。
【選択図】図２－１



【特許請求の範囲】
【請求項１】
瀉血針であって：
組織を貫通するように構成された尖った遠位端を有する遠位の針部分と、採血管のストッパを貫通するように構成された尖った近位端を有する近位の針部分とを有し、該遠位の針部分と該近位の針部分が流体チャンネルを画定する、針；
該針上に支持される筐体であって、受動通気孔を含み、該筐体が該筐体中に血液を観察するための観察領域を画定する、筐体；および
該近位の針部分の周りに位置決めされるエラストマーのシールドであって、該エラストマーのシールドおよび該近位の針部分が該筐体中への流体の流路を画定する、エラストマーのシールド、を備える、瀉血針。
【請求項２】
前記筐体内に位置決めされる縦溝のある部材をさらに含み、該縦溝のある部材が複数の流体チャンネルを画定する、請求項１に記載の瀉血針。
【請求項３】
前記縦溝のある部材が、前記エラストマーのシールドを超えて遠位方向に延びる、請求項２に記載の瀉血針。
【請求項４】
前記縦溝のある部材の流体チャンネルが血液の通過を可能にするように構成されている、請求項２に記載の瀉血針。
【請求項５】
前記筐体内に支持される親水性材料をさらに含む、請求項２に記載の瀉血針。
【請求項６】
前記流路が、血液を、前記針の近位端から前記縦溝のある部材の流体チャンネル中に、および前記親水性材料との接触に向ける、請求項５に記載の瀉血針。
【請求項７】
前記縦溝のある部材の一部分が、前記親水性材料によって取り囲まれる、請求項５に記載の瀉血針。
【請求項８】
前記縦溝のある部材の近位端が前記エラストマーのシールドによって取り囲まれ、そして該縦溝のある部材の遠位端が前記親水性材料によって取り囲まれる、請求項５に記載の瀉血針。
【請求項９】
前記筐体の近位部分が、内方に延びる環状のリブを含む、請求項５に記載の瀉血針。
【請求項１０】
前記エラストマーのシールドが環状のフランジを含む開いた遠位端を有し、前記筐体の環状のリブが該フランジを係合し、該エラストマーのシールドの遠位端を該筐体内に保持する、請求項９に記載の瀉血針。
【請求項１１】
前記エラストマーのシールドのフランジが、前記親水性材料に隣接して位置決めされる、請求項１０に記載の瀉血針。
【請求項１２】
前記エラストマーシールドの遠位端が前記筐体中に受容され、そして該エラストマーシールドの近位端が該筐体から近位方向に延びる、請求項１に記載の瀉血針。
【発明の詳細な説明】
【技術分野】
【０００１】
（１．技術分野）
本開示は、フラッシュバックの可視化を容易にする構造を有する医療用針に関する。より詳細には、本開示は、フラッシュバックの可視化を容易にする構造を含む通気型瀉血針

に関する。
【背景技術】
【０００２】
（２．関連技術の背景）
患者から血液を抜き取る医療用デバイスは周知である。これらのデバイスは、標準的な針－注射器、蝶型針セット、および瀉血針を含む。通常、蝶型針セットは、尖った遠位端および針ハブに固定された近位端を有する中空の針を含む。針ハブの近位部分は、可撓性の配管に接続されている。針ハブは、配管と連通する流体導管を画定し、一対の可撓性の、半径方向に延びるウィングを含み、該ウィングは、医療従事者による蝶型針セットの把持を容易にする。一般に、可撓性の配管は、医療従事者が、針ハブに直近の配管を通る血流、すなわちフラッシュバックを可視化することを可能にする透明の材料で形成される。フラッシュバックの可視化は、針が患者の中に正しく挿入されたことを、医療従事者が確認することを可能にする。
【０００３】
一部の臨床医は、血液サンプルを採取するために、透明の針ハブを備えた皮下針－注射器を利用する。挿入の間、これらの臨床医たちは通常、針ハブの中のフラッシュバックを観察する。
【０００４】
一般に、瀉血針は、フラッシュバックを可視化するための構造を含んでいない。瀉血針にフラッシュバックを可視化するための構造がないことは、より経験のある医療従事者にとっては大きな欠点ではないが、瀉血針によって血液を抜き取る経験をほとんど有しない医療従事者にとっては、針が正しく患者の中に位置決めされたことを確認するいかなる手段もないことは、血液を抜き取るために必要な時間を増加させ得、患者の不快を増加させ得る。
【０００５】
上記の不利を克服する試みとして、Ｎｏｒｒｉｓらへの特許文献１は、瀉血針を開示し、該瀉血針は、採血管に取り付け可能であり、外側針、内側針、およびそれらの間にバルブ（ｂｕｌｂ）を含む。バルブは、透明であり、外側針が正しく患者の静脈内に位置決めされたとき、医療従事者が血液を可視化することを可能にする。バルブは、針内から空気を通気するために医療従事者によって押し下げられ得るボタンも含む。針内の空気は、血液が針を通って流れることを妨げ、通気されなければならない。
【先行技術文献】
【特許文献】
【０００６】
【特許文献１】米国特許第５，４５０，８５６号明細書
【発明の概要】
【発明が解決しようとする課題】
【０００７】
Ｎｏｒｒｉｓの瀉血針は、フラッシュバックの可視化を容易にするが、フラッシュバックの可視化を容易にするより安価な、より簡単な瀉血針が望まれる。
【課題を解決するための手段】
【０００８】
本開示は瀉血針に関し、該瀉血針は、組織を貫通するように構成された尖った遠位端を有する遠位の針部分と、採血管のストッパを貫通するように構成された尖った近位端を有する近位の針部分と、および開口部を画定する中央の針部分とを含む。遠位の針部分、近位の針部分および中央の針部分は、開口部と連通する流体チャンネルを画定する。材料が、開口部に隣接して位置決めされる。材料は、空気が開口部を通って流体チャンネルを出ることを可能にし、一方、血液の通過を防止するタイプのものである。一実施形態において、材料は、開口部に隣接する血流、すなわちフラッシュバックの可視表示を提供する。
【０００９】

一実施形態において、材料は疎水性材料を含む。代替の実施形態において、材料は親水性毛管作用材料を含む。さらに別の実施形態において、材料は疎水性のプラグを含む。あるいは、材料は開口部の周りに位置決めされたカラー部を画定し得る。

【００１０】

一実施形態において、開口部は円形である。あるいは、開口部は様々な構成、例えば長方形またはスロット形状であることが想定されている。

【００１１】

一実施形態において、透明の筐体が開口部の周りに位置決めされ、フラッシュバックの可視化を容易にする。筐体はまた、材料を包含するように位置決めされ得、針から空気を通気するための通気孔を含み得る。

【００１２】

一実施形態において、瀉血針は、針ホルダーと係合するように構成された係合構造を含む。

【００１３】

一実施形態において、空気が開口部を通って流体チャンネルの中に入ることを阻止するために、逆止弁が提供される。さらに別の実施形態において、瀉血針は、針ホルダーを含む。

例えば、本発明は以下の項目を提供する。

（項目１）

瀉血針であって、

組織を貫通するように構成された尖った遠位端を有する遠位の針部分と、

採血管のストッパを貫通するように構成された尖った近位端を有する近位の針部分と、

開口部を画定する中央の針部分であって、該遠位の針部分、該近位の針部分および該中央の針部分は、該開口部と連通する流体チャンネルを画定する、中央の針部分と、

該開口部に隣接して位置決めされた材料であって、空気が該開口部を通って該流体チャンネルを出ることを可能にし、一方、血液の通過を防止するタイプのものであり、血流の可視表示をさらに可能にする、材料と

を備えている、瀉血針。

（項目２）

上記材料は疎水性材料を含む、項目１に記載の瀉血針。

（項目３）

上記材料は親水性毛管作用材料を含む、項目１に記載の瀉血針。

（項目４）

上記材料は、上記開口部の方に向かう親水性材料の内側層と、疎水性材料の外側層とを含む、項目１に記載の瀉血針。

（項目５）

上記開口部は円形である、項目１に記載の瀉血針。

（項目６）

上記開口部は細長いスロットを画定する、項目１に記載の瀉血針。

（項目７）

上記開口部の周りに位置決めされた透明の筐体をさらに含む、項目１に記載の瀉血針。

（項目８）

上記瀉血針で支持された係合構造であって、針ホルダーと係合するように構成された、係合構造をさらに含む、項目１に記載の瀉血針。

（項目９）

上記材料は、上記開口部を覆い上記針の周りに位置決めされたカラー部を画定する、項目１に記載の瀉血針。

（項目１０）

上記カラー部の材料の周りに位置決めされた透明の筐体をさらに含む、項目９に記載の瀉血針。

（項目１１）
空気が、上記開口部を通って上記流体チャンネルの中に入ることを阻止するための逆止弁をさらに含む、項目１に記載の瀉血針。
（項目１２）
針ホルダーをさらに含む、項目１に記載の瀉血針。
（項目１３）
上記材料は、上記開口部を通る血流の可視表示を提供する、項目１に記載の瀉血針。
（項目１４）
瀉血針であって、
組織を貫通するように構成された尖った遠位端を有する遠位の針部分と、
採血管のストッパを貫通するように構成された尖った近位端を有する近位の針部分と、
開口部を画定する中央の針部分であって、該遠位の針部分、該近位の針部分および該中央の針部分は、該開口部と連通する流体チャンネルを画定する、中央の針部分と、
該開口部に隣接して位置決めされた疎水性材料であって、空気が該開口部を通って該流体チャンネルを出ることを可能にし、一方、血液の通過を防止するタイプのものであり、血流の可視表示をさらに可能にする、疎水性材料と、
該開口部の周りに位置決めされた透明の筐体と、
該瀉血針で支持された係合構造であって、針ホルダーと係合するように構成された、係合構造と
を備えている、瀉血針。
（項目１５）
上記針ホルダーをさらに含む、項目１４に記載の瀉血針。
（項目１６）
瀉血針であって、
組織を貫通するように構成された尖った遠位端を有する遠位の針部分と、
採血管のストッパを貫通するように構成された尖った近位端を有する近位の針部分と、
開口部を画定する中央の針部分であって、該遠位の針部分、該近位の針部分および該中央の針部分は、該開口部と連通する流体チャンネルを画定する、中央の針部分と、
該開口部に隣接して位置決めされた親水性毛管作用材料であって、空気が該開口部を通って該流体チャンネルを出ることを可能にし、一方、血液の通過を防止するタイプのものであり、血流の可視表示をさらに可能にする、親水性毛管作用材料と、
該開口部の周りに位置決めされた透明の筐体と、
該瀉血針で支持された係合構造であって、針ホルダーと係合するように構成された、係合構造と
を備えている、瀉血針。
（項目１７）
上記針ホルダーをさらに含む、項目１６に記載の瀉血針。
（項目１８）
瀉血針であって、該瀉血針は、
針であって、組織を貫通するように構成された尖った遠位端を有する遠位の針部分と、採血管のストッパを貫通するように構成された尖った近位端を有する近位の針部分とを含み、該遠位の針部分および該近位の針部分は、流体チャンネルを画定する、針と、
該針で支持された筐体であって、受動通気孔を含み、該筐体の血液を可視化するための観察領域を画定する、筐体と
を備えている、瀉血針。
（項目１９）
上記近位の針部分の周りに位置決めされたエラストマーのシールドをさらに含み、該エラストマーのシールドおよび該近位の針部分が、上記筐体の中への流体の流路を画定する、項目１８に記載の瀉血針。
（項目２０）

上記筐体内に位置決めされた縦溝のある部材をさらに含み、該縦溝のある部材は、複数の流体チャンネルを画定する、項目１８および項目１９のうちのいずれか一項に記載の瀉血針。

（項目２１）

上記筐体内に支持された親水性材料をさらに含む、項目１８～項目２０のうちのいずれか一項に記載の瀉血針。

（項目２２）

上記針は、上記筐体の中への開口部を画定する中央部分を有する、項目１８～項目２１のうちのいずれか一項に記載の瀉血針。

【図面の簡単な説明】

【００１４】

フラッシュバックチャンバを備えた本開示の通気型瀉血針の実施形態が、図面を参照して本明細書に開示される。

【図１－１】図１は、針ホルダー、保護針カバーおよび幻影で示された採血管を備えた「従来技術」の瀉血針の斜視図であり、部品は分離されている。

【図１－２】図１Ａは、組み立てられた「従来技術」の瀉血針、針ホルダー、および幻影で示された採血管の側面断面図であり、瀉血針の遠位部分は静脈内に位置決めされている。

【図２－１】図２は、本開示の瀉血針の一実施形態の側面斜視図である。図２Ａは、図２で示された瀉血針の断面図である。図２Ｂは、図２Ａの切断線２Ｂ－２Ｂに沿った断面図である。

【図２－２】図２Ｃは、本開示の瀉血針の別の実施形態の側面断面図である。

【図３】図３は、本開示の瀉血針の代替の実施形態の側面断面図である。図３Ａは、図３の切断線３Ａ－３Ａに沿った断面図である。

【図４】図４は、本開示の瀉血針の別の実施形態の側面斜視切取り図である。図４Ａは、図４の切断線４Ａ－４Ａに沿った断面図である。

【図５】図５は、本開示の瀉血針の別の実施形態の側面斜視切取り図である。

【図６】図６は、本開示の瀉血針の別の実施形態の側面断面図である。

【図７】図７は、図６の切断線７－７に沿った断面図である。

【発明を実施するための形態】

【００１５】

（実施形態の詳細な記述）

フラッシュバックチャンバを備えた本開示の通気型瀉血針の実施形態がここで、図面を参照して詳細に記述され、該図面においては、同様の参照番号は、幾つかの図面の各々において同一のまたは対応する要素を示す。

【００１６】

図１は、公知の瀉血針１０、針ホルダー１２、ならびに針カバー１４および１６を示す。採血管１７が幻影で示されている。瀉血針１０は、遠位の針部分２０と、近位の針部分２２と、係合部分２４を備えた中間の針ハブ２３とを含む。係合部分２４は、瀉血針１０を針ホルダー１２に接続することを容易にするように提供される。一実施形態において、係合部分は、雄継手２４ａを含み、雄継手２４ａは、雌継手または係合部材２６と係合するように構成され、係合部材２６は、針ホルダー１２の遠位端に提供される。あるいは、ねじ、スナップ型コネクタ、その他を含む他の係合構造が使用され得る。下にさらに詳細に記述されるように、エラストマーのシールド２８が近位の針部分２２を覆い位置決めされ、近位の針部分２２をシールする。

【００１７】

針ホルダー１２は、実質的に円筒状の本体３０を含み、実質的に円筒状の本体３０は、係合部材２６を含む遠位端および一対のフランジ部材３２を含む近位端を有する。フランジ部材３２は、医療従事者による採血管１７の把持および挿入を容易にする。円筒状の本体３０は、採血管１７を受け入れるための空洞３４（図１Ａ）を画定する。通常、採血管

１７は、貫通可能ストッパ１７ａによってシールされ、低圧の空洞１７ｂ（図１Ａ）を画定する。ホルダー１２の遠位端は、係合部材２６を通る開口部３６を画定し、開口部３６は、近位の針部分２２を受け入れる大きさとされる。

【００１８】

図１Ａに示されるように、使用に際して、針１０は、係合部分２４および係合部材２６を介して針ホルダー１２の遠位端に固定される。針１０が針ホルダー１２に固定されると、近位の針部分２２は、針ホルダー１２の本体３０の空洞３４内に位置決めされ、エラストマーのシールド２８は、近位の針部分２２を覆い位置決めされる。次に、貫通可能ストッパ１７ａを含む採血管１７（幻影で示される）が、空洞３４内に位置決めされる。採血管１７が空洞３４の中に挿入されると、近位の針部分２２が、ストッパ１７ａと係合し、シールド２８を貫通する。近位の針部分２２が、ストッパ４０を貫通し、採血管１７の空洞１７ｂに入るように、シールド２８は下向きに圧縮（図１Ａ）される。遠位の針部分２０が患者の静脈３８に正しく位置決めされ、採血管１７が空洞３４内に位置決めされると、血液が、針１０を通って採血管１７の中に流入するように、通常、採血管１７は、真空に維持される。採血管１７が針ホルダー１２から取り外されると、弾力的なエラストマーのシールド２８は、その元の構成に戻り、近位の針部分２２を被覆し、近位の針部分２２をシールする。

【００１９】

図２および図２Ａは、概して１００として示されるフラッシュバックチャンバを備えた本開示の瀉血針の一実施形態を示す。針１００は、遠位端１０２と、近位端１０４と、中央部分１０６とを含む。遠位端１０２は、患者の組織を貫通するように構成された尖った端１０２ａを有し、近位端１０４は、採血管１７（図１Ａを参照）のストッパ１７ａを貫通するように構成された尖った端１０４ａを有する。中央部分１０６は、上に論議されたように、係合部材１０８を含み、係合部材１０８は針ホルダー（図１）と係合するように構成される。中央部分１０６はまた、開口部または穴１１０と、開口部１１０を画定する部分の中央部分１０６の周りに位置決めされた半透明または透明の筐体１１２とを含む。開口部１１０は円形として示されているが、他の構成、例えば長方形、正方形、楕円形、細長いスロット３９（図５）、その他が想定されている。透明の筐体１１２は、血液レザバ１１２ａを画定する。通気開口部１１３は好ましくは、透明の筐体１１２に形成される。通気開口部１１３が針１００の通気を容易にし、針１００を通る血流を可能にする。下に論議されるように、筐体１１２の通気開口部１１３は、空気の通過は許すが、例えば血液のような液体の通過は許さない材料によって被覆され得る。

【００２０】

図２Ａおよび図２Ｂを参照して、通気開口部１１３は、フィルタ１１６で被覆され得る。フィルタ１１６は好ましくは、親水性材料の内側層１１６ａと、疎水性材料の外側層１１６ｂとを含む。好ましくは、層１１６ａおよび層１１６ｂのうちの少なくとも１つは、０．４５ミクロンを下回る孔サイズを有する。かかる孔サイズは、空気の通過は可能にするが、バクテリアが筐体１１２の中に入ることを防止する。

【００２１】

図２Ｃを参照して、代替の実施形態において、フィルタ１１６は、例えばフラップ弁１５０のような疎水性逆止弁によって置き換えられ得る。図示のように、フラップ弁１５０は、筐体１１２の中に血液が流入し始めると、筐体１１２から外向きに曲がり、通気開口部１１３を露出させ、筐体１１２を通気するように構成される。逆止弁が開いたとき、血液が通気開口部１１３から出ることを防止するために、疎水性シート１５２が開口部１１３を覆い位置決めされる。血液が筐体１１２の中に流入し始めるのに先立って、フラップ弁１５０は開口部１１３をシールし、物質が筐体１１２の中に入ることを防止する。あるいは、フラップ弁１５０は、親水性材料の孔サイズが血液成分の通過を遮るサイズである場合は、該親水性材料から形成され得る。

【００２２】

針１００の遠位端１０２が患者の静脈内に正しく位置決めされたとき、すなわち、血液

が針１００を通って流れ、空気が通気されて、血液が開口部１１０を通ってレザバ１１２ａの中に入るとき、透明の筐体１１２は、医療実施者が針１００を通る血流を可視化することを可能にする。これによって、医療実施者は、針１００の遠位端１０２が、血液を抜き取るために患者の静脈内に正しく位置決めされたことを確認することができる。これは、患者から血液を抜き取ろうと試みる医療実施者に対して、特に瀉血針によって患者から血液を抜き取ることについて限られた経験しか有しないような実施者に対して大きな利益を提供する。

【００２３】

図３は、概して２００として示されるフラッシュバックチャンバを備えた本開示の通気型瀉血針の代替の実施形態を示す。針２００は、下に記述されるとおりを除いて、針１００と実質的に同様である。針２００は、遠位端２０２と、近位端２０４と、中央部分２０６とを含む。遠位端２０２は、患者の組織を貫通するように構成された尖った端２０２ａを有し、近位端２０４は、採血管（図１Ａを参照）のストッパを貫通するように構成された尖った端２０４ａを有する。中央部分２０６は、開口部または穴２１０と係合部材２１２ａとを含む。材料２１４は、穴２１０を覆い位置決めされている。医療従事者が針２００を通る血流を容易に識別し得るように、材料２１４は、材料の中に血液を毛管作用で吸い込む親水性の材料であり得る。針２００の通気を容易にするために、材料２１４は、空気に対しては透過性があるが、例えば血液のように液体に対しては透過性がない親水性材料であり得る。一実施形態において、親水性材料は、血液と接触したとき、色が変わるタイプのものであり得る。材料は、カラー２５０（図３）またはプラグ２５２（図４）の形であり得る。さらに、材料は、透明の筐体もしくはハブ２１２内に位置決めされ得るか、または代替的に、いかなる筐体もなく開口部２１０に隣接して位置決めされ得る。代替の実施形態において、材料は、空気は通すが血液は通さない疎水性の材料である。通気開口部２２６は筐体２１２に提供され得、筐体の通気を容易にし得ることに留意される。通気孔は、筐体２１２における開口部の形であり得、該開口部は、血液が入ると筐体２１２から空気が流れ出ることを可能にする。

【００２４】

図３および図３Ａでさらに示される代替の実施形態において、材料２１４は、膨張可能な材料で形成され得、該膨張可能な材料が血液と接触する前に、空気が通気開口部２２６を通ることを可能にする。材料２１４は、血液と接触すると膨張し得、通気開口部２２６を閉じ得る。

【００２５】

本明細書において、親水性材料および疎水性材料のみが開示されたが、血液の通過を防止しながら空気の通過を容易にし、血流の表示を提供する他の材料が、本開示の瀉血針に対して使用され得る。材料は、本明細書に開示されていない他の構成を有し得る。例えば、材料は、開口部を被覆するパッドを画定し得る。

【００２６】

図６および図７は、概してデバイス３９８として示されるフラッシュバックチャンバを備えた本開示の瀉血針の別の実施形態を示す。瀉血針３９８は、針４００と段付き筐体４０８とを含む。針４００は、遠位端４０２と、近位端４０４と、中央部分４０６とを含む。遠位端４０２は、患者の組織を貫通するように構成された尖った端４０２ａを有し、近位端４０４は、採血管（図示されず）のストッパ（図示されず）を貫通するように構成された尖った端４０４ａを有する。

【００２７】

段付き筐体４０８は、遠位部分４０８ａおよびより大きな直径の近位部分４０８ｂを有する。段付き筐体４０８は、中央部分４０６で支持されている。遠位部分４０８ａは、針の中央部分４０６を受け入れる大きさとされた通し穴４１２を画定する。遠位部分４０８ａは、例えば接着剤４１０を使用して、針４００にシールされ、固定される。あるいは、他の公知の技術、例えばクリンプ加工、クランプ、ねじ、溶接その他が使用され得、針４００を筐体４０８に固定し得る。近位部分４０８ｂは、透明の材料または半透明の材料で

形成され、筐体４０８の近位部分４０８ｂ内の可視化を容易にする。近位部分４０８ｂはまた、通し穴４１４を画定し、通し穴４１４は通し穴４１２と連通するが、通し穴４１２よりも直径が大きい。近位部分４０８ｂは、部分４０８ｂと針４００の近位端４０４との間に環状のリセス４１６を画定する。リセス４１６は、親水性材料４１８および内側の縦溝のある部材４２０を受け入れるような大きさとされる。内側の縦溝のある部材４２０が、針４００の近位端４０４の周りに位置決めされ、親水性材料４１８と連通する複数のチャンネル４２２を画定する。通気開口部４０９は、筐体４０８を通して提供される。

【００２８】

エラストマーのシールド４２８は、針４００の近位端４０４を覆い位置決めされる。上に論議されたように、エラストマーのシールド４２８は弾力的であり得、針４００の近位端４０４が採血管（図示されず）に接続されていないとき、針４００の近位端４０４をシールするように機能する。エラストマーのシールド４２８は、閉じた近位端４２８ａと開いた遠位端４２８ｂとを含む。開いた遠位端４２８ｂは環状のフランジ４３０を含み、環状のフランジ４３０は、筐体４０８のリセス４１６内で材料４１８に隣接して位置決めされる。筐体４０８の近位部分４０８ｂは、内向きに延びる環状のリブ４３２を含み、内向きに延びる環状のリブ４３２は、エラストマーのシールド４２８のフランジ４３０と係合し、シールド４２８の遠位端４２８ｂを筐体４０８のリセス４１６内に保持するように位置決めされる。矢印４３４によって示されるように、流路４３６は、エラストマーのシールド４２８と針４００の近位端４０４との間に画定される。流路４３６は、針４００の近位端４０４から縦溝のある部材４２０の縦溝のあるチャンネル４２２の中に血液を導き、親水性材料４１８と接触させる。使用に際して、血液が材料４１８と接触すると、材料４１８は、筐体４０８の近位部分４０８ｂを通して目視可能となる血流の可視表示を提供する。

【００２９】

フィルタ１１６と共に画定された（図２Ａ～図２Ｂ）、フィルタ２５２と共に画定された（図４～図４Ａ）、もしくはフィルタ３９と共に画定された（図５）、または逆止弁１５０と共に画定された（図２Ｃ）通気開口部１１３、ならびに開口部２２６（図３～図３Ａ）および開口部４０９（図６）はすべて、受動通気開口部として記述され得、該受動通気開口部は、針カニューレ内において大気圧よりも大きな圧力の気体が大気中に自動的に漏れることを可能にする。これらの受動通気開口部は、本発明によるデバイスのユーザによるいかなる行動も必要としない。

【００３０】

本明細書に開示された実施形態には、様々な変更がなされ得ることは理解される。したがって、上述は、限定するものとして解釈されるべきではなく、好ましい実施形態の単なる例示として解釈されるべきである。当業者は、本明細書に添付された請求項の範囲および精神内で他の変更に想到する。

【図１－１】

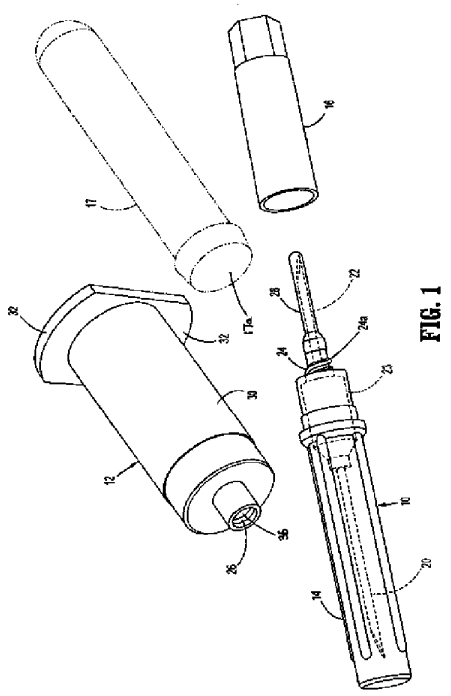


FIG. 1

【図１－２】

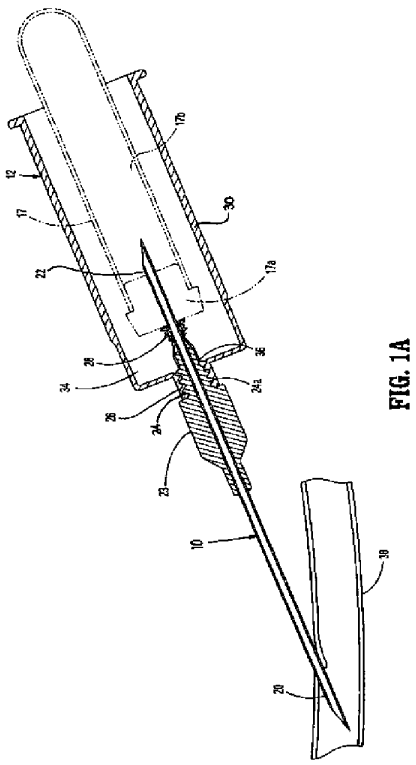


FIG. 1A

【図２－１】

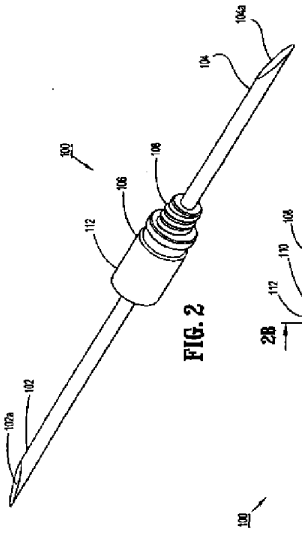


FIG. 2

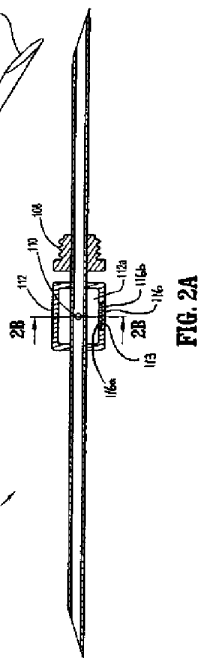


FIG. 2A



FIG. 2B

【図２－２】

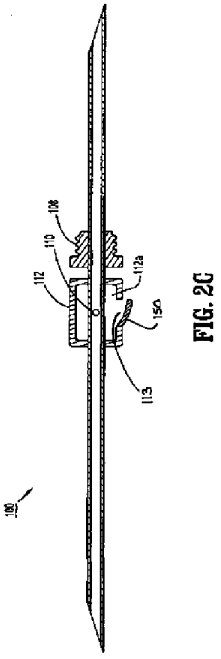


FIG. 2C

【図３】

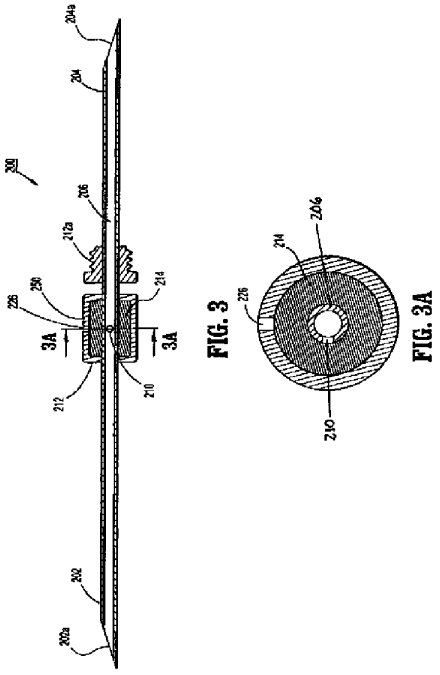


FIG. 3

FIG. 3A

【図４】

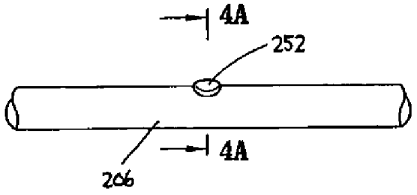


FIG. 4



FIG. 4A

【図５】

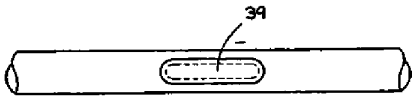


FIG. 5

【図６】

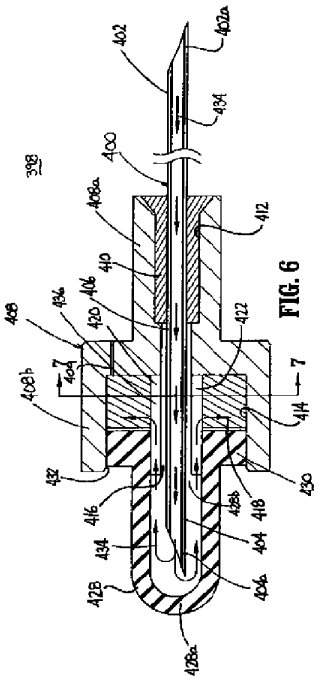


FIG. 6

【図７】

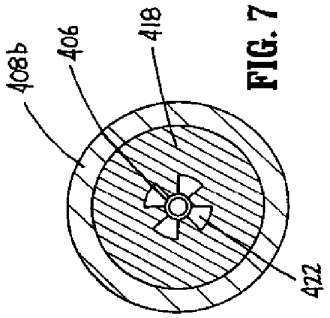


FIG. 7

フロントページの続き

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DEVICE AND METHOD FOR PREPARING BLOOD

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The invention relates to a preparation device (100) for treating suspension samples, especially for preparing blood cryobanks. Said device comprises an arrangement of at least two containers for receiving suspension samples, sample parts and/or additives. Said containers are formed as chambers (13 to 15, 90) having fixed walls and are arranged in a fixed manner in relation to each other. A transfer device comprising at least one connecting line (22) is provided, by which means the chambers (13 to 15) can be interconnected.

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DESCRIPTION DE10134913A1

[0001]

13 The invention relates to a device for sample preparation, in particular a device for handling and treating blood samples, such as. B. for separating blood samples by centrifugation and for modifying blood samples by additives in preparation for cryopreservation of the blood samples, and methods for blood preparation, in particular for preparing blood samples for cryopreservation.

[0002]

21 It is known, for the cryopreservation of blood samples, to first prepare a blood unit from a blood donation for the state ready for freezing.

23 The preparation comprises in particular firstly a separation of the blood donation into an erythrocyte suspension which is to be cryopreserved and residual components and secondly the addition of a cryoadditive to the erythrocyte suspension. In conventional methods, blood samples are handled using flexible blood bags, as illustrated schematically in FIG. A blood donation is provided in a first blood bag 1' and centrifuged. After centrifugation, the blood donation is separated into the sediment and the supernatant (plasma). If necessary, the supernatant is drawn off into a waste container 4'. The erythrocyte suspension is transferred into another blood bag 2', to which a cryo-additive is added to provide the preserved product ready for freezing. The illustrated use of blood bags, described for example in DE 298 05 538 and WO 00/38762, has the following disadvantages.

[0003]

36 A major problem relates to the handling of the blood bags.

37 Since the blood bags do not have a fixed shape, careful handling of the blood bags must be

provided, in particular to preserve the phase boundary after centrifugation. In the conventional systems mentioned, devices for holding and transporting the blood bags are provided. However, these devices can only be automated to a very limited extent. The devices must be loaded manually and the operation must be continuously monitored. Furthermore, in the conventional devices, the blood bags are connected to one another via flexible hoses. To separate the erythrocyte suspension and supernatant, the phase boundary on the blood bag or tube must be detected. Due to the flexibility of the respective containers, there is a risk of incorrect detection and thus a malfunction during preparation.

[0004]

49 Further disadvantages result from sterility problems when handling the blood bags.

50 The hose connections must be connected to the blood bags in a sterile manner and separated and sealed after the respective process step. In each step of the preparation, complex precautions must be taken to maintain the sterility and freedom from pyrogens of the blood samples. The conventional blood bag preparation is also problematic because of the risk of mix-ups. If a blood bag is mixed up during preparation or cross-contamination occurs between blood bags, the consequences for the recipient of the blood donation can be devastating. Extensive safety measures have to be implemented in conventional systems to rule out the risk of confusion.

[0005]

61 Another disadvantage of the technique described in WO 00/38762 is its specific tailoring to stem cell preparation.

63 When separating stem cells from biological fluid samples, only a very small amount of stem cells has to be separated from the samples. This allows for the use of special centrifugation techniques and less sensitivity to the use of blood bags.

[0006]

69 In modern medicine and in civil protection there is an interest in enlarged blood banks with a wide range of different blood types.

71 Automating the preparation of the canned goods is necessary for the production of modern blood banks. Because of the need for automation, the applicability of conventional preparation devices is limited.

[0007]

77 The problems illustrated in handling blood samples are not unique to the preparation of preserves for cryopreservation.

79 There is also a corresponding need for sterile, automated and safe sample handling when

processing biological cell suspensions for therapeutic purposes.

[0008]

84 The object of the invention is to provide an improved device for the preparation of suspended biological samples, with which the disadvantages of conventional systems are overcome and which is particularly suitable for automated and safe handling of a large number of samples.

87 The object of the invention is in particular to provide an improved system for the preparation of cryopreserves such. B. Blood cryopreserves. The object of the invention is also to specify a novel method for handling biologically suspended samples which can be automated and carried out safely.

[0009]

94 These objects are achieved with a preparation device, a preparation station and a method having the features according to patent claims 1, 9 and 12.

96 Advantageous embodiments and applications of the invention result from the dependent claims.

[0010]

100 The basic idea of the invention is to provide a preparation device that has at least two containers for receiving the suspension samples to be treated, the containers, in contrast to conventional systems, being formed by chambers with fixed walls that are positioned stationary relative to one another.

104 The chambers are connected to one another via line connections that can be actuated individually or are equipped with connecting pieces for the optional formation of line connections between the chambers. According to a first embodiment, the preparation device according to the invention is formed by an integral structure in which the chambers are formed in a chamber body, at one end of which the line connections can be attached or adjusted. According to a second embodiment, the preparation device comprises a framework into which the chambers can be inserted individually. The connection pieces of the individual chambers are all on one (e.g. B. lower) side of the rack arranged. Depending on requirements, the connecting pieces, which are initially sealed with a septum, are opened and connected in pairs via line connections. According to a third embodiment, the design with individual chambers is such that the framework is equipped with a valve plate with line connections via which the individual chambers can be connected in pairs.

116 The design of the preparation device as an integral structure or as a frame structure with at least two chambers has the advantages that the preparation device represents an object that can be safely gripped and manipulated within the scope of an automated process sequence and that the sample handling, in particular the independent pre-filling of the chambers, the treatment of samples in the chambers and the transfer of the samples between the chambers, is simplified. When using the preparation device according to the invention for the production

of blood samples for cryopreservation, at least three chambers are preferably provided.

[0011]

126 According to said first embodiment of the invention, the chambers are preferably formed in the form of right circular cylinders in a plastic body, at one end of which is attached a valve plate which contains at least one line connection for coupling two chambers each.

129 The construction with an integral plastic body has the advantage that the preparation device can be manufactured as a disposable product, so that problems with sterility and mix-ups can be ruled out. A further advantage is the high stability of the preparation device, particularly during centrifugation processes.

[0012]

136 The second and third embodiments of the invention mentioned each represent a modular structure.

138 The chambers can be used as disposable products. An additional advantage is the relatively low weight of the frame construction.

[0013]

143 The transfer of samples between the chambers is preferably effected by hydrostatic pressure applied as gas pressure or preferably with plungers located in each chamber.

145 Alternatively, it is possible to transfer the pressure with a mechanically actuated piston (e.g. B. with a connecting rod rod). In this configuration, the chambers of the preparation device according to the invention form piston pressure generators, which are set up both to receive the respective samples and to transfer the samples to adjacent chambers.

[0014]

152 According to a further preferred embodiment, the preparation device, in particular the chambers as the main components, consists at least partially of a transparent plastic material.

154 If non-transparent material is used, the chambers preferably have at least one transparent window for optical detection. A reliable and reproducible optical detection of sample properties, in particular the position of the phase boundary after centrifugation, is made possible.

[0015]

160 The invention also relates to a preparation station that is equipped with the preparation device according to the invention and also has a pressure device for transferring samples between the chambers, a detector device for measuring sample properties in the chambers and an actuating device for selectively coupling chambers.

[0016]

167 The invention also relates to a method for the preparation of suspensions containing biologically relevant components, such as e.g.

169 B. cells, cell components or macromolecules, using the preparation device according to the invention.

171 The method is characterized in particular by the fact that all preparation steps are carried out with the entire preparation device, which contains different chambers for receiving samples at different stages of preparation.

[0017]

177 The invention has the following advantages for sample preparation, particularly for the manufacture of cryopreserved blood.

179 The preparation process is designed to increase productivity in canning, i. H. to achieve the highest possible canning throughput, can be automated, while at the same time increasing the production quality and maintaining it independently of the manual skills of an operator. A blood unit produced according to the invention already experiences an increase in quality through the use of the preparation device, without the preparation becoming significantly more expensive.

[0018]

188 The preparation device according to the invention is completely closed off from the outside during the preparation procedure.

190 It only comes into contact with the environment once during filling and emptying. For example, the pre-treatment of a preserve is absolutely sterile until it is ready for freezing. Advantageously, the opening, connecting and closing of bags and connecting tubes according to the conventional systems is avoided. The suspension sample does not leave the preparation device during the preparation steps. A mix-up e.g. B. blood from different donors or contamination by foreign blood or microorganisms are excluded. The identity of the donor blood is guaranteed. The preparation process is greatly accelerated, since work steps that may be necessary several times in conventional systems can be completely eliminated according to the invention. Partial or complete sample loss or contamination of the working environment, including the laboratory staff, through leaking tube connections are ruled out with the preparation device according to the invention.

[0019]

204 The preparation device according to the invention forms a solid container which, in comparison with conventionally used blood bags, enables the device and the valves and/or nozzles

attached to it to be gripped and manipulated in a defined and reproducible manner.

207 There is no need to grip or position and clamp connecting hoses if the at least one connecting line is integrated into the preparation device and thus enables the individual chambers to be connected repeatedly and reproducibly over the shortest possible route. The short distances and the choice of a suitable cross-section for the respective connecting line allow the transfer time for transferring samples between the chambers to be optimized. The construction of the device enables a defined positioning of the at least one connecting line. Accidental connection of currently non-cooperating chambers is excluded. Deformation or squeezing of the chambers is avoided according to the invention. a z. B. set by centrifugation phase separation of sample components can not be blurred by a gripping process.

[0020]

219 The fixed and preferably symmetrical arrangement of the chambers in a preparation device according to the invention enables rapid and defined positioning of the chamber of interest in a preparation system, independently of the process step.

222 All sensors and actuators are automatically positioned correctly. Increased, error-free throughput is achieved. For example, with a preparation device according to the invention, around three times as many cryopreserves can be prepared per unit of time. The preparation device allows a free choice of material and dimensioning of the outer shape of the chamber arrangement. Advantageously, the device can be readily used with conventional centrifuge equipment.

[0021]

231 By manufacturing the preparation device from inexpensive plastic materials, large numbers of the device can be manufactured using injection molding or extrusion techniques.

233 This is advantageous for the use according to the invention of the solidly walled chambers as disposable products.

[0022]

238 The following additional advantages result in particular in the preparation of blood samples.

239 When using the preparation device according to the invention, there is no significant additional effort for blood donation services. No multiple bag systems are required. The preparation device can be coupled directly to a simple donation bag (single blood bag). The supernatant (plasma and buffy coat) which in conventional methods ends up in the waste or can only be obtained with great effort is available according to the invention as an additional end product if required. The preparation device also provides advantages when filling freezing bags after preparation. When docked to the preparation device, a filled freezing bag can be vented in a simple and sterile manner with this device by subjecting the respective chamber to negative pressure.

[0023]

251 Further advantages and details of the invention result from the following description of the accompanying drawings.

253 Show it:

[0024]

257 1 shows a schematic phantom view of an embodiment of a preparation device according to the invention in a partially expanded state,

[0025]

262 FIG. 2 shows an illustration of the integration of the preparation device according to FIG. 1 into a device for the production of blood reserves,

[0026]

267 3 shows an enlarged partial view of a chamber end of the preparation device according to FIG. 1,

[0027]

272 4 illustration of a modified embodiment of a preparation device according to the invention,

[0028]

276 5 shows a schematic sectional view of a single chamber used according to the invention, and

[0029]

280 6 shows an illustration of a conventional preparation technique (prior art).

[0030]

284 1 shows an embodiment of a preparation device 100 according to the invention in a schematic phantom view.

286 The preparation device 100 comprises a chamber body 10, in which three chambers are formed for receiving suspension samples, a transfer device 20, consisting of a valve plate 21 and at least one connecting line 22, a stamp device 30 with several pressure stamps 31 to 33 and a cover plate 40, which upper end of the chamber body 10 forms.

290 The chamber body 10 is integrally formed of a transparent plastic material (e.g.
291 B. PMMA, cycloolefin copolymers, polyamide, polycarbonate, PCHP, polyester or polysulfone).
292 It has the external shape of a right circular cylinder with a flat upper side 11 and a flat lower side 12.
294 In the interior of the chamber body 10, the three cylindrical chambers 13, 14 and 15 for receiving samples are formed.
296 At the upper end of the chamber body 10, the chambers open out freely into the top 11.
297 At the lower end, each chamber has a taper 16 with a connecting piece 17, as illustrated in FIG. 3 on an enlarged scale. The connecting piece 17 opens into the underside 12 of the chamber body 10.

[0031]

303 For use in the preparation of blood samples, the preparation device 100 has, for example, a diameter of approximately 18 to 20 cm, the height of the chamber body 10 being approximately 10 to 12 cm and the chambers 13 to 15 each having an internal diameter of approximately 6 to own 8 cm.
307 A chamber preferably has a volume in the range 400 ml to 600 ml. The chambers 13 to 15 are preferably distributed symmetrically relative to the axis of the chamber body 10 .

[0032]

312 The transfer device 20 is set up to transfer samples between the chambers 13 to 15 .
313 The valve plate 21 is rotatably attached to the bottom 12 of the chamber body 10 . The connecting line 22, which forms an overflow channel, is integrated into the valve plate 21, which is also made of plastic material. Sealing rings made of an elastic material (e.g. B. PTFE) attached. In addition to the sealing function, the sealing rings (not shown) can also serve as latching devices. Upon rotation of the connecting plate 21, the sealing rings snap into place at the desired positions of the connecting pieces or the mouth of the connecting pipe 22 when these are straightly aligned with one another.

[0033]

323 The valve plate 21 has a valve function since liquid is generally only ever pumped in one direction from one chamber to the adjacent chamber.
325 To rule out incorrect operation, a device for forced specification of a specific direction of rotation and/or a repeat lock can be provided on the valve plate 21 or on the chamber body 10 . This device includes, for example, teeth that prevent reverse rotation and/or an additional locking aid.

[0034]

332 The structure of the valve plate 21 can be modified depending on the application (see FIG. 4).
333 Several connecting lines can be provided. The at least one connecting line can be equipped with a blocking or valve device. Additional through-openings for charging the chambers can preferably be provided in the valve plate. However, loading can also take place from the top.

[0035]

339 Pressure is applied to the samples to transport the samples between the chambers.
340 The sample is transferred via the overflow channel in the valve plate 21 under the effect of an overpressure in the chamber from which the transfer originates. The transfer pressure is applied with a pressure device which is part of the preparation station (see FIG. 2) in which the preparation device according to the invention is preferably used. According to an advantageous embodiment of the invention, the pressure is transmitted using a stamp device 30 which has a pressure stamp 31 to 33 in each of the chambers 13 to 15 . The plunger 31 to 33 consist of plastic bodies z. B. in the form of a cylinder, which are fitted in a form-fitting manner into the respective chamber. Each plunger has at least one circumferential sealing lip, which seals any gaps that may occur between the plungers and the inner walls of the chamber. The sealing lips prevent the piston from passing through the liquid samples when pressure is applied. The pistons with the sealing lips are made of a plastic material (e.g.
351 e.g. PTFE). The use of the plungers 31 to 33 in the chambers has the advantage that when the preparation device 100 moves, a sample movement in the chambers is prevented when the plungers are respectively placed on the liquids. After a centrifugation, the phase boundary between the fractions is advantageously avoided.

[0036]

358 According to a preferred embodiment, the plungers 31 to 33 can each have a central bore (shown in dashed lines) with a closure (e.g.
360 B. a septum). This allows access to the samples or supplemental liquids in the chambers from the top of the device 100.

[0037]

365 According to a modified embodiment of the invention, the use of the plunger can also be dispensed with.
367 In this case, the transfer pressure is applied directly to the liquid surface in the respective chamber. In this design, the upper ends of the chambers are preferably equipped with a sterile filter insert at the top, which is only suitable for the sterile pressure medium used (e.g. B. air, inert gas) is permeable. The structure without a plunger has the advantages of an increased internal volume and a simplified structure of the chambers and thus cost savings.

[0038]

375 The upper cover plate 40 serves to close off the preparation device 100.

376 It is fixedly mounted on the chamber body 10 and has through openings or ports 41 aligned with the upper ends of the chambers 13-15, respectively. The connecting pieces 41 serve to connect individual chambers or all chambers at the same time to the pressure device and/or charging devices.

[0039]

383 The process sequence for producing a blood cryopreservation using a preparation device according to the invention is explained below with reference to FIG.

385 FIG. 2 shows the preparation device 100 analogous to the representation according to FIG. 1 in combination with parts of the preparation station.

[0040]

390 The components of the preparation device 100 are provided with the same reference symbols as in FIG. 1 .

[0041]

395 The preparation station includes, in particular, the printing device 50, a detector device 60, an actuating device 70 and a control device 80.

397 The pressure device 50 preferably comprises a pressure generator 51 with a motor 52 and a pump part 53.

399 Alternatively, the pressure device 50 comprises a lever device with a connecting rod. The mechanical power transmission has the advantage that the positioning of the plunger can be done with increased precision. According to alternative embodiments of the invention, the pressure generator can also be supplied by a pressure source (e.g. B. compressed gas cylinder) are formed with a control valve.

[0042]

407 The detector device 60 comprises, in particular, at least one light-sensitive element 61 for detecting the phase boundary.

409 Depending on the application, the light-sensitive element 61 can be equipped with filter devices (not shown). A plurality of light-sensitive elements can also be arranged corresponding to the positions of the chambers. Depending on the application, other detectors for detecting sample properties can also be provided, as are known from analytics (e.g. B. spectrophotometer, resistivity meter for density determination). The chambers can also each have a scale extending over their length for optical control of the filling level, the position of the plunger or the position of the phase boundary. The detectors can also be attached to other components

of the preparation device, e.g. B. be provided on a connecting line in the valve plate.

[0043]

420 To adjust the valve plate 21 explained above, the adjusting device 70 comprises an actuating element 71 and a servomotor 72.

422 The actuating element 71 has the form of a plate with at least one projection 73 which cooperates with at least one corresponding recess (not shown) on the underside of the valve plate 21. The projection 73 engages in the recess and rotates the valve plate 21 into the desired position when the servomotor 72 is actuated, so that one chamber can be opened or emptied, two chambers are connected via the connecting line 22 or all three chambers are closed.

[0044]

431 The control device 80 is connected to the components 50, 60 and 70 of the preparation system.

432 Depending on the operating state and the detector signal supplied by the detector device 60, the pressure generator 50 and the actuating device 70 are actuated in the following manner. In the case of semi-automatic or manual operation, the corresponding steps are at least partially carried out by an operator.

[0045]

439 In a starting state, the chambers of the preparation device 100 according to the invention are loaded as follows.

441 In the first chamber 13 there is a blood donation. The blood donation is poured into the first chamber 13 from a donor bag, which may be carried out with the application of a supporting negative pressure. The second chamber 14 is filled with a washing solution. A cryoadditive is located in the third chamber 15 . In the starting state, the first chamber 13 is completely filled, while the remaining chambers 14, 15 are only partially filled. There is as much free volume in these chambers as is required to take over the erythrocyte suspension after centrifugation (see below). After the starting state (all closed), the valve plate 21 is set in such a way that, for example, the first and second chambers 13, 14 are connected. Advantageously, there is essentially no liquid exchange via the connecting line despite the connection in the pressure-free state.

[0046]

454 In a first preparation step, the chamber body with the filled chambers is centrifuged using a centrifugation device.

456 The centrifugation device (not shown) has the design of a large centrifuge known per se with individual centrifuge buckets in which a large number of preparation devices can be

centrifuged at the same time. During centrifugation, the blood donation is only separated into fractions. The plungers 31 to 33 are not shifted. The chambers are sealed during centrifugation.

[0047]

464 The state of the preparation device after centrifugation is shown in FIG.

465 In the first chamber 13, the formed fractions of the blood donation with the erythrocyte sediment 1 of the so-called "Buffy Coat" layer 2 and the plasma supernatant 3 illustrated. Depending on the operation, the erythrocyte sediment 1 comprises a volume proportion of approx. 45% of the chamber 13. The volume fraction depends in particular on the centrifugation speed. A higher speed results in a higher packing density of the erythrocytes and thus a lower volume fraction. The “buffy coat” layer 2 is a greyish-colored coating containing thrombocytes and leukocytes, which forms between the deep red erythrocyte sediment 1 and the bright red plasma supernatant 3 after centrifugation.

[0048]

476 After the centrifugation, the preparation device 100 is inserted into the preparation station.

477 The valve plate 21 is rotated between the first and second chambers 13, 14 in the passage direction. This is done manually, e.g. B. with a knob wrench or with the adjusting device 70 (see above). The first chamber 13 is pressurized. Under the action of hydrostatic or mechanical pressure, the plunger 31 moves downwards and the plunger 32 moves upwards. The separated blood donation is transferred to the second chamber 14 . This preparation step is terminated as soon as the detector device 60 arranged at the lower end of the first chamber 13 detects the "buffy coat" layer 2 . In this state it is ensured that only erythrocyte sediment is still present in the narrowed area 16 (see FIG. 3) and the connecting line. When the buffy coat layer 2 has been detected, the print transfer is stopped. Then the valve plate is brought into the closed position. This occurs either immediately upon detection of the layer 2 or with a time delay, so that concentrate residues from the narrowed area 16 can still get into the connecting line.

[0049]

492 The erythrocytes transferred to the second chamber 14 mix with the washing solution.

493 The washing solution includes, for example, physiological saline. Another centrifugation follows, as a result of which the treated erythrocytes again collect as a concentrate in the lower part of the second chamber 14, while the remaining washing solution forms the supernatant.

[0050]

499 In a further preparation step, the washed erythrocyte sediment is transferred to the third

chamber 15 analogously to the manner described.

501 For this purpose, the valve plate 21 is rotated in such a way that the connecting line 22 is arranged between the second and third chambers 14 , 15 . In addition, the pressure distributor 56 is adjusted accordingly. The pressure transmission is in turn controlled as a function of the detector signal from the detector device 60 . A further sensor (not shown) can be provided on the second chamber 14 . Alternatively, it is possible to rotate the preparation device 100 towards the sensor 61 so that the phase boundary in the second chamber 14 can be detected.

[0051]

510 After the washed erythrocyte sediment has been transferred to the third chamber 15, it is mixed with the cryoadditive there.

512 The additives known per se are used as cryoadditive. For example, the cryoadditive comprises a solution of water-soluble starch derivative.

[0052]

517 After the washed erythrocytes have been transferred to the third chamber 15 and mixed with the cryoadditive, the cryopreserve is ready to be frozen.

519 This is followed by the transfer to the container selected depending on the application, e.g. B. a cryobag in which the freezing process takes place. After completion of the preparation, the plasma supernatant is advantageously present in the first chamber 13 as a donor-specific residual product. Depending on the application, the plasma can be used for other purposes.

[0053]

526 Details of a design of the preparation device according to the invention that is modified compared to FIG. 1 are shown in FIG.

528 The differences relate to the design of the valve plate 21. The lower side 12 of the chamber body 10 with the chambers 13 to 15 is illustrated in the top partial image of FIG. Each chamber has an inlet and outlet opening in the form of a connecting piece 17 (see FIG. 3). An O-ring seal 18 is provided on each connecting piece 17 . In the middle of the chamber body 10, corresponding to the cylinder axis, there is a threaded hole 19 for fastening the valve plate 21.

[0054]

536 In the middle part of Fig. 4, the valve plate 21 is shown individually.

537 In this design, two connecting lines (or overflow channels) 22, 23 are provided, which are arranged such that two chambers can be connected to one of the connecting lines 22 or 23, while the other connecting line 22 or 23 is closed. The use of two connecting lines has the advantage of shorter adjustment paths when setting the chamber connections in the individual preparation steps. Three inlet and outlet bores 24 are provided in the valve plate, which are

arranged in such a way that when one of the inlet and outlet bores 24 is aligned with one of the connecting pieces 17, the other connecting pieces remain closed.

[0055]

547 The valve plate 21 has a circumferential O-ring 25 which provides an additional seal against the underside 12 of the chamber body 10.

549 The reference number 26 refers to the axis of rotation and the bearing of the valve plate 21.

[0056]

553 In the lower partial image of FIG. 4, the valve plate 21 and the underside 12 of the chamber body 10 are shown in the assembled state.

555 If the valve plate 21 is turned to the left from the state shown, the chambers 13 and 14 are first connected to the connecting line 22 and the chambers 14 and 15 are connected via the connecting line 23 as the adjustment continues. The two preparation steps explained above can thus be carried out with a short travel distance.

[0057]

562 The embodiment of the invention illustrated in FIGS. 1 to 4 can be modified in many ways depending on the task at hand.

564 For example, further chambers for accommodating further additives can be provided in the chamber body in order to carry out further preparation steps. Instead of the 120° arrangement, the chambers can also be arranged differently in the chamber body or a frame (see below). Depending on the application, the chambers can be loaded from the top or bottom. This is preferably done using tubing or pipetting systems. According to a preferred embodiment of the invention, the inlet openings of the chambers are adapted to the outer diameter of standardized liquid pipettes or tube adapters, so that they can be easily attached and operated for loading. Depending on the application, the size of the preparation device can be scaled as desired. The transmission device with the valve plate can be replaced by a fixed arrangement of several connecting lines with valves that can be actuated.

[0058]

577 Additional gripping or fastening devices for handling the chamber body and/or for use in a centrifuge can be provided on the outside of the chamber body.

[0059]

582 According to the invention, the chamber body with the integrated chambers can be replaced by an arrangement of individual chambers in a frame.

584 This configuration has advantages with regard to separate filling of the individual chambers before composition for the preparation device and disposal of the chambers after use.

586 Any suitable structure can be used as the framework, into which the chambers can be inserted in a fixed manner in accordance with the desired arrangement and which has sufficient stability during centrifugation. Depending on the design of the chambers, the structure of the frame is adjusted.

[0060]

593 If ready-made plunger syringes with suitable plunger diameters are used as chambers, then the frame has recesses to accommodate the syringe plunger.

595 If the individual chambers are formed by straight tubular bodies, the recesses in the framework are adjusted accordingly. If necessary, conically preformed chamber floors are provided on the floor of the framework, as illustrated in FIG.

[0061]

601 5 shows a single chamber in a schematic sectional view.

602 Two or more such individual chambers (e.g. B. according to the above design three individual chambers) are provided on a frame (not shown). The single chamber 90 comprises a chamber wall 91 in the shape of a right circular cylinder and a tapered portion 92 which rests in a correspondingly shaped support base 93 which is part of the framework. Inside the single chamber 90 is the plunger (see above). In this configuration, the pressure ram is not cylindrical, but is designed as a ram plate 94 with a sealing ring 97 running around it on the outside. The stamp plate 94 consists of PMMA, for example. The sealing ring 97 is a z. B. made of PTFE molded part that is pulled positively over the outer edge of the stamp plate 94. The cross section of the sealing ring 97 has a U-shape, the open ends of which form two sealing lips. This shape ensures that the sealing lips lie tightly against the chamber wall. The upper side of the individual chamber 90 is closed with a cover plate 95, which has a passage opening 96 for the passage of the pressure medium.

[0062]

617 The individual chamber 90 has, for example, a volume of 470 ml with a diameter of approx. 80 mm, a length of the chamber wall 91 of approx. 110 mm and a height of the support base 93 of approx. 30 mm.

620 The partial area 92 delimits a partial volume of approximately 30 ml.

[0063]

624 In a method according to the invention for blood preparation, the following single-chamber centrifugation can be provided in deviation from the centrifugation of the entire preparation

device explained above.

627 The individual chamber of interest (e.g. B. according to FIG. 5) removed from the frame and centrifuged separately. Before or after centrifugation, the individual chamber is arranged in the frame for carrying out the remaining steps of sample preparation. This method is particularly advantageous if no suitable centrifuge is available for centrifugation.

[0064]

634 The features of the invention disclosed in the above description, the claims and the drawings can be important both individually and in any combination for the implementation of the invention in its various configurations.

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CLAIMS DE10134913A1

1.

13 Preparation device (100) for treating suspension samples, in particular for preparing cryopreserved blood, with an arrangement of at least two containers for holding suspension samples, sample parts and/or additives, characterized in that the containers are designed as chambers (13 to 15, 90) are formed with solid walls and are arranged in a fixed position relative to one another, a transmission device (20) having at least one connecting line (22) being provided, via which the chambers (13 to 15) can be connected to one another.

2.

22 Preparation device according to claim 1, wherein the chambers (13 to 15) are formed in a one-piece chamber body (10).

3.

27 Preparation device according to Claim 1, in which the chambers (90) are detachably fastened as individual chambers in a framework.

4.

32 Preparation device according to one of the preceding claims, in which the walls of the chambers or the chamber body (10) consist of a transparent material.

5.

37 Preparation device according to one of the preceding claims 1 or 2, in which the chambers (13

to 15) have the shape of straight hollow cylinders which run from an upper side (11) to an underside (12) of the chamber body (10), the underside (12) each chamber (13 to 15) has a connecting piece (17) to which one end of the at least one connecting line (22) can be connected.

6.

45 Preparation device according to one of the preceding claims, in which a pressure plunger (31 to 33) is provided in each chamber.

7.

50 Preparation device according to Claim 6, in which each pressure plunger (31 to 33) has a peripheral sealing lip.

8.

55 Preparation device according to one of the preceding claims, in which the transmission device (20) is formed by a valve plate (21) in which at least one connecting line (22) is integrated, the valve plate (21) being arranged rotatably.

9.

61 Preparation station for preparing suspension samples, comprising: at least one preparation device (100) according to one of the preceding claims, a printing device (50), a detector device (60), an actuating device (70), and a control device (80).

10.

67 Preparation station according to Claim 9, in which the pressure device (50) comprises a pneumatic pressure generator or a mechanical pressure generator with connecting rods.

11.

72 Preparation station according to Claim 9 or 10, in which the adjusting device (70) has an actuating element (71) with which the transmission device (20) can be adjusted in such a way that two chambers are connected via the at least one connecting line (22).

12.

78 A method for preparing suspension samples using a preparation device (100) according to any one of claims 1 to 8, in which treatment of a sample in at least one of the chambers (13 to 15,

90) and transfer of at least part of the sample between two chambers are alternated he follows.

13.

84 Method according to Claim 12, in which the sample treatment comprises centrifugation of the sample and/or treatment of the sample with additives.

14.

89 Method according to claim 13, in which the entire preparation device (100) or an individual chamber (90) is centrifuged during the centrifugation of the sample.

15.

94 A method according to any one of claims 12 to 14, in which a cryopreserved blood is prepared.

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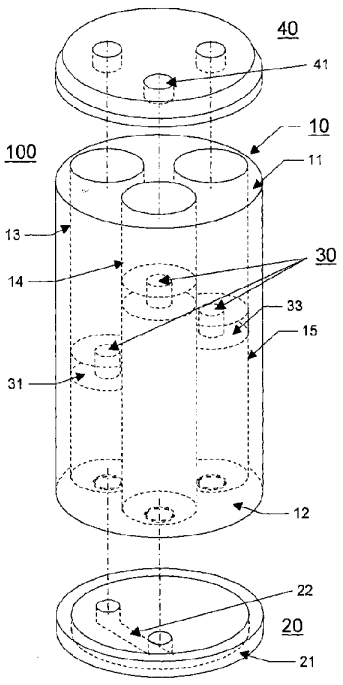
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Die folgenden Angaben sind den vom Anmelder eingereichten Unterlagen entnommen

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(54) Vorrichtung und Verfahren zur Blutpräparation

(57) Es wird eine Präparationsvorrichtung (100) zur Behandlung von Suspensionsproben, insbesondere zur Präparation von Blut-Kryokonserven, mit einer Anordnung von mindestens zwei Behältnissen zur Aufnahme von Suspensionsproben, Probenteilen und/oder Zusatzstoffen beschrieben, wobei die Behältnisse als Kammern (13 bis 15, 90) mit festen Wänden gebildet und relativ zueinander ortsfest angeordnet sind, wobei eine Übertragungseinrichtung (20) mit mindestens einer Verbindungsleitung (22) vorgesehen ist, über die die Kammern (13 bis 15) miteinander verbunden werden können.



DE 101 34 913 A 1

Beschreibung

[0001] Die Erfindung betrifft eine Vorrichtung zur Probenpräparation, insbesondere eine Vorrichtung zur Handhabung und Behandlung von Blutproben, wie z. B. zum Trennen von Blutproben durch Zentrifugation und zur Modifizierung von Blutproben durch Zusatzstoffe zur Vorbereitung einer Kryokonservierung der Blutproben, und Verfahren zur Blutpräparation, insbesondere zur Vorbereitung von Blutproben für die Kryokonservierung.

[0002] Es ist bekannt, zur Kryokonservierung von Blutproben zunächst aus einer Blutspende eine Blutkonserve für den einfrierfertigen Zustand zu präparieren. Die Präparation umfasst insbesondere erstens eine Auftrennung der Blutspende in eine Erythrozytensuspension, die kryokonserviert werden soll, und Restbestandteile und zweitens den Zusatz eines Kryoadditives zur Erythrozytensuspension. Bei herkömmlichen Verfahren erfolgt die Handhabung der Blutproben unter Verwendung von flexiblen Blutbeuteln, wie es schematisch in **Fig.** 6 illustriert ist. Eine Blutspende wird in einem ersten Blutbeutel **1'** bereitgestellt und zentrifugiert. Nach dem Zentrifugieren ist die Blutspende in das Sediment und den Überstand (Plasma) getrennt. Der Überstand wird ggf. in einen Abfallbehälter **4'** abgezogen. Die Erythrozytensuspension wird in einen weiteren Blutbeutel **2'** umgefüllt, dem zur Bereitstellung der einfrierfertigen Konserve ein Kryoadditiv zugesetzt wird. Die illustrierte Verwendung von Blutbeuteln, die bspw. in DE 298 05 538 und WO 00/38762 beschrieben wird, besitzt die folgenden Nachteile.

[0003] Ein Hauptproblem betrifft die Handhabung der Blutbeutel. Da die Blutbeutel keine feste Form besitzen, muss insbesondere zur Erhaltung der Phasengrenze nach der Zentrifugation ein schonender Umgang mit den Blutbeuteln vorgesehen sein. Bei den genannten herkömmlichen Systemen sind zwar Vorrichtungen zur Halterung und zum Transport der Blutbeutel vorgesehen. Diese Vorrichtungen sind jedoch nur sehr eingeschränkt automatisierbar. Es müssen eine manuelle Beschickung der Vorrichtungen und eine laufende Überwachung des Betriebes erfolgen. Des Weiteren sind die Blutbeutel bei den herkömmlichen Vorrichtungen über flexible Schläuche miteinander verbunden. Zur Trennung von Erythrozytensuspension und Überstand muss die Phasengrenze am Blutbeutel oder am Schlauch detektiert werden. Wegen der Flexibilität der jeweiligen Behältnisse besteht das Risiko einer Fehldetektion und damit einer Fehlfunktion bei der Präparation.

[0004] Weitere Nachteile ergeben sich aus Sterilitätsproblemen beim Umgang mit den Blutbeuteln. Die Schlauchverbindungen müssen steril an die Blutbeutel angeschlossen und nach dem jeweiligen Verfahrensschritt abgetrennt und verschweißt werden. Bei jedem Präparationsschritt müssen aufwendige Vorkehrungen zur Erhaltung der Sterilität und Pyrogenfreiheit der Blutproben getroffen werden. Die herkömmliche Blutbeutelpräparation ist auch wegen der Verwechslungsgefahr problematisch. Wenn während der Präparation ein Blutbeutel verwechselt wird oder eine Kreuzkontamination zwischen Blutbeuteln auftritt, so kann dies verheerende Folgen für den Empfänger der Blutspende haben. Zum Ausschluss der Verwechslungsgefahr müssen bei herkömmlichen Systemen aufwendige Sicherheitsmaßnahmen realisiert werden.

[0005] Ein weiterer Nachteil der in WO 00/38762 beschriebenen Technik besteht in deren spezifischen Zuschnitt auf die Stammzellenpräparation. Bei der Trennung von Stammzellen aus biologischen Flüssigkeitsproben ist lediglich ein sehr geringer Stammzellengehalt aus den Proben abzutrennen. Dies ermöglicht den Einsatz spezieller Zentrifugationstechniken und eine geringere Empfindlichkeit in Bezug auf die Verwendung von Blutbeuteln.

[0006] In der modernen Medizin und im Katastrophenschutz besteht ein Interesse an vergrößerten Blutbanken mit einem breiten Spektrum verschiedenster Bluttypen. Zur Herstellung moderner Blutbanken ist eine Automatisierung der Konservenpräparation erforderlich. Wegen des Automatisierungsbedarfes ist die Anwendbarkeit herkömmlicher Präparationsvorrichtungen eingeschränkt.

[0007] Die illustrierten Probleme bei der Handhabung von Blutproben bestehen nicht nur bei der Vorbereitung von Konserven für die Kryokonservierung. Ein entsprechender Bedarf nach steriler, automatisierter und sicherer Probenhandhabung besteht auch bei der Bearbeitung von biologischen Zeilsuspensionen für therapeutische Zwecke.

[0008] Die Aufgabe der Erfindung ist es, eine verbesserte Vorrichtung zur Präparation suspendierter biologischer Proben bereitzustellen, mit der die Nachteile herkömmlichen Systeme überwunden werden und die insbesondere für eine automatisierbare und sichere Handhabung einer Vielzahl von Proben geeignet ist. Die Aufgabe der Erfindung besteht insbesondere in der Schaffung eines verbesserten Systems zur Präparation von Kryokonserven, wie z. B. Blut-Kryokonserven. Die Aufgabe der Erfindung ist es auch, ein neuartiges Verfahren zur Handhabung biologischer suspendierter Proben anzugeben, das insbesondere automatisierbar und sicher durchführbar ist.

[0009] Diese Aufgaben werden mit einer Präparationsvorrichtung, einer Präparationsstation und einem Verfahren mit den Merkmalen gemäß den Patentansprüchen 1, 9 und 12 gelöst. Vorteilhafte Ausführungsformen und Anwendungen der Erfindung ergeben sich aus den abhängigen Ansprüchen.

[0010] Die Grundidee der Erfindung ist es, eine Präparationsvorrichtung bereitzustellen, die mindestens zwei Behältnisse zur Aufnahme der zu behandelnden Suspensionsproben aufweist, wobei die Behältnisse im Unterschied zu herkömmlichen Systemen durch relativ zueinander ortsfest positionierte Kammern mit festen Wänden gebildet werden. Die Kammern sind über einzeln betätigbare Leitungsverbindungen miteinander verbunden oder mit Anschlussstücken zur optionalen Ausbildung von Leitungsverbindungen zwischen den Kammern ausgestattet. Die erfindungsgemäße Präparationsvorrichtung ist gemäß einer ersten Ausführungsform durch einen integralen Aufbau gebildet, bei dem die Kammern in einem Kammerkörper geformt sind, an dessen einem Ende die Leitungsverbindungen ansetzbar oder einstellbar sind. Gemäß einer zweiten Ausführungsform umfasst die Präparationsvorrichtung ein Rahmengestell, in das die Kammern einzeln einsetzbar sind. Die Anschlussstücke der einzelnen Kammern sind sämtlich auf einer (z. B. unteren) Seite des Rahmengestells angeordnet. Je nach Bedarf werden die zunächst mit einem Septum verschlossenen Anschlussstücke geöffnet und über Leitungsverbindungen paarweise in Verbindung gebracht. Die Gestaltung mit einzelnen Kammern ist gemäß einer dritten Ausführungsform derart ausgebildet, dass das Rahmengestell mit einer Ventilplatte mit Leitungsverbindungen ausgestattet ist, über die die einzelnen Kammern paarweise verbunden werden können. Die Ausbildung der Präparationsvorrichtung als integraler Aufbau oder als Gestellaufbau mit mindestens zwei Kammern besitzt die Vorteile, dass die Präparationsvorrichtung im Rahmen eines automatisierten Verfahrensablaufes einen sicher greif- und manipulierbaren Gegenstand darstellt und dass die Probenhandhabung, insbesondere die unabhängige Vorbefüllung der Kammern, die Behandlung von Proben in den Kammern und die Überführung der Proben zwischen den Kammern, vereinfacht wird. Bei Anwendung der erfindungsgemäßen Präparationsvorrichtung zur Her-

stellung von Blutproben für die Kryokonservierung sind vorzugsweise mindestens drei Kammern vorgesehen.

[0011] Gemäß der genannten ersten Ausführungsform der Erfindung sind die Kammern vorzugsweise in Form von geraden Kreiszylindern in einem Kunststoffkörper gebildet, an dessen einem Ende eine Ventilplatte angebracht ist, die mindestens eine Leitungsverbindung zur Kopplung von jeweils zwei Kammern enthält. Der Aufbau mit einem integralen Kunststoffkörper besitzt den Vorteil, dass die Präparationsvorrichtung als Einwegprodukt herstellbar ist, so dass Sterilitäts- und Verwechslungsprobleme ausgeschlossen werden können. Als weiterer Vorteil ergibt sich eine hohe Stabilität der Präparationsvorrichtung insbesondere bei Zentrifugationsvorgängen.

[0012] Die genannten zweiten und dritten Ausführungsformen der Erfindung stellen jeweils einen modularen Aufbau dar. Die Kammern können als Einwegprodukte verwendet werden. Als zusätzlicher Vorteil ergibt sich beim Rahmenaufbau ein relativ geringes Gewicht.

[0013] Die Übertragung von Proben zwischen den Kammern erfolgt vorzugsweise durch einen hydrostatischen Druck, der als Gasdruck oder vorzugsweise mit Druckstempeln ausgeübt wird, die jeweils in den Kammern angeordnet sind. Alternativ ist es möglich, den Druck mit einem mechanisch betätigbaren Kolben zu übertragen (z. B. mit einem Pleuelgestänge). Die Kammern der erfindungsgemäßen Präparationsvorrichtung bilden bei dieser Gestaltung Kolben-Druckerzeuger, die sowohl zur Aufnahme der jeweiligen Proben als auch zur Übertragung der Proben in benachbarte Kammern eingerichtet sind.

[0014] Gemäß einer weiteren bevorzugten Gestaltung besteht die Präparationsvorrichtung, insbesondere die Kammern als Hauptkomponenten, zumindest teilweise aus einem transparenten Kunststoffmaterial. Bei Verwendung von nicht-transparentem Material besitzen die Kammern vorzugsweise mindestens ein transparentes Fenster zur optischen Detektion. Es wird eine zuverlässige und reproduzierbare optische Detektion von Probeneigenschaften, insbesondere der Lage der Phasengrenze nach einer Zentrifugation, ermöglicht.

[0015] Gegenstand der Erfindung ist auch eine Präparationsstation, die mit der erfindungsgemäßen Präparationsvorrichtung ausgestattet ist und des Weiteren eine Druckeinrichtung zur Probenübertragung zwischen den Kammern, eine Detektoreinrichtung zur Messung von Probeneigenschaften in den Kammern und eine Stelleinrichtung zur selektiven Kopplung von Kammern aufweist.

[0016] Gegenstand der Erfindung ist auch ein Verfahren zur Präparation von Suspensionen, die biologisch relevante Komponenten, wie z. B. Zellen, Zellbestandteile oder Makromoleküle, enthalten, unter Verwendung der erfindungsgemäßen Präparationsvorrichtung. Das Verfahren zeichnet sich insbesondere dadurch aus, dass alle Präparationsschritte mit der gesamten Präparationsvorrichtung durchgeführt werden, die verschiedene Kammern zur Aufnahme von Proben in verschiedenen Präparationsstadien enthält.

[0017] Die Erfindung besitzt die folgenden Vorteile für die Probenpräparation, insbesondere für die Herstellung von Blut-Kryokonserven. Der Präparationsprozess ist zur Erhöhung der Produktivität bei der Konservenherstellung, d. h. zur Erzielung eines möglichst hohen Konservendurchsatzes, automatisierbar, wobei gleichzeitig die Herstellungsqualität gesteigert und unabhängig von der Handfertigkeit eines Bedieners aufrechterhalten wird. Eine erfindungsgemäß hergestellte Blutkonserve erfährt bereits durch die Verwendung der Präparationsvorrichtung eine Qualitätssteigerung, ohne dass die Präparation wesentlich verteuert wird.

[0018] Die erfindungsgemäße Präparationsvorrichtung ist während der Präparationsprozedur nach außen hin absolut abgeschlossen. Sie tritt lediglich einmalig jeweils beim Befüllen und beim Entleeren in Kontakt mit der Umgebung. Beispielsweise erfolgt die Vorbehandlung einer Konserve bis zum Erlangen des einfrierfertigen Zustandes absolut steril. Vorteilhafterweise wird das Öffnen, Verbinden und Verschließen von Beuteln und Verbindungsschläuchen entsprechend den herkömmlichen Systemen vermieden. Die Suspensionsprobe verlässt während der Präparationsschritte nicht die Präparationsvorrichtung. Eine Verwechslung z. B. von Blut verschiedener Spender oder eine Kontamination durch Fremdblut oder Mikroorganismen sind ausgeschlossen. Die Identität des Spenderblutes ist garantiert. Der Präparationsvorgang wird stark beschleunigt, da Arbeitsschritte, die bei herkömmlichen Systemen ggf. mehrfach notwendig sind, erfindungsgemäß vollständig entfallen können. Ein teilweiser oder vollständiger Probenverlust oder eine Kontamination der Arbeitsumgebung einschließlich des Laborpersonals durch undichte Schlauchverbindungen werden bei der erfindungsgemäßen Präparationsvorrichtung ausgeschlossen.

[0019] Die erfindungsgemäße Präparationsvorrichtung bildet ein festes Behältnis, das im Vergleich mit herkömmlich verwendeten Blutbeuteln ein definiertes und reproduzierbares Greifen und Handhaben der Vorrichtung und der an dieser angebrachten Ventile und/oder Stutzen ermöglicht. Das Greifen oder Positionieren und Klemmen von Verbindungsschläuchen entfällt, wenn die mindestens eine Verbindungsleitung in die Präparationsvorrichtung integriert ist und somit ein reproduzierbares und mehrfaches Verbinden der einzelnen Kammern auf kürzestem Weg ermöglicht. Durch die kurzen Wege und die Wahl eines geeigneten Querschnittes der jeweiligen Verbindungsleitung lässt sich die Transferzeit zur Übertragung von Proben zwischen den Kammern optimieren. Der Aufbau der Vorrichtung ermöglicht ein definiertes Positionieren der mindestens einen Verbindungsleitung. Ein versehentliches Verbinden von aktuell nicht kooperierenden Kammern wird ausgeschlossen. Ein Deformieren oder Quetschen der Kammern wird erfindungsgemäß vermieden. Eine z. B. durch Zentrifugation eingestellte Phasentrennung von Probenbestandteilen kann durch einen Greifvorgang nicht verwischt werden.

[0020] Die feste und vorzugsweise symmetrische Anordnung der Kammern in einer erfindungsgemäßen Präparationsvorrichtung ermöglicht ein schnelles und definiertes Positionieren der jeweils interessierenden Kammer in einem Präparationssystem unabhängig vom Verfahrensschritt. Alle Sensoren und Aktoren sind automatisch korrekt positioniert. Es wird ein erhöhter, fehlerfreier Durchsatz erzielt. Beispielsweise lassen sich mit einer erfindungsgemäß Präparationsvorrichtung rund dreifach mehr Kryokonserven pro Zeiteinheit präparieren. Die Präparationsvorrichtung ermöglicht eine freie Materialwahl und Dimensionierung der Außenform der Kammeranordnung. Vorteilhafterweise kann die Vorrichtung ohne Weiteres mit herkömmlichen Zentrifugiereinrichtungen verwendet werden.

[0021] Durch die Herstellung der Präparationsvorrichtung aus kostengünstigen Kunststoffmaterialien können große Stückzahlen der Vorrichtung in Spritzgieß- oder Extrusionstechniken hergestellt werden. Dies ist für die erfindungsgemäße Verwendung der fest bewandeten Kammern als Einwegprodukte von Vorteil.

[0022] Insbesondere bei der Präparation von Blutproben ergeben sich zusätzlich die folgenden Vorteile. Für Blutspendedienste entsteht bei Einsatz der erfindungsgemäßen Präparationsvorrichtung kein wesentlicher Zusatzaufwand. Es werden keine Mehrfachbeutelsysteme erforderlich. Die Präparationsvorrichtung kann direkt mit einem einfachen

Spendebeutel (Einfachblutbeutel) gekoppelt werden. Der bei herkömmlichen Verfahren ggf. in den Abfall gelangende oder nur mit großem Aufwand gewinnbare Überstand (Plasma und "Buffy Coat") steht erfindungsgemäß bei Bedarf als zusätzliches Endprodukt zur Verfügung. Die Präparationsvorrichtung liefert auch Vorteile bei der nach der Präparation vorgesehenen Befüllung von Einfrierbeuteln. Ein befüllter Einfrierbeutel kann im angedockten Zustand an der Präparationsvorrichtung mit dieser einfach und steril entlüftet werden, in dem die jeweilige Kammer mit einem Unterdruck beaufschlagt wird.

[0023] Weitere Vorteile und Einzelheiten der Erfindung ergeben sich aus der folgenden Beschreibung der beigefügten Zeichnungen. Es zeigen:

[0024] **Fig.** 1 eine schematische Phantomansicht einer Ausführungsform einer erfindungsgemäßen Präparationsvorrichtung in teilweise auseinander gezogenem Zustand,

[0025] **Fig.** 2 eine Illustration der Einbindung der Präparationsvorrichtung gemäß **Fig.** 1 in eine Vorrichtung zur Herstellung von Blutkonserven,

[0026] **Fig.** 3 eine vergrößerte Teilansicht eines Kammerendes der Präparationsvorrichtung gemäß **Fig.** 1,

[0027] **Fig.** 4 Illustration einer abgewandelten Ausführungsform einer erfindungsgemäßen Präparationsvorrichtung,

[0028] **Fig.** 5 eine schematische Schnittansicht einer erfindungsgemäß verwendeten Einzelkammer, und

[0029] **Fig.** 6 eine Illustration einer herkömmlichen Präparationstechnik (Stand der Technik).

[0030] In **Fig.** 1 ist eine Ausführungsform einer erfindungsgemäßen Präparationsvorrichtung **100** in schematischer Phantomansicht dargestellt. Die Präparationsvorrichtung **100** umfasst einen Kammerkörper **10**, in dem drei Kammern zur Aufnahme von Suspensionsproben gebildet sind, eine Übertragungseinrichtung **20**, bestehend aus einer Ventilplatte **21** und mindestens einer Verbindungsleitung **22**, eine Stempeleinrichtung **30** mit mehreren Druckstempeln **31** bis **33** und eine Deckplatte **40**, die den oberen Abschluss des Kammerkörpers **10** bildet. Der Kammerkörper **10** ist einstückig aus einem transparenten Kunststoffmaterial (z. B. PMMA, Cycloolefin-Copolymere, Polyamid, Polycarbonat, PCHP, Polyester oder Polysulfone) geformt. Er besitzt die äußere Form eines geraden Kreiszylinders mit einer ebenen Oberseite **11** und einer ebenen Unterseite **12**. Im Inneren des Kammerkörpers **10** sind die drei zylinderförmigen Kammern **13**, **14** und **15** zur Probenaufnahme gebildet. Am oberen Ende des Kammerkörpers **10** münden die Kammern frei in die Oberseite **11**. Am unteren Ende besitzt jede Kammer eine Verjüngung **16** mit einem Anschlussstutzen **17**, wie es vergrößert in **Fig.** 3 illustriert ist. Der Anschlussstutzen **17** mündet jeweils in die Unterseite **12** des Kammerköpers **10**.

[0031] Zur Anwendung bei der Präparation von Blutproben besitzt die Präparationsvorrichtung **100** bspw. einen Durchmesser von ca. 18 bis 20 cm, wobei die Höhe des Kammerkörpers **10** ca. 10 bis 12 cm beträgt und die Kammern **13** bis **15** jeweils einen Innendurchmesser von ca. 6 bis 8 cm besitzen. Eine Kammer besitzt vorzugsweise ein Volumen im Bereich von 400 ml bis 600 ml. Die Kammern **13** bis **15** sind vorzugsweise relativ zur Achse des Kammerkörpers **10** symmetrisch verteilt angeordnet.

[0032] Die Übertragungseinrichtung **20** ist zur Übertragung von Proben zwischen den Kammern **13** bis **15** eingerichtet. Die Ventilplatte **21** ist drehbar an der Unterseite **12** des Kammerkörpers **10** befestigt. In die ebenfalls aus Kunststoffmaterial hergestellte Ventilplatte **21** ist die Verbindungsleitung **22** integriert, die einen Überströmkanal bildet. An den Mündungen der Verbindungsleitungen **22** auf der inneren Seite der Verbindungsplatte **21**, die an die Unterseite **12** des Kammerkörpers **10** angrenzt, oder an den Anschlussstutzen **17** der einzelnen Kammern (siehe **Fig.** 3) sind Dichtungsringe aus einem elastischen Material (z. B. PTFE) angebracht. Neben der Dichtfunktion können die Dichtungsringe (nicht dargestellt) auch als Rasteinrichtungen dienen. Bei Drehung der Verbindungsplatte **21** rasten die Dichtungsringe an den gewünschten Positionen der Anschlussstutzen oder der Mündung der Verbindungsleitung **22** ein, wenn diese gerade zueinander ausgerichtet sind.

[0033] Die Ventilplatte **21** besitzt eine Ventilfunktion, da in der Regel Flüssigkeit immer nur in einer Richtung von einer Kammer zur benachbarten Kammer gepumpt wird. Zum Ausschluss einer Fehlbedienung kann an der Ventilplatte **21** oder am Kammerkörper **10** eine Vorrichtung zur erzwungenen Vorgabe einer bestimmten Drehrichtung und/oder eine Wiederholsperre vorgesehen sein. Diese Vorrichtung umfasst bspw. eine Verzahnung, die eine Rückwärtsdrehung ausschließt, und/oder eine zusätzliche Arretierhilfe.

[0034] Der Aufbau der Ventilplatte **21** kann anwendungsabhängig abgewandelt werden (siehe **Fig.** 4). Es können mehrere Verbindungsleitungen vorgesehen sein. Die mindestens eine Verbindungsleitung kann mit einer Sperr- oder Ventileinrichtung ausgestattet sein. In der Ventilplatte können vorzugsweise zusätzliche Durchgangsöffnungen zur Beschickung der Kammern vorgesehen sein. Die Beschikkung kann aber auch von der oberen Seite her erfolgen.

[0035] Zum Probentransport zwischen den Kammern werden die Proben mit einem Druck beaufschlagt. Unter der Wirkung eines Überdruckes in der Kammer, von der die Übertragung ausgeht, wird die Probe über den Überströmkanal in der Ventilplatte **21** übertragen. Der Übertragungsdruck wird mit einer Druckeinrichtung aufgebracht, die Teil der Präparationsstation (siehe **Fig.** 2) ist, in der die erfindungsgemäße Präparationsvorrichtung vorzugsweise verwendet wird. Gemäß einer vorteilhaften Ausführungsform der Erfindung wird der Druck mit einer Stempeleinrichtung **30** übertragen, die in den Kammern **13** bis **15** jeweils einen Druckstempel **31** bis **33** aufweist. Die Druckstempel **31** bis **33** bestehen aus Kunststoffkörpern z. B. in Zylinderform, die formschlüssig in die jeweilige Kammer eingepasst sind. Jeder Druckstempel weist mindestens eine umlaufende Dichtlippe auf, die ggf. auftretende Spalte zwischen den Druckstempeln und den Kammerinnenwänden abdichtet. Die Dichtlippen verhindern ein Durchlauf des Kolbens durch die flüssigen Proben bei Druckbeaufschlagung. Die Kolben mit den Dichtlippen bestehen aus einem Kunststoffmaterial (z. B. PTFE). Der Einsatz der Druckstempel **31** bis **33** in den Kammern besitzt den Vorteil, dass bei einer Bewegung der Präparationsvorrichtung **100** eine Probenbewegung in den Kammern verhindert wird, wenn die Druckstempel jeweils auf den Flüssigkeiten aufgesetzt sind. Nach einer Zentrifugation wird vorteilhafterweise eine Aufhebung der Phasengrenze zwischen den Fraktionen vermieden.

[0036] Die Druckstempel **31** bis **33** können gemäß einer bevorzugten Ausführungsform jeweils eine zentralen Bohrung (gestrichelt eingezeichnet) mit einem Verschluss (z. B. einem Septum) aufweisen. Dies ermöglicht einen Zugriff zu den Proben oder Zusatzflüssigkeiten in den Kammern von der Oberseite der Vorrichtung **100** her.

[0037] Gemäß einer abgewandelten Ausführungsform der Erfindung kann auf die Verwendung der Druckstempel auch verzichtet werden. In diesem Fall wird der Übertragungsdruck direkt auf die Flüssigkeitsoberfläche in der jeweiligen Kammer gegeben. Bei dieser Gestaltung sind die oberen Enden der Kammern an der Oberseite vorzugsweise mit einem Sterilfiltereinsatz ausgestattet, der nur für das jeweilig verwendete sterile Druckmedium (z. B. Luft, inertes Gas)

durchlässig ist. Der Aufbau ohne Druckstempel besitzt die Vorteile eines vergrößerten Innenvolumens und vereinfachten Aufbaus der Kammern und damit einer Kostenersparnis.

[0038] Die obere Deckplatte **40** dient dem Abschluss der Präparationsvorrichtung **100**. Sie ist fest auf dem Kammerkörper **10** angebracht und besitzt Durchtrittöffnungen oder Anschlussstutzen **41**, die jeweils mit den oberen Enden der Kammern **13** bis **15** ausgerichtet sind. Die Anschlussstutzen **41** dienen der Verbindung von einzelnen oder gleichzeitig allen Kammern mit der Druckeinrichtung und/oder Beschickungseinrichtungen.

[0039] Der Verfahrensablauf zur Herstellung einer Blut-Kryokonserve unter Verwendung einer erfindungsgemäßen Präparationsvorrichtung wird im Folgenden unter Bezug auf **Fig.** 2 erläutert. **Fig.** 2 zeigt die Präparationsvorrichtung **100** analog zur Darstellung gemäß **Fig.** 1 in Kombination mit Teilen der Präparationsstation.

[0040] Die Komponenten der Präparationsvorrichtung **100** sind mit den gleichen Bezugszeichen wie in **Fig.** 1 versehen.

[0041] Zur Präparationsstation gehören insbesondere die Druckeinrichtung **50**, eine Detektoreinrichtung **60**, eine Stelleinrichtung **70** und eine Steuereinrichtung **80**. Die Druckeinrichtung **50** umfasst vorzugsweise einen Druckerzeuger **51** mit einem Motor **52** und einem Pumpenteil **53**. Alternativ umfasst die Druckeinrichtung **50** eine Hebeleinrichtung mit einer Pleuelstange. Die mechanische Kraftübertragung besitzt den Vorteil, dass die Positionierung der Druckstempel mit einer erhöhten Präzision erfolgen kann. Gemäß alternativen Ausführungsformen der Erfindung kann der Druckerzeuger auch durch eine Druckquelle (z. B. Druckgasflasche) mit einem Regelventil gebildet werden.

[0042] Die Detektoreinrichtung **60** umfasst insbesondere mindestens ein lichtempfindliches Element **61** zur Erkennung der Phasengrenze. Das lichtempfindliche Element **61** kann anwendungsabhängig mit (nicht dargestellten) Filtereinrichtungen ausgestattet sein. Es können auch mehrere lichtempfindliche Elemente entsprechend den Positionen der Kammern angeordnet sein. Anwendungsabhängig können auch andere Detektoren zur Erfassung von Probeneigenschaften vorgesehen sein, wie sie an sich aus der Analytik bekannt sind (z. B. Spektralphotometer, Widerstandsmesser zur Dichtebestimmung). Die Kammern können auch eine sich jeweils über ihre Länge erstreckende Skalierung zur optischen Kontrolle des Füllstandes, der Position der Druckstempel oder der Position der Phasengrenze aufweisen. Die Detektoren können ferner an anderen Komponenten der Präparationsvorrichtung, z. B. an einer Verbindungsleitung in der Ventilplatte, vorgesehen sein.

[0043] Zur Verstellung der oben erläuterten Ventilplatte **21** umfasst die Stelleinrichtung **70** ein Betätigungselement **71** und einen Stellmotor **72**. Das Betätigungselement **71** besitzt die Form einer Platte mit mindestens einem Vorsprung **73**, der mit mindestens einer entsprechenden Ausnehmung (nicht dargestellt) auf der Unterseite der Ventilplatte **21** zusammenwirkt. Der Vorsprung **73** greift in die Ausnehmung ein und verdreht die Ventilplatte **21** bei Betätigung des Stellmotors **72** in die gewünschte Position, so dass jeweils eine Kammer geöffnet oder geleert werden kann, jeweils zwei Kammern über die Verbindungsleitung **22** verbunden sind oder alle drei Kammern verschlossen sind.

[0044] Die Steuereinrichtung **80** ist mit den Komponenten **50**, **60** und **70** des Präparationssystems verbunden. Je nach Betriebszustand und dem von der Detektoreinrichtung **60** gelieferten Detektorsignal werden in der folgenden Weise der Druckerzeuger **50** und die Stelleinrichtung **70** betätigt. Bei halbautomatischem oder manuellem Betrieb werden die entsprechenden Schritte zumindest teilweise durch einen Bediener durchgeführt.

[0045] In einem Startzustand sind die Kammern der erfindungsgemäßen Präparationsvorrichtung **100** wie folgt beschickt. In der ersten Kammer **13** befindet sich eine Blutspende. Die Blutspende wird aus einem Spenderbeutel in die erste Kammer **13** gefüllt, was ggf. unter Ausübung eines unterstützenden Unterdruckes erfolgt. Die zweite Kammer **14** ist mit einer Waschlösung gefüllt. In der dritten Kammer **15** befindet sich ein Kryoadditiv. Im Startzustand ist die erste Kammer **13** vollständig gefüllt, während die übrigen Kammern **14**, **15** lediglich teilweise befüllt sind. In diesen Kammern ist so viel Volumen frei, wie es zur Übernahme der Erythrozytensuspension nach der Zentrifugation (siehe unten) erforderlich ist. Die Ventilplatte **21** wird nach dem Startzustand (alle verschlossen) so eingestellt, dass bspw. die erste und zweite Kammer **13**, **14** verbunden sind. Vorteilhafterweise ist trotz der Verbindung im druckfreien Zustand über die Verbindungsleitung im Wesentlichen kein Flüssigkeitsaustausch gegeben.

[0046] In einem ersten Präparationsschritt wird der Kammerkörper mit den befüllten Kammern mit einer Zentrifugationseinrichtung zentrifugiert. Die (nicht dargestellte) Zentrifugationseinrichtung besitzt die Bauform einer an sich bekannten Großzentrifuge mit einzelnen Zentrifugenbechern, in denen eine Vielzahl von Präparationsvorrichtungen gleichzeitig zentrifugiert werden können. Während der Zentrifugation erfolgt lediglich die Auftrennung der Blutspende in die Fraktionen. Eine Verschiebung der Druckstempel **31** bis **33** erfolgt nicht. Während der Zentrifugation sind die Kammern verschlossen.

[0047] Der Zustand der Präparationsvorrichtung nach der Zentrifugation ist in **Fig.** 2 dargestellt. In der ersten Kammer **13** sind die gebildeten Fraktionen der Blutspende mit dem Erythrozytensediment **1** der sog. "Buffy Coat"-Schicht **2** und dem Plasmaüberstand **3** illustriert. Das Erythrozytensediment **1** umfasst betriebsabhängig einen Volumenanteil von ca. 45% der Kammer **13**. Der Volumenanteil hängt insbesondere von der Zentrifugationsgeschwindigkeit ab. Bei einer höheren Geschwindigkeit ergibt sich eine höhere Packungsdichte der Erythrozyten und damit ein geringerer Volumenanteil. Die "Buffy-Coat"-Schicht **2** ist ein thrombozyten- und leukozytenhaltiger Belag mit einer gräulichen Färbung, der sich nach der Zentrifugation zwischen den tiefroten Erythrozytensediment **1** und dem hellroten Plasmaüberstand **3** ausbildet.

[0048] Nach der Zentrifugation wird die Präparationsvorrichtung **100** in die Präparationsstation eingesetzt. Die Ventilplatte **21** wird in Durchlassrichtung zwischen die erste und zweite Kammer **13**, **14** gedreht. Dies erfolgt manuell, z. B. mit einem Noppenschlüssel oder mit der Stelleinrichtung **70** (siehe oben). Die erste Kammer **13** wird mit einem Überdruck beaufschlagt. Unter der hydrostatischen oder mechanischen Druckeinwirkung bewegen sich der Druckstempel **31** nach unten und der Druckstempel **32** nach oben. Die aufgetrennte Blutspende wird in die zweite Kammer **14** übertragen. Dieser Präparationsschritt wird beendet, sobald die am unteren Ende der ersten Kammer **13** angeordnete Detektoreinrichtung **60** die "Buffy Coat"-Schicht **2** erfasst. In diesem Zustand ist sichergestellt, dass in dem verjüngtem Bereich **16** (siehe **Fig.** 3) und der Verbindungsleitung noch ausschließlich Erythrozytensediment vorhanden ist. Wenn die "Buffy Coat"-Schicht **2** erfasst worden ist, wird die Druckübertragung gestoppt. Danach wird die Ventilplatte in Verschlussstellung gebracht. Dies erfolgt entweder unmittelbar bei Detektion der Schicht **2** oder zeitlich verzögert, so dass Konzentratreste aus dem verjüngten Bereich **16** noch in die Verbindungsleitung gelangen können.

[0049] Die in die zweite Kammer **14** übertragenen Ery-

throzyten vermengen sich mit der Waschlösung. Die Waschlösung umfasst bspw. physiologische Kochsalzlösung. Es folgt eine weitere Zentrifugation, in deren Ergebnis sich die behandelten Erythrozyten als Konzentrat wiederum im unteren Teil der zweiten Kammer **14** sammeln, während die übrige Waschlösung den Überstand bildet.

[0050] In einem weiteren Präparationsschritt wird analog zu der beschriebenen Weise das gewaschene Erythrozytensediment in die dritte Kammer **15** übertragen. Hierzu wird die Ventilplatte **21** so verdreht, dass die Verbindungsleitung **22** zwischen der zweiten und dritten Kammer **14**, **15** angeordnet ist. Außerdem wird der Druckverteiler **56** entsprechend verstellt. Die Druckübertragung wird wiederum in Abhängigkeit vom Detektorsignal der Detektoreinrichtung **60** gesteuert. Es kann an der zweiten Kammer **14** ein weiterer Sensor (nicht dargestellt) vorgesehen sein. Alternativ ist es möglich, die Präparationsvorrichtung **100** zu dem Sensor **61** hin zu verdrehen, so dass die Phasengrenze in der zweiten Kammer **14** erfasst werden kann.

[0051] Nach Übertragung des gewaschenen Erythrozytensedimentes in die dritte Kammer **15** erfolgt dort die Vermengung mit dem Kryoadditiv. Als Kryoadditiv werden die an sich bekannten Zusatzstoffe verwendet. Das Kryoadditiv umfasst bspw. eine Lösung aus wasserlöslichem Stärkederivat.

[0052] Nach Übertragung der gewaschenen Erythrozyten in die dritte Kammer **15** und Vermengung mit dem Kryoadditiv ist die Kryokonserve einfrierfertig. Es folgt die Übertragung in den anwendungsabhängig gewählten Behälter, z. B. einen Kryobeutel, in dem der Einfriervorgang erfolgt. Vorteilhafterweise ist nach Abschluss der Präparation in der ersten Kammer **13** der Plasmaüberstand als spenderspezifisches Restprodukt vorhanden. Anwendungsabhängig kann das Plasma einer weiteren Verwendung zugeführt werden.

[0053] Einzelheiten einer gegenüber **Fig.** 1 abgewandelten Gestaltung der erfindungsgemäßen Präparationsvorrichtung sind in **Fig.** 4 dargestellt. Die Unterschiede beziehen sich auf die Ausbildung der Ventilplatte **21**. Im obersten Teilbild von **Fig.** 4 ist die Unterseite **12** des Kammerkörpers **10** mit den Kammern **13** bis **15** illustriert. Jede Kammer besitzt eine Ein- und Auslassöffnung in Form eines Anschlussstutzens **17** (siehe **Fig.** 3). An jedem Anschlussstutzen **17** ist ein O-Dichtring **18** vorgesehen. In der Mitte des Kammerkörpers **10** befindet sich entsprechend der Zylinderachse eine Gewindebohrung **19** zur Befestigung der Ventilplatte **21**.

[0054] Im mittleren Teilbild von **Fig.** 4 ist die Ventilplatte **21** einzeln dargestellt. Bei dieser Gestaltung sind zwei Verbindungsleitungen (oder Überströmkanäle) **22**, **23** vorgesehen, die so angeordnet sind, dass mit einer der Verbindungsleitungen **22** oder **23** jeweils zwei Kammern verbunden werden können, während die jeweils andere Verbindungsleitung **22** oder **23** verschlossen ist. Die Verwendung von zwei Verbindungsleitungen besitzt den Vorteil geringerer Verstellwege bei der Einstellung der Kammerverbindungen bei den einzelnen Präparationsschritten. In der Ventilplatte sind drei Ein- und Auslassbohrungen **24** vorgesehen, die so angeordnet sind, dass wenn eine der Ein- und Auslassbohrungen **24** mit einem der Anschlussstutzen **17** ausgerichtet ist, die anderen Anschlussstutzen jeweils verschlossen bleiben.

[0055] Die Ventilplatte **21** besitzt einen umlaufenden O-Dichtring **25**, der eine zusätzliche Dichtung gegenüber der Unterseite **12** des Kammerkörpers **10** bereitstellt. Das Bezugszeichen **26** bezieht sich auf die Drehachse und das Lager der Ventilplatte **21**.

[0056] Im unteren Teilbild von **Fig.** 4 ist die Ventilplatte **21** und die Unterseite **12** des Kammerkörpers **10** im zusammenmontierten Zustand dargestellt. Wird die Ventilplatte **21** vom dargestellten Zustand nach links gedreht, so werden zunächst mit der Verbindungsleitung **22** die Kammern **13** und **14** verbunden und bei der weiteren Verstellung werden die Kammern **14** und **15** über die Verbindungsleitung **23** verbunden. Damit können mit einem kurzen Stellweg die beiden oben erläuterten Präparationsschritte ausgeführt werden.

[0057] Die in den **Fig.** 1 bis 4 illustrierte Ausführungsform der Erfindung kann je nach Aufgabenstellung vielfältig modifiziert werden. So können bspw. zur Durchführung weiterer Präparationsschritte im Kammerkörper weitere Kammern zur Aufnahme weiterer Zusatzstoffe vorgesehen sein. Anstelle der 120°-Anordnung können die Kammern auch anderweitig im Kammerkörper oder einem Rahmengestell (siehe unten) angeordnet werden. Die Beschickung der Kammern kann anwendungsabhängig von der Ober- oder Unterseite her erfolgen. Dies erfolgt vorzugsweise unter Verwendung von Schlauch- oder Pipettiersystemen. Gemäß einer bevorzugten Gestaltung der Erfindung sind die Einlassöffnungen der Kammern gerade an die Außendurchmesser von standardisierten Flüssigkeitspipetten oder Schlauchadapter angepasst, so dass diese zur Beschickung einfach angesetzt und betätigt werden können. Die Präparationsvorrichtung kann anwendungsabhängig in ihrer Größe beliebig skaliert werden. Die Übertragungseinrichtung mit der Ventilplatte kann durch eine fest eingestellte Anordnung mehrerer Verbindungsleitungen mit betätigbaren Ventilen ersetzt werden.

[0058] An der Außenseite des Kammerkörpers können zusätzliche Greif- oder Befestigungseinrichtungen zur Handhabung des Kammerkörpers und/oder zum Einsatz in eine Zentrifuge vorgesehen sein.

[0059] Der Kammerkörper mit den integrierten Kammern kann erfindungsgemäß durch eine Anordnung einzelner Kammern in einem Rahmengestell ersetzt werden. Diese Gestaltung besitzt Vorteile in Bezug auf eine separate Befüllung der einzelnen Kammern vor der Zusammensetzung zur Präparationsvorrichtung und die Entsorgung der Kammern nach Verwendung. Als Rahmengestell kann jede geeignete Struktur verwendet werden, in die die Kammern entsprechend der gewünschten Anordnung fixiert einsetzbar sind und die eine genügende Stabilität bei der Zentrifugation besitzt. Je nach der Gestaltung der Kammern ist die Struktur des Rahmengestells angepasst.

[0060] Werden als Kammern fertige Kolbenspritzen mit geeigneten Kolbendurchmessern verwendet, so besitzt das Rahmengestell Ausnehmungen zur Aufnahme der Spritzenkolben. Wenn die Einzelkammern durch gerade Rohrkörper gebildet sind, werden die Ausnehmungen des Rahmengestells entsprechend angepasst. Am Boden des Rahmengestells sind ggf. konisch vorgeformte Kammerböden vorgesehen, wie dies in **Fig.** 5 illustriert ist.

[0061] **Fig.** 5 zeigt eine Einzelkammer in schematischer Schnittansicht. Zwei oder mehr derartige Einzelkammern (z. B. entsprechend der obigen Gestaltung drei Einzelkammern) sind an einem Rahmengestell (nicht dargestellt) vorgesehen. Die Einzelkammer **90** umfasst eine Kammerwand **91** in Form eines geraden Kreiszylinders und einen sich verjüngenden Teilbereich **92**, der in einem entsprechend geformten Stützsockel **93** ruht, der Teil des Rahmengestells ist. Im Inneren der Einzelkammer **90** befindet sich der Druckstempel (siehe oben). Der Druckstempel ist bei dieser Gestaltung nicht zylinderförmig, sondern als Stempelplatte **94** mit einem außen umlaufenden Dichtring **97** ausgebildet. Die Stempelplatte **94** besteht beispielsweise aus PMMA. Der Dichtring **97** ist ein z. B. aus PTFE bestehendes Formteil, das formschlüssig über den äußeren Rand der Stempelplatte **94** gezogen ist. Der Querschnitt des Dichtringes **97** besitzt

eine U-Form, deren offenen Enden zwei Dichtlippen bilden. Durch diese Formgebung wird ein dichtendes Anlegen der Dichtlippen an die Kammerwand sicherstellt. Die Oberseite der Einzelkammer **90** ist mit einer Deckplatte **95** verschlossen, die eine Durchtrittsöffnung **96** zum Durchlass des Druckmediums aufweist.

[0062] Die Einzelkammer **90** besitzt bspw. ein Volumen von 470 ml bei einem Durchmesser von ca. 80 mm, einer Länge der Kammerwand **91** von ca. 110 mm und einer Höhe des Stützsockels **93** von ca. 30 mm. Der Teilbereich **92** grenzt ein Teilvolumen von ca. 30 ml ab.

[0063] Bei einem erfindungsgemäßen Verfahren zur Blutpräparation kann abweichend von der oben erläuterten Zentrifugation der gesamten Präparationsvorrichtung die folgende Einzelkammerzentrifugation vorgesehen sein. Dabei wird die jeweils interessierende Einzelkammer (z. B. gemäß **Fig.** 5) aus dem Rahmengestell entnommen und separat zentrifugiert. Vor oder nach der Zentrifugation ist die Einzelkammer im Rahmengestell zur Durchführung der übrigen Schritte der Probenpräparation angeordnet. Dieses Verfahren ist besonders vorteilhaft, falls zur Zentrifugation keine passende Zentrifuge zur Verfügung steht.

[0064] Die in der vorstehenden Beschreibung, den Ansprüchen und den Zeichnungen offenbarten Merkmale der Erfindung können sowohl einzeln als auch in beliebiger Kombination für die Verwirklichung der Erfindung in ihren verschiedenen Ausgestaltungen von Bedeutung sein.

Patentansprüche

1. Präparationsvorrichtung (**100**) zur Behandlung von Suspensionsproben, insbesondere zur Präparation von Blut-Kryokonserven, mit einer Anordnung von mindestens zwei Behältnissen zur Aufnahme von Suspensionsproben, Probenteilen und/oder Zusatzstoffen, **dadurch gekennzeichnet**, dass die Behältnisse als Kammern (**13** bis **15**, **90**) mit festen Wänden gebildet und relativ zueinander ortsfest angeordnet sind, wobei eine Übertragungseinrichtung (**20**) mit mindestens einer Verbindungsleitung (**22**) vorgesehen ist, über die die Kammern (**13** bis **15**) miteinander verbunden werden können.

2. Präparationsvorrichtung gemäß Anspruch 1, bei der die Kammern (**13** bis **15**) in einem einstückigen Kammerkörper (**10**) gebildet sind.

3. Präparationsvorrichtung gemäß Anspruch 1, bei dem die Kammern (**90**) als Einzelkammern lösbar in einem Rahmengestell befestigt sind.

4. Präparationsvorrichtung gemäß einem der vorhergehenden Ansprüche, bei der die Wände der Kammern oder der Kammerkörper (**10**) aus einem transparenten Material bestehen.

5. Präparationsvorrichtung gemäß einem der vorhergehenden Ansprüche 1 oder 2, bei der die Kammern (**13** bis **15**) die Gestalt gerader Hohlzylinder besitzen, die von einer Oberseite (**11**) bis zu einer Unterseite (**12**) des Kammerkörpers (**10**) verlaufen, wobei an der Unterseite (**12**) jede Kammer (**13** bis **15**) einen Anschlussstutzen (**17**) aufweist, mit dem jeweils ein Ende der mindestens einen Verbindungsleitung (**22**) verbunden werden kann.

6. Präparationsvorrichtung gemäß einem der vorhergehenden Ansprüche, bei der in jeder Kammer ein Druckstempel (**31** bis **33**) vorgesehen ist.

7. Präparationsvorrichtung gemäß Anspruch 6, bei der jeder Druckstempel (**31** bis **33**) eine umlaufende Dichtlippe aufweist.

8. Präparationsvorrichtung gemäß einem der vorhergehenden Ansprüche, bei der die Übertragungseinrichtung (**20**) durch eine Ventilplatte (**21**) gebildet wird, in der mindestens eine Verbindungsleitung (**22**) integriert ist, wobei die Ventilplatte (**21**) verdrehbar angeordnet ist.

9. Präparationsstation zur Präparation von Suspensionsproben, die umfasst:
mindestens eine Präparationsvorrichtung (**100**) gemäß einem der vorhergehenden Ansprüche,
eine Druckeinrichtung (**50**),
eine Detektoreinrichtung (**60**),
eine Stelleinrichtung (**70**), und
eine Steuereinrichtung (**80**).

10. Präparationsstation gemäß Anspruch 9, bei der die Druckeinrichtung (**50**) einen pneumatischen Druckerzeuger oder einen mechanischen Druckerzeuger mit Pleuelstangen umfasst.

11. Präparationsstation gemäß Anspruch 9 oder 10, bei der die Stelleinrichtung (**70**) ein Betätigungselement (**71**) aufweist, mit dem die Übertragungseinrichtung (**20**) derart einstellbar ist, dass jeweils zwei Kammern über die mindestens eine Verbindungsleitung (**22**) verbunden sind.

12. Verfahren zur Präparation von Suspensionsproben unter Verwendung einer Präparationsvorrichtung (**100**) gemäß einem der Ansprüche 1 bis 8, bei dem abwechselnd eine Behandlung einer Probe in mindestens einer der Kammern (**13** bis **15**, **90**) und eine Übertragung mindestens eines Teils der Probe zwischen zwei Kammern erfolgt.

13. Verfahren gemäß Anspruch 12, bei dem die Probenbehandlung eine Zentrifugation der Probe und/oder eine Behandlung der Probe mit Zusatzstoffen umfasst.

14. Verfahren gemäß Anspruch 13, bei dem bei der Zentifugation der Probe die gesamte Präparationsvorrichtung (**100**) oder eine Einzelkammer (**90**) zentrifugiert wird.

15. Verfahren gemäß einem der Ansprüche 12 bis 14, bei dem eine Blut-Kryokonserve herstellt wird.

Hierzu 5 Seite(n) Zeichnungen

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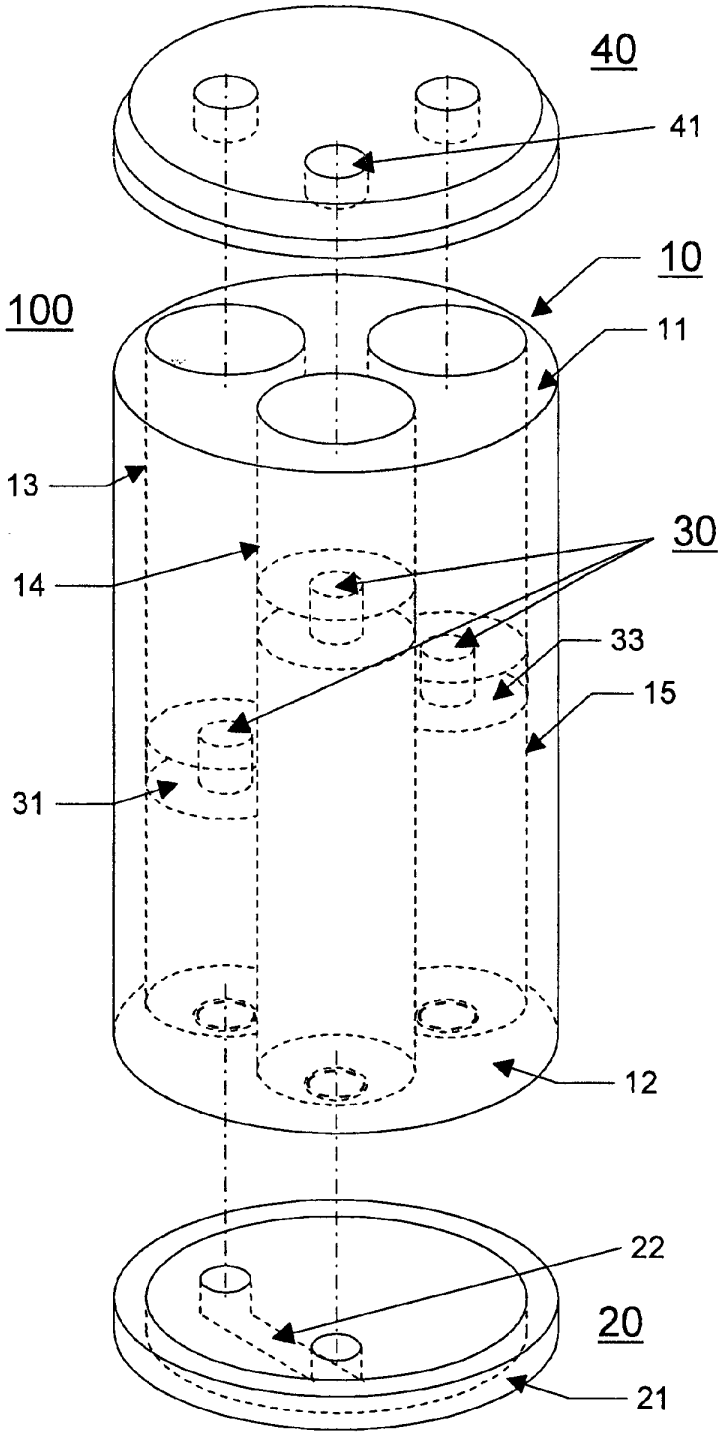


Fig. 1

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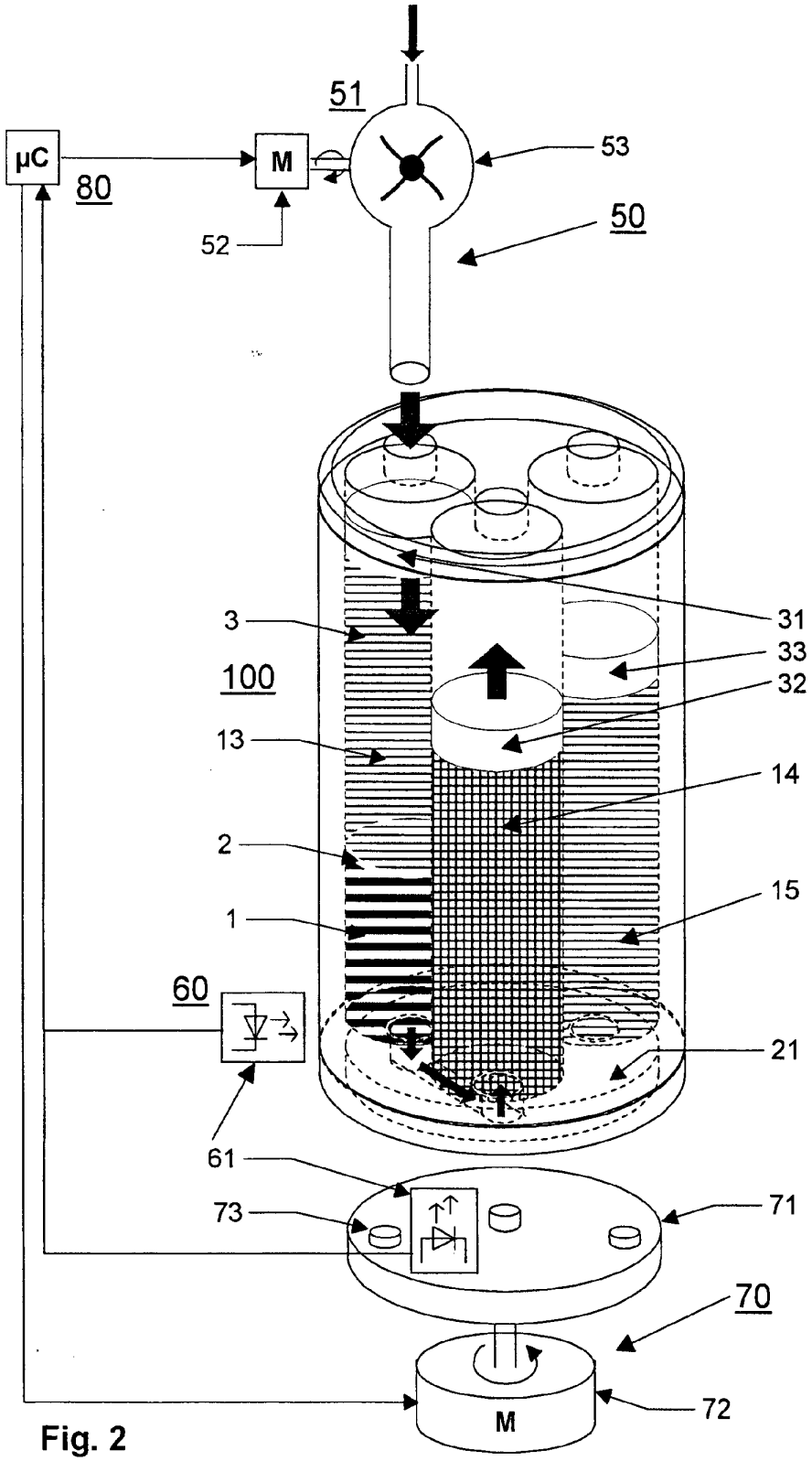


Fig. 2

102 680/59

Nummer: DE 101 34 913 A1
Int. Cl.[7]: A 61 M 1/00
Offenlegungstag: 20. Februar 2003

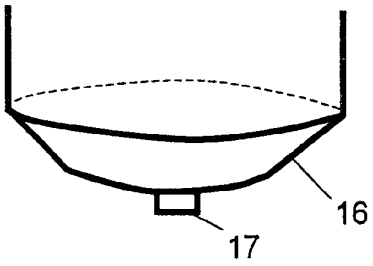


Fig. 3

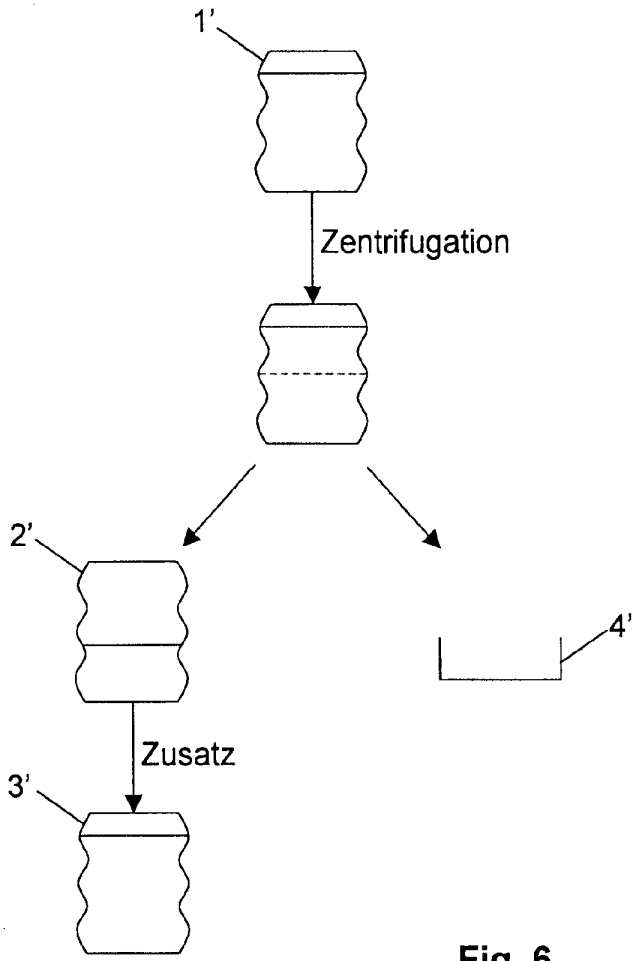
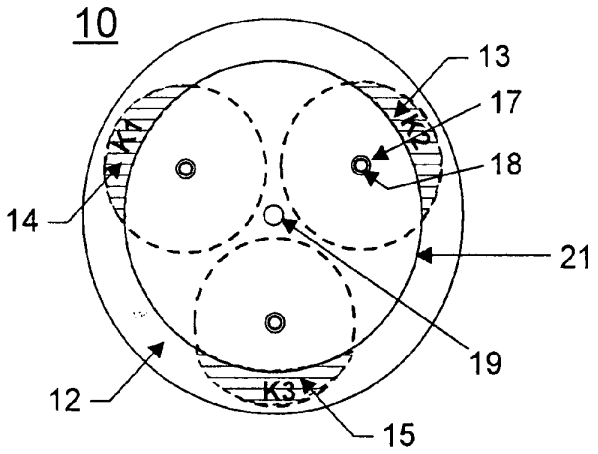
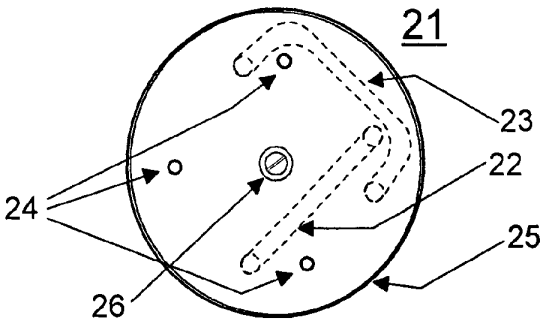


Fig. 6
(Stand der Technik)

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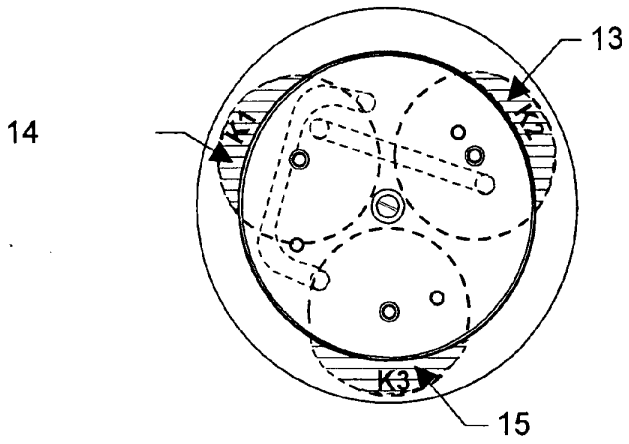


Fig. 4

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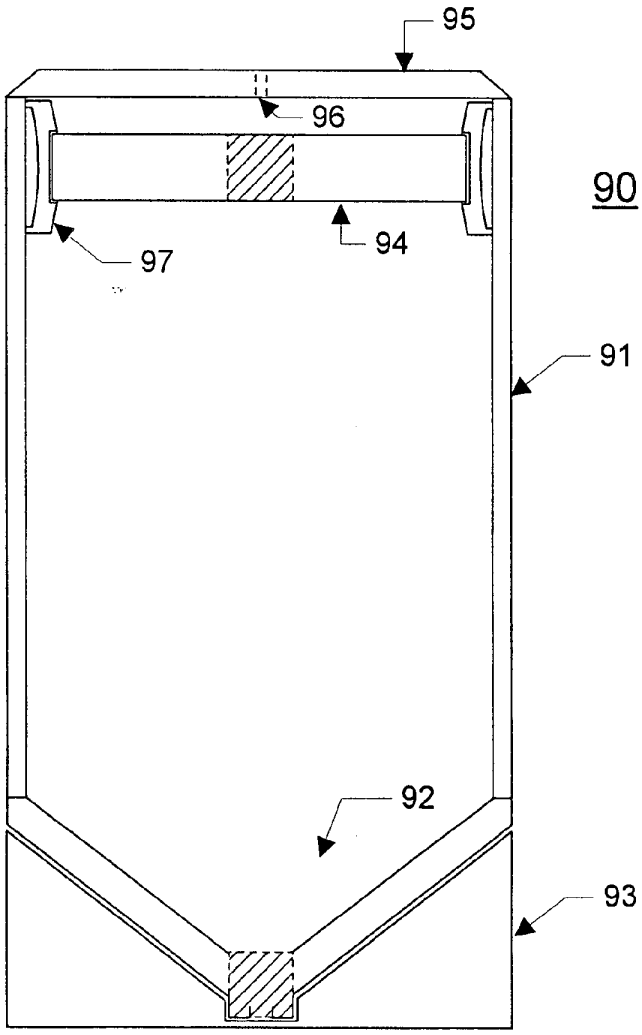


Fig. 5

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Literature display help

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Japanese Patent Application Laid-Open No. 57-089869

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primary literature

The scope of the claims open

[Claims]

1. A single sample needle assembly adapted to recognize insertion of the needle into a blood vessel when collecting a blood sample from a patient into the evacuated vessel, the single sa mple needle assembly having at least a forward end, a rearward end and an interior chamber. a housing having a transparent portion surrounding the chamber so that a user can see the ch amber; a first opening formed in a front end of the housing and communicating with the cham ber; and a first opening extending outwardly into the chamber. a first puncture needle that co mmunicates and is inserted into a patient; a second opening that is formed in the rear end of the housing and communicates with the chamber; a second cannula closed and having two sp aced apart transverse holes, and a plug of air permeable blood impermeable material in fluid t ight sliding contact with the housing enclosing the chamber and the second puncture needle. said plug initially in a position covering a first side hole remote from said second opening and not covering the other second side hole from a first puncture needle under constant tournique t pressure; Blood entering the chamber is prevented by the plug from flowing out into the sec ond cannula, allowing only the air in the chamber to flow out so that the user can see through the transparent housing that the first needle has entered the blood vessel. , wherein a negativ e pressure gradient acting on the second opening causes the plug to slide to open the first lat

eral hole, allowing blood to flow from the chamber through the first lateral hole and the secon d cannula to the second opening. A single sample needle assembly, characterized in that it is collected externally.

2. 2. A needle assembly according to claim 1, wherein the distance between said lateral holes is greater than the longitudinal length of said plug so that said plug does not simultaneously c over said lateral holes.

3. 3. The needle assembly of claim 1, wherein only a portion of said plug outer surface is in fl uid tight contact with a housing enclosing a chamber.

4. The plug includes an air and blood impermeable material in combination with the air and bl ood impermeable material, the impermeable material being in fluid tight contact with the hou sing surrounding the chamber and the second cannula. of patent claimsThe needle assembly of claim 1.

5. 5. The needle assembly of claim 4, wherein only a portion of the outer surface of said impe rmeable plug material is in liquid-tight contact with the housing surrounding the chamber.

6. 6. The needle assembly of claim 5, wherein only a portion of the surface of said impermeab le plug material is in fluid tight contact with the second cannula.

7. 7. A needle assembly according to claim 6, wherein said impermeable material is a membe r surrounding the outside of the air permeable material and has at least one opening in which the air permeable material communicates directly with the chamber.

8. 8. The needle assembly of claim 7, wherein said impermeable material includes a plurality of apertures communicating air permeable material with the chamber.

9. 5. The needle assembly of claim 4, wherein said impermeable material is flexible.

10. 10. The needle assembly of claim 9, wherein said impermeable material is elastomeric.

11. 11. The needle assembly of claim 10, wherein said impermeable material is silicone rubbe r.

12. 3. A needle assembly as in claim 1, wherein said plug is in the shape of a hollow cylinder.

13. 3. The needle assembly of claim 1, wherein said plug material is porous.

14. 14. The needle assembly of claim 13, wherein said plug material is sintered polyethylene and the average pore diameter is about 10 microns.

15. 3. The needle assembly of claim 1, wherein the end of the second cannula extending into said chamber is sealed with an adhesive.

16. 3. The needle assembly of claim 1, including an exit needle in communication with said se cond cannula and extending outwardly from a second opening through a blood sample collecti on evacuated vessel.

17. 17. The needle assembly of claim 16, wherein said second cannula and exit needle are joi ned to form a unitary construction.

18. 4. The needle assembly of claim 1, wherein said entire housing is transparent.

19. 3. The needle assembly of claim 1, including a vacuum vessel holder connected to said ho using.

20. A single sample needle assembly adapted to be in fluid communication when collecting a f luid sample from a fluid supply to a vacuum collector, the assembly defining a chamber therei n and first and second openings communicating with the chamber. a housing having solution v iewing means and a second opening in communication with the vacuum collection device; a d evice for placing two openings in a closed relationship with a chamber and slidingly sealing sai d chamber to prevent liquid from flowing into one of the holes and permitting air to flow into o ne of the holes in a first position. a plug device for making the liquid within the chamber visibl e by visual means, said plug device being slidable by a negative pressure gradient acting on t he second opening to force the liquid through one of the holes at the second location within th e chamber. A single sample needle assembly, characterized in that the liquid is allowed to flow into the second opening and collect from the second opening.

21. A needle assembly adapted to be in fluid communication when collecting a fluid sample fr om a fluid supply into a vacuum collection device, the needle assembly defining a chamber th erein and first and second openings communicating with the chamber, the chamber contents. a housing having liquid viewing means and a second opening in communication with a vacuu m collection device; an extension device extending into said chamber for directing gas and liq uid to said second opening; and operatively sealing said chamber. a plug device for preventing liquid from flowing into the extension device and allowing gas to flow into the extension devic e at a first position within the chamber, the liquid within the chamber being visible by visual m eans, the plug device A needle assembly as characterized in that when moved to a second pos ition, fluid is allowed to flow into the extension device to allow fluid to be collected from the se cond opening.

22. A single sample needle assembly adapted to recognize a vascular puncture when collectin g a blood sample from a patient into an evacuated vessel, the assembly comprising a transpar ent housing having a front end, a rear end and an internal chamber; A first needle in commun ication extending outwardly from the front end of the housing for insertion into the patient, an d an outer portion extending outwardly from the rear end of the housing for penetrating the bl ood sample collection evacuated vessel. a second puncture needle with an inner portion exten ding into the chamber and having a closed end and two spaced apart transverse holes;and a plug slidable within the chamber as a composite member of an air permeable blood impermea ble material and an elastic impermeable material, the impermeable material forming an outer member surrounding the air permeable material. a plurality of apertures providing an air per meable material in direct communication with the chamber, said impermeable material being i n fluid tight contact with a housing surrounding the chamber and an inner portion of the seco nd needle; , the plug initially covers the first lateral hole furthest from the trailing end and op ens the other second lateral hole to the chamber, thereby providing a constant tourniquet pre ssure from the first needle. blood flowing into the chamber below is prevented by the plug fro m flowing into the second needle to allow room air flow to allow blood to be visualized throug h the transparent housing to indicate that the first needle has entered the vessel; The plug sli

des due to the negative pressure gradient acting on the second needle from the vacuum vess el to open the first lateral hole, and the blood that has flowed into the chamber is collected in the vacuum vessel through the first lateral hole and the second needle. A single sample needl e assembly, characterized in that:

detailed description open —

DETAILED DESCRIPTION OF THE INVENTION

The present invention relates to a needle assembly for collecting fluid from a patient, and mor e particularly to a needle assembly having means for collecting a single sample of blood from a patient and recognizing when the needle has entered the patient's blood vessel. Regarding s olids.

In collecting bodily fluids, such as blood, from a patient, a nurse or clinician must locate or ori entate the patient's blood vessels as the fluid is being collected, but even with the application of tourniquet pressure, the vessels are narrow. In some cases, or if the blood vessel is remote from the skin surface, it may not be possible to insert the needle directly into the patient's blo od vessel. In this case, the needle may be punctured at a location other than the location of t he blood vessel, or may penetrate the small vessel completely. As a result, the flow of blood t hrough the needle and into the evacuated blood collection tube is uncomfortable and extremel y slow because it does not flow out of the patient's blood vessel. Nurses have to start over an d often have to use another evacuated blood collection tube in this case, increasing equipmen t, cost and patient anxiety.

To reduce wastage of evacuated blood collection tubes when a nurse needs to locate a vessel, many blood collection devices have been proposed that have an indicator to show when the n eedle has entered the vessel. This visual indicator system usually has an antechamber and is i solated by some valve system from a needle through which blood is collected in an evacuated tube. When the nurse locates the vessel and the needle enters the vessel, it indicates that the blood has entered the antechamber through the needle and into the vessel in the correct posit ion. The blood collection process is now started, the evacuated blood collection tube is plugge d into the blood collection holder, the valve is opened and blood flows into the collection tube. Examples of blood collection devices with visual indicators are U.S. Pat. Nos. 4,166,450 and 3, 585,984.

In theory, antechamber structures for viewing blood flow are operable and sometimes work w ell, but there are inherent problems. That is, the anterior chamber is normally filled with air w hen the front end of the needle is inserted into the patient's blood vessel. Due to the valve clo sure between the second needle passing through the evacuated blood collection tube, the air i

n the antechamber has no escape and forms stagnant air. Thus, even if the nurse knows the l ocation of the vessel and the needle is well within the vessel, the constant tourniquet pressur e will not allow blood flow from the patient through the needle and into the antechamber. That is, the stagnant air in the anterior chamber prevents blood from entering the anterior chambe r through the needle even under constant tourniquet pressure. As a result, the nurse conclude s that the required endovascular insertion was not performed because no blood was visible in the anterior chamber. An unnecessary second vascular puncture is performed, which is not onl y uncomfortable for the patient, but also inefficient and wasteful.

Therefore, there is a need for new visual indicators for users of blood collection devices. Thus, there is a need for an improved blood collection device of the type that will know when the ne edle has been inserted into the patient's blood vessel prior to inserting the evacuated blood co llection tube into the blood collection holder, as per normal blood collection procedures.

A needle assembly capable of recognizing the arrival of liquid when collecting a liquid sample f rom a liquid source into a vacuum collection device in accordance with the present invention c omprises a housing having an interior chamber and a chamber in communication with the cha mber. and a first and second opening device. The housing includes means for viewing the cont ents of the chamber and the second opening means is communicable with the vacuum collecti on system. Extending into the room with gasand an extension device for directing the liquid to the second opening device. There is a plug device in operative engagement within the chambe r to prevent liquid from flowing into the extension device and permit gas to flow into the exte nsion device at a first position within the chamber. When the plug device is moved to the seco nd position fluid is allowed to flow into the extension device and is collected through the secon d opening device.

In the preferred embodiment of the needle assembly according to the invention described abo ve, the housing is transparent and provides a front end, a rear end and an interior chamber. A first cannula extends forwardly from the front end of the housing and communicates with the chamber. A second cannula has an outer portion extending outwardly from the rearward end o f the housing and an inner portion extending into the chamber having a closed end and first a nd second longitudinally spaced transverse bores. The plug device is a combination plug of an air permeable, blood impermeable material and an elastic impermeable material, slidable with in the chamber, the impermeable material forming an outer member surrounding the air perm eable material. A plurality of openings extend through the impermeable material and commun icate the air permeable material directly to the chamber. The impermeable material is in liquid -tight contact with the inner housing wall surrounding the chamber and the inner portion of th e second sleeve. In the first position, the plug covers the first cross-bore of the second bushin g, remote from the rear end of the housing, and the second cross-bore communicates with th e chamber. Blood flowing through the first cannula into the chamber under constant tournique t pressure is prevented by the plug from flowing into the second cannula and is visible to the user, and air passes through the plug to the second cannula. 2 cannula. A negative pressure g

radient acting on the second cannula causes the plug to slide open the first crossbore and mo ve toward the second crossbore. Blood in the chamber therefore flows from the first lateral ho le through the second cannula and into the blood collection container.

The components and characteristics of the needle assembly according to the invention differ si gnificantly from known ones of this type. For example, the plug material within the housing ch amber acts as a valve to prevent blood from flowing out of the chamber when the needle is in serted into the patient's vessel. At this stage of the blood collection procedure, the evacuated blood collection tube is normally not plugged in. Therefore, it is necessary to prevent blood fro m escaping the needle assembly at this stage. However, when a nurse punctures a patient's bl ood vessel, blood flows through the front needle and into the chamber of the needle assembly housing. The plug material is essentially blood impermeable, thus preventing blood from flowi ng through the chamber. However, because the plug material of the present invention is air pe rmeable, air originally present in the chamber and front needle escapes from the chamber. Th erefore, there is no air stagnation as with known needle assemblies with visual indicators. In addition, the plug is slidable within the chamber, and when a vacuum blood collection tube is attached to the rear of the needle assembly, the negative pressure gradient will cause the plu g to slide within the chamber to bring the front lateral port of the collection cannula into the bl ood flow path. expose. Thus, when a negative pressure blood collection tube is attached, the plug immediately moves to create an opening effect and blood flows through the needle asse mbly and into the blood collection container.

As noted above, the present invention solves the problem of air stagnation in known needle a ssemblies. That is, the needle assembly of the present invention allows the user to see blood entering the housing chamber as soon as the needle assembly is correctly inserted into the bl ood vessel. Since air within the needle assembly is free to escape, blood flows freely into the housing chamber.

Embodiments and drawings illustrating the invention will now be described. The present inven tion can be modified in various ways, and the examples and drawings are examples for facilita ting understanding of the present invention and do not limit the invention.

FIG. 1 shows an embodiment of a single sample needle assembly 10 according to the present invention. The basic components of the needle assembly 10 include a housing 12, a first punct ure needle 14 for insertion into the patient, and a second puncture needle 15 for puncturing a vacuum vessel 16 on the opposite side of the housing 12 from which a blood sample is collect ed. include. A threaded portion 18 of the housing 12 is adjacent to the second puncture needl e 15 and threads into internal threads 20 at the front end of the container holder 19 . By slidi ngly engaging the vacuum container 16 within the holder 19 the second puncture needle 15 p enetrates the pierceable stopper 21 at the front end of the container 16 . Blood sample collect ion in the general configuration described above is well known.

Figures 2, 3 and 4 show the detailed construction of the needle assembly 10 according to the present invention. The housing 12 has a forward end 24 and a rearward end 25 which are sep

arated so that a slidable pillar 26 can be placed in place within the housing.make it The front end 24 is cylindrical in the illustrated example, and a hole 29 into which the puncture needle 1 4 is slidably fitted extends from the front end to a partial depth. Hole 29 does not extend thro ugh front end 24, but a small diameter passageway 30 extends from hole 29 to form an openi ng 31 at the trailing edge of front end 24. As shown in FIG. A shoulder 33 is formed between t he hole 29 and the passageway 30 . The puncture needle 14 comes into contact with the shou lder 33 and comes to a predetermined position. After the puncture needle 14 is at a predeter mined position, it is fixed with an adhesive or the like.

The front end 24 of the housing 12 is formed with a plurality of longitudinal ribs 28 surroundin g the puncture needle. A needle shield, not shown, covers the outwardly projecting needle an d has internal ribs that match ribs 28 . Inner and outer ribs between the needle shield and the needle assembly facilitate attachment and detachment of the needle assembly from holder 19 by the user. An annular flange 32 formed on the front end 24 forms a joining surface for the h ousing halves. Both parts 24, 25 are secured together using any desired attachment means, s uch as adhesive.

The rear end 25 is also cylindrical in the illustrated example, with a large hole partially extendi ng from one end in the direction of the second puncture needle. This large hole defines a cha mber 40 within housing 12, described in more detail below. A small hole 41 extending through the rear end portion of rear end 25 is substantially similar to hole 29 in the front end. The hol e 41 is sized to allow the diameter of the second puncture needle 15 to pass through, and the puncture needle 15 is fixed to the hole 41 with an adhesive or the like. External threads 18 ar e formed on the outer surface of the rear end surrounding the bore 41 to provide a connectio n to the holder as previously described. The outer surface 42 of the rear end 25 surrounding t he chamber 40 is smooth and transparent to allow the user to see inside the housing. In man y instances, it is preferred that the entire trailing and leading ends be made of a transparent material for ease of manufacture and to minimize the variety of materials used to manufactur e the needle assembly. A transparent rigid synthetic resin is the preferred material for manufa cturing the needle assembly. However, it could also be constructed with closed windows or por ts where desired. The window or port closure is configured so that blood entering chamber 40 will not leak out when the needle enters the vessel.

The distal end of the second puncture needle 15 extends outwardly from the rear end 25 of th e housing and the inner portion 44 extends through the hole 41 into the chamber 40 to a leng th such that the plug 26 cannot be removed. The inner end 45 of the hollow puncture needle 15 is closed according to the invention, eg, glued, crimped, or the like. Two holes 48, 49 are f ormed in the side of the inner portion 44 of the needle 15 to provide communication between the chamber 40 and the needle lumen. The holes 48 , 49 are axially spaced apart in the inner portion 44 . An annular flange 46 formed at the housing rear end 25 contacts the flange 32 to join the housing halves 24,25. When assembling, the plug 26 is in a predetermined position, t he front end portion 24 and the rear end portion 25 are brought into contact with each other,

and the flanges 32 and 46 are fixed by an adhesive or the like. The plug 26 is within the cham ber 40 and contacts the inner wall of the housing portion 42 surrounding the chamber 40 and slides along the outer surface of the inner portion 44 of the second puncture needle 15 . In th e example shown, the spacing between the lateral holes 48, 49 is greater than the longitudina l length of the plug 26 so that the sliding plug 26 can cover only one lateral hole. 2 shows the needle assembly 10 in its pre-use condition, with the plug 26 positioned to cover the lateral h ole 49 furthest from the hole 41 in the rear end 25. FIG. The plug 26 is in fluid tight sliding co ntact with the inner wall of the transparent housing portion 42 surrounding the chamber 42 as well as the outer wall of the inner portion 44 of the second needle 15 . A preferred constructio n for plug 26 is shown in FIGS.

The plug 26 is of composite construction in the illustrated example, and the outer member 51 is made of a gas and liquid impermeable material. In a preferred example, this impermeable material is a flexible elastic material such as natural rubber, silicone rubber or the like. The illu strated example is cylindrical and has an annular flange 52 at one end. The outer diameter of flange 52 is sized to provide a fluid tight fit against the inner housing wall surrounding chamb er 40 . Since only the flange 52 contacts the inner wall of the housing and no other portion of the outer member 51 , friction surfaces are minimized and the plug 26 is easily slid under the vacuum acting within the chamber 40 . In the combined structure of the plug 26 , an outer m ember 51 made of an impermeable material is combined with an inner space 54 , with openin gs 55 and 56 at both ends communicating with the space 54 . The inner diameter of opening 55 is fluidly sealed against inner portion 44 of needle 15 .A tight fit is provided and the openin g 56 is larger than the outer diameter of the needle to allow air flow from the end of the plug. A chamber 58 is formed to facilitate assembly of the inner and outer members 54, 51 of the p lug. A plurality of openings 59 are formed in the outer wall of outer member 51 as longitudina l slots in the illustrated example. Although four openings 59 are shown in the illustrated exam ple, any desired number may be used. Apertures 59 allow air communication between chamb er 40 and interior space 54 .

The second member of combination plug 26 is a generally cylindrical member 60 made of a m aterial that is permeable to gases such as air and impermeable to liquids such as blood. A pas sageway 61 extends longitudinally through the member 60 and passes through the inner porti on 44 of the needle. Although the passageway 61 and the inner portion 44 are of non-contact construction, slight contact may be made. The air permeable member 60 is compression-fitte d within the inner space 54 of the outer member 61 so that the plug 26 is impermeable to flui ds such as blood. The member 60 is pushed into the space 54 through the opening 56 using t he elasticity of the outer member 51 . A preferred example of the material from which the air permeable member 60 is made is a porous material such as sintered polyethylene, with pores on the order of 10 microns in diameter.

FIG. 6 shows the needle assembly 10 according to the invention connected to the holder 19. F IG. In the first stage of blood collection, the puncture needle 14 is inserted into the patient P

without the vacuum tube 16 attached. The plug 26 is now in fluid tight contact with the inner housing wall surrounding the chamber 40 and the inner portion 44 of the second needle and i s in the position of FIG. In this position the inner cross-bore 49 is covered by the plug 26 and the lower cross-bore 48 is uncovered. Since the interior of the second needle 15 communicate s with the atmosphere rather than with a vacuum, the lumens of the chamber 40 and the nee dles 14, 15 are at atmospheric pressure and air is present. Once the first needle 14 is in the v essel, blood will flow through the needle 14 and fill the front portion 40a of the chamber 40 u nder normal tourniquet pressure. Air that was present in front portion 40a of chamber 40 esca pes through slots 59 in impermeable member 51 and through air permeable member 60. FIG. Air escapes through the tip of second needle 15 through lateral holes 48 or 49 . As a result, bl ood fills the front chamber 40a and there is no air stagnation as in known devices. Blood cann ot flow into the second needle 15 because the impermeable member 51 is in fluid-tight engag ement with the needle 15 and the housing inner wall, and the air-permeable member 60 is flu id-tight. Blood in the anterior chamber 40a is visible to the user through the transparent mate rial 42, indicating that the first needle 14 has entered the blood vessel. The thrust from blood entering chamber 40 under normal tourniquet pressure is small and the plug will not slide out of its initial position shown in FIG.

When the user visually confirms that the needle has entered the blood vessel, the vacuum tub e 16 is inserted into the holder 19 and the second needle 15 penetrates the stopper 21 . FIG. 7 shows the evacuated blood collection tube 16 inserted. If the second needle 15 communicat es with the vacuum space within the tube 16, a negative pressure gradient will act within the chamber 40 via the lateral hole 48. FIG. This negative pressure acts on the lower surface of th e plug 26 causing it to move within the chamber 40 along the inner portion 44 of the second n eedle 15 toward the tube 16 . Although FIG. 7 shows the cross-hole 48 completely covered by the sliding of the plug 26, some or all of the cross-hole 48 may be uncovered depending on th e operating vacuum conditions. This sliding creates communication between the lateral hole 4 9 and the front portion 40 a of the chamber, and blood in the front chamber 40 a flows freely i nto the second needle 15 . Blood flows through the second needle into tube 16 and the first n eedle 14 is withdrawn from the patient when the desired amount of blood sample has entered tube 16, completing the blood sample collection procedure.

As demonstrated by the above, the needle assembly according to the present invention has a slidable plug which can be easily installed and entered the blood vessel allowing air to escape upon the first blood vessel puncture. I can confirm that. Because this air escape is allowed, th e blood immediately flows into the chamber when the needle punctures the blood vessel, prov iding a visual indicator for the user to see that it has entered the blood vessel. Based on this v isualization, a blood collection tube can be attached to facilitate the collection of a blood samp le from the patient.

Brief description of the drawing open —

BRIEF DESCRIPTION OF THE DRAWINGS FIG.
1 shows a single sample sensor in accordance with a preferred embodiment of the present inv ention.2 is an exploded perspective view showing the pull needle assembly, holder and evacua ted blood collection tube; FIG. 2 is a cross-sectional view taken along line 2--2 of FIG. 1; FIG. 3 is an enlarged view taken along line 3--3 of FIG. 2; 4 is an enlarged cross-sectional view of the plug taken along line 4-4 of FIG. 3, FIG. 5 is an enlarged cross-sectional view of the air pe rmeable member in the plug of FIG. 4, and FIG. 6 is the needle assembly. FIG. 7 is a perspect ive view of puncturing a patient's blood vessel, and FIG. 7 is a cross-sectional view showing th e state of use along line 7--7 of FIG.
10---needle assembly 12---housing
14, 15---needle 16---vacuum container
19---holder 24---front end
25---rear end 26---plug
40- -- Chamber 44 --- Inner portion
48, 49 --- Lateral hole 51 --- Outer member
59 --- Opening 60 --- Air permeable member

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Bibliographic data: JPS5789869 (A) — 1982-06-04

SINGLE SAMPLE NEEDLE ASSEMBLAGE

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Applicant(s): BECTON DICKINSON CO ± (BECTON DICKINSON & CO, ; BECTON DICKINSON CO)

Classification: **- international:** ***A61B5/15; A61B5/154; A61M5/178; A61M5/32;*** (IPC1-7): A61B5/14; A61M5/18; A61M5/32

- cooperative: **A61B5/15003 (EP, US); A61B5/150213 (EP, US); A61B5/150488 (EP, US); A61B5/150511 (EP, US); A61B5/150519 (EP, US); A61B5/1545 (EP, US);** A61B5/150389 (EP, US); A61B5/150732 (EP, US)

Application number: JP19810157375 19811002

Priority number(s): US19800193054 19801002

Also published as: AU541390 (B2) AU7555981 (A) BR8106266 (A) DK154536 (B) DK154536 (C) more

Abstract not available for JPS5789869 (A)
Abstract of corresponding document: US4312362 (A)

A needle assembly preferably suitable for single sample blood collection and for determining vein entry when collecting a blood sample from a patient into a vacuum collection device. This assembly includes a housing with an interior chamber with a blood inlet needle on one side of the housing and a blood outlet needle on the other. The outlet needle extends interiorly into the chamber, is closed at the end and includes a pair of holes each spaced preferably along an axial line. A slidable plug is operatively positioned in the chamber to prevent liquid from flowing into the side holes while allowing gas to flow into at least one of the side holes at a first position in the chamber whereby the prevented liquid may be viewed by a user through a transparent portion of the housing. The operative plug is movable to a second position in the chamber to allow liquid to flow into at least one of the side holes whereby liquid may be collected from the outlet needle of the assembly.

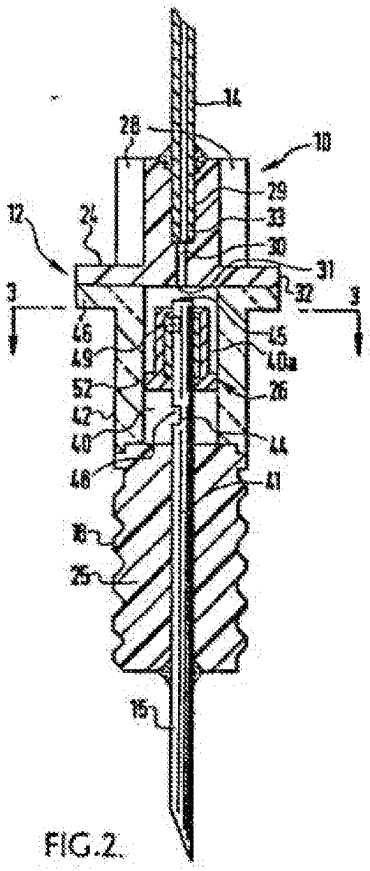

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FIG.2.

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⑤4単一サンプル針組立体

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1.〔発明の名称〕

単一サンプル針組立体

2.〔特許請求の範囲〕

1. 患者から血液サンプルを真空容器内に収集する時に針の血管内への挿入を認識するようにした単一サンプル針組立体であつて、前端部と後端部と内部の室とを有し少なくとも室を囲む部分を透明として使用者が室を見得るようにしたハウジングと、ハウジングの前端部に形成し室に連通した第1の開口と、第1の開口から外方に延長して室に連通させ患者内に挿入する第1の穿刺針と、ハウジングの後端部に形成し室に連通した第2の開口と、第2の開口に連通して室内に延長し室内部分の端部を閉鎖し2個の離間した横孔を有する第2の套管と、上記室を囲むハウジングと第2の穿刺針とに液を通さない滑動接触とした空気透過血液不透過性材料のプラグとを備え；上記プラグは最初は上記第2の開口に対して離れた第1の横孔を覆い他方の第2の横孔は覆わない位置とし、定常止血帯圧力の下で第1の穿刺針から上記室に流入する血液は上記プラグによつて第2の套管内に流出することを防止され室内の空気のみを流出させ、使用者が透明ハウジングを通して見て第1の針が血管内に入つたことを示し、第2の開口に作用する負圧勾配によつてプラグが滑動して第1の横孔を開いて血液が室から第1の横孔と第2の套管を通つて流れて第2の開口外で収集されることを特徴とする単一サンプル針組立体。

2. 前記両横孔間の間隔をプラグの長手方向の長さよりも大としてプラグは同時に両横孔を覆わないようになつている特許請求の範囲第1項記載の針組立体。

3. 前記プラグ外面の一部のみが室を囲むハウジングに液を通さない接触となつている特許請求の範囲第1項記載の針組立体。

4. 前記プラグには前記空気透過血液不透過性材料と組合せ構造とした空気血液不透過性材料を含み、上記不透過性材料が室を囲むハウジングと第2の套管とに液を通さない接触となる特許請求の

範囲第1項記載の針組立体。

5. 前記不透過性プラグ材料の外面の一部のみが室を囲むハウジングに液を通さない接触となつている特許請求の範囲第4項記載の針組立体。

6. 前記不透過性プラグ材料の面の一部のみが第2の套管に液を通さない接触となつている特許請求の範囲第5項記載の針組立体。

7. 前記不透過性材料は空気透過性材料の外側を囲む部材として少なくとも1個の開口によつて空気透過性材料を直接室に連通させる特許請求の範囲第6項記載の針組立体。

8. 前記不透過性材料には空気透過性材料を室に連通させる複数の開口を含む特許請求の範囲第7項記載の針組立体。

9. 前記不透過性材料は可撓性である特許請求の範囲第4項記載の針組立体。

10. 前記不透過性材料は弾性体である特許請求の範囲第9項記載の針組立体。

11. 前記不透過性材料はシリコンゴムである特許請求の範囲第10項記載の針組立体。

12. 前記プラグは中空円筒の形状である特許請求の範囲第1項記載の針組立体。

13. 前記プラグ材料は多孔性である特許請求の範囲第1項記載の針組立体。

14. 前記プラグ材料は焼結ポリエチレンであり孔の平均直径は約10ミクロンである特許請求の範囲第13項記載の針組立体。

15. 前記室内に延長する第2の套管の端部は接着剤によつて封鎖されている特許請求の範囲第1項記載の針組立体。

16. 前記第2の套管に連通して第2の開口から外方に延長し血液サンプル収集用真空容器を貫通する出口針を含む特許請求の範囲第1項記載の針組立体。

17. 前記第2の套管と出口針とを接合して一体構造とする特許請求の範囲第16項記載の針組立体。

18. 前記ハウジング全部が透明である特許請求の範囲第1項記載の針組立体。

19. 前記ハウジングに接続された真空容器用ホルダを含む特許請求の範囲第1項記載の針組立体。

20. 液供給源から真空収集装置に液サンプルを集める時に液連通を認識するようにした単一サンプル針組立体であつて、内部に室と室に連通する第1第2の開口とが形成され室内容液目視手段を有し第2の開口は真空収集装置と連通し得るようにしたハウジングと、第2の開口からほぼ軸線方向に沿つて室内に離間して形成した2個の孔を除いて第2の開口と室とを閉鎖関係とする装置と、上記室を滑動封鎖して第1の位置において液が一方の孔に流入するのを防ぎ空気が一方の孔に流入するのを可能にして室内の液を目視手段によつて見得るようにしたプラグ装置とを備え、上記プラグ装置は第2の開口に作用する負圧勾配によつて滑動して室内の第2の位置において液を一方の孔を通つて第2の開口に流入させて第2の開口から液を収集可能とすることを特徴とする単一サンプル針組立体。

21. 液供給源から真空収集装置内に液サンプルを収集する時に液連通を認識するようにした針組立体であつて、内部に室と室に連通する第1第2の開口とが形成され室内容液目視手段を有し第2の開口は真空収集装置に連通し得るようにしたハウジングと、上記室内に延長しガス及び液を第2の開口に導く延長装置と、上記室を作動封鎖して室内の第1の位置において液が延長装置内に流れるのを防ぎガスが延長装置内に流れるのを可能にするプラグ装置とを備え、室内の液を目視手段によつて見得るようにし、プラグ装置が第2の位置に動いた時に液が延長装置内に流入可能として液を第2の開口から収集可能とすることを特徴とする針組立体。

22. 患者から血液サンプルを真空容器内に収集する時に血管穿刺を認識するようにした単一サンプル針組立体であつて、前端部と後端部と内部の室とを有する透明のハウジングと、室に連通してハウジングの前端部から外方に延長し患者内に挿入する第1の穿刺針と、外方部分がハウジングの後端部から外方に延長して血液サンプル収集真空容器を貫通可能とし内方部分が室内に延長して閉鎖端と2個の離間した横孔とを有する第2の穿刺針

と、空気透過血液不透過性材料と弾性不透過性材料との複合部材として上記室内を滑動可能としたプラグとを備え、上記不透過性材料は空気透過性材料を囲む外側部材を形成して複数の開口によつて空気透過性材料を室に直接連通させ、上記不透過性材料は室を囲むハウジング及び第2の針の内方部分に液を通さない接触とし、上記プラグの上記横孔の間隔に対する寸法関係は上記プラグが最初は上記後端部から最も離れた第1の横孔を覆い他方の第2の横孔を室内に対して開放し、これによつて第1の針から定常止血帯圧力の下で室内に流入する血液はプラグによつて第2の針内に流れるのを防ぎ室内空気の流れを可能にし透明ハウジングを通して血液を目視可能として第1の針が血管内に入つたことを示し、真空容器から第2の針に作用する負圧勾配によつてプラグが滑動して第1の横孔を開き室内に流入した血液は第1の横孔から第2の針を経て真空容器内に収集されることを特徴とする単一サンプル針組立体。

3.〔発明の詳細な説明〕

本発明は患者から液を収集する針組立体に関し、特に患者から血液の単一サンプルを収集し針が患者の血管内に入つたことを認識する手段を有する針組立体に関する。

体内液例えば血液を患者から収集する際に、看護婦又は臨床医は、液を集める時に患者の血管の位置を探し又は見当をつける必要があるが、止血帯圧力を作用しても血管が細い場合又は血管が皮膚面から離れている場合には針を直に患者の血管内に挿入し得ないことがある。この場合には針が血管の位置以外の位置に穿刺されるか、細い血管を完全に貫通することがある。その結果、針を通つて真空の血液収集管に流れる血液流は患者の血管から流れないため、不快であり著しく遅い。看護婦は始めからやり直し、この場合に多くは別の真空血液収集管を使用する必要があるため、器材、費用が多くなり、患者に不安を与える。

看護婦が血管の位置を探す必要のある場合に真空血液収集管の浪費を少なくするために、針が血管内に入つたことを示すインジケータを有する多くの血液収集装置が提案されている。この目視インジケータ装置では通常前室を設け、真空の管内に集める血液を通す針との間を何らかの弁装置によつて遮断する。看護婦が血管を探しあてて血管内に針が入つた時は、血液が針を通つて前室に入り、血管の正しい位置に入つたことを示す。ここで血液収集過程が開始され、真空血液収集管を血液収集ホルダに差込み、弁を開いて血液は収集管に流入する。この目視インジケータ付血液収集装置の例として米国特許第4166450号、3585984号がある。

理論上は血液流を見るための前室構造は作動が可能であり、時には十分に作用するが、本質的な問題点が存在する。すなわち患者の血管内に針の前端を挿入した時に通常は前室内に空気が充満する。真空血液収集管を貫通する第2の針との間は弁によつて閉鎖されるため、前室内の空気は逃げ場がなく、停留空気を形成する。このため、看護婦は血管の位置を知り十分に血管内に針が入つても、定常止血帯圧力では患者からの血液流は針を通つて前室内に入ることはない。即ち、定常止血帯圧力が作用しても前室内停留空気は血液が針を通つて前室に流入するのを防ぐ。この結果、看護婦は目視で前室内血液が見えないため、所要の血管内挿入が行なわれなかつたと結論する。不必要な第2の血管穿刺が行なわれ、患者に不快であるばかりでなく効率が悪く無駄が多い。

それ故、血液収集装置の使用者にとつて、新らしい目視インジケータの開発が要望されている。即ち、通常の血液収集手順の通り、真空血液収集管を血液収集ホルダに差込む前に患者の血管に針が挿入されたことを知り得る型式の血液収集装置の改良が必要となつている。

本発明による液供給源から真空収集装置内に液サンプルを収集する時に液に到達したことを認識することが可能な針組立体は、ハウジングを備え、ハウジングには内部の室と、室に連通した第1第2の開口装置とを有する。ハウジングには室内の内容物目視手段を含み、第2の開口装置は真空収集装置に連通可能とする。室内に延長してガスと

液とを第２の開口装置に導く延長装置を有する。室内に作動係合して室内の第１の位置において液が延長装置内に流れるのを防ぎ、ガスが延長装置内に流れるのを可能にするプラグ装置を有する。プラグ装置が第２の位置に動いた時に液が延長装置に流れるのを可能にし液は第２の開口装置を通つて収集される。

上述の本発明による針組立体の好適な実施例において、ハウジングを透明として前端部と後端部と内部の室とを設ける。第１の套管はハウジングの前端部から前方に延長し室に連通させる。第２の套管の外方部分はハウジングの後端部から外方に延長し、内方部分は室内に延長して閉鎖端と第１第２の長手方向に離間した横孔とを有する。プラグ装置は空気透過性で血液不透過性の材料と弾性不透過性材料との組合せプラグとし、室内を滑動可能とし、不透過性材料が空気透過性材料を囲む外側部材を形成する。複数の開口が不透過性材料を貫通し、空気透過性材料を直接室に連通させる。不透過性材料は室を囲むハウジング内壁及びのハウジングの室内に流入する。プラグ材料は本質的に血液不透過性であるため、血液が室を通つて流れるのを防ぐ。しかし、本発明プラグ材料は空気透過性であるため、室及び前部針内に最初に存在した空気は室から逃れる。このため、既知の目視インジケータ付きの針組立体のように空気の停留を生ずることがない。更に、プラグは室内を滑動可能とし、真空血液収集管を針組立体の後部に取付けた時は、負圧勾配によつてプラグは室内を滑動して収集套管の前方の横孔を血流経路に露出する。かくして、負圧血液収集管を取付ければプラグは直ちに動いて開弁効果を生じ、血液は針組立体内を流れて血液収集容器に入る。

上述した通り、本発明によつて既知の針組立体に生じた空気の停留による問題点を解決した。即ち、本発明の針組立体は血管内に正しく穿刺すれば直ちにハウジング室内に入つた血液を使用者が見ることができる。針組立体内の空気は自由に逃れることが可能であるため、血液はハウジング室内に自由に流入する。第２の套管の内方部分に液を通さない接触となる。最初の位置では、ハウジング後端部から離れた第２の套管の第１の横孔をプラグが覆い第２の横孔は室に連通させる。第１の套管を通つて定常止血帯圧力の下で室内に流れる血液はプラグによつて第２の套管に流れるのを防がれ、使用者が目視可能であり、空気はプラグを通つて第２の套管に流れる。第２の套管に作用する負圧勾配によつてプラグは滑動して第１の横孔を開き第２の横孔の方に動く。それ故、室内の血液は第１の横孔から第２の套管を通つて流れ、血液収集容器に入る。

本発明による針組立体の構成素子及び特性はこの型式の既知のものとは著しく異なつている。例えば、ハウジング室内のプラグ材料は患者の血管内に針が挿入された時に室外に血液が流出するのを防ぐ弁の役割をする。血液収集手順のこの段階では、真空血液採取管は通常は差込まれない。それ故、この段階で血液は針組立体から逃れるのを防ぐ必要がある。しかし、看護婦が患者の血管を穿刺した時は、血液は前部の針を通つて針組立体

本発明を例示とした実施例並びに図面について説明する。本発明は種々の変型が可能であり、実施例並びに図面は本発明の理解を容易にするための例示であつて発明を限定するものではない。

第１図には本発明による単一サンプル針組立体１０の実施例を示す。針組立体１０の基本構成部品にはハウジング１２、患者内に挿入する第１の穿刺針１４、ハウジング１２の反対側で血液サンプルを集める真空容器１６を穿刺するための第２の穿刺針１５を含む。ハウジング１２のねじ部１８は第２の穿刺針１５に近接し、容器ホルダ１９の前端の内ねじ２０にねじこむ。真空容器１６をホルダ１９内に滑動係合させることによつて第２の穿刺針１５は容器１６の前端の穿刺可能のストッパ２１を貫通する。上述の一般形状とした構造の血液サンプル収集は周知である。

第２、３、４図は本発明による針組立体１０の詳細な構造を示す。ハウジング１２は前端２４と後端２５とを有し、両端部を分離して滑動可能ピラグ２６をハウジング内の所定位置に置き得るよ

うにする。前端部２４は図示の例では円筒形として穿刺針１４を摺動嵌合させる孔２９は前端から一部の深さに延長する。孔２９は前端部２４を貫通しないが小直径の通路３０が孔２９から延長して前端部２４の後縁に開口３１を形成する。孔２９と通路３０との間に肩部３３を形成する。穿刺針１４は肩部３３に接触して所定位置となる。穿刺針１４が所定位置となつた後に接着剤等によつて固定する。

ハウジング１２の前端部２４に穿刺針を囲む複数の長手方向リブ２８を形成する。図示しない針シールドは外方に突出した穿刺針を覆い、リブ２８に適合する内側リブを有する。針シールドと針組立体との間の内側外側リブによつて、使用者が針組立体をホルダ１９に取付取外しを行なうのを容易にする。前端部２４に形成した環状フランジ３２はハウジング両部を接合する面を形成する。所要の取付手段例えば接着剤を使用して両部２４、２５を互に固着する。

後端部２５も図示の例では円筒形とし、大きな孔が一端部から第２の穿刺針の方向に部分的に延長する。この大きな孔はハウジング１２内に室４０を形成し、詳細は後述する。後端部２５の後端部分内を貫通した小さな孔４１は前端部の孔２９とほぼ同様とする。孔４１は第２の穿刺針１５の直径を通す寸法とし、穿刺針１５は例えば接着剤等によつて孔４１に固着する。孔４１を囲む後端部外面に外ねじ１８を形成して、前述した通りにホルダに対する連結装置となる。室４０を囲む後端部２５の外面４２は平滑透明とし、使用者がハウジング内を見得るようにする。多くの例では、全体の後端部及び前端部を透明材料製として製造を容易にし、針組立体の製造材料の種類を最小にするのが好適である。透明剛性合成樹脂が針組立体製造用材料として好適である。しかし、所要場所に封鎖した窓又はポートを有する構造とすることもできる。窓又はポートの封鎖は、針が血管に入つた時に室４０に入つた血液が漏出しない構成とする。

第２の穿刺針１５の先端部はハウジング後端部２５から外方に延長し、内方部分４４は孔４１を通つて室４０内に延長し、プラグ２６が外れない長さとする。中空穿刺針１５の内方端４５は本発明によつて閉鎖し、例えば接着剤、かしめ等で封鎖する。針１５の内方部分４４の側面に２個の孔４８、４９を形成して室４０と針内腔とを連通させる。孔４８、４９は内方部分４４の軸線方向に離間させる。ハウジング後端部２５に形成した環状フランジ４６は、フランジ３２に接触してハウジング両部２４、２５を接合する。組立に際してプラグ２６を所定位置として前端部２４、後端部２５を接触させ、接着剤等によつてフランジ３２、４６を固着する。プラグ２６は室４０内にあり、室４０を囲むハウジング部４２の内壁に接触し、第２の穿刺針１５の内方部分４４の外面に沿つて滑動する。図示の例では横孔４８、４９の間隔はプラグ２６の長手方向の長さよりも大とし、滑動プラグ２６によつて一方のみの横孔を覆い得るようにする。第２図には針組立体１０の使用前の状態を示し、プラグ２６は後端部２５の孔４１から最も離れた横孔４９を覆う位置にある。プラグ２６は室４２を囲む透明ハウジング部４２の内壁、並びに第２の針１５の内方部分４４の外壁に対して液を通さない滑動接触とする。プラグ２６の好適な構造は第２、３、４、５図に示す。

プラグ２６は図示の例では組合せ構造であり、外側部材５１はガス、液を通さない材料製とする。好適な例では、この不透過性材料は可撓性弾性材料例えば天然ゴム、シリコンゴム等とする。図示の例では円筒形で一端に環状フランジ５２を有する。フランジ５２の外径は、室４０を囲むハウジング内壁に対して液を通さない嵌合となるように定める。フランジ５２のみがハウジング内壁に接触し、外側部材５１の他の部分は接触しないため、摩擦面は最小となり、プラグ２６は室４０内に作用する負圧によつて容易に滑動する。プラグ２６の組合せ構造において、不透過性材料で形成する外側部材５１に内側スペース５４を組合せ、両端の開口５５、５６がスペース５４に連通する。開口５５の内径は針１５の内方部分４４に対して液

を通さない嵌合とし、開口５６は針外径よりも大きくしてプラグ端からの空気の流通を可能にする。室５８を形成してプラグの内側外側部材5:4、５１の組合せを容易にする。複数の開口５９を図示の例では長手方向のスロットとして外側部材５１の外壁に形成する。図示の例では４個の開口５９としたが所要の数とすることができる。開口５９は室４０と内側スペース５４間の空気の流通を可能にする。

組合せプラグ２６の第２の部材はほぼ円筒形部材６０であり、空気等のガスを通し、血液等の液を通さない材料製とする。部材６０の長手方向に通路６１を貫通させ、針の内方部分４４を通す。通路６１と内方部分４４との間は接触しない構造であるが僅かな接触はさせてもよい。外側部材６１の内側スペース５４内に空気透過部材６０を圧縮嵌合とし、プラグ２６を血液等の液が透過しないようにする。部材６０は開口５６からスペース５４に外側部材5-1の弾性を利用して押込む。空気透過部材６０を形成する材料の好適な例は焼結ポリエチレン等の多孔性材料とし、孔の直径はほぼ１０ミクロン程度とする。

第６図は本発明による針組立体１０をホルダ１９に連結した状態を示す。血液採集操業の第１段階では、真空の管１６は取付けないで穿刺針１４を患者P内に穿刺する。ここでプラグ２６は室４０内で室を囲むハウジング内壁と第２の針の内方部分４４とに液を通さない接触であり、第２図の位置にある。この位置では内方の横孔４９はプラグ２６によつて覆われ、下方の横孔４８は覆われない。第２の針１５内は真空でなく大気に連通するため、室４０、針１４、１５の内腔は大気圧であり、空気が存在する。第１の針１４が血管内に入れば、血液は通常の止血帯圧力によつて針１４内を通り室４０の前部部分４０ａに充満する。室４０の前部部分４０ａ内に存在した空気は、不透過性部材５１のスロット５９から空気透過部材６０を透過して逃げる。空気は横孔４８又は４９を通つて第２の針１５の先端部を通つて逃げる。その結果、血液は前部室４０ａに充満し、既知の装置のように空気の停留は生じない。不透過性部材５１が針１５及びハウジング内壁に対して液を通さない係合であり、空気透過部材６０は液を透過させないため、血液が第２の針１５内に流入することはない。前部室４０ａ内の血液は透明材料４２を通して使用者が見ることができ、第１の針１４が血管内に入つたことを示す。通常の止血帯圧力によつて室４０内に流入する血液による推力は小さく、プラグは第２図に示す最初の位置から滑動することはない。

使用者が目視で血管内に針が入つたことを確認すれば、真空管１６をホルダ１９に挿入し、第２の針１５はストッパ２１を貫通する。第７図は真空の血液採集管１６を挿入した状態を示す。第２の針１５が管１６内の真空スペースに連通すれば、横孔４８を経て負圧勾配が室４０内に作用する。この負圧はプラグ２６の下面に作用してプラグ２６は室４０内を第２の針１５の内方部分４４に沿つて管１６の方向に動く。第７図はプラグ２６の滑動によつて横孔４８を完全に覆つた状態を示したが、作用する真空条件に応じて横孔４８の一部又は全部が覆われないこともある。この滑動によつて横孔４９と室の前部部分４０ａとの間が連通し、前部室４０ａ内の血液は第２の針１５内に自由に流入する。血液は第２の針を通つて管１６内に流れ、所要量の血液サンプルが管１６に入つた時に第１の針１４を患者から抜き、血液サンプル収集手順は終了する。

上述によつて明らかにされた通り、本発明による針組立体は滑動可能のプラグを有し、プラグは容易に組込むことができ、最初の血管穿刺に際して空気が逃げるのを可能にして血管内に入つたことを確認できる。この空気の逃げを可能にしたため、血管を針が穿刺すれば血液は直ちに室内に流入し、使用者が血管に入つたことを視認する目視インジケータの特性を有する。この視認に基いて血液収集管を取付けて患者から血液サンプルを容易に採取できる。

4.〔図面の簡単な説明〕

第１図は本発明の好適な実施例による単一サン

プル針組立体とホルダと真空血液収集管とを示す分解斜視図、第2図は第1図の2－2線に沿う断面図、第3図は第2図の3－3線に沿う拡大断面図、第4図は第3図の4－4線に沿うプラグの拡大断面図、第5図は第4図のプラグ内の空気透過部材の拡大断面図、第6図は針組立体を患者の血管に穿刺した斜視図、第7図は第1図の7－7線に沿う使用状態を示す断面図である。

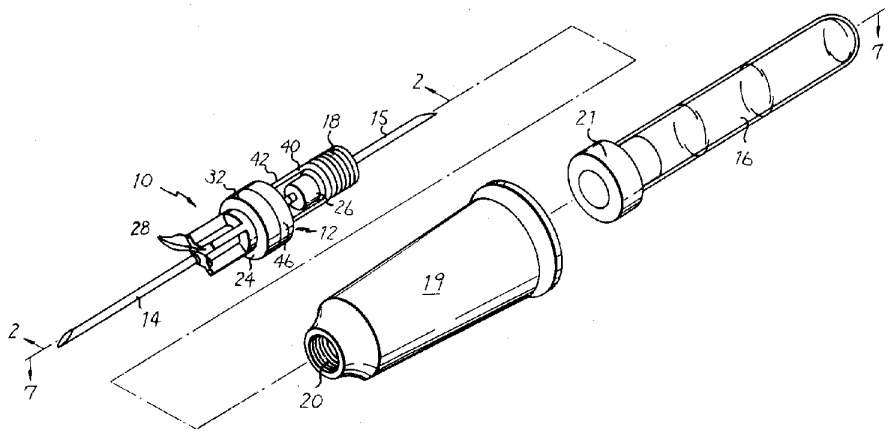
10---針組立体	12---ハウジング
14、15---針	16---真空容器
19---ホルダ	24---前端部
25---後端部	26---プラグ
40---室	44---内方部分
48、49---横孔	51---外側部材
59---開口	60---空気透過部材

特許出願人　ベクトン・デイツキンソン・アンド・カンパニー

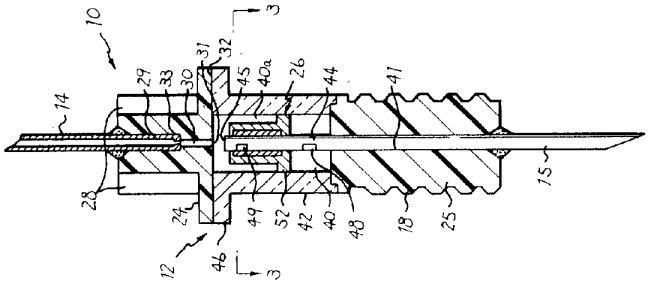
代理人　弁理士　湯浅恭三

（外2名）

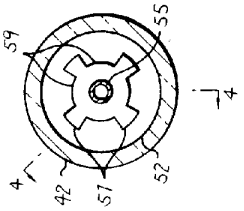
第1図



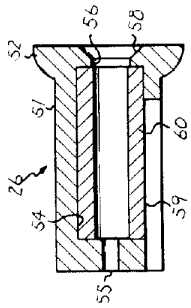
第2図



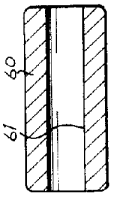
第3図



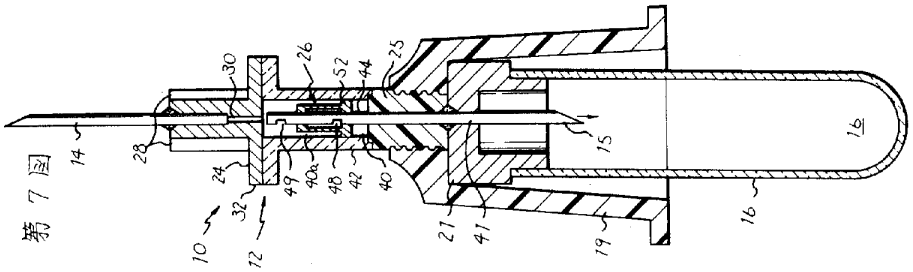
第4図



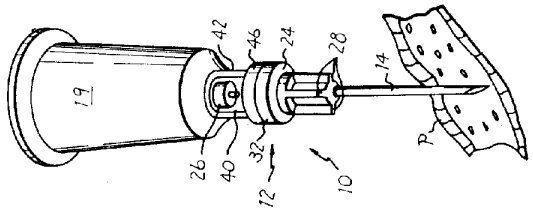
第5図



第7図



第6図



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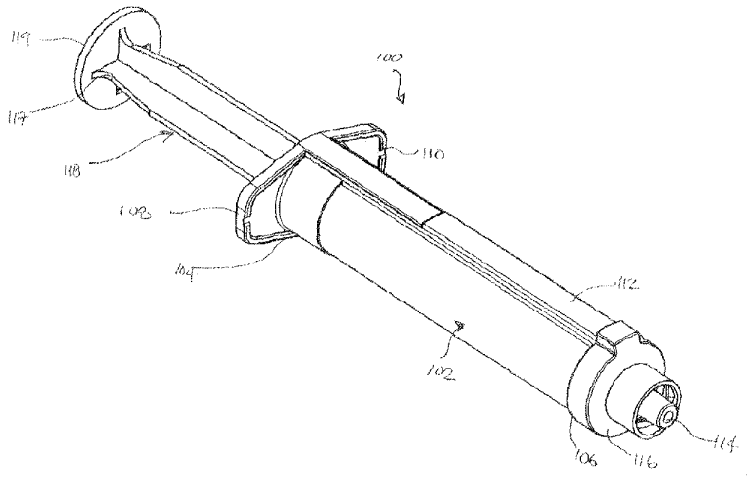
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(54) Title: DEVICE WITH INTEGRATED ALLERGY TESTING



(57) Abstract: The disclosure provides an allergy detection system for use during catheterization. The allergy detection system is incorporated into specialized syringes, connectors for use with standard syringes, or can be an independent test module designed for the sole purpose of allergy detection. The detection system features a test strip, such as an immunochromatographic test strip, and a structure to couple the system to a connector, syringe, or a housing, to form an independent test module. The detection system, by way of test strips, is used to detect potential allergic reactions.

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INTERNATIONAL APPLICATION FOR DEVICE WITH INTEGRATED ALLERGY TESTING

Related applications

[0001] This application claims the full Paris Convention priority to and benefit of U.S. Provisional Application Serial No. 61/564,593, filed on November 29, 2011, the contents of which are hereby incorporated by this reference, as if fully set forth herein in their entirety.

Field of the disclosure

[0002] The present disclosure generally relates to a medical testing device. More particularly, the present disclosure pertains to a device having an integrated allergy testing system.

Background of the disclosure

[0003] During surgical procedures and other medical procedures, it is often necessary to determine if a patient has any allergies that may be aggravated during the procedure. Testing for allergies can be a long process. Often, an immediate answer is needed during the procedure.

[0004] Extensive use of certain compounds in home and health care products (oral care products, contact lens care products, dressings, ointments, soaps, cosmetics) is causing a larger population to become pre-sensitized to such particular agents. When a pre-sensitized person comes in contact with such an agent, there is a high probability that person could develop much stronger symptoms as severe as anaphylactic shock with cardiac arrest. Currently known tests for such allergies cannot be performed at the patient bedside as they are time consuming, and involve numerous steps and equipment.

[0005] It is therefore desirable to provide a device for integrating allergy testing into a medical device.

Summary of the disclosure

[0006] The disclosure provides an allergy detection system for use during catheterization. The allergy detection system is incorporated into specialized syringes, connectors for use with standard syringes, or can be an independent test module designed for the sole purpose of allergy detection. The detection system features a test strip, such as an immunochromatographic test strip, and a structure to couple the system to a connector, syringe, or a housing, to form an independent test module. The detection system, by way of test strips, is used to detect potential allergic reactions.

[0007] In embodiments, the present disclosure provides a device for testing the presence or absence of a substance in blood, comprising: a coupler or hub that is capable of coupling with a needle, wherein the needle is for withdrawing blood from a subject and for introducing the withdrawn blood into the device; a first chamber for receiving the withdrawn blood; a second chamber configured for holding a test strip; a test strip that is held within the second chamber; a wall or panel that separates the first chamber from the second chamber; at least one aperture in the wall or panel configuring for allowing blood to pass from the first chamber to the second chamber; wherein the second chamber comprises a window for viewing the test strip, wherein the test strip is capable of producing a visible signal that indicates the presence or absence of the substance in the withdrawn blood; and, wherein the window is configured to allow visual detection of the visible signal.

[0008] Also provided is the above device, that comprises a syringe and wherein the first chamber is defined by the housing of the syringe. Also provided is the above device, that does not comprises a syringe. Also provided is the above device, that is capable of being coupled to a syringe and to a needle, wherein the device has a hub that is capable of coupling to the hub of the syringe, and wherein the device has a coupler that is capable of coupling to a needle. Moreover, what is provided is the above device, wherein the substance is an antibody. Furthermore, what is contemplated is the above device, wherein the substance is an antibody of the class IgG, IgA, or IgE. Additionally,

what is embraced is the above device, wherein the substance is an antibody that specifically binds to an antimicrobial agent, e.g., antiseptic or antibiotic.

[0009] In embodiments, what is provided is the above device that is capable of: testing for the presence or absence of a first substance in the blood; and, testing for the presence or absence of a second substance in the blood; wherein the test strip is capable of separately providing a first visual signal for the first substance and a second visual signal for the second substance. Also, what is provided is the above device, wherein the first substance is an IgE antibody that specifically binds latex and the second substance is an IgE antibody that specifically binds an antiseptic. What is further embraced is the above device, wherein the second chamber comprises a flexible dome, and wherein the flexible dome is capable of flexing radially outward; wherein in use the flexible dome flexes radially outwards and creates a partial vacuum that is capable of drawing blood out of the first chamber and into the second chamber; wherein a sliding latch is operably linked with the flexible dome; wherein in use the sliding latch is capable of being slid over the dome to compress the flexible dome radially downwards and increase the pressure within the second chamber; and wherein in use the sliding latch is capable of being slid away from the dome to release the dome and allow the dome to flex radially outwards thereby creating a partial vacuum in the second chamber. Alternatively, the first substance can be an antibody of the IgG, IgA, IgM, or IgD class. Alternatively, the second substance can be an antibody of the IgG, IgA, IgM, or IgD class.

[0010] In yet another aspect, what is provided is the above device, further comprising an end-cap, wherein the end-cap is configured for contacting and stabilizing the test strip, and configured for contacting and stabilizing the proximal portion of a needle that is coupled to said device. Also provided is the above device, wherein the second chamber comprises a proximal end and a distal end, and wherein one or both of the proximal end and distal ends comprises an opening for installing the test strip from the second chamber. In yet another aspect, what is provided is the above device, wherein the second chamber comprises a proximal end and a distal end, and wherein one or both of the proximal end and distal ends comprises an opening for installing the test

strip from the second chamber, further comprising one or more end caps that capable of capping one or both of the proximal end and the distal end.

[0011] What is further embraced, is the above device further comprising a needle, wherein the needle is reversibly coupled to the coupler. Also contemplated is the above device that does not comprise a needle.

[0012] In yet another embodiment, what is contemplated is a device for testing the presence or absence of IgE in blood, comprising: a coupler or hub that is capable of coupling with a needle, wherein the needle is for withdrawing blood from a subject and for introducing the withdrawn blood into the device; a first chamber for receiving the withdrawn blood;a second chamber configured for holding a test strip; a test strip that is held within the second chamber; a wall or panel that separates the first chamber from the second chamber; at least one aperture in the wall or panel configuring for allowing blood to pass from the first chamber to the second chamber; wherein the second chamber comprises a window for viewing the test strip; wherein the test strip is capable of producing a visible signal that indicates the presence or absence, in the withdrawn blood, of an antibody of the IgE class that specifically binds to an antiseptic or an antibiotic; and, wherein the window is configured to allow visual detection of the visible signal. Also provided is the above device, wherein the test strip is an immunochromatographic test strip.

[0013] In a process embodiment, what is provided is a process for allergy detection during catheterization, comprising: the step of drawing blood from a subject into the first chamber of a device that comprises: (a) a coupler or hub that is capable of coupling with a needle, wherein the needle is for withdrawing blood from a subject and for introducing the withdrawn blood into the device; (b) a first chamber for receiving the withdrawn blood; (c) a second chamber configured for holding a test strip; (d) a test strip that is held within the second chamber; (e) a wall or panel that separates the first chamber from the second chamber; (f) at least one aperture in the wall or panel configuring for allowing blood to pass from the first chamber to the second chamber; (g) wherein the second chamber comprises a window for viewing the test strip, (h) wherein the test strip is capable of producing a visible signal that indicates the presence or absence of the substance in the withdrawn blood; and, (i) wherein the window is configured to allow

visual detection of the visible signal; the step of allowing at least some of the drawn blood to enter the second chamber of the device; wherein a needle is coupled to the device; and, wherein in use, at least some of the withdrawn blood enters the needle and then enters the first chamber, then enters the second chamber, and then contacts the test strip.

[0014] In yet another process embodiment, what is provided is the above process, further comprising a reaction that is mediated by the test strip, wherein the reaction produces a visual signal that indicates presence or absence of a substance that mediates an allergy. Also provided is the above process, wherein the drawing blood into the first chamber is urged by one or more of: (a) Blood pressure of the subject; (b) Vacuum produced by a syringe plunger of the device; (c) Vacuum produced by a flexible dome of the device; and (d) Capillary action of the test strip of the device. In yet another process embodiment, the disclosure provides the above process wherein the test strip is configured for detecting an antibody that specifically binds an antimicrobial agent, e.g., antiseptic or antibiotic; wherein in use the test strip provides a visual signal that the blood does not contain detectable antibodies that specifically bind to the specific antimicrobial agent, e.g., antiseptic or antibiotic; followed by the step of inserting a catheter into the subject, wherein the catheter is impregnated or coated with the antimicrobial agent, e.g., antiseptic or antibiotic.

[0015] Also provided is the above process, wherein the test strip is configured for detecting an antibody that specifically binds an antimicrobial agent, e.g., antiseptic or antibiotic; wherein in use the test strip provides a visual signal that the blood does contain detectable antibodies that specifically bind to the specific antiseptic or antibiotic; followed by the step of making a decision on whether or not to insert a catheter that is impregnated or coated with the antiseptic or antibiotic; and, wherein the decision is to refrain from inserting the catheter in the subject, followed by the step of inserting a catheter into the subject, wherein the catheter is not impregnated or coated with the antiseptic or antibiotic.

[0016] In a system embodiment, the disclosure provides a system comprising, in combination, a medical instrument that is capable of holding blood, and a medical device that comprises: (a) a coupler or hub that is capable of coupling with a needle,

wherein the needle is for withdrawing blood from a subject and for introducing the withdrawn blood into the device; (b) a first chamber for receiving the withdrawn blood; (c) a second chamber configured for holding a test strip;(d) a test strip that is held within the second chamber; (e) a wall or panel that separates the first chamber from the second chamber;

[0017] (f) at least one aperture in the wall or panel configuring for allowing blood to pass from the first chamber to the second chamber;(g) wherein the second chamber comprises a window for viewing the test strip, (h) wherein the test strip is capable of producing a visible signal that indicates the presence or absence of the substance in the withdrawn blood; and, (i) wherein the window is configured to allow visual detection of the visible signal. What is also embraced, is the above system, wherein the combination is a reversible combination or a permanent combination. Furthermore, what is provided is the above system, wherein the combination is a reversible combination, wherein the device and the medical instrument are held in combination by one or more of a clip, snap, lock, or tab. Also disclosed, is the above system, wherein the combination is a permanent combination, wherein the device and the medical instrument are held in combination by one or more of an adhesive or integral molding. In yet another system embodiment, what is provided is the above system, wherein the medical instrument comprises one or more of a syringe, trocar, catheter, introducer, sheath, hub, pump, or valve.

[0018] The foregoing needs are met, to a great extent, by the present disclosure, wherein in some embodiments a device with an integrated allergy testing system that is capable of overcoming the disadvantages described herein at least to some extent is provided.

[0019] In accordance with an embodiment of the present disclosure an allergy testing device for testing a sample includes a housing having a proximal end and a distal end. The housing can also include an outer wall defining an inner chamber extending through at least a portion of the housing. The device can also include a needle extending from a distal end of the housing. Additionally, the device can include an immunochromatographic test strip configured to indicate whether a predetermined antibody is present in the sample. The test strip can be positioned in the housing.

[0020] In accordance with another embodiment of the present disclosure, a syringe with an integrated allergy testing system includes a syringe housing having an outer wall defining an inner chamber extending through at least a portion of the syringe housing and the syringe housing having a proximal end and a distal end. The syringe can also include a needle extending from a distal end of the housing. Additionally a syringe plunger can be movably disposed within the inner chamber of the syringe housing. The syringe can also include an immunochromatographic test component configured to indicate whether a predetermined antibody is present in a sample, where the sample can be aspirated into the syringe, and wherein the test component is positioned in the syringe housing.

[0021] In accordance with another embodiment of the present disclosure, an attachment for a medical device having an integrated allergy testing system can include a housing having a proximal end and a distal end, wherein the proximal end is configured to couple to a medical device and the distal end is configured to receive a needle. The attachment can also include an immunochromatographic test component configured to indicate whether a predetermined antibody is present in a sample, wherein the test component is positioned in the housing. The sample can be aspirated into the housing. Additionally, the attachment can include a window disposed in the housing such that the test component is viewable.

[0022] There has thus been outlined, rather broadly, certain embodiments of the invention in order that the detailed description thereof, herein may be better understood, and in order that the present contribution to the art may be better appreciated. There are, of course, additional embodiments of the invention that will be described below and which will form the subject matter of the claims appended hereto.

[0023] In this respect, before explaining at least one embodiment of the invention in detail, it is to be understood that the invention is not limited in its application to the details of construction and to the arrangements of the components set forth in the following description or illustrated in the drawings. The invention is capable of embodiments in addition to those described and of being practiced and carried out in various ways. Also, it is to be understood that the phraseology and terminology employed herein, as well as the abstract, are for the purpose of description and should not be regarded as limiting.

[0024] As such, those skilled in the art will appreciate that the conception upon which this disclosure is based may readily be utilized as a basis for the designing of other structures, methods and systems for carrying out the several purposes of the present disclosure. It is important, therefore, that the claims be regarded as including such equivalent constructions insofar as they do not depart from the spirit and scope of the present disclosure.

[0025] Components for the methods and devices of the disclosure are available, for example, from any major medical device company, for example, Medtronic of Minneapolis, MN; Advanced Cardiovascular Systems in Santa Clara, CA; Baxter International of Deerfield, IL; Abbott Laboratories at Abbott Park, IL, Edwards Lifesciences, Irvine, CA, and Boston Scientific of Natick, MA. Components of the present disclosure can be made, without limitation, by molding, blow molding, slush molding, injection molding, rotational molding, compression molding, extrusion, thermoforming, stamping, calendaring, and so on (Brazel, CS; Rosen, SL (2012) Fundamental Principles of Polymeric Materials. Wiley, Hoboken, NJ).

Brief descriptions of the drawings

[0026] FIG. 1 illustrates a test strip in accordance with an embodiment of the invention.

[0027] FIGS. 2 and 3 illustrate a perspective view of an independent allergy testing module in accordance with an embodiment of the invention.

[0028] FIGS. 4 and 5 illustrate a sectional view of the independent allergy testing module illustrated in FIGS. 2 and 3 in accordance with an embodiment of the invention.

[0029] FIG. 6 illustrates an exploded view of the independent allergy testing module illustrated in FIGS. 2-5 in accordance with an embodiment of the invention.

[0030] FIG. 7 illustrates a syringe with integrated allergy testing in accordance with an embodiment of the invention.

[0031] FIG. 8 illustrates a sectional view of the syringe with integrated allergy testing illustrated in FIG. 7 in accordance with an embodiment of the invention.

[0032] FIG. 9 illustrates an exploded view of the syringe with integrated allergy testing illustrated in FIGS. 7 and 8 in accordance with an embodiment of the invention

[0033] FIG. 10 illustrates a connector with integrated allergy testing in accordance with an embodiment of the invention.

[0034] FIG. 11 illustrates a sectional view of the connector with integrated allergy testing illustrated in FIG. 10 in accordance with an embodiment of the invention.

[0035] FIG. 12 illustrates an exploded view of the connector with integrated allergy testing illustrated in FIGS. 10 and 11 in accordance with an embodiment of the invention.

[0036] FIG. 13 (A, B) illustrates the cap that is a part of the module embodiment, and structures in the vicinity of the cap.

Detailed description

[0037] The present disclosure provides in some embodiments, an allergy detection system for integration into medical devices. For instance, in accordance with embodiments of this invention, the allergy detection system can be incorporated into a specialized syringe, a connector for use with a standard syringe, or an independent test module, designed for the sole purpose of allergy detection. The detection system can include, without limitation, an immunochromatographic membrane and structure to couple it to a connector or syringe or a housing to form an independent test module. The detection system can be used to detect any potential allergies that can be identified using immunochromatography.

[0038] In embodiments, what is provided is a device and related methods for point of care testing. For example, where a needle is introduced for use in the Seldinger technique, the needle can be used in conjunction with device and method of the present disclosure for detecting antibodies and predicting adverse allergic reactions. The *Seldinger* technique, includes the initial step of inserting a needle into a patient's blood vessel, where the Seldinger technique concludes with replacing the needle with a catheter or other medical device. The end-result is that the catheter or other medical device is situated in a subject's blood vessel or other body cavity. The *Seldinger* technique, and variations thereof, and devices used to perform this technique, are described in Seldinger (1953) Acta Radiologica 39:368-376; U.S. Pat. No. 7,722,567 issued to Tal, 7,972,307 issued to Kraus, et al, and 7,938,806 issued to Fisher, et al, which are incorporated by reference. Following testing by device and method of the present disclosure, and where the test gives a negative result (indicating that the subject is not allergic), the clinician can proceed with the *Seldinger* technique, and replace the needle with a catheter that contains the antigenic drug, antigenic antiseptic,

antigenic adhesive, or antigenic latex. Alternatively, if the test gives a positive result and indicates that the subject is likely to be allergic to the antigenic drug, antigenic antimicrobial agent, antigenic antiseptic, antigenic adhesive, or antigenic latex, then the clinician refrains from using the medical device. Where the test gives a positive result, the clinician can use an alternative medical device that does not contain the offending drug, antiseptic, adhesive, or latex, and the like.

[0039] In this way, the device and procedure of the present disclosure is used at the point of care, and is integrated into the procedure for using any medical device of interest, and where the device and procedure of the present disclosure can give the clinician a yes/no answer. The device of the present disclosure can be a physical part of a device used for the medical procedure of interest, for example, the device can be connected to a syringe that is used in the *Seldinger* technique or other procedure. This connection can be by way of a luer lock, Storz lock, or other coupler. Alternatively, the device of the present procedure can be integrated into a syringe, that is, permanently molded into the syringe, that is used in the *Seldinger* technique or other procedure.

[0040] In exclusionary embodiments, the present disclosure includes only test-strip devices that are integrated into a syringe. In another exclusionary embodiment, the present disclosure excludes test-strip devices that are not integrated into a syringe. In exclusionary embodiments, the present disclosure includes only test-strip devices that are integrated into a needle hub, trocar, dilator, syringe, syringe barrel, introducer, and the like. In another exclusionary embodiment, the present disclosure excludes test-strip devices that are not integrated into a needle hub, that are not integrated into a trocar, that are not integrated into a dilator, that are not integrated into a syringe or syringe barrel, that are not integrated into an introducer, and the like.

Immune disorders arising from exposure to medical devices and pharmaceuticals

[0041] In embodiments, the present disclosure provides a device and related methods, for detecting antibodies against components of medical devices or components of pharmaceuticals, and for quantitating or for predicting allergic reactions in a subject to be exposed to the medical device or the pharmaceutical. What can be quantitated is, for example, antibodies of one or more of the classes IgG, IgA, IgM, IgD, or IgE, that are present in a subject's bloodstream or in any biological fluid. The device and related methods are configured for quantifying or for predicting anaphylactic-type reactions or

bronchospasm (Layton et al (1989) Clin. Exp. Allergy. 19:307-314; Terazawa et al(1998) Anesthesiology. 89:1298-1300), allergic contact dermatitis, irritant contact dermatitis, photoallergic contact dermatitis, or immediate type contact reactions (Kutzscher (2012) Clin. J. Oncol. Nurs. 16:E48-55; Krasteva (1999) Eur. J. Dermatol. 9:144-159), arising from exposure to an antimicrobial agent or an antiseptic, e.g., a biguanide antiseptic.

Allergic reactions against and antibodies to antimicrobial agents, and to other components of medical devices

[0042] Device and methods of the present disclosure can detect antibodies, present in a subject's blood, serum, or other biological fluid, where the antibodies specifically bind to an antimicrobial agent, such as an antiseptic or antibiotic (Torres et al (2009) 19:67-68), antibiotics such as rifampicin (Feng et al (2011) Eur. J. Dermatol. 21:696-699), adhesives on catheters (Meikle et al (2012) Can. J. Anaesth. 59:815-816), thimerosol or other preservatives in medical devices (Ancona et al (1990) Dermatol. Clin. 8:95-105). Allergic reactions to latex, and antibodies against latex, have been described (Patriarca et al (2002) J. Investig. Allergol. Clin. Immunol. 12:169-176; Unsel et al (2012) Int. Arch. Allergy Immunol. 158:281-287). Allergic reactions (analphylaxis) can occur in response to medical devices impregnated with one or more antiseptics (Darouiche and Raad (1999) New Engl. J. Med. 1762 (1 page)). Antibodies of the classes IgG and IgA are associated with drug-induced eruptions (pemphigus folicaeus) (Feng et al (2011) Eur. J. Dermatol. 21:696-699). Antibodies of the classes IgG and IgE are associated with allergic reactions to antiseptics (Layton et al (1987) Mol. Immunol. 24:133-141). Antibodies of the IgE class have been identified that are responsible for hypersensitivity to various beta-lactam antibiotics (Gunez et al (2012) J. Investig. Allergol. Clin. Immunol. 22:41-47). IgE antibodies have also been identified that specifically react against latex (Galindo et al (2011) J. Investig. Allergol. Clin. Immunol. 21:459-465).

[0043] The term "antimicrobial" encompasses, but is not limited to, antiseptics and antibiotics.

Detecting antibodies and other molecules that can provoke adverse events

[0044] Antibodies in blood or in other biological fluids can be detected, for example, by way of reagents in a test strip. The reagents can be covalently or non-covalently attached to the surface of a test strip, the reagents can be adsorbed to a test strip, the

reagents can be absorbed to a test strip, the reagents can be covalently or non-covalently bound to interior of test strip, such as porous interior or fibrous interior, or any combination of the above. Reagents, test strips, substrates, for immune assays, including color reactions, and the like, are provided, for example, from US 7,544,324 issued to Tung et al, US 7,438,852 issued to Tung et al, US 7,989,217 issued to Yee et al, 7,910,381 of Ford et al, each of which is individually incorporated herein by reference, each in its entirety. The present disclosure encompasses detection of antibodies, such as IgG, IgA, IgM, IgD, or IgE, detecting B cells that express IgE or other classes of antibodies, by way of test strip technology. Several antibody classes can be simultaneously expressed in the body, and that recognize the same antigen. Accordingly, the present disclosure provides a test strip that can detect antibodies two or more of the classes IgG, IgA, IgM, IgA, IgD, or IgE. In one embodiment, the test strip detects two different classes, and provides two different colors. In another embodiment, the test strip detects two different classes, and provides the same color for both of the respective color reactions, but at different locations in the test strip. In yet another embodiment, the test strip detects a plurality of different antibody classes (or detects a plurality of different specific antibodies that bind to respective different antigens, where all of these specific antibodies are in one particular class). Combinations of the previous embodiments are also provided, e.g., detecting IgG that binds to an antibiotic, and detecting IgE that binds to latex, or detecting an antibody that binds to an antimicrobial and an antibody that binds to a pathogen. Color reaction can be provided by a label that comprises a metal, a colloidal particle such as colloidal gold, a dye particle, or results from a reaction catalyzed by peroxidase or alkaline phosphatase (see US 7,262019 issued to Kovalenko, US 5,200,312 issued to Oprandy, US 5,637,468 issued to Mason, and US 6,503,726 issued to Anne, which are each incorporated herein in their entirety). Where a gold labeled anti-IgE antibody is used, for example, a test sample (e.g., blood) reacts with the gold labeled anti-IgE antibody, forming a complex. The complex travels across a membrane where immobilized allergens capture the complex, resulting in a colored line (see US 7,629,127 issued to Hubscher, which is incorporated herein by reference).

[0045] The following provides a non-limiting example. For detection of anti-antiseptic antibodies, blood can be deposited at a sample receiving area located at a first end of

the test strip. Flow of solvent from the first end of the test strip towards the opposite end of the test strip draws any antibodies towards the test strip, and draws the antibodies over a region of the test strip that contains conjugates of gold-antiseptic. When the antibodies migrate over the area that contains gold-antiseptic, the result is an insoluble complex that forms a visually detectable line. Conjugates of gold-antiseptic that are not trapped as part of this insoluble complex continue to migrate on the test strip, and do not contribute to the visual signal of the line. As an alternative to using a conjugate of gold-antiseptic, what can be used is a conjugate of gold with an antibody that specifically binds to anti-antiseptic antibodies (anti-idiotype antibodies). The above narrative applies to anti-antiseptic antibodies, but also to embodiments where the antigen is an antibiotic, a pharmaceutical, a drug, latex, an adhesive, and the like.

[0046] In a non-limiting embodiment, what is provided is a device that encompasses an immunoassay with all reagents embedded on a test strip that performs without the use of instruments. Total IgE in a biological fluid is bound by anti-human IgE immobilized on test strips in the IgE reactive field of the test strip. Visualization of captured IgE is indicated by colloidal gold labeled anti-human IgE. Excess labeled antibodies are captured by antibodies in the control field. A control line appears in the control field and determines when enough of the biological fluid has been collected. The presence of IgE in the sample is visualized by the appearance of a dark-colored line, e.g., a red line, in the reactive field and the control field. Absence of a line in the control field, regardless of the presence of line in the reactive field, indicates an invalid assay result. The area on the support identifying the reactive field and control field are on the back surface of the support in two colors. A sample with IgE in the normal reference range lacks a line in the reactive field but has a line in the control field. The presence of lines in the reactive and control fields indicates a sample with elevated total IgE levels. The device provides a qualitative/semi-quantitative measure of total IgE in the biological fluid when the intensity of color on the test strip is visually observed. The skilled artisan can divide or classify the different intensities of signal as negative or as positive, and the skilled artisan can prepare a standard operating procedure (SOP) that sets forth these different intensities. What is also provided is the above embodiment, but where it applies to other antibody classes, e.g., IgG, IgA, IgM, or IgD.

[0047] In a non-limiting embodiment, what is provided is a device that comprises a series of capillary beds (elements), for example, made of cellulose. The first element (a sample pad) acts as a sponge and can hold an excessive amount of biological fluid. Then, the fluid migrates to the second element (conjugate pad). The second element is manufactured with a conjugate, a dried format of particles in a soluble matrix that contains reagents that promote the desired chemical reaction between the target molecule (antigen) and its binding partner (antibody) that has been immobilized on the surface of the particle. At the time that the sample fluid dissolves the soluble matrix, it also dissolves the particles and the sample and conjugate mix while flowing through the porous structure. In this way, the analyte binds to the particles while migrating further through the third capillary bed. This material has one or more regions or stripes where a third molecule has been immobilized. By the time the sample-conjugate mix has migrated to these stripes, analyte has been bound on the particle and the third capture molecule binds the complex. When additional fluid passes the stripes, particles accumulate and the stripe-area changes color. In embodiments, there can be two stripes: one (the control) that captures any particle and demonstrates that reaction is in working order, the second contains a specific capture molecule and only captures those particles on which an analyte molecule has been immobilized.

Duration of detection

[0048] In embodiments, what is provided is a device that is capable of detecting an antibody responsible for an allergic reaction, for example, to an antibiotic or antiseptic,
(1) During a blood draw that is dedicated to this detection;

(2) Only during a blood draw that is dedicated to this detection, with no capability during subsequent procedures, e.g., during insertion of a catheter or other medical instrument. This is an exclusionary embodiment;

(3) During a period of time when a catheter or other medical instrument is indwelling in a subject, that is, when a catheter or other medical instrument is operably linked to a subject. This period of time can be, e.g., at least ten minutes, at least one hour, at least one day, at least one week, at least one month, and the like;

(4) Only during a period of time when a catheter or other medical instrument is indwelling in a subject, but not capable of detecting the antibody during a blood draw

that is solely dedicated to the detection of the antibody. This is an exclusionary embodiment.

Antibodies and other reagents

[0049] "Specifically" or "selectively" binds, when referring to a ligand/receptor, nucleic acid/complementary nucleic acid, antibody/antigen, or other binding pair (e.g., a cytokine to a cytokine receptor) indicates a binding reaction which is determinative of the presence of the protein in a heterogeneous population of proteins and other biologics. Thus, under designated conditions, a specified ligand binds to a particular receptor and does not bind in a significant amount to other proteins present in the sample. Specific binding can also mean, e.g., that the binding compound, nucleic acid ligand, antibody, or binding composition derived from the antigen-binding site of an antibody, of the contemplated method binds to its target with an affinity that is often at least 25% greater, more often at least 50% greater, most often at least 100% (2-fold) greater, conventionally at least ten times greater, more normally at least 20-times greater, more typically at least 100-times greater, and most typically at least 1000-fold than the affinity with any other binding compound (see, e.g., US 2012/0121643 of Dubensky, which is incorporated by reference).

[0050] In a typical embodiment an antibody will have an affinity that is greater than about 10^9 liters/mol, as determined, e.g., by Scatchard analysis (Munsen, et al. (1980) Analyt. Biochem. 107:220-239). It is recognized by the skilled artisan that some binding compounds can specifically bind to more than one target, e.g., an antibody specifically binds to its antigen, binds to lectins by way of the antibody's oligosaccharide, and also binds to an Fc receptor by way of the antibody's Fc region.

[0051] In embodiments, the disclosure provides test strip that is capable of detecting antibodies in blood, where the antibodies specifically bind to a pathogen. Anti-pathogen antibodies have been characterized. Reagents and kits are available for detecting antibodies that specifically bind to viruses (e.g., HIV, HCV,HBV), fungi, and bacteria (see, e.g., Novack et al (2006) J. Clin. Microbiol. 44:2909-2913; Hennessey et al (2009) J. Urban Health. 86:93-105; Thurman et al (2009) Clin. Infect. Dis. 48:1244-1249; Alexander et al (1996) J. Clin. Microbiol. 34:1180-1183).

[0052] "Sample" refers to a sample from a human, animal, placebo, or research sample, e.g., a cell, tissue, organ, fluid, gas, aerosol, slurry, colloid, or coagulated material. The "sample" may be tested in vivo, e.g., without removal from the human or animal, or it may be tested in vitro. The sample may be tested after processing, e.g., by histological methods. "Sample" also refers, e.g., to a cell comprising a fluid or tissue sample or a cell separated from a fluid or tissue sample. "Sample" may also refer to a cell, tissue, organ, or fluid that is freshly taken from a human or animal, or to a cell, tissue, organ, or fluid that is processed or stored.

[0053] A composition that is "labeled" is detectable, either directly or indirectly, by spectroscopic, photochemical, biochemical, immunochemical, isotopic, or chemical methods. For example, useful labels include ^{32}P, ^{33}P, ^{35}S, ^{14}C, ^{3}H, ^{125}I, stable isotopes, epitope tags fluorescent dyes, electron-dense reagents, substrates, or enzymes, e.g., as used in enzyme-linked immunoassays, or fluorettes (see, e.g., Rozinov and Nolan (1998) Chem. Biol. 5:713-728).

Detailed descriptions of the figures

[0054] The invention will now be described with reference to the drawing figures, in which like reference numerals refer to like parts throughout. As illustrated in FIG. 1, the allergy detection system can include an immunochromatographic membrane 2 (PVDF or nitrocellulose material) in strip or cassette format that can detect elevated levels of an allergen by employing a highly sensitive detecting antibody and a carrier-protein conjugated hapten. The antibody is labeled with a signal generator (e.g., colloidal gold), which is placed in the dry state at a predetermined site on the membrane. Using this novel approach the clinician (catheter inserters) would be able to determine if a patient is at risk of developing an allergic reaction before potentially introducing an allergen into a patient's system. The system also provides ease of use to the hospital staff as it does not require any additional step, equipment or time other than what is needed for standard procedures.

[0055] FIGS. 2 and 3 illustrate an independent testing module in accordance with an embodiment of this invention. FIG. 2 illustrates the independent testing module 10 in its inactive state and FIG. 3 illustrates the independent testing module 10 in its active state. The independent testing module 10 includes a housing 12 having a proximal end 14 and a distal end 16. A needle 18 can extend from the distal end 16 of the housing 12.

The needle 18 can include a sharpened distal end 20 and a proximal end 22 that extends into the housing 12. The needle 18 can be generally configured as a hypodermic-type needle with a bore 24 extending through its length. The testing module 10 can also include a viewing window 26, through which test strip 28 can be observed. The test strip 28 is disposed within the housing 12 behind the window 26, such that the operator can view any changes in the strip 28 during use. The testing module 10 can also include a slide 30 and a vacuum button 32 (as illustrated in FIGS. 4-6). In the inactive state illustrated in FIG. 2, the slide 30 is positioned toward the distal end of the testing module 10. When the needle 18 is inserted into the patient and testing is required the slide 30 can be moved from its distal, forward position to a proximal position. Slot 34, positioned on a side 36 of housing 12 in FIGS. 2 and 3, is configured to lock the slide 30 into place after it has been activated into the proximal position.

[0056] The button can comprise an elastic material, for example, silicone, latex, or polyurethane. In one non-limiting embodiment, button is thinner at the peak of the button's dome, and is thicker at the base of the dome.

[0057] FIGS. 4 and 5 illustrate a sectional view of the independent testing module 10 illustrated in FIGS. 2 and 3. FIG. 4 is a sectional view of the independent testing module 10 in the inactive position, as illustrated in FIG. 2, and FIG. 5 is a sectional view of the independent testing module 10 in the active position, as illustrated in FIG. 3. The housing 12 can define an inner space 38 near the proximal end 14 of the testing module 10. The test strip 28 can be disposed in this inner space 38. In addition, an absorbent pad 40 can be integrated into the bottom of the test strip 28 in this inner space 38. The test strip 28 can include a proximal end 42 and a distal end 44. Cap 46 is positioned on top of the junction between the proximal end of the needle 22 and the distal end 44 of the test strip 28.

[0058] The following concerns non-limiting embodiments of cap (46). The cap holds or positions the test strip. The cap holds or positions the proximal end of the needle. Also, the cap creates or defines small vacuum pathways from the vacuum button to the proximal end of the needle. In a preferred embodiment, the cap (46), is not removable.

[0059] In a non-limiting embodiment of the present disclosure, the absorbent pad is an integrated part of the test strip. In another non-limiting embodiment, the absorbent pad

is separate from, and does not occupy the same space as, the test strip. The absorbent pad increases the total volume of sample that enters the test strip. The absorbent pad can block the migration of blood cells, and thereby provide a clean field for development and detection (by clinician's eyes) of the color reaction. In addition, or alternatively, the absorbent pad can draw the biological fluid by way of capillary attraction, resulting in wetting of a broad area of the test strip. In another embodiment, the device comprises only a test strip and does not contain any absorbent pad. In one embodiment that does not contain an absorbent pad, the test strip does not disperse fluid by way of capillary attraction, and the biological fluid is sufficiently dispersed without capillary attraction. In another embodiment, the test strip is sufficiently thick (or thin but sufficiently opaque) that it blocks passage of red blood cells to the viewable area where the color reaction takes place. In yet another embodiment, the test strip has capillary attraction and is also sufficiently thick (or thin but sufficiently opaque) to block passage of red blood cells, and to prevent the red blood cells from residing in the viewable area where the color reaction takes place). Absorbent pad can comprise cellulose, polyvinylidene fluoride (PVDF), nitrocellulose, and the like. Filter material suitable as a matrix for test strips, and for serving as a reaction area for color reagents, and optionally for blocking red blood cells, and optionally for serving as a capillary attractant for attracting and dispersing a biological fluid, are available (EMD Millipore, Darmstadt, Germany; Millipore, Billerica, MA; Membrane Solutions, Plano, TX). US 4,855,240 of Rosenstein, US 4,703,017 of Campbell, and US 4,376,110 of David et al, disclose absorbent materials, capillary materials, test strips, labels, and immunoassays, are incorporated herein by reference in their entirety.

[0060] FIGS. 4 and 5 also illustrate a vacuum button 32 of the independent testing module 10. In the inactivated position illustrated in FIG. 4, the vacuum button 32 is depressed by slide 30. This keeps the vacuum button 32 depressed until the needle 18 is inserted and ready to extract blood. As illustrated in FIG. 5, once the device is in position, the slide 30 is retracted to the active position, releasing vacuum button 32, thus creating a vacuum and allowing blood to flow into the bore 24 of the needle 18. Locking the slide 30 in the active position prevents depression of the vacuum button 32, when the needle 18 is inserted into a vein of the patient, in turn preventing air from potentially being pushed into the access point or blood being squirted from the device

after it has been used. The blood aspirated into the testing module 10 is absorbed from the bottom end of the testing strip 28. The absorbent pad 40 can absorb the plasma sample after the completion of the signal detection reaction. The absorbent pad 40 can also include a porous backing and an absorbent dispersed, adsorbed, or coated into the pores of the porous backing. A color signal can appear within approximately 10 minutes within the viewing window 26, but could take less time or more time depending on the detecting antibodies contained in the test strip.

[0061] FIG. 6 illustrates an exploded view of the independent testing module 10 as shown in FIGS. 2-5. As shown in FIG. 6, the testing module includes the housing 12 and a needle 18 coupled to a distal end 16 of the housing 12. The housing 12 also defines the inner space 38 near the proximal end 14 of the testing module 10. The test strip 28 can be disposed in this inner space 38. In addition, an absorbent pad 40 can be integrated into the test strip 28 in this inner space 38. The test strip 28 can include a proximal end 42 and a distal end 44. Cap 46 is positioned on top of the junction between the proximal end of the needle 22 and the distal end 44 of the absorbent pad 40. FIG. 6 also illustrates the slide 30 and the vacuum button 32 which work together to release the vacuum for the independent testing module such that it can aspirate the blood sample. The slide 30 and vacuum button 32 also prevent the vacuum button from being re-depressed to prevent pushing any air into the entry site or allowing any blood to spurt out after use. The vacuum button 32 sits within an opening 48 defined by the housing 12. The slide 30 can lock into position via the slot 34, also illustrated in FIGS. 2 and 3. As illustrated, tab 31 interacts with a notch 31' in the architecture of slot 34 in order to lock the slide 30 into place. However, any suitable means of locking the slide into place can be used. Locking the slide 30 in the active position prevents depression of the vacuum button 32, when the needle 18 is inserted into a vein of the patient, in turn preventing air from potentially being pushed into the access point or blood being squirted from the device after it has been used. Cap 46 is also shown and is placed over the junction between the testing strip 28 and the proximal end 22 of the needle 18.

[0062] FIG. 7 illustrates a syringe with integrated allergy testing, in accordance with another embodiment of the integrated allergy testing system. As shown in FIG. 7, the syringe 100 includes a housing 102 having a proximal end 104 and a distal end 106. The proximal end 104 of the housing 102 can include flanges 108, 110 which can serve

as finger rests during use of the syringe 100. The housing 102 can include a window 112 positioned such that test strip positioned below the window is visible to a user of the syringe 100. The test strip resides within its own lumen or channel, such that only the distal end of the test strip is exposed to the blood that is aspirated within the syringe housing 102. A needle hub 114 can be positioned at the distal end 106 of the housing 102 and can be configured to couple to a hypodermic-type needle for aspirating blood into a lumen of the syringe 100. A syringe housing cap 116 can be coupled to the distal end 106 to hold the test strip in the housing 102. The syringe 100 can also include a plunger 118 extending into the lumen of the housing 102 for creating negative pressure to aspirate blood into the lumen of the syringe. The plunger 118 can include a thumb rest 119 positioned at a proximal end 117 of the plunger 118.

[0063] In embodiments, where test strip resides in its own lumen or channel, blood or other biological sample enters channel through a hole, slit, passage, or crevice, that is about 5% the distal-to-proximal length of the channel, about 10% the distal-to-proximal length of the channel, about 15%, about 20%, about 25%, about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, about 100%, or longer, than the distal-to-proximal length of the channel. Where the slit or crevice is about 100% the distal-to-proximal length of the channel, the result is that blood entering the syringe, or entering a corresponding structure in the module (10), contacts that entire test strip essentially simultaneously.

[0064] Regarding the orientation of the channel with respect to the hole, slit, passage, or crevice, the hole, slit, or crevice, can start at a point corresponding to the distal-most portion of the channel, and then migrate proximally. Alternatively, the hole, slit, or crevice, can start at a point corresponding to the proximal-most portion of the channel, and then migrate distally. In yet another alternative, the hole, slit, passage, or crevice, can be situated entirely between the distal-most and proximal-most portions of the channel. For example, the hole or passage can be situated near the half-way point of the channel, where blood entering the hole migrates both in the proximal and in the distal directions.

[0065] In embodiments where the hole, slit, passage, or crevice, is about 5% the distal-to-proximal length of the channel, it may be the case that only about 5% of the

test strip is wetted by the blood or other biological sample. Alternatively, in embodiments where the hole, silt, passage, or crevice, is about 5% the distal-to-proximal length of the channel, it may be the case that greater than about 5% of the test strip is wetted by the blood or other biological sample, where this greater than amount results from migration of the biological sample through the test strip. Migration can by via diffusion, capillary force, or by a combination of diffusion and capillary force. The above narrative also applies to configurations where the hole, slit, passage, or crevice, is less than 90%, less than 80%, less than 70%, less than 60%, less than 50%, less than 40%, less than 30%, less than 20%, less than 10%, less than 5%, of the length of the distal-to-proximal length of the channel.

[0066] FIG. 8 illustrates a sectional view of the syringe illustrated in FIG. 7. As shown in FIG. 8, the syringe 100 includes the housing 102 defining a lumen 120, extending therethrough. The plunger 118 is shown extending into the lumen 120 of the housing 102. Additionally, FIG. 8 illustrates test strip 122 positioned within the housing 102 beneath window 112. The syringe housing cap 116 holds the test strip 122 in place beneath the window 112 for observation by the practitioner. Alternately, the test strip 122 can take the form of a cassette or any other appropriate form for positioning within the syringe 100. In addition, an absorbent pad 124 can be integrated into the test strip 122. The absorbent pad 124 can absorb the plasma sample after the completion of the signal detection reaction. The absorbent pad 124 can also include a porous backing and an absorbent dispersed, adsorbed, or coated into the pores of the porous backing. A color signal can appear within approximately 10 minutes within the viewing window 112, but could take less time or more time depending on the antibodies contained in the test strip.

[0067] FIG. 9 illustrates an exploded view of the syringe illustrated in FIGS. 7 and 8. FIG. 9 shows the housing 102 having a window 112 for the test strip 122. The syringe housing cap 116 can be used to hold the test strip in place, such that it does not move during testing. The plunger 118 can be configured to slide within the lumen 120 of the housing 112.

[0068] FIG. 10 illustrates a connector design for the integrated testing system in accordance with an embodiment of the invention. The connector 200, includes a housing 201, having a proximal end 202 and a distal end 204, and can be configured for

placement between a syringe body and a needle for the syringe. The connector 200 can be connected to the syringe body in a variety of different ways such as frictional hold, tabs, or any other suitable coupling. As illustrated in FIG. 10, the connector 200 can be coupled to the syringe via luer threads 206 positioned at the proximal end 202 of the connector 200. The connector 200 can also include a coupling 208 for coupling the connector 200 to a needle. The needle can take the form of a hypodermic-type needle or any other needle suitable for aspirating blood through the connector 200. The connector also includes a window 210 through which test strip (not shown) can be visualized.

[0069] FIG. 11 illustrates a sectional view of the embodiment shown in FIG. 10 and FIG. 12 illustrates an exploded view of the embodiment illustrated in FIGS. 10 and 11. FIGS. 11 and 12 illustrate the test strip 214 disposed within the connector housing 201. As illustrated, the test strip 214 is spirally wound within the connector housing 201. The test strip 214 can be viewed through window 210 in the housing 201. Blood can be aspirated into a lumen 212 defined by housing 201, when testing is required. In addition, an absorbent pad 216 can be positioned beneath the test strip 214. The absorbent pad 216 integrated into the test strip 228 can absorb the plasma sample after the completion of the signal detection reaction. The absorbent pad 216 can also include a porous backing and an absorbent dispersed, adsorbed, or coated into the pores of the porous backing. A color signal can appear within approximately 10 minutes within the viewing window 210, but could take less time or more time depending on the antibodies contained in the blood sample.

[0070] Alternately test strip, for example, an immunochromatographic test strip, can be incorporated into a number of different medical devices. One such example is an test strip incorporated into a "hemo-hopper," such as a blood reservoir in a medical tray or kit. The blood aspirated during access to the vessel would be disposed into the hemo-hopper. The sample could then be absorbed into the test strip. In addition, an absorbent pad can be positioned beneath the test strip. The absorbent pad can absorb the plasma sample after the completion of the signal detection reaction. The absorbent pad can also include a porous backing and an absorbent dispersed, adsorbed, or coated into the pores of the porous backing. A color signal can appear within

approximately 10 minutes, but could take less time or more time depending on the antibodies contained in the blood sample.

[0071] FIG. 13 (A, B) illustrates the end-cap that is a part of the module embodiment, and structures in the vicinity of the cap. The end-cap (346) is in contact with needle (318). The end-cap (346) defines part of cavity (348) where the vacuum button (32) can fit. A non-limiting embodiment of vacuum button (32) is shown in FIGS. 4-6. FIG. 13(A) shows cap without test strip, and FIG. 13 (B) shows cap with test strip.

[0072] While the method and apparatus have been described in terms of what are presently considered to be the most practical and preferred embodiments, it is to be understood that the disclosure need not be limited to the disclosed embodiments. It is intended to cover various modifications and similar arrangements included within the spirit and scope of the claims, the scope of which should be accorded the broadest interpretation so as to encompass all such modifications and similar structures. The present disclosure includes any and all embodiments of the following claims.

[0073] It should also be understood that a variety of changes may be made without departing from the essence of the invention. Such changes are also implicitly included in the description. They still fall within the scope of this invention. It should be understood that this disclosure is intended to yield a patent covering numerous aspects of the invention both independently and as an overall system and in both method and apparatus modes.

[0074] Further, each of the various elements of the invention and claims may also be achieved in a variety of manners. This disclosure should be understood to encompass each such variation, be it a variation of an embodiment of any apparatus embodiment, a method or process embodiment, or even merely a variation of any element of these.

[0075] Particularly, it should be understood that as the disclosure relates to elements of the invention, the words for each element may be expressed by equivalent apparatus terms or method terms -- even if only the function or result is the same.

[0076] Such equivalent, broader, or even more generic terms should be considered to be encompassed in the description of each element or action. Such terms can be

substituted where desired to make explicit the implicitly broad coverage to which this invention is entitled.

[0077] It should be understood that all actions may be expressed as a means for taking that action or as an element which causes that action.

[0078] Similarly, each physical element disclosed should be understood to encompass a disclosure of the action which that physical element facilitates.

[0079] Any patents, publications, or other references mentioned in this application for patent are hereby incorporated by reference.

[0080] Finally, all references listed in the Information Disclosure Statement or other information statement filed with the application are hereby appended and hereby incorporated by reference; however, as to each of the above, to the extent that such information or statements incorporated by reference might be considered inconsistent with the patenting of this/these invention(s), such statements are expressly not to be considered as made by the applicant.

[0081] In this regard it should be understood that for practical reasons and so as to avoid adding potentially hundreds of claims, the applicant has presented claims with initial dependencies only.

[0082] Support should be understood to exist to the degree required under new matter laws -- including but not limited to United States Patent Law 35 USC §132 or other such laws -- to permit the addition of any of the various dependencies or other elements presented under one independent claim or concept as dependencies or elements under any other independent claim or concept.

[0083] To the extent that insubstantial substitutes are made, to the extent that the applicant did not in fact draft any claim so as to literally encompass any particular embodiment, and to the extent otherwise applicable, the applicant should not be understood to have in any way intended to or actually relinquished such coverage as the applicant simply may not have been able to anticipate all eventualities; one skilled in the art, should not be reasonably expected to have drafted a claim that would have literally encompassed such alternative embodiments.

[0084] Further, the use of the transitional phrase "comprising" is used to maintain the "open-end" claims herein, according to traditional claim interpretation. Thus, unless the context requires otherwise, it should be understood that the term "compromise" or variations such as "comprises" or "comprising", are intended to imply the inclusion of a stated element or step or group of elements or steps but not the exclusion of any other element or step or group of elements or steps.

[0085] Such terms should be interpreted in their most expansive forms so as to afford the applicant the broadest coverage legally permissible.

[0086] The many features and advantages of the invention are apparent from the detailed specification, and thus, it is intended by the appended claims to cover all such features and advantages of the invention which fall within the true spirit and scope of the invention. Further, because numerous modifications and variations will readily occur to those skilled in the art, it is not desired to limit the invention to the exact construction and operation illustrated and described, and accordingly, all suitable modifications and equivalents may be resorted to falling within the scope of the invention.

What is claimed is:

Claim 1. A device for testing the presence or absence of a substance in blood, comprising:

a coupler or hub that is capable of coupling with a needle, wherein the needle is for withdrawing blood from a subject and for introducing the withdrawn blood into the device;

a first chamber for receiving the withdrawn blood;

a second chamber configured for holding a test strip;

a test strip that is held within the second chamber;

a wall or panel that separates the first chamber from the second chamber;

at least one aperture in the wall or panel configuring for allowing blood to pass from the first chamber to the second chamber;

wherein the second chamber comprises a window for viewing the test strip,

wherein the test strip is capable of producing a visible signal that indicates the presence or absence of the substance in the withdrawn blood; and,

wherein the window is configured to allow visual detection of the visible signal.

Claim 2. The device of claim 1, that comprises a syringe and wherein the first chamber is defined by the housing or barrel of the syringe.

Claim 3. The device of claim 1 that is capable of being coupled to a syringe and to a needle, wherein the device has a hub that is capable of coupling to the hub of the syringe, and wherein the device has a coupler that is capable of coupling to a hub of a needle.

Claim 4. The device of claim 1, wherein the substance is an antibody that specifically binds to an antimicrobial agent.

Claim 5. The device of claim 1, wherein the substance is an antibody of the class IgG, IgA, IgM, or IgE.

Claim 6. The device of claim 1, wherein the second chamber comprises a flexible dome, and

wherein the flexible dome is capable of flexing radially outward;

wherein in use the flexible dome flexes radially outwards and creates a partial vacuum that is capable of drawing blood out of the first chamber and into the second chamber;

wherein a sliding latch is operably linked with the flexible dome;

wherein in use the sliding latch is capable of being slid over the dome to compress the flexible dome radially downwards and increase the pressure within the second chamber; and

wherein in use the sliding latch is capable of being slid away from the dome to release the dome and allow the dome to flex radially outwards thereby creating a partial vacuum in the second chamber.

Claim 7. The device of claim 1, further comprising an end-cap, wherein the end-cap is configured for contacting and stabilizing the test strip, and configured for contacting and stabilizing the proximal portion of a needle that is coupled to said device.

Claim 8. The device of claim 1, further comprising a needle, wherein the needle is reversibly coupled to the coupler.

Claim 9. The device of claim 1 that does not comprise a needle.

Claim 10. The device of claim 1, wherein the test strip is an immunochromatographic test strip.

Claim 11. A device for testing the presence or absence of an antibody in blood, wherein the antibody specifically binds to an antimicrobial agent, comprising:

a coupler that is capable of coupling with a hub of a needle, wherein the needle is for withdrawing blood from a subject and for introducing the withdrawn blood into the device;

a first chamber for receiving the withdrawn blood;

a second chamber configured for holding a test strip;

a test strip that is held within the second chamber;

a wall or panel that separates the first chamber from the second chamber;

at least one aperture in the wall or panel configuring for allowing blood to pass from the first chamber to the second chamber;

wherein the second chamber comprises a window for viewing the test strip;

wherein the test strip is capable of producing a visible signal that indicates the presence or absence, in the withdrawn blood, of the antibody that specifically binds to the antimicrobial agent; and,

wherein the window is configured to allow visual detection of the visible signal.

Claim 12. A process for allergy detection during catheterization, comprising:

the step of drawing blood from a subject into the first chamber of a device that comprises:

(a) a coupler or hub that is capable of coupling with a needle, wherein the needle is for withdrawing blood from a subject and for introducing the withdrawn blood into the device;

(b) a first chamber for receiving the withdrawn blood;

(c) a second chamber configured for holding a test strip;

(d) a test strip that is held within the second chamber;

(e) a wall or panel that separates the first chamber from the second chamber;

(f) at least one aperture in the wall or panel configuring for allowing blood to pass from the first chamber to the second chamber;

(g) wherein the second chamber comprises a window for viewing the test strip,

(h) wherein the test strip is capable of producing a visible signal that indicates the presence or absence of the substance in the withdrawn blood; and,

(i) wherein the window is configured to allow visual detection of the visible signal;

the step of allowing at least some of the drawn blood to enter the second chamber of the device;

wherein a needle is coupled to the device; and,

wherein in use, at least some of the withdrawn blood enters the needle and then enters the first chamber, then enters the second chamber, and then contacts the test strip.

Claim 13. The process of claim 12, further comprising a reaction that is mediated by the test strip, wherein the reaction produces a visual signal that indicates presence or absence of a substance that mediates an allergy.

Claim 14. The process of claim 12, wherein the drawing blood into the first chamber is urged by one or more of: (a) Blood pressure of the subject; (b) Vacuum produced by a syringe plunger of the device; (c) Vacuum produced by a flexible dome of the device; and (d) Capillary action of the test strip of the device.

Claim 15. The process of claim 12, wherein the test strip is configured for detecting an antibody that specifically binds an antimicrobial agent;

wherein in use the test strip provides a visual signal that the blood does not contain detectable antibodies that specifically bind to the specific antimicrobial agent;

followed by the step of inserting a catheter into the subject, wherein the catheter is impregnated or coated with the antimicrobial agent.

Claim 16. The process of claim 12, wherein the test strip is configured for detecting an antibody that specifically binds an antimicrobial agent;

wherein in use the test strip provides a visual signal that the blood does contain detectable antibodies that specifically bind to the specific antimicrobial agent;

followed by the step of making a decision on whether or not to insert a catheter that is impregnated or coated with the antimicrobial agent; and,

wherein the decision is to refrain from inserting the catheter in the subject,

followed by the step of inserting a catheter into the subject, wherein the catheter is not impregnated or coated with the antimicrobial agent.

Claim 17. A system comprising, in combination, a medical instrument that is capable of holding blood, and a medical device that comprises:

(a) a coupler or hub that is capable of coupling with a needle, wherein the needle is for withdrawing blood from a subject and for introducing the withdrawn blood into the device;

(b) a first chamber for receiving the withdrawn blood;

(c) a second chamber configured for holding a test strip;

(d) a test strip that is held within the second chamber;

(e) a wall or panel that separates the first chamber from the second chamber;

(f) at least one aperture in the wall or panel configuring for allowing blood to pass from the first chamber to the second chamber;

(g) wherein the second chamber comprises a window for viewing the test strip,

(h) wherein the test strip is capable of producing a visible signal that indicates the presence or absence of the substance in the withdrawn blood; and,

(i) wherein the window is configured to allow visual detection of the visible signal.

Claim 18. The system of claim 17, wherein the combination is a reversible combination or a permanent combination.

Claim 19. The system of claim 17, wherein the combination is a reversible combination, wherein the device and the medical instrument are held in combination by one or more of a clip, snap, lock, or tab.

Claim 20. The system of claim 17, wherein the medical instrument comprises one or more of a syringe, trocar, catheter, introducer, sheath, hub, pump, or valve.

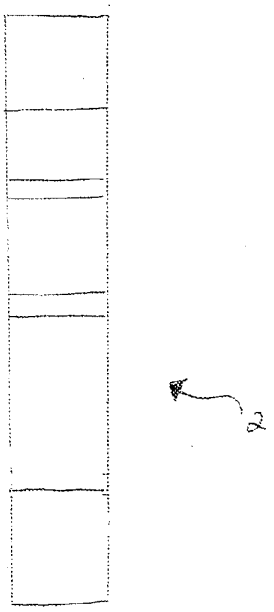


FIG. 1

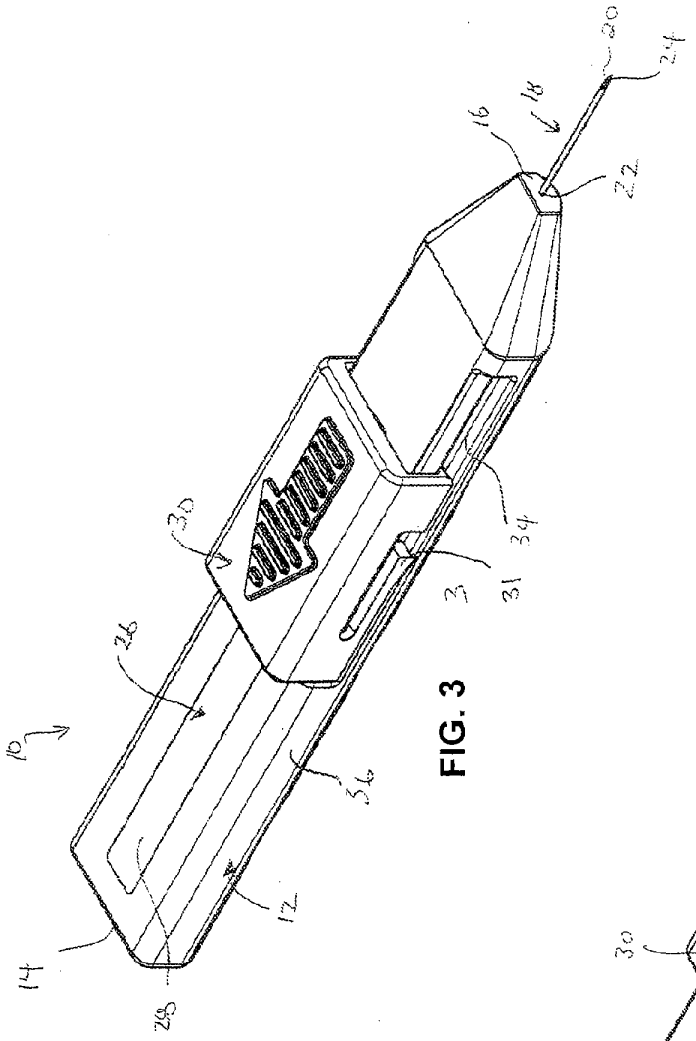

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FIG. 3

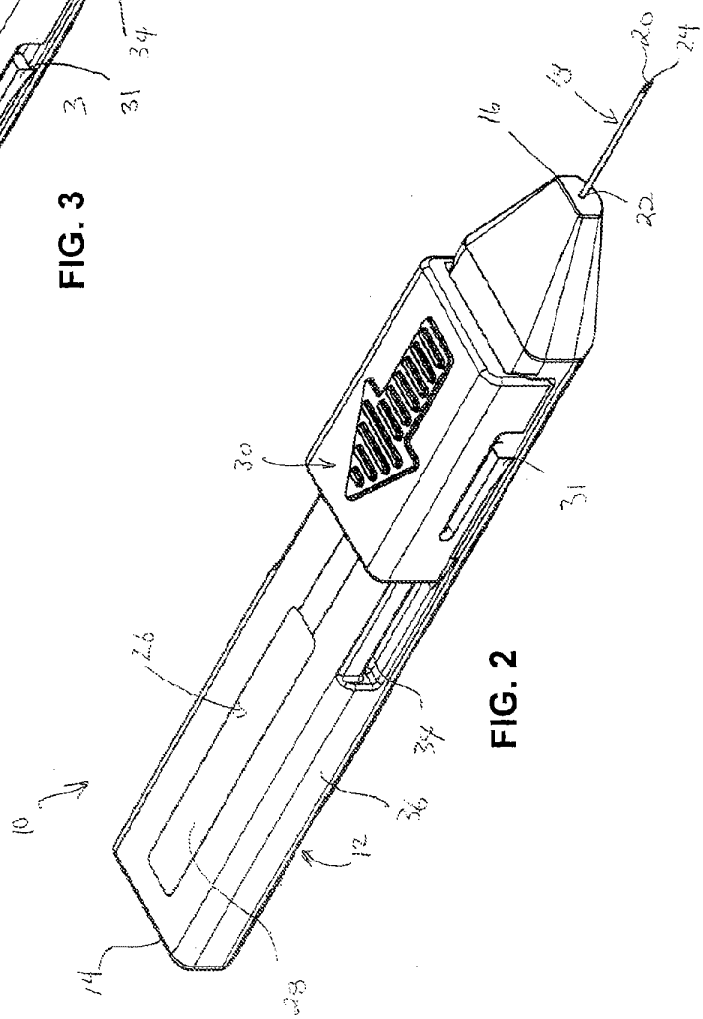

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FIG. 2

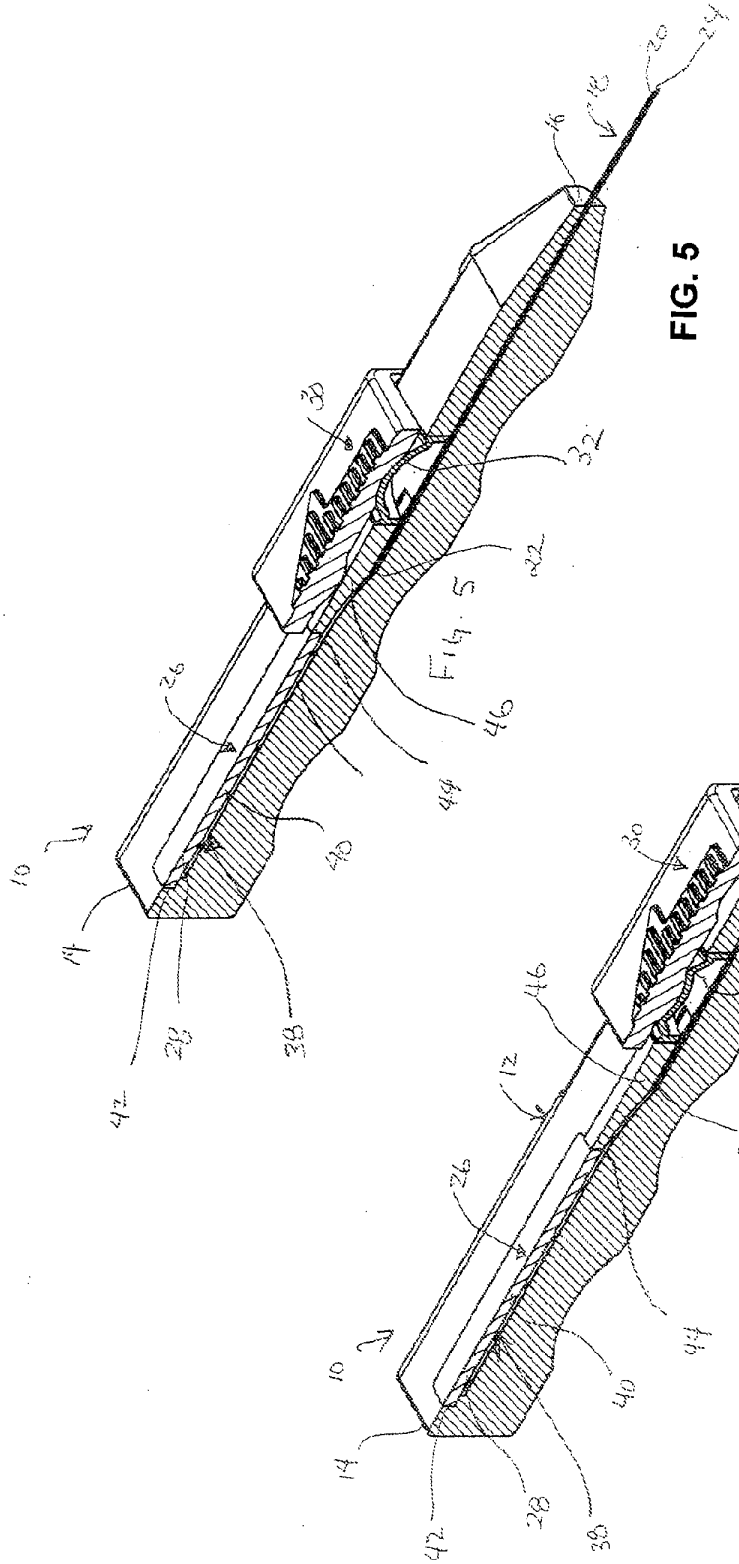

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FIG. 5

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FIG. 4

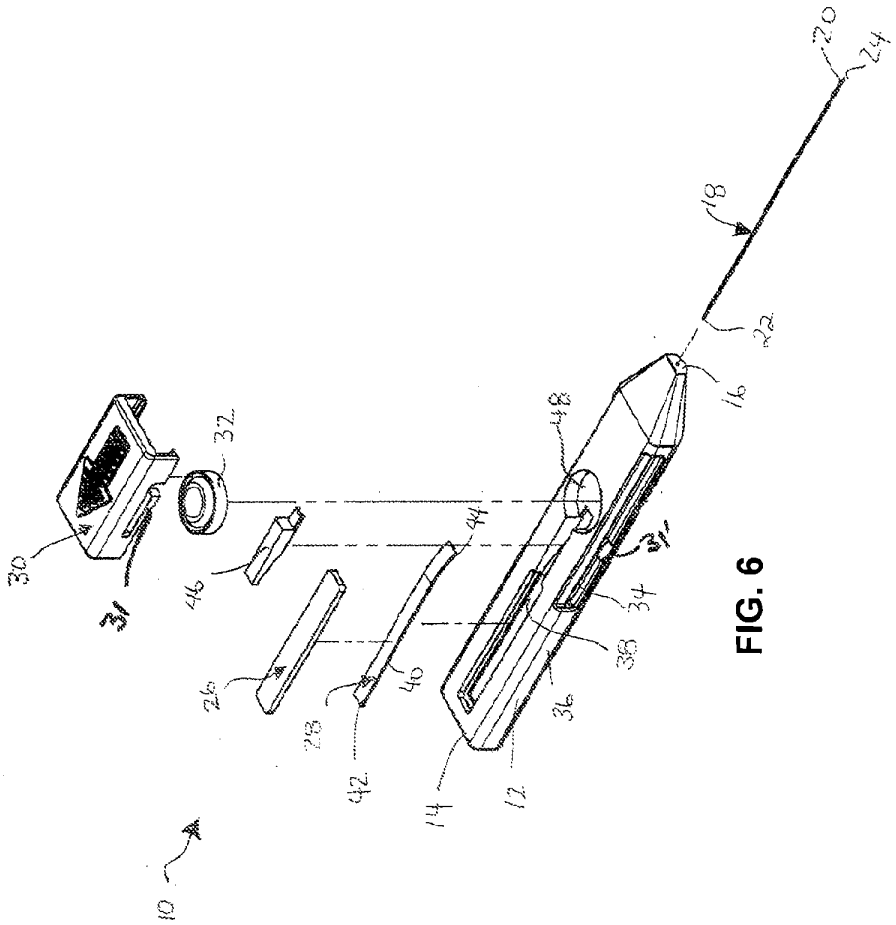


FIG. 6

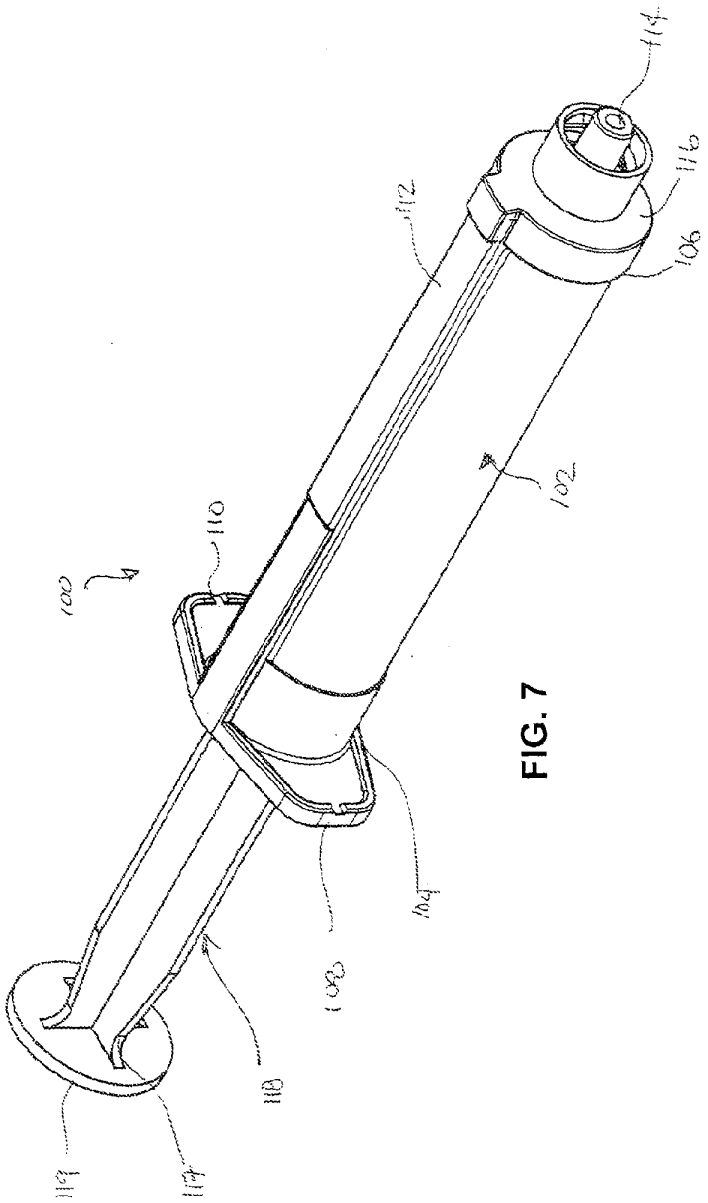


FIG. 7

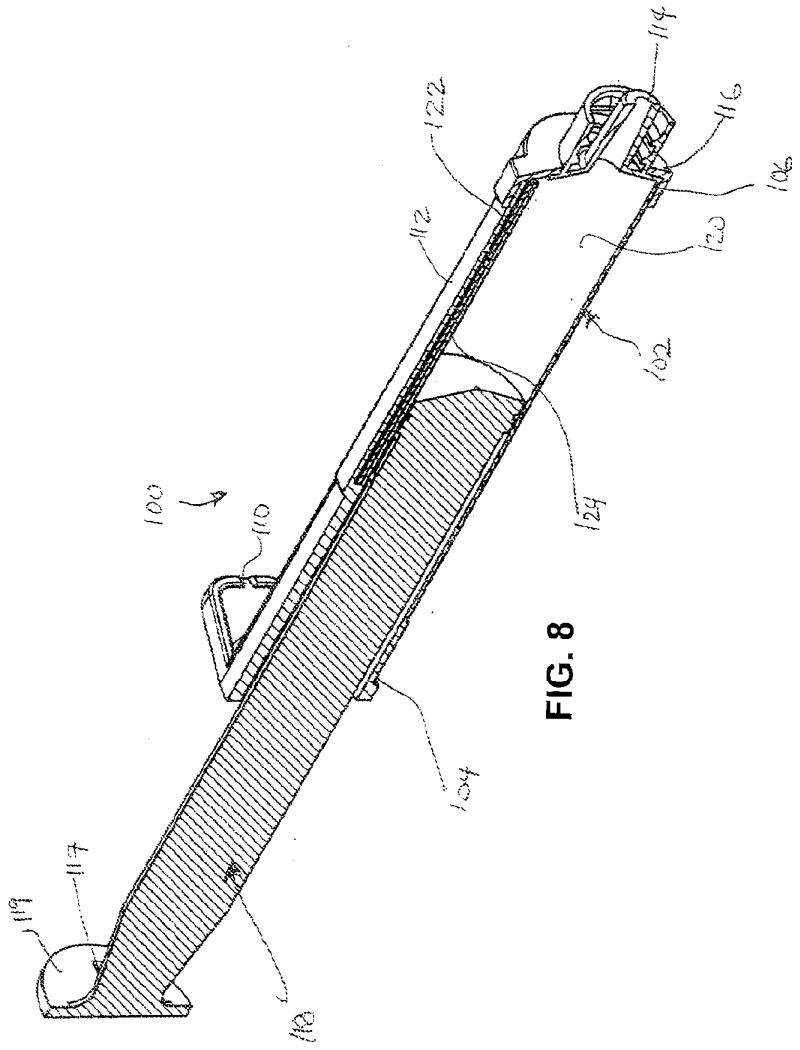


FIG. 8

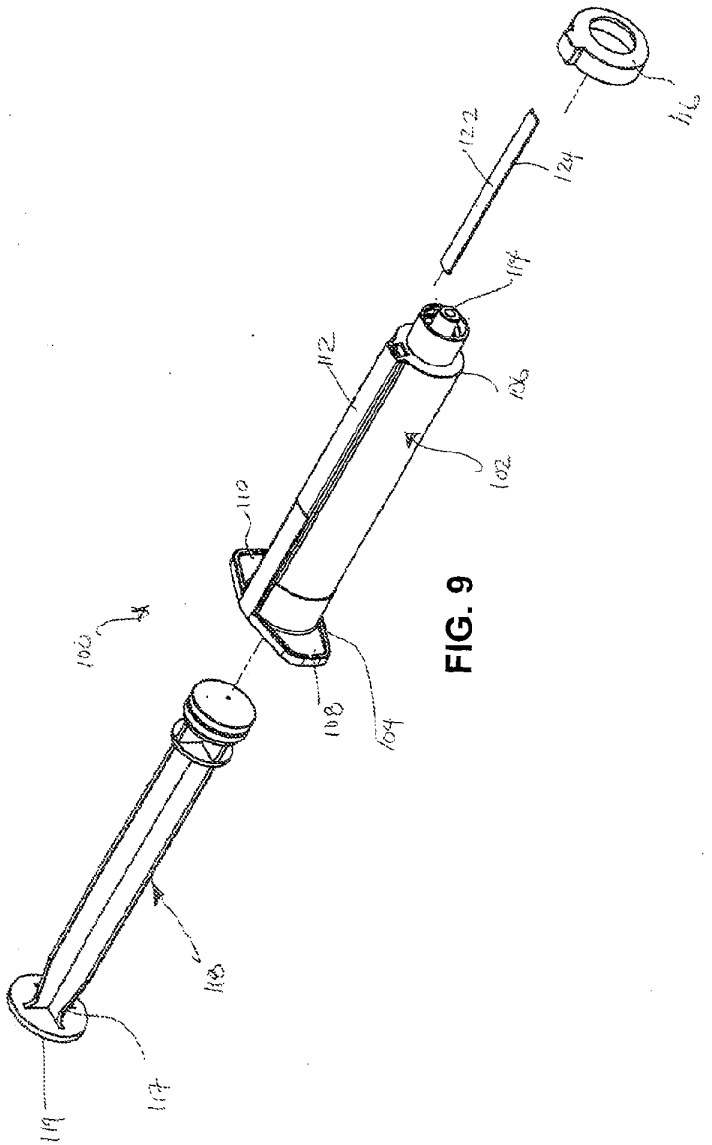


FIG. 9

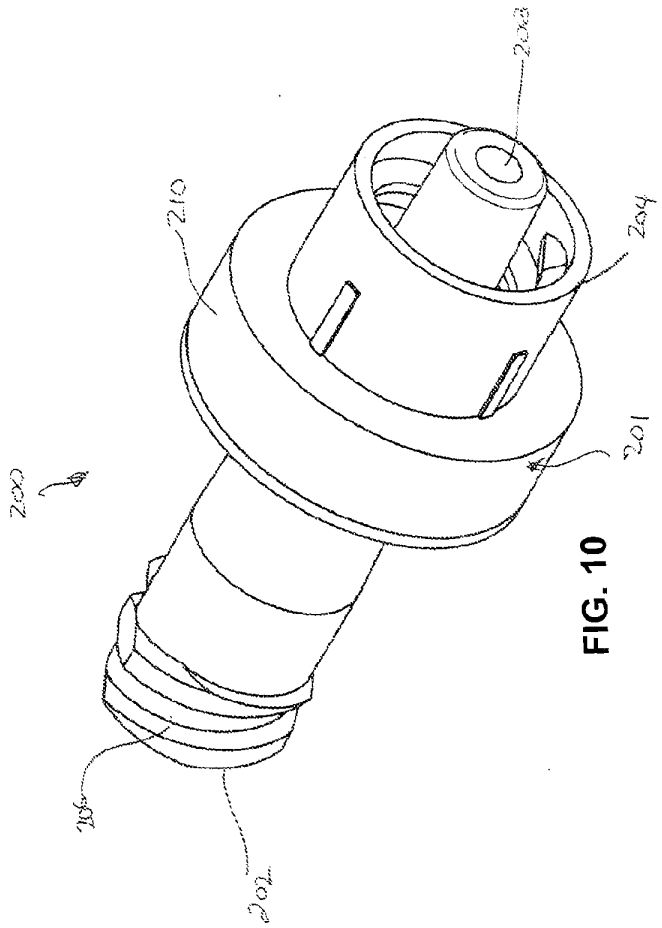


FIG. 10

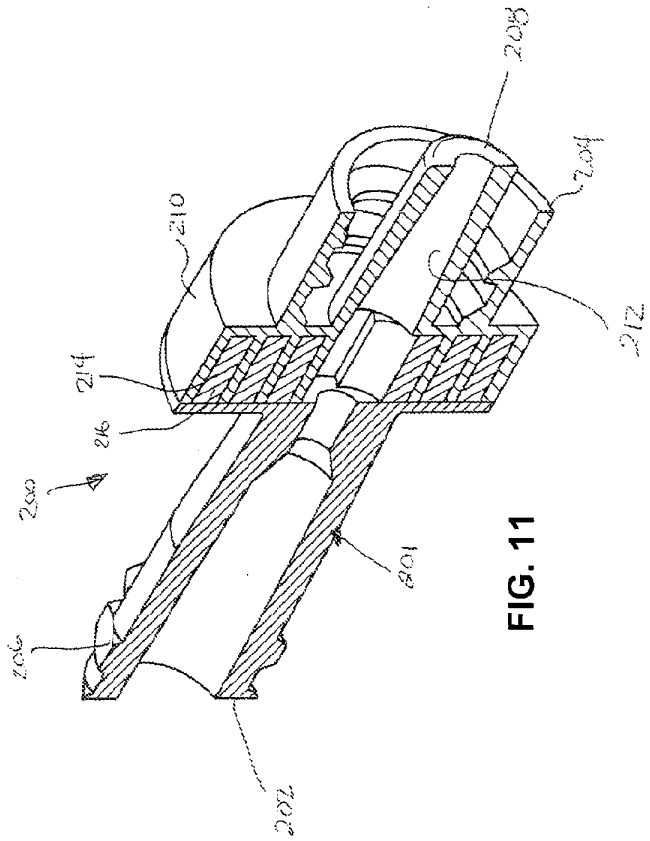


FIG. 11

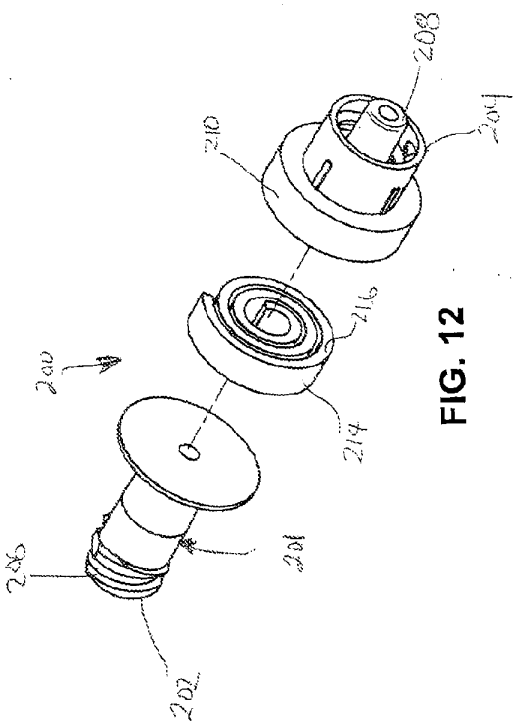
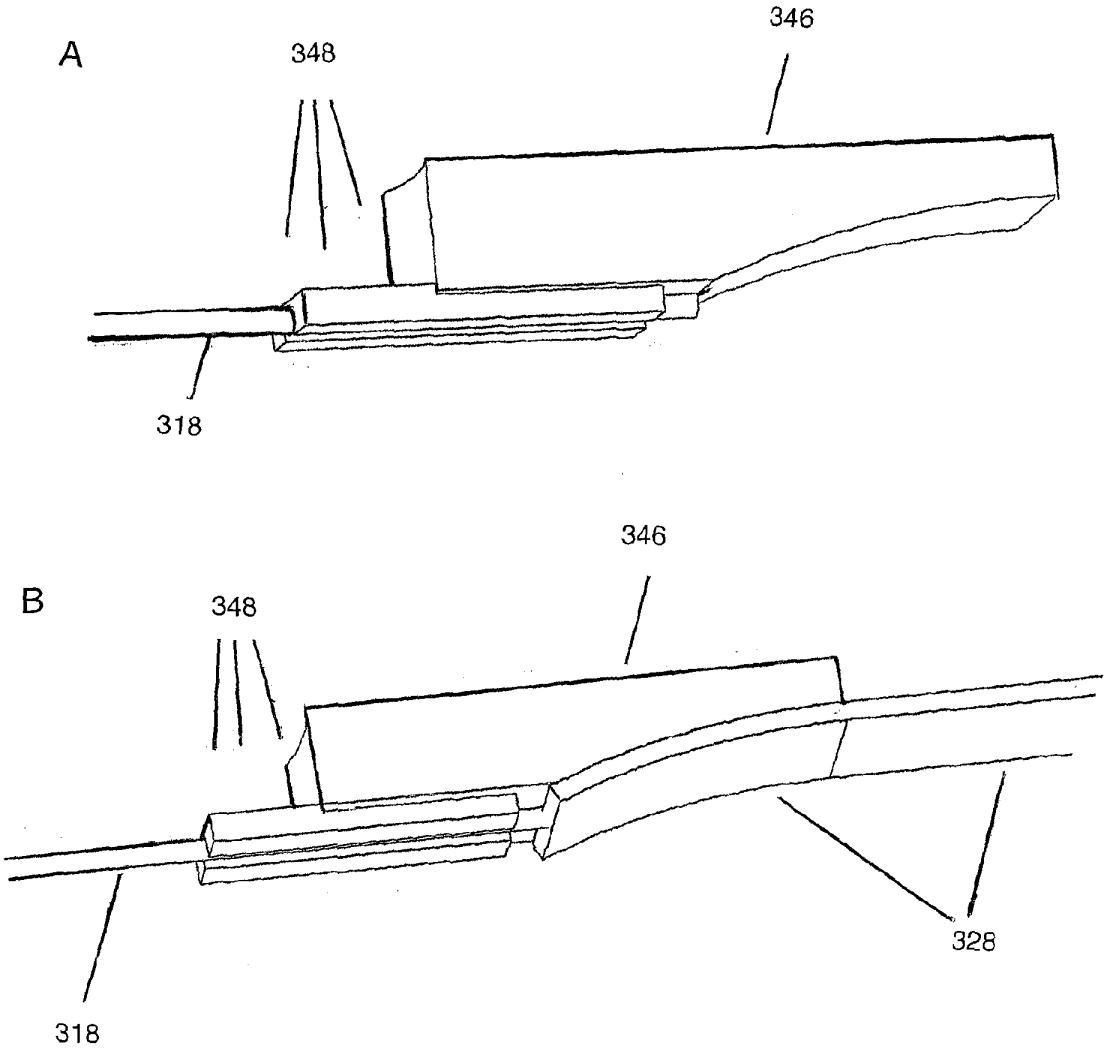


FIG. 12

Fig. 13



INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2012/067095

A. CLASSIFICATION OF SUBJECT MATTER

G01N 33/50(2006.01)i, G01N 33/52(2006.01)i, G01N 33/53(2006.01)i

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

G01N 33/50; C25C 3/02; A61B 5/151; G01N 17/00; B32B 38/04; A61B 5/00

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Korean utility models and applications for utility models
Japanese utility models and applications for utility models

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

eKOMPASS(KIPO internal) & keywords: test strip, coupling, needle, chamber, window

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 2009-0112125 A1 (TAMIR, NILI) 30 April 2009 See paragraph [0100]; claims 1 and 5-6; figure 5.	1-20
A	US 2003-0109777 A1 (KLOEPFER, HANS G. et al.) 12 June 2003 See paragraph [0107]; claim 1; figures 1 and 5.	1-20
A	US 2003-0150745 A1 (TEODORCZYK, MARIA et al.) 14 August 2003 See claims 1, 8 and 13; figure 3.	1-20
A	US 2007-0161926 A1 (IMAMURA, TAKESHI et al.) 12 July 2007 See paragraph [0032]; claim 1; figure 2A.	1-20
A	US 2011-0046453 (KEIL, MICHAEL) 24 February 2011 See paragraphs [0017] and [0019]; claims 14-16; figures 1 and 7.	1-20

☐ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

* Special categories of cited documents:
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Date of the actual completion of the international search	Date of mailing of the international search report
28 FEBRUARY 2013 (28.02.2013)	**04 MARCH 2013 (04.03.2013)**
Name and mailing address of the ISA/KR Facsimile No. 82-42-472-7140	Authorized officer LEE, Dong Yun Telephone No. 82-42-481-8734

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Information on patent family members

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(54) Title: FLUID CONTROL DEVICES AND METHODS OF USING THE SAME

(57) Abstract: A fluid control device (200) includes an inlet (212) configured to be placed in fluid communication with a bodily fluid source and an outlet (216) configured to be placed in fluid communication with a fluid collection device, which can produce a negative pressure differential between the outlet and the inlet. A sequestration portion (214) is in fluid communication with the inlet and includes a first flow controller (222) configured to transition from a first state to a second state to place the sequestration portion in fluid communication with the outlet when the negative pressure differential has a first magnitude. A sampling portion (224) is in fluid communication with an outlet and includes a second flow controller (221) configured to transition from a first state to a second state to place the sampling portion in fluid communication with the inlet when the negative pressure differential has a second magnitude greater than the first magnitude.

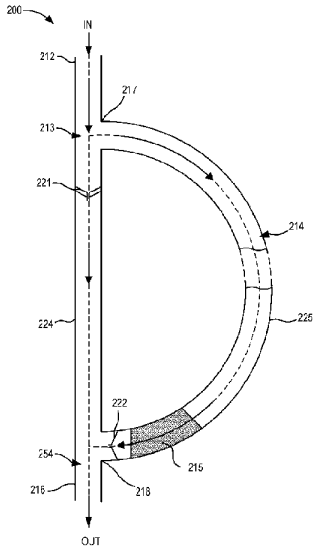


FIG. 2

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[Continued on next page]

Declarations under Rule 4.17:

— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*

Published:

— *with international search report (Art. 21(3))*

FLUID CONTROL DEVICES AND METHODS OF USING THE SAME

Cross-Reference to Related Applications

[0001] This application claims priority to and the benefit of U.S. Provisional Patent Application Serial No. 62/678,637 entitled, "Fluid Control Devices and Methods of Using the Same," filed May 31, 2018, the disclosure of which is incorporated herein by reference in its entirety.

Background

[0002] Embodiments described herein relate generally to the procurement of bodily fluid samples, and more particularly to fluid diversion, sequestration, and/or isolation devices and methods for procuring bodily fluid samples with reduced contaminants such as dermally residing microbes and/or other contaminants exterior to the bodily fluid source.

[0003] Health care practitioners routinely perform various types of microbial as well as other broad diagnostic tests on patients using parenterally obtained bodily fluids. As advanced diagnostic technologies evolve and improve, the speed, accuracy (both sensitivity and specificity), and value of information that can be provided to clinicians continues to improve. Maintaining the integrity of the bodily fluid sample during and/or after collection also ensures that analytical diagnostic results are representative of the in vivo conditions of a patient. Examples of diagnostic technologies that are reliant on high quality, non-contaminated, and/or unadulterated bodily fluid samples include but are not limited to microbial detection, molecular diagnostics, genetic sequencing (e.g., deoxyribonucleic acid (DNA), ribonucleic acid (RNA), next-generation sequencing (NGS), etc.), biomarker identification, and/or the like.

[0004] Inaccurate results from such testing can be due to the presence biological matter including cells external to the intended sample source and/or other external contaminants that inadvertently are included in the bodily fluid sample being analyzed. In short, when the purity of the bodily fluid sample is compromised during the specimen procurement process, resultant analytical test results may be inaccurate, distorted, adulterated, falsely positive, falsely negative, and/or otherwise not representative of the actual condition of the patient. In turn, these results can lead to faulty, inaccurate, confused, unsure, low-confidence, and/or otherwise undesired clinical decision making.

[0005] In some instances, devices and/or systems can be used to reduce the likelihood of contamination, adulteration, and/or the like of bodily fluid samples for testing. For example, some known devices can be configured to collect, divert, separate, and/or sequester (e.g., isolate) an initial volume of bodily fluid that may be more likely to contain contaminants such as dermally residing microbes or the like. Some such devices, however, can be cumbersome, non-intuitive, perceived as difficult to use, inappropriate or unusable for a target patient population, etc. In addition, some such devices can require training, user observation, intervention by more than one user, and/or can otherwise present challenges that can lead to limited efficacy. In some instances, these and/or other challenges can complicate the collection of consistently high quality samples that are non-contaminated, sterile, unadulterated, etc., which in turn, can influence the validity of test result outcomes.

[0006] As such, a need exists for fluid control and/or diversion devices and methods for procuring bodily fluid samples with reduced contaminants such as dermally residing microbes and/or other contaminants exterior to the bodily fluid source that result in consistent bodily fluid collection (e.g., from a general patient population and/or a challenging patient population). In addition, a need exists for devices and methods that can include, for example, bodily fluid collection with the assistance of various sources of external energy and/or negative pressure.

Summary

[0007] Devices and methods for procuring bodily fluid samples with reduced contaminants such as dermally residing microbes and/or other contaminants exterior to the bodily fluid source are described herein. In some embodiments, a fluid control device includes an inlet and an outlet. The inlet is configured to be placed in fluid communication with a bodily fluid source and the outlet is configured to be placed in fluid communication with a fluid collection device. The coupling of the outlet to the fluid collection device can produce a negative pressure differential within the fluid control device between the outlet and the inlet. The fluid control device has a sequestration portion in fluid communication with the inlet and a sampling portion in fluid communication with the outlet. The sequestration portion includes a first flow controller configured to transition from a first state in which the sequestration portion is sequestered from the outlet to a second state in which the sequestration portion is in fluid communication with the outlet when the negative pressure differential has a first magnitude. The sampling portion includes a second flow controller configured to transition from a first

state in which the sampling portion is sequestered from the inlet to a second state in which the sampling portion is in fluid communication with the inlet when the negative pressure differential has a second magnitude greater than the first magnitude.

Brief Description of the Drawings

[0008] FIG. 1 is a schematic illustration of a fluid control device according to an embodiment.

[0009] FIG. 2 is a schematic illustration of a fluid control device according to an embodiment.

[0010] FIG. 3 is a schematic illustration of a fluid control device according to an embodiment.

[0011] FIG. 4 is a schematic illustration of a fluid control device according to an embodiment.

[0012] FIGS. 5-7 are each a schematic illustration of a flow controller included in a fluid control device according to various embodiments.

[0013] FIG. 8 is a schematic illustration of a fluid control device according to an embodiment.

[0014] FIGS. 9 and 10 are schematic cross-sectional illustrations of the fluid control device illustrated in FIG. 8, taken along the line A-A, and shown in a first state and a second state, respectively.

[0015] FIGS. 11 and 12 are schematic cross-sectional illustrations of a fluid control device in a first state and a second state, respectively, according to an embodiment.

[0016] FIGS. 13 and 14 are schematic cross-sectional illustrations of a fluid control device in a first state and a second state, respectively, according to an embodiment.

[0017] FIGS. 15 and 16 are flowcharts, each of which illustrates a method of using a fluid control device to divert an initial volume of bodily fluid to procure bodily fluid samples with reduced contamination, according to different embodiments.

Detailed Description

[0018] Devices and methods for collecting, diverting, sequestering, isolating, etc. an initial volume of bodily fluid to reduce contamination in subsequently procured bodily fluid samples

are described herein. Any of the fluid control devices described herein can be configured to receive, procure, and/or transfer a flow, bolus, volume, etc., of bodily fluid. A first reservoir, channel, flow path, chamber, and/or portion of the device can receive an initial amount of the bodily fluid flow, which then can be substantially or fully sequestered therein (e.g., contained or retained, circumvented, isolated, segregated, vapor-locked, separated, and/or the like). In some instances, contaminants such as dermally residing microbes or the like can be included and/or entrained in the initial amount of the bodily fluid and likewise are sequestered in or by the first reservoir, flow path, or portion of the device. Once the initial amount is sequestered, any subsequent amount of the bodily fluid flow can be diverted, channeled, directed, and/or otherwise allowed to flow to or through a second portion of the device and/or any additional flow path(s) thereof. Based at least in part on the initial amount being sequestered, subsequent amount(s) of bodily fluid can be substantially free from contaminants that may otherwise produce inaccurate, distorted, adulterated, and/or false results in some diagnostics and/or testing. In some instances, the initial amount of bodily fluid also can be used, for example, in other testing such as those less affected by the presence of contaminants, can be discarded as a waste volume, can be infused back into the patient, and/or can be used for any other suitable clinical application.

[0019] In some embodiments, a feature of the fluid control devices and/or methods described herein is the use of an external negative pressure source (e.g., provided by a fluid collection device or any other suitable means) that can (1) overcome physical patient challenges which can limit and/or prevent a sufficient pressure differential to fully engage the sequestration chamber or sequestration portion of the control device and/or to transition fluid flow to the fluid collection device; (2) result in proper filling of the sequestration chamber with a clinically validated and/or desirable volume of bodily fluid; (3) result in efficient, timely, and/or user-accepted consistency with bodily fluid collection process; and/or (4) provide a means of transitioning fluid flow (e.g., automatically or by manipulation to move any number of physical components of the system or by changing, switching, engaging, and/or otherwise providing desired fluid flow dynamics) to enable sequestration and/or isolation of the initial amount (e.g., pre-sample) and collection of a subsequent sample.

[0020] In some embodiments, a fluid control device includes an inlet and an outlet. The inlet is configured to be placed in fluid communication with a bodily fluid source and the outlet is configured to be placed in fluid communication with a fluid collection device. The coupling of the outlet to the fluid collection device can produce a negative pressure differential within

the fluid control device between the outlet and the inlet. The fluid control device has a sequestration portion in fluid communication with the inlet and a sampling portion in fluid communication with the outlet. The sequestration portion includes a first flow controller configured to transition from a first state in which the sequestration portion is sequestered from the outlet to a second state in which the sequestration portion is in fluid communication with the outlet when the negative pressure differential has a first magnitude. The sampling portion includes a second flow controller configured to transition from a first state in which the sampling portion is sequestered from the inlet to a second state in which the sampling portion is in fluid communication with the inlet when the negative pressure differential has a second magnitude greater than the first magnitude.

[0021] In some embodiments, a fluid control device includes a housing, a first flow controller, and a second flow controller. The housing has an inlet configured to establish fluid communication with a bodily fluid source and an outlet configured to be coupled to a fluid collection device. The housing defines a sequestration flow path that is in fluid communication with the inlet and a sampling flow path that is in fluid communication with the outlet. The first flow controller has a flow state in which the sequestration flow path is in fluid communication with the outlet and a non-flow state in which the sequestration flow path is sequestered from the outlet. The second flow controller has a flow state in which sampling flow path is in fluid communication with the inlet and a non-flow state in which the sampling flow path is sequestered from the inlet. The first flow controller configured to be in the flow state when a negative pressure differential generated by coupling the outlet to the fluid collection device has a first magnitude such that an initial volume of bodily fluid flows through the sequestration flow path toward the first flow controller. The first flow controller is configured to transition to the non-flow state when the initial volume of bodily fluid is received in the sequestration flow path such that (1) the sequestration flow path is sequestered from the outlet and (2) the negative pressure differential is increased to a second magnitude operable to transition the second flow controller from the non-flow state to the flow state.

[0022] In some embodiments, a method of using a fluid control device to obtain a bodily fluid sample with reduced contamination includes coupling a fluid collection device to an outlet of the fluid control device. The coupling of the fluid collection device to the outlet is configured to produce a negative pressure differential within at least a portion of the fluid control device. A first flow controller is transitioned from a first state to a second state when the negative pressure differential has a first magnitude. The first flow controller is configured

to sequester a sequestration portion of the fluid control device from the outlet when in the first state and to establish fluid communication between the sequestration portion and the outlet when in the second state. An initial volume of bodily fluid is received from an inlet of the fluid control device into the sequestration portion in response to the negative pressure differential when the first flow controller is in the second state. The first flow controller is configured to transition from the second state to a third state in response to the sequestration portion receiving the initial volume of bodily fluid. When the first flow controller is in the third state, the first flow controller sequesters the sequestration portion from the outlet the negative pressure differential increases from the first magnitude to a second magnitude. A second flow controller is transitioned from a first state to a second state when the negative pressure differential has the second magnitude. The second flow controller is configured to sequester a sampling portion of the fluid control device from the inlet when in the first state and to establish fluid communication between the sampling portion and the inlet when in the second state. A subsequent volume of bodily fluid is transferred from the inlet to the fluid collection device via the sampling portion and the outlet.

[0023] In some embodiments, a fluid control device includes an inlet and an outlet. The inlet is configured to be placed in fluid communication with a bodily fluid source or an intermediary bodily fluid transfer device. The outlet is configured to be placed in fluid communication with a fluid collection device such as, for example, a sample reservoir (bottle, container, dish, vial, etc.), a culture bottle, and evacuated container, a syringe, a lumen-containing device, and/or any other suitable bodily fluid collection and/or transfer device. The fluid control device has a first state in which a negative pressure differential produced from an external source (e.g., the fluid collection device such as a sample reservoir, a syringe, a vessel, and/or any suitable intermediary fluid reservoir) is applied to the fluid control device to draw an initial volume of bodily fluid from the bodily fluid source, through the inlet, and into a sequestration and/or diversion portion of the fluid control device (which can be formed by or in the fluid control device or coupled thereto). The fluid control device has a second state in which (1) the sequestration and/or diversion portion sequesters the initial volume, and (2) the negative pressure differential draws a subsequent volume of bodily fluid, being substantially free of contaminants, from the bodily fluid source, through the fluid control device, and into the fluid collection device.

[0024] Any of the embodiments and/or methods described herein can be used in the procurement of clean or substantially unadulterated bodily fluid samples such as, for example,

blood samples. In some instances, bodily fluid samples (e.g., blood samples) can be tested for the presence of one or more potentially undesirable microbes, such as bacteria (e.g., Gram-Positive bacteria and/or Gram-Negative bacteria), fungi, yeast (e.g., Candida), and/or other undesirable microbes. Various technologies can be employed to assist in the detection of the presence of microbes as well as other types of biological matter, specific types of cells, biomarkers, proteins, antigens, enzymes, blood components, and/or the like during diagnostic testing. Examples include but are not limited to molecular polymerase chain reaction (PCR), magnetic resonance and other magnetic analytical platforms, automated microscopy, spatial clone isolation, flow cytometry, whole blood ("culture free") specimen analysis (e.g., NGS) and associated technologies, morphokinetic cellular analysis, and/or other common or evolving and advanced technologies to characterize patient specimens and/or to detect, identify, type, categorize, and/or characterize specific organisms, antibiotic susceptibilities, and/or the like.

[0025] For example, in some instances, microbial testing and/or detection can include incubating blood samples in one or more vessels that may contain culture media (e.g., a nutrient rich and/or environmentally controlled medium to promote growth and/or any number of other mediums), common additives, and/or other types of solutions conducive to microbial growth. Any of the microbes and/or organisms present in the blood sample flourish and/or grow over time in the culture medium (e.g., a variable amount of time from less than an hour to more than several days – which can be longer or shorter depending on the diagnostic technology employed). The presence of the microbes and/or organisms can be detected by automated, continuous monitoring, and/or other methods specific to the analytical platform and/or technology used for detection, identification, and/or the like (e.g., by observing carbon dioxide levels and/or any other suitable methods of detection).

[0026] The presence of microbes and/or organisms in the culture medium suggests the presence of the same microbes and/or organisms in the blood sample, which in turn, suggests the presence of the same microbes and/or organisms in the bodily fluid of the patient from whom the sample was obtained. In other instances, a bodily fluid sample may be analyzed directed (i.e., not incubated) for the presence of the microbes and/or organisms. Accordingly, when the microbes and/or organisms are determined to be present in the blood sample, the patient may be diagnosed and prescribed one or more antibiotics or other treatments specifically designed to treat or otherwise remove the undesired microbes and/or organisms from the patient.

[0027] Patient samples, however, can become contaminated during procurement and/or otherwise can be susceptible to false results. For example, microbes from a bodily surface (e.g., dermally residing microbes) that are dislodged during the specimen procurement process (e.g., either directly or indirectly via tissue fragments, hair follicles, sweat glands, and other skin adnexal structures) can be subsequently transferred to a culture medium, test vial, or other suitable specimen collection or transfer vessel with the patient sample and/or otherwise included in the specimen that is to be analyzed. Another possible source of contamination is from the person drawing the patient sample (e.g., a doctor, phlebotomist, nurse, technician, etc.) and/or the equipment used for drawing the patient sample. For example, equipment, supplies, and/or devices used during a patient sample procurement process often include multiple fluidic interfaces (e.g., patient to needle, needle to transfer adapter, transfer adapter to sample vessel, catheter hub to syringe, syringe to transfer adapter, needle/tubing to sample vessels, and/or any other fluidic interface or any combination(s) thereof) that can each introduce points of potential contamination. In some instances, such contaminants may thrive in a culture medium and/or may be otherwise identified, thereby increasing a risk or likelihood of false, compromised, and/or erroneous microbial test results, which may inaccurately reflect the presence or lack of such microbes within the patient (i.e., in vivo).

[0028] Such inaccurate results because of contamination and/or any other sources of adulteration are a concern when attempting to diagnose or treat a wide range of suspected illnesses, diseases, infections, patient conditions, and/or other maladies. For example, false results from microbial tests may result in a misdiagnosis and/or delayed treatment of a patient illness (which could result in the harm to and/or death of the patient or, on the other hand, may result in the patient being unnecessarily subjected to one or more anti-microbial therapies, which may cause serious side effects to and/or consequences for the patient including, for example, death. As such, false results produce an unnecessary burden and expense on the health care system due to extended length of patient stay and/or other complications associated with erroneous treatments. The use of diagnostic imaging equipment to arrive at these false results is also a concern from both a cost perspective and a patient safety perspective as unnecessary exposure to concentrated radiation associated with a variety of imaging procedures (e.g., CT scans) has many known adverse effects on long-term patient health.

[0029] As used in this specification and/or any of the claims included herein, the singular forms "a," "an" and "the" include plural referents unless the context clearly dictates otherwise.

Thus, for example, the term "a member" is intended to mean a single member or a combination of members, "a material" is intended to mean one or more materials, or a combination thereof.

[0030] As used herein, the terms "about," "approximately," and/or "substantially" when used in connection with a stated value(s) and/or a geometric structure(s) or relationship(s) is intended to convey that the value or characteristic so defined is nominally the value stated and/or characteristic described. In some instances, the terms "about," "approximately," and/or "substantially" can generally mean and/or can generally contemplate a value or characteristic stated within a desirable tolerance (e.g., plus or minus 10% of the value or characteristic stated). For example, a value of about 0.01 would include 0.009 and 0.011, a value of about 0.5 would include 0.45 and 0.55, a value of about 10 would include 9 to 11, and a value of about 1000 would include 900 to 1100. While a value, structure, and/or relationship stated may be desirable, it should be understood that some variance may occur as a result of, for example, manufacturing tolerances or other practical considerations (such as, for example, the pressure or force applied through a portion of a device, conduit, lumen, etc.). Accordingly, the terms "about," "approximately," and/or "substantially" can be used herein to account for such tolerances and/or considerations.

[0031] As used herein, "bodily fluid" can include any fluid obtained directly or indirectly from a body of a patient. For example, "bodily fluid" includes, but is not limited to, blood, cerebrospinal fluid, urine, bile, lymph, saliva, synovial fluid, serous fluid, pleural fluid, amniotic fluid, mucus, sputum, vitreous, air, and the like, or any combination thereof.

[0032] As used herein, the words "proximal" and "distal" refer to the direction closer to and away from, respectively, a user who would place the device into contact with a patient. Thus, for example, the end of a device first touching the body of the patient would be the distal end, while the opposite end of the device (e.g., the end of the device being manipulated by the user) would be the proximal end of the device.

[0033] As used herein, the terms "pre-sample," "first," and/or "initial," can be used interchangeably to describe an amount, portion, or volume of bodily fluid that is collected and/or sequestered prior to procuring the "sample" volume. A "pre-sample," "first," and/or "initial" volume can refer to a predetermined, defined, desired, and/or given volume of bodily fluid. For example, a predetermined and/or desired pre-sample volume of bodily fluid can be a drop of bodily fluid, a few drops of bodily fluid, and/or a volume of bodily fluid equal to about 0.1 milliliter (mL), about 0.2 mL, about 0.3 mL, about 0.4 mL, about 0.5 mL, about 1.0

mL, about 2.0 mL, about 3.0 mL, about 4.0 mL, about 5.0 mL, about 10.0 mL, about 20.0 mL, about 50.0 mL, and/or any volume or fraction of a volume therebetween. Alternatively, a pre-sample volume can be greater than 50.0 mL or less than 0.1 mL. In some specific embodiments, a predetermined and/or desired pre-sample volume can be between about 0.1 mL and about 5.0 mL. In other embodiments, a pre-sample volume can be, for example, a combined volume of any number of lumen (e.g., lumen that form at least a portion of a flow path from the bodily fluid source to an initial collection chamber, portion, reservoir, etc...

[0034] As used herein, the terms "sample," "second," and/or "subsequent" can be used interchangeably to describe a volume, portion, or amount of bodily fluid that is used, for example, in one or more sample or diagnostic tests. A "sample" volume can be either a random volume or a predetermined or desired volume of bodily fluid collected after collecting, sequestering, and/or isolating a pre-sample volume of bodily fluid. A desired sample volume of bodily fluid can be, for example, between about 10.0 mL to about 60.0 mL. Alternatively, a desired sample volume of bodily fluid can be less than 10.0 mL or greater than 60.0 mL. In some embodiments, for example, a sample volume can be at least partially based on one or more tests, assays, analyses, and/or processes to be performed on the sample volume.

[0035] The embodiments described herein can be configured to transfer bodily fluid with reduced contamination and/or substantially free from contamination to one or more fluid collection device(s). In some embodiments, a fluid collection device can include, but is not limited to, any suitable vessel, container, reservoir, bottle, adapter, dish, vial, syringe, device, diagnostic and/or testing machine, and/or the like. In some embodiments, a fluid collection device can be substantially similar to or the same as known sample containers such as, for example, a Vacutainer ® (manufactured by Becton Dickinson and Company (BD)), a BacT/ALERT ® SN or BacT/ALERT ® FA (manufactured by Biomerieux, Inc.), and/or any suitable reservoir, vial, microvial, microliter vial, nanoliter vial, container, microcontainer, nanocontainer, and/or the like. In some embodiments, a fluid collection device can be similar to and/or substantially the same as any of those described in U.S. Patent No. 8,197,420 entitled, "Systems and Methods for Parenterally Procuring Bodily-Fluid Samples with Reduced Contamination," filed December 13, 2007 ("the '420 Patent"), the disclosure of which is incorporated herein by reference in its entirety.

[0036] In some embodiments, a fluid collection device can be devoid of contents prior to receiving a sample volume of bodily fluid. For example, in some embodiments, a fluid collection device or reservoir can define and/or can be configured to define or produce a

vacuum or suction such as, for example, a vacuum-based collection tube (e.g., a Vacutainer ®), a syringe, and/or the like. In some embodiments, a sample reservoir can include, for example, any suitable additives, substances, enzymes, oils, fluids, compounds, chemicals, etc. (e.g., heparin, citrate, acid citrate dextrose (ACD), ethylenediaminetetraacetic acid (EDTA), oxalate, sodium polyanethol sulfonate (SPS), and/or the like). In other embodiments, a sample reservoir can contain, for example, an aerobic culture medium or an anaerobic culture medium. The sample reservoir (e.g., culture bottle) can receive a bodily fluid sample, which can then be tested (e.g., after incubation via in vitro diagnostic (IVD) tests and/or any other suitable test) for the presence of, for example, Gram-Positive bacteria, Gram-Negative bacteria, yeast, fungi, and/or any other organism. If testing of the culture medium yields a positive result, the culture medium can be subsequently tested using, for example, a PCR-based system to identify a specific organism.

[0037] While the term "culture medium" can be used to describe a substance configured to react with organisms in a bodily fluid (e.g., microorganisms such as bacteria) and the term "additive" can be used to describe a substance configured to react with portions of the bodily fluid (e.g., constituent cells of blood, serum, synovial fluid, etc.), it should be understood that a sample reservoir can include any suitable substance, liquid, solid, powder, lyophilized compound, gas, etc. Moreover, when referring to an "additive" within a sample reservoir, it should be understood that the additive could be a culture medium, an additive, and/or any other suitable substance, and/or any combination(s) thereof. That is to say, the embodiments described herein can be used with any suitable fluid collection device, reservoir, and/or the like containing any suitable substance.

[0038] While some of the embodiments are described herein as being used for procuring bodily fluid for one or more culture sample testing, it should be understood that the embodiments are not limited to such a use. Any of the embodiments and/or methods described herein can be used to transfer a flow of bodily fluid to any suitable device that is placed in fluid communication therewith. Thus, while specific examples are described herein, the devices, methods, and/or concepts are not intended to be limited to such specific examples.

[0039] The embodiments described herein and/or portions thereof can be formed or constructed of one or more biocompatible materials. In some embodiments, the biocompatible materials can be selected based on one or more properties of the constituent material such as, for example, stiffness, toughness, durometer, bioreactivity, etc. Examples of suitable biocompatible materials include metals, glasses, ceramics, or polymers. Examples of suitable

metals include pharmaceutical grade stainless steel, gold, titanium, nickel, iron, platinum, tin, chromium, copper, and/or alloys thereof. A polymer material may be biodegradable or non-biodegradable. Examples of suitable biodegradable polymers include polylactides, polyglycolides, polylactide-co-glycolides (PLGA), polyanhydrides, polyorthoesters, polyetheresters, polycaprolactones, polyesteramides, poly(butyric acid), poly(valeric acid), polyurethanes, and/or blends and copolymers thereof. Examples of non-biodegradable polymers include nylons, polyesters, polycarbonates, polyacrylates, polysiloxanes (silicones), polymers of ethylene-vinyl acetates and other acyl substituted cellulose acetates, non-degradable polyurethanes, polystyrenes, polyvinyl chloride, polyvinyl fluoride, poly(vinyl imidazole), chlorosulphonate polyolefins, polyethylene oxide, and/or blends and copolymers thereof.

[0040] The embodiments described herein and/or portions thereof can include components formed of one or more parts, features, structures, etc. When referring to such components it should be understood that the components can be formed by a singular part having any number of sections, regions, portions, and/or characteristics, or can be formed by multiple parts or features. For example, when referring to a structure such as a wall or chamber, the structure can be considered as a single structure with multiple portions, or multiple, distinct substructures or the like coupled to form the structure. Thus, a monolithically constructed structure can include, for example, a set of substructures. Such a set of substructures may include multiple portions that are either continuous or discontinuous from each other. A set of substructures can also be fabricated from multiple items or components that are produced separately and are later joined together (e.g., via a weld, an adhesive, and/or any other suitable method).

[0041] Referring now to the drawings, FIG. 1 is a schematic illustration of a fluid control device 100 according to an embodiment. Generally, the fluid control device 100 (also referred to herein as "control device" or "device") is configured to withdrawal bodily fluid from a patient. A first portion or amount (e.g., an initial amount) of the withdrawn bodily fluid is sequestered from a second portion or amount (e.g., a subsequent amount) of the withdrawn bodily fluid which can be subsequently used for additional testing, discarded, and/or reinfused into the patient. In this manner, contaminants or the like can be sequestered within the first portion or amount, leaving the second portion or amount substantially free of contaminants. The second portion or amount of bodily fluid can then be used as a biological sample in one or more tests for the purpose of medical diagnosis and/or treatment (e.g., a blood culture test or the like), as described in more detail herein. The first portion or amount of bodily fluid can be

discarded as waste or can be used in any suitable test that is less likely to produce false, inaccurate, distorted, inconsistent, and unreliable results as a result of potential contaminants contained therein. In some circumstances, for example in patients with limited supply of the bodily fluid such as blood, the first portion or amount of bodily fluid can be reinfused back into the patient via any suitable method.

[0042] The control device 100 can be any suitable shape, size, and/or configuration. For example, in some embodiments, the control device 100 can have a size that is at least partially based on a volume of bodily fluid at least temporarily stored, for example, in a sequestration, diversion, isolation, and/or storage portion of the control device 100. As described in further detail herein, the control device 100 can be configured to transition between operating modes such that (1) the first portion or amount of bodily fluid selectively flows through at least a first portion of the fluid control device and is subsequently sequestered therein, and (2) the second portion or amount of bodily fluid selectively flows through at least a second portion of the fluid control device and into a fluid collection device or the like. In some embodiments, the control device 100 can be configured to transition between operating modes automatically (e.g., based on pressure differential, time, electronic signal or instruction, saturation of a membrane or member, an absorbent and/or barrier material, etc.) or via and/or in response to intervention (e.g., user intervention, mechanical intervention, or the like).

[0043] The control device 100 includes an inlet 112, at least one outlet 116, and a sequestration chamber 114. In addition, the control device 100 defines one or more fluid flow paths 113 between the inlet 112 and at least the sequestration chamber 114 and/or one or more fluid flow paths 154 between the inlet 112 and the outlet(s) 116.

[0044] The inlet 112 of the control device 100 is configured to be placed in fluid communication with a bodily fluid source such as, for example, the vasculature of a patient. In some embodiments, the inlet 112 can be coupled to and/or can include an inlet device such as, for example, an intravenous (IV) catheter, a needle, a peripherally inserted central catheter (PICC), a syringe, one or more pieces of sterile tubing, and/or any other suitable lumen-containing device and/or intermediary transfer device. In some embodiments, the inlet 112 can be a port, a valve, and/or the like such as, for example, a Luer Lok ® or any other suitable coupler. In such embodiments, the inlet 112 (e.g., port or coupler) can be configured to couple to an access or inlet device in fluid communication with a patient (e.g., a placed or indwelling IV catheter or needle). In some embodiments, the inlet 112 can be physically and fluidically coupled to the access or inlet device via a lock, coupler, port, etc. In other embodiments, the

inlet 112 can be in fluid communication with the access or inlet device via an intermediate lumen-containing device such as, for example, sterile tubing or the like. In still other embodiments, the inlet 112 of the control device 100 can form and/or can be integrally or monolithically formed with the access or inlet device.

[0045] The sequestration chamber 114 is at least temporarily placed in fluid communication with the inlet 112 via the fluid flow path(s) 113. As described in further detail herein, the sequestration chamber 114 is configured to (1) receive a flow and/or volume of bodily fluid from the inlet 112 and (2) sequester (e.g., separate, segregate, contain, retain, isolate, etc.) the flow and/or volume of bodily fluid therein.

[0046] Although not shown in FIG.1, in some embodiments, the fluid control device 100 can have one or more flow path(s) 113 that include one or more flow modulating features (e.g., flow restrictors, fluid flow retardants, etc.) that selectively modulate the flow of bodily fluid drawn therethrough. In some embodiments, the flow modulating features can be structural and built into the fluid control device 100. In other embodiments, the flow modulating features can be separately formed or can be a material that can be introduced within the fluid control device 100, for example within the sequestration chamber 114, as described in further detail herein.

[0047] The sequestration chamber 114 can be any suitable shape, size, and/or configuration. For example, in some embodiments, the sequestration chamber 114 can be at least partially formed by a body portion of the control device 100 (not shown in FIG. 1). In other embodiments, the sequestration chamber 114 can be a reservoir placed and/or disposed within a portion of the control device 100. In other embodiments, the sequestration chamber 114 can be formed and/or defined by a portion of the fluid flow path 113. That is to say, the control device 100 can define one or more lumen and/or can include one or more lumen-defining device(s) configured to receive a flow of bodily fluid from the inlet 112, thereby defining the fluid flow path 113. In such embodiments, at least a portion of the lumen and/or a portion of the lumen-defining device(s) can form and/or can define the sequestration chamber 114.

[0048] The sequestration chamber 114 can have any suitable volume and/or fluid capacity. For example, in some embodiments, the sequestration chamber 114 can have a volume and/or fluid capacity between about 0.25 milliliters (mL) and about 5.0 mL. In some embodiments, the sequestration chamber 114 can have a volume measured in volumes as small as a microliter or less of bodily fluid (e.g., a volume as small as 20 drops of bodily fluid, 10 drops of bodily

fluid, 5 drops of bodily fluid, a single drop of bodily fluid, or any suitable volume therebetween). In other embodiments, the sequestration chamber 114 can have a volume up to, for example, about 5.0 mL, 10.0 mL, 15.0 mL, 20.0 mL, 30.0 mL, 40.0 mL, 50.0 mL, or more. In some embodiments, the sequestration chamber 114 can have a volume that is equal to and/or that is based at least in part on the volumes of a lumen of the inlet device coupled to and/or included in the control device 100, the lumen of the inlet 112, and a portion of the fluid flow path 113 defined between the inlet 112 and the sequestration chamber 114 and/or any combination thereof. In other embodiments, the sequestration chamber 114 can have a volume that is equal to and/or that is based at least in part on the individual and/or combined volumes of a portion of the inlet device, the inlet 112 of the control device 100, and the portion of the fluid flow path 113 defined between the inlet 112 and the sequestration chamber 114.

[0049] Although not shown in FIG. 1, in some embodiments, the fluid control device 100 and/or the sequestration chamber 114 can include and/or can be formed of one or more features or materials configured to interact with a portion of the bodily fluid transferred into the sequestration chamber 114. For example, in some embodiments, the fluid control device 100 and/or the sequestration chamber 114 can include and/or define a valve, a membrane, a diaphragm, a restrictor, a vent, a selectively permeable member (e.g., a fluid impermeable barrier or seal that at least selectively allows the passage of air or gas therethrough), a port, a junction, an actuator, and/or the like, or any suitable combination thereof (collectively referred to herein as a "flow controller"). Such flow controllers can be configured to selectively control (at least in part) a flow of fluids into and/or out of the sequestration chamber 114 and/or any other suitable portion of the fluid control device 100. In this context, the flow of fluids, for example, can be a liquid such as water, oil, dampening fluid, bodily fluid, and/or any other suitable liquid, and/or can be a gas such as air, oxygen, carbon dioxide, helium, nitrogen, ethylene oxide, and/or any other suitable gas.

[0050] In some embodiments, one or more openings and/or one or more flow controllers can be configured to facilitate air displacement into or out of the sequestration chamber 114. In some embodiments, the air displacement from the sequestration chamber 114 as an initial portion of the bodily fluid is transferred into the sequestration chamber 114 can allow for a redistribution of pressure in the sequestration chamber 114 and/or between the sequestration chamber 114 and, for example, the fluid source and/or a portion of the fluid flow path outside of the sequestration chamber 114, or a pressure of an ambient environment into which the sequestration chamber 114 is vented. In some embodiments, the redistribution of pressure can

be a factor in determining and/or defining how bodily fluid flows through the control device 100 and/or the amount or volume of bodily fluid to be transferred into the sequestration chamber 114.

[0051] In other embodiments, the sequestration chamber 114 and/or control device 100 can include a flow controller operable to selectively control a flow of bodily fluid through the fluid flow paths 113 in any suitable manner. For example, in some embodiments, the control device 100 can be configured to selectively transfer a volume of bodily fluid to the sequestration chamber 114 or to the outlet 116 based at least in part on a pressure differential between two or more portions of the control device 100. In some embodiments, the pressure differential can result from fluidically coupling the outlet 116 to an evacuated fluid collection device 160 (e.g., a sample reservoir, a syringe, a pressure charged canister, and/or other source or potential energy to create a vacuum or pressure differential). In other embodiments, the pressure differential can result from a change in volume and/or temperature. In still other embodiments, the pressure differential can result from at least a portion of the control device 100, and/or other portions of the flow paths 113 and/or 154 being evacuated and/or charged (e.g., the sequestration chamber 114 and/or any other suitable portion). In some embodiments, the pressure differential can be established automatically or via direct or indirect intervention and/or manipulation (e.g., by the user). Moreover, a flow of a fluid (e.g., gas and/or liquid) resulting from a pressure differential can be selectively controlled via one or more flow controllers that can, for example, transition between one or more operating conditions to control the fluid flow. It should be understood that the flow controllers included in the embodiments described herein are presented by way of example and not limitation. Thus, while specific flow controllers are described herein, it should be understood that fluid flow can be controlled through the control device 100 by any suitable means.

[0052] In some embodiments, a wall or structure of the fluid control device 100 can define an opening, aperture, port, orifice, and/or the like that is in fluid communication with the sequestration chamber 114. In some embodiments, the control device 100 can include a semi-permeable member, film, membrane, or material such as a hydrophobic or hydrophilic membrane disposed in or about the opening or elsewhere in the flow paths 113 to selectively allow a flow of air or gas through the opening while limiting or substantially preventing a flow of fluid (e.g., bodily fluid such as blood) through the opening.

[0053] In some embodiments, for example, the control device 100 can include an absorbent and/or hydrophilic material disposed within the sequestration chamber 114. Accordingly,

when bodily fluid is transferred into the sequestration chamber 114, the absorbent and/or hydrophilic material can absorb, attract, retain, expand, and/or otherwise interact with at least a portion of the bodily fluid, which in turn, can sequester and/or retain at least an initial portion of the bodily fluid within the sequestration chamber 114, as described in further detail herein.

[0054] In some embodiments, the fluid control device 100 can include one or more self-sealing vent materials that permit the flow of air or air pressure (e.g., vacuum) but not the flow of fluid (i.e., liquid). For example, the self-sealing material when wetted or when in contact with a fluid may absorb or otherwise become saturated and transition to a sealed configuration such that the self-sealing material does not permit air or liquid therethrough. The transitioning of the self-sealing material (e.g., vent) may be associated with the fluid control device 100 moving from a first state (e.g., wherein an initial portion of the bodily fluid is being transferred into the sequestration chamber 114) to a second state (e.g., after the initial portion of the bodily fluid is transferred into the sequestration chamber 114).

[0055] In some embodiments, the sequestration chamber 114 or any other portion of the fluid control device 100 can include and/or can be formed of an expandable or collapsible material configured to transition between a first state (e.g., while an initial portion of the bodily fluid is being transferred into the sequestration chamber 114) to a second state (e.g., after the initial portion of the bodily fluid is transferred into the sequestration chamber 114). For example, the collapsible material can be in the form of a dissolvable substance that initially blocks the flow path 113 within which it is present and does not permit the flow of fluid (e.g., gas or liquid) therethrough. Upon coming into contact with a predetermined amount of fluid, however, the material can be dissolved or otherwise transitioned to a dissolved configuration to release the obstruction of the fluid flow path 113 in which the material is disposed. In some embodiments, the change in configuration resulting from such a material expanding, collapsing, dissolving, etc. can be operable to transition the control device 100 and/or any suitable portion of the control device 100 from a first state, mode, position, configuration, etc., to a second state, mode, position, configuration, etc., as described in further detail herein.

[0056] In some embodiments, the control device 100 and/or the sequestration chamber 114 can include a valve such as, for example, a duckbill valve, a butterfly valve, a one-way check valve, etc. and can be made from any suitable material with any suitable cracking pressure (e.g., an amount of pressure or force sufficient to open the valve) to be used to direct fluid flow as desired. For example, the fluid control device 100 can include two or more valves with varying cracking pressure such that they open sequentially with increasing pressure. Such a

configuration can be used, for example, in conjunction with a suitable source of negative pressure and suitable flow controllers to direct fluid flow.

[0057] The outlet(s) 116 is/are in fluid communication with and/or is/are configured to be placed in fluid communication with the fluid flow paths 113 and/or 154. The outlet 116 can be any suitable outlet, opening, port, stopcock, lock, seal, coupler, valve (e.g., a one-way check valve, duckbill valve, umbrella valve, and/or the like), etc. and is configured to be fluidically coupled to the fluid collection device 160. In some embodiments, the outlet 116 can be monolithically formed with the collection device 160, a syringe, and/or other intermediary bodily-fluid transfer device. In other embodiments, the outlet 116 can be at least temporarily coupled to the collection device 160 via an adhesive, a resistance fit, a mechanical fastener, a threaded coupling, a piercing or puncturing arrangement, any number of mating recesses, and/or any other suitable coupling or combination thereof. Similarly stated, the outlet 116 can be physically (e.g., mechanically) and/or fluidically coupled to the collection device 160 such that an interior volume defined by the collection device 160 is in fluid communication with the outlet 116. In still other embodiments, the outlet 116 can be operably coupled to the collection device 160 via an intervening structure (not shown in FIG. 1), such as a flexible sterile tubing. In still other embodiments, the outlet 116 can be fluidically coupled to a downstream source of negative pressure that suitably directs the flow of fluid into the collection device 160.

[0058] In some embodiments, the arrangement of the outlet 116 can be such that the outlet 116 is physically and/or fluidically sealed prior to coupling to the collection device 160. In some embodiments, the outlet 116 can be transitioned from a sealed configuration to an unsealed configuration in response to being coupled to the collection device 160 and/or in response to a negative pressure differential between an environment within the outlet 116 and/or control device 100 and an environment within the collection device 160.

[0059] The fluid collection device 160 can be any suitable device for at least temporarily containing a bodily fluid, such as, for example, those described above. For example, in some embodiments, the fluid collection device 160 can be a single-use disposable collection tube(s), a syringe, a vacuum-based collection tube(s), an intermediary bodily-fluid transfer device, and/or the like. In some embodiments, the fluid collection device 160 can be substantially similar to or the same as known sample containers such as, for example, a Vacutainer ®, a BacT/ALERT ® SN or BacT/ALERT ® FA, and/or any other suitable reservoir, vial, microvial, microliter vial, nanoliter vial, container, microcontainer, nanocontainer, and/or the like. In some embodiments, the collection device 160 can be a sample reservoir that includes

a vacuum seal that maintains negative pressure conditions (vacuum conditions) inside the sample reservoir, which in turn, can facilitate withdrawal of bodily fluid from the patient, through the fluid control device 100, and into the sample reservoir, via a vacuum or suction force, as described in further detail herein. In embodiments in which the fluid collection device 160 is an evacuated container or the like, the user can couple the collection device 160 to the outlet 116 to initiate a flow of bodily fluid from the patient such that a first or initial portion of the bodily fluid is transferred into and sequestered by the sequestration chamber 114 and such that any subsequent portion or volume of bodily fluid bypasses and/or is otherwise diverted away from the sequestration chamber 114 and flows into the fluid collection device 160.

[0060] Although the outlet 116 of the control device 100 is described above as being fluidically coupled to and/or otherwise placed in fluid communication with the fluid collection device 160 (e.g., a sample reservoir, syringe, etc.), in other embodiments, the control device 100 can be used in conjunction with any suitable bodily fluid collection device, system, and/or the like. For example, in some embodiments, the fluid control device 100 can be used in any suitable fluid transfer device such as those described in U.S. Patent Publication No. 2015/0342510 entitled, "Sterile Bodily-Fluid Collection Device and Methods," filed June 2, 2015 (referred to herein as the "'510 publication"), the disclosure of which is incorporated herein by reference in its entirety. More particularly, the control device 100 can be used in an "all-in-one" or pre-assembled device (e.g., such as those described in the '510 publication) to receive and sequester an initial volume of bodily fluid such that contaminants in subsequent volumes of bodily fluid are reduced and/or eliminated. In other embodiments, the outlet 116 can include and/or can be coupled to an adapter, outlet needle, and/or the like. For example, in some embodiments, the outlet 116 can be coupled to and/or can include a transfer adapter and/or the like such as, for example, the transfer adapters described in U.S. Patent Publication No. 2015/0246352 entitled, "Apparatus and Methods for Disinfection of a Specimen Container," filed March 3, 2015 (referred to henceforth as the "'352 publication"), the disclosure of which is incorporated herein by reference in its entirety.

[0061] As described above, the device 100 can be used to procure a bodily fluid sample having reduced contamination from microbes such as, for example, dermally residing microbes and/or the like. For example, in some instances, a user such as a doctor, physician, nurse, phlebotomist, technician, etc. can manipulate the device 100 to establish fluid communication between the inlet 112 and the bodily fluid source (e.g., a vein of a patient, cerebral spinal fluid (CSF) from the spinal cavity, urine collection, and/or the like). As a specific example, in some

instances, the inlet 112 can be coupled to and/or can include a needle or the like that can be manipulated to puncture the skin of the patient and to insert at least a portion of the needle in the vein of the patient, thereby placing the inlet 112 in fluid communication with the bodily fluid source (e.g., the vein, an IV catheter, a PICC, etc.).

[0062] In some embodiments, once the inlet 112 is placed in fluid communication with the bodily fluid source (e.g., the portion of the patient), the outlet 116 can be fluidically coupled to the collection device 160. As described above, the collection device 160 can be any suitable reservoir, container, and/or collection system configured to receive a volume of bodily fluid. More particularly, the collection device 160 can be, for example, an evacuated reservoir or container that defines a negative pressure and/or can be a syringe that can be manipulated to produce a negative pressure. In some instances, coupling the outlet 116 to the collection device 160 selectively exposes at least a portion of the fluid flow paths 113 and/or 154 to the negative pressure, thereby resulting in a negative pressure differential operable in drawing bodily fluid from the bodily fluid source (e.g., the patient), through the inlet 112, and into the fluid control device 100.

[0063] In some embodiments, the arrangement of the control device 100 is such that when a volume of bodily fluid is transferred to and/or through the inlet 112, an initial portion of the volume of bodily fluid (also referred to herein as an "initial volume" or a "first volume") flows from the inlet 112, through at least a portion of the fluid flow path 113, and into the sequestration chamber 114. That is to say, in some embodiments, the control device 100 can be in first or initial state in which the initial portion or volume of bodily fluid can flow in or through at least a portion the fluid flow path 113 and into the sequestration chamber 114. For example, in some embodiments, the initial state of the control device 100 can be one in which one or more flow controllers (e.g., valves, membranes, diaphragms, restrictors, vents, air permeable and fluid impermeable barriers, ports, and/or the like) are in a first state in which the fluid flow path 113 is exposed to the negative pressure differential via the sequestration chamber 114. In other words, the negative pressure within the sample reservoir 160 (or created by a syringe or other source of negative pressure) can result in a negative pressure (or negative pressure differential) within at least a portion of the sequestration chamber 114 that is operable in drawing an initial flow of bodily fluid into the sequestration chamber 114 when one or more flow controllers is in a first or initial state.

[0064] For example, in some embodiments, the control device 100 can include one or more flow controller(s) such as those described above that is at least temporarily fluidically coupled

to a flow path between the fluid collection device 160 and the sequestration chamber 114. In some embodiments, the flow controller(s) can be at least temporarily fluidically coupled to a flow path between the fluid collection device 160 and the inlet 112. While in some embodiments the flow controller examples noted above can be, for example, known off-the-shelf components that are used in medical devices to control the flow of fluids and air, in other embodiments, the flow controller can be a custom, proprietary, and/or specifically tailored component integrated into the device 100. When the flow controller is in the first or initial state, the flow controller can allow a flow of fluid therethrough in response to the negative pressure of the collection device 160. In some embodiments, the flow controller is configured to allow only a flow of air or gas through the flow controller and is configured to limit and/or substantially prevent a flow of liquid (e.g., bodily fluid) through the flow controller. As such, the collection device 160 can produce a negative pressure differential that is operable to draw an initial portion and/or amount of bodily fluid into the sequestration chamber 114 when the flow controller is in a first or initial state without allowing the initial portion of bodily fluid to flow into the fluid flow path 154 and/or otherwise out of the sequestration chamber 114.

[0065] Although not shown in FIG. 1, in some embodiments, the control device 100 can include a member, device, mechanism, etc. configured to modulate a magnitude of the negative pressure to which the sequestration chamber 114 is exposed. For example, in some embodiments, the control device 100 can include a valve, a membrane, a porous material, a restrictor, and/or any other suitable member and/or device configured to modulate pressure. In some embodiments, modulating and/or controlling a magnitude of the pressure to which the sequestration chamber 114 is exposed can, in turn, modulate a magnitude of pressure exerted on the bodily fluid and/or within a vein of a patient. In some instances, such pressure modulation can reduce, for example, hemolysis of a blood sample and/or a likelihood of collapsing a vein (e.g., which is particularly important in fragile patients needing microbial and/or other diagnostic testing associated with use of the control device 100). In addition, the modulation of the negative pressure can, for example, at least partially control a rate at which the fluid control device 100 transitions between a first configuration or state and a second configuration or state. In some embodiments, modulating the negative pressure can act like a timer. For example, a time between the introduction of the negative pressure differential and the transitioning of the diverter from the first state to the second state can be known, predetermined, calculated, and/or controlled. As such, in some instances, modulating the negative pressure can at least partially control an amount or volume of bodily fluid transferred

into the sequestration chamber 114 (e.g., can control a volume of the initial amount of bodily fluid).

[0066] The initial portion and/or amount of bodily fluid can be any suitable volume of bodily fluid, as described above. For example, in some instances, the control device 100 can remain in the first state until a predetermined and/or desired volume (e.g., the initial volume) of bodily fluid is transferred to the sequestration chamber 134. In some embodiments, the initial volume can be associated with and/or at least partially based on a volume of the sequestration chamber 114. In other embodiments, the initial volume can be associated with and/or at least partially based on an amount or volume of bodily fluid that can be transferred into the device prior to one or more portions of the control device 100 transitioning from a first operating state or mode to a second operating state or more (e.g., an amount of bodily fluid that can be absorbed by an absorbent, expandable, hydrophilic, and/or a wicking material, an amount of bodily fluid sufficient to fully wet or saturate a vent material or semi-permeable member or membrane, an amount sufficient to equalize one or more pressure differentials within the control device 100, an amount sufficient to transition a valve or actuator, and/or the like).

[0067] After the initial volume of bodily fluid is transferred and/or diverted into the sequestration chamber 114, the initial volume is sequestered, segregated, retained, contained, isolated, etc. in the sequestration chamber 114. For example, in some embodiments, the transitioning of the one or more flow controllers from a first state to a second state can be operable to sequester and/or retain the initial portion of the bodily fluid in the sequestration chamber 114. As described in further detail herein, in some instances, contaminants such as, for example, dermally residing microbes or the like dislodged during the venipuncture event, other external sources of contamination, colonization of catheters and PICC lines that are used to collect samples, and/or the like can be entrained and/or included in the initial volume of the bodily fluid and thus, are sequestered in the sequestration chamber 114 when the initial volume is sequestered therein.

[0068] With the initial volume transferred and/or diverted into the sequestration chamber 114, the device 100 can transition to the second state in which a subsequent volume(s) of bodily fluid can flow through at least a portion the fluid flow paths 113 and/or 154 from the inlet 112 to the outlet 116. In some embodiments, the control device 100 can passively and/or automatically transition (e.g., without user intervention) from the first state to the second state once the initial volume of bodily fluid is sequestered in the sequestration chamber 114. For

example, in some embodiments, filling the sequestration chamber 114 to capacity and/or fully saturating, wetting, and/or impregnating an absorbent or similar material disposed between the sequestration chamber 114 and the sample reservoir 160 can be such that further transfer of bodily fluid into the sequestration chamber 114 is limited and/or substantially prevented due to a removal or diversion of the negative pressure. In other embodiments, the control device 100 can be manually transitioned or transitioned in response to at least an indirect interaction by a user. For example, in some embodiments, a user can at least partially obstruct the opening and/or vent. In other embodiments, the user can actuate an actuator or the like (not shown in FIG. 1) to transition the control device 100 from the first state to the second state. In still other embodiments, at least a portion of the initial volume of bodily fluid can transition the control device 100 from the first state to the second state. For example, the control device 100 can include a bodily fluid activated switch, valve, port, and/or the like. In other embodiments, a volume of bodily fluid can move and/or displace one or more actuators or the like that can, for example, open a port, flow path, and/or outlet. In still other embodiments, a user can manipulate such a switch, valve, port, actuator, etc. to transition the control device 100 from the first state to the second state.

[0069] With the collection device 160 fluidically coupled to the outlet 116 and with the control device 100 being in the second state (e.g., the initial volume of bodily fluid is sequestered in or by the sequestration chamber 134), any subsequent volume(s) of the bodily fluid can flow from the inlet 112, through at least one of the fluid flow paths 113 and/or 154, through the outlet 116, and into the collection device 160. Thus, as described above, sequestering the initial volume of bodily fluid in the sequestration chamber 114 prior to collecting or procuring one or more sample volumes of bodily fluid reduces and/or substantially eliminates and amount of contaminants in the one or more sample volumes. Moreover, in some embodiments, the arrangement of the control device 100 can be such that the control device 100 cannot transition to the second state prior to collecting and sequestering the initial volume in the sequestration chamber 114.

[0070] FIG. 2 illustrates a cross-sectional side-view of a fluid control device 200 according to an embodiment. The fluid control device 200 can be similar in at least form and/or function to the fluid control device 100 described above with reference to FIG. 1. Accordingly, portions of the fluid control device 200 that can be similar to portions of the fluid control device 100 are not described in further detail herein.

[0071] As shown in FIG. 2, the fluid control device 200 (also referred to herein as "control device" or "device") includes an inlet 212, an outlet 216, and a sequestration chamber 214. As described above with reference to the control device 100, the inlet 212 is configured to be placed in fluid communication with a bodily fluid source to receive a flow of bodily fluid therefrom (e.g., via a lumen-containing device such as a needle, IV catheter, PICC line, or the like). The outlet 216 is configured to be fluidically coupled to a fluid collection device, a syringe, and/or other intermediary bodily fluid transfer device or vessel (not shown in FIG. 2) such as, for example, a transfer device similar to those described in the '510 publication.

[0072] As described above with reference to the fluid control device 100, the control device 200 includes one or more fluid flow paths 213 between the inlet 212 and a sequestration chamber 214 and/or one or more fluid flow paths 254 between the inlet 212 and the outlet 216. The device 200 can have any suitable shape, size, and/or configuration. For example, in some embodiments, the device 200 can be substantially similar in at least form and/or function to the device 100 described above with reference to FIG. 1. In some embodiments, the device 200 can include a first portion 224 and a second portion 225. As shown in FIG. 2, in some embodiments, the second portion 225 can be, for example, a bypass and/or diversion portion that is physically coupled to and selectively in fluid communication with the first portion 224. Moreover, the device 200 includes and/or forms a first junction 217 at a position where a first end (e.g., an inlet end) of the second portion 225 is coupled to the first portion 224 and includes and/or forms a second junction 218 at a position where a second end (e.g., an outlet end) of the second portion 225 is coupled to the first portion 224. That is to say, the device 200 can be configured to have and/or form a bifurcation (e.g., the second portion 225) at the first junction 217 which is rejoined at, for example, the second junction 218. In some embodiments, the second portion 225 can form and/or can have a D-shaped configuration and/or arrangement. In other embodiments, the first portion 224 and/or the second portion 225 can form and/or can have any suitable configuration and/or arrangement (e.g., a serpentine configuration, a looping configuration, a spiraled configuration, any suitable geometric configuration, and/or the like). In some embodiments, the first portion 224 and/or the second portion 225 of the device 200 can include and/or can be formed by flexible tubing or the like having any suitable shape and/or size and being reconfigurable or movable to be placed in any suitable configuration and/or arrangement.

[0073] In some embodiments, the sequestration chamber 214 of the device 200 can be formed by and/or included in the second portion 225 of the device 200. The coupling of the

second portion 225 to the first portion 224 (e.g., at the first junction 217) is such that the sequestration chamber 214 can be selectively placed in fluid communication with the inlet 212 via the fluid flow path 213 and the first junction 217. Similarly, the coupling of the second portion 225 to the first portion 224 (e.g., at the second junction 218) is such that the sequestration chamber 214 can be selectively placed in fluid communication with the outlet 216 and/or a fluid collection device coupled to the outlet 216 via the fluid flow path 254 and the second junction 218,.

[0074] As described in further detail herein, the sequestration chamber 214 is configured to (1) selectively receive a flow and/or volume of bodily fluid from the inlet 212 and (2) sequester (e.g., separate, segregate, contain, retain, isolate, etc.) the flow and/or volume of bodily fluid therein. The sequestration chamber 214 can have any suitable shape, size, and/or configuration. For example, in some embodiments, the sequestration chamber 214 can have any suitable size, volume, and/or fluid capacity such as, for example, those described above with reference to the sequestration chamber 114. In some embodiments, at least a portion of the fluid flow path 213 can extend through a portion of the device 200 and/or the first junction 217 to form and/or define at least a portion of the sequestration chamber 214. In other embodiments, the first junction 217 and/or the sequestration chamber 214 can include a flow control mechanism and/or the like that can at least temporarily separate the fluid flow path 213 from the sequestration chamber 214. In some embodiments, the device 200 can include, form, and/or define one or more flow controllers such as flow controllers 221, 222, and/or 215. The flow controllers 221, 222, and/or 215 can be, for example, a valve, membrane, diaphragm, restrictor, vent, a selectively permeable member (e.g., a fluid impermeable barrier or seal that allows at least selective passage of gas or air such as, for example, a blood barrier like Porex ®, and/or the like), port, etc. (collectively referred to herein as a "flow controller") placed in one or more desired positions and configured to selectively control (at least in part) a flow of fluids into and/or out of the sequestration chamber 214 and/or any other suitable portion of the device 200.

[0075] More particularly, in the embodiment shown in FIG. 2, the flow controllers 221 and 222 each can be a valve configured to have a specific, desired, and/or predetermined cracking pressure or the like. The valves 221 and/or 222 can be, for example, inline or Lined Pipe Insert (LP) valves that can configured to be suitably placed in any position along pipe or tubing systems. In some embodiments, the valves 221 and/or 222 can be configured to stay in a closed state, limiting or substantially preventing the flow of air or liquid, until a specific amount of

pressure greater than the cracking pressure is applied on the valves 221 and/or 222 to transition the valve 221 and/or 222, respectively, from a closed state to an open state.

[0076] In some embodiments, the valves 221 and/or 222 and other additional valves (not shown) each can be configured to have a variable cracking pressure and to be placed in any suitable position in and/or along the device 200. For example, in some embodiments, as shown in FIG.2, the valve 221 can be disposed in the first portion 224 of the device 200 and downstream of the first junction 217 and the valve 222 can be disposed in the second portion 225 of the device 200 upstream and/or before the second junction 218. In some embodiments, the device 200 can be configured such that the valve 221 has a greater cracking pressure than the valve 222 such that an applied vacuum source may be used to result in a sequential opening of the valves 221 and 222. For example, the cracking pressure of each of the valves 221 and 222 and the pressure exerted by the source of negative pressure can be collectively configured to achieve a sequential and/or otherwise desired first flow of bodily fluid towards and/or into the sequestration chamber 214 and then a desired second flow of bodily fluid towards the outlet 216 and the fluid collection device.

[0077] By way of specific example, in some embodiments, a source of negative pressure (e.g., a fluid collection device and/or the like) can define a vacuum having a magnitude of approximately 8 pounds per square inch (psi). Thus, when the source of negative pressure is coupled to the outlet 216, the pressure is communicated to both valves 221 and 222. In some embodiments, the valve 221 may have, for example, a cracking pressure of 3.4 psi and the valve 222 may have, for example, a cracking pressure of 0.017 psi. As such, the negative pressure differential produced as a result of coupling the negative pressure source to the outlet 216, in turn, can transition the valve 222 (having the lower cracking pressure) from a substantially closed configuration or state to a substantially open configuration or state prior to transitioning the valve 221 (having the higher cracking pressure) from a substantially closed configuration or state to a substantially open configuration or state. In some instances, this sequential opening of the valves (i.e., valve 222 before valve 221), can be operable to direct a flow of fluid (e.g., a first flow) towards the sequestration chamber 214 and then direct the flow of fluid (e.g., a second flow) towards the fluid collection device and/or negative pressure source coupled to the outlet 216, as described further below.

[0078] The device 200, can in some embodiments, include one or more flow controllers in the form of materials that are selectively permeable to air but impermeable or at least selectively permeable to fluid (e.g., liquid). For example, the device 200 can include one or

more membranes made of material that permit the flow of air or convey a vacuum from a source of negative pressure but do not permit or convey a flow of bodily fluid (e.g., hydrophobic). In some embodiment, the device 200 can include flow controllers that can be in a first or initial state or configuration before interaction with a bodily fluid or any other suitable form of actuation, and then transition and/or be transitioned to a second state or configuration upon interaction with the bodily fluid or a suitable form of actuation. For example, in some embodiments, such flow controllers can be in an initial or first state that selectively permits a flow of air therethrough while substantially limiting and/or preventing a flow of bodily fluid therethrough. Upon interaction with a bodily fluid (or any other suitable fluid), the flow controller can transition to a second state, in which the flow controller can be substantially impermeable to the flow of air and the flow of bodily fluid therethrough.

[0079] As shown in the embodiment illustrated in FIG.2, the device 200 can include a flow controller 215 in the form of a membrane, porous material, absorbent material, etc. The flow controller 215 can be any suitable shape, size, and/or configuration. In some embodiments, the flow controller 215 can be formed of a porous material having any suitable pore size to, for example, permit a flow of air therethrough while limiting and/or substantially preventing a flow of liquid therethrough. For example, in some embodiments, the flow controller 215 can be a membrane or the like having a diameter of about 17 mm and having a pore size of about 0.45 micrometers (μm). In other embodiments, the flow controller 215 can be a membrane and/or the like having any suitable diameter (e.g., 1 mm, 2 mm, 3 mm ,4 mm, 5 mm, 10 mm, 15 mm, 20 mm, 30 mm, or more, and/or any diameter therebetween). Likewise, in other embodiments, the flow controller 215 can be a membrane and/or the like having any suitable pore size. In some embodiments, a pore size for a flow controller, membrane, and/or the like can be based on, for example, the type of fluid (e.g., bodily fluid) to be withdrawn, collected, and/or sequestered, the amount or type of particulate matter expected in the fluid flow (e.g., in the flow of the bodily fluid and/or the flow of air), the vacuum source to be used and/or a magnitude of an expected negative pressure differential, and/or any other suitable factor or consideration.

[0080] As shown, the flow controller 215 is positioned within the device 200 to selectively establish fluid communication between the second portion 225 and/or the sequestration chamber 214 and the outlet 216 via the junction 218. Thus, with the flow controller 215 being configured as a semi-permeable member, the flow controller 215 can be configured to at least temporarily allow a gas or air to transfer from the second portion 225 of the device 200 and/or the sequestration chamber 214, through the flow controller 215 and the junction 218, and into

the fluid flow path 254 and can be configured to limit and/or substantially prevent a flow of liquid (e.g., bodily fluid) between the second portion 225 and/or the sequestration chamber and the fluid flow path 254 (e.g., via the junction 218), as described in further detail herein. Although not shown, in some embodiments, the device 200 can include one or more actuators or the like configured to control and/or transition the state of the flow controller 215. The outlet 216 of the device 200 is in fluid communication with and/or is configured to be placed in fluid communication with the fluid flow paths 213 and/or 254. The outlet 216 can be any suitable outlet, opening, port, lock, seal, coupler, etc. and is configured to be fluidically coupled to a fluid collection device, such as a sample reservoir, a syringe, container, and/or other sample vessel. In some embodiments, the outlet 216 can be monolithically formed with the fluid collection device or can be at least temporarily coupled to the fluid collection device, as described above with reference to the outlet 116 of the device 100. The fluid collection device can be any suitable collection system for containing a bodily fluid, such as, for example, any of those described in detail above with reference to the collection device 160. More particularly, in some embodiments, the outlet 216 can be configured to couple to an evacuated sample reservoir. In some other embodiments, the outlet 216 can be configured to couple to a source of negative pressure downstream of the outlet 216, while also coupled to the fluid collection device. As such, the user can couple the fluid collection device to the outlet 216 to initiate a flow of bodily fluid from the patient such that a first or initial portion of the bodily fluid is transferred into and sequestered by the sequestration chamber 214 and such that any subsequent portion or volume of bodily fluid bypasses and/or is otherwise diverted away from the sequestration chamber 214 and flows into the fluid collection device.

[0081] In operation, the device 200 can be used to procure a bodily fluid sample having reduced contamination from microbes such as, for example, dermally residing microbes and/or the like. For example, in some instances, a user such as a doctor, physician, nurse, phlebotomist, technician, etc. can manipulate the device 200 to establish fluid communication between the inlet 212 and the bodily fluid source (e.g., a vein of a patient). Once the inlet 212 is placed in fluid communication with the bodily fluid source (e.g., the portion of the patient), the outlet 216 can be fluidically coupled to the fluid collection device. As described above, in the embodiment shown in FIG. 2, the fluid collection device can be a negative pressure source and/or can be configured to produce a negative pressure differential. For example, the fluid collection device can be an evacuated reservoir or container that defines a negative pressure, a syringe, a pump, and/or any other negative pressure source. In other embodiments, the fluid

collection device can be a container, reservoir, or device configured to be coupled to a separate negative pressure source.

[0082] Coupling the outlet 216 to the fluid collection device and/or the source of negative pressure selectively exposes at least a portion of the fluid flow path 254 to the negative pressure within or passing through the fluid collection device. As described above, the flow controller 215 and/or the valves 221 and 222 can be configured to selectively control the flow of fluid through the device 200. More particularly, coupling the outlet 216 to the fluid collection device and/or source of negative pressure results in a negative pressure differential within the fluid flow path 254, which in turn, exposes the valves 221 and 222 to the negative pressure. As described above, in some embodiments, the valve 221 can have a greater cracking pressure (e.g., 3.4 psi) compared to that of the valve 222 (e.g., 0.017 psi). Furthermore, the flow controller 215 upstream of the valve 222 can be a membrane in an initial or first state, in which the flow controller 215 is permeable to a flow of air or gas. In some instances, such an arrangement results in the valve 222 being transitioned from a closed state to an open state such that the negative pressure is communicated through the valve 222 and the flow controller 215 and into the sequestration chamber 214.

[0083] Accordingly, a negative pressure differential is produced that is operable in drawing bodily fluid from the bodily fluid source (e.g., the patient), through the inlet 212, and into the fluid flow path 213. Moreover, with the valve 222 in the open state and the valve 221 in the closed state, the bodily fluid can flow through the fluid flow path 213 and into the sequestration chamber 214 (e.g., via the junction 217). As described above with reference to the control device 100, the arrangement of the device 200 is such that when a volume of bodily fluid is transferred to and/or through the inlet 212, an initial portion of the volume of bodily fluid (also referred to herein as an "initial volume" or a "first volume") flows from the inlet 212, through at least a portion of the fluid flow path 213 and/or the junction 217, and into the sequestration chamber 214. That is to say, in some embodiments, the control device 200 can be in first or initial state in which the initial portion or volume of bodily fluid can flow in or through at least a portion the fluid flow path 213 and/or junction 217 and into the sequestration chamber 214. When the device 200 is in the first or initial state, the valve 221 is in a closed state and as such, the bodily fluid does not pass through the valve 221 nor substantially enter the fluid flow path 254.

[0084] As described above, the control device 200 can be in the initial state when the flow controller 222 (valve) is in an open state, which in turn, allows the negative pressure differential

to draw the initial amount of bodily fluid into the sequestration chamber 214. In some instances, the bodily fluid can flow through the second portion 225 (e.g., the sequestration chamber 214) until the flow reaches the flow controller 215 (e.g., a selectively permeable membrane or member, as described above). The membrane 215 can be in its initial or first state and therefore can be permeable to air but impermeable to liquids. As such, the membrane 215 isolates, separates, segregates, sequesters and/or otherwise prevents direct liquid communication between the fluid flow paths 213 and the sequestration chamber 214. In addition, the inlet 212 is exposed to the negative pressure differential via the sequestration chamber 214. In other words, the negative pressure within the fluid collection device can result in a negative pressure (or negative pressure differential) within at least the second portion 225 of the device 200 (e.g., the sequestration chamber 214) that is operable in drawing an initial flow of bodily fluid from the inlet 212, through at least a portion of the fluid flow path 213 and/or the junction 217, and into the sequestration chamber 214 when the control device 200 is in the first or initial state.

[0085] When the flow controller 215 is in the first or initial state, the flow controller 215 can allow a flow of fluid (e.g., a gas or air) therethrough in response to the negative pressure of the sample reservoir (or a syringe or other source of potential energy used to create negative pressure), as described above with reference to the device 100. The flow controller 215 (e.g., selectively permeable membrane or member) can be configured to transition from the first state of being permeable to air and impermeable to liquid, to a second state of being impermeable to air and liquid in response to the flow of the initial amount of bodily fluid into the sequestration chamber 214. For example, the filling of the sequestration chamber 214 to capacity can correspond to and/or otherwise result in the bodily fluid saturating, wetting, and/or impregnating the flow controller 215 (e.g., membrane material), which can transition the flow controller 215 from the first state to the second state. In the second state the flow controller 215 is impermeable to air and liquid, thereby limiting and/or substantially preventing fluid communication between the sequestration chamber 214 and the source of negative pressure (e.g., the fluid collection device). In other words, the sequestration chamber 214 can be sequestered from the negative pressure source in response to initial volume of bodily fluid filling the sequestration chamber 214.

[0086] The initial portion and/or amount of bodily fluid can be any suitable volume of bodily fluid, as described in detail above with reference to the control device 100. For example, in some instances, the initial volume can be associated with and/or at least partially based on

an amount or volume of bodily fluid that is sufficient to fully wet or saturate the flow controller 215 (e.g., selectively permeable membrane or member). In other words, in some embodiments, the initial volume of bodily fluid can be a volume sufficient to transition the flow controller 215 to a second state (e.g., a saturated or fully wetted state). In some embodiments, the flow controller 215 is placed in a sealed configuration when transitioned to the second state. That is to say, saturating and/or fully wetting the flow controller 215 (e.g., the semi-permeable material) places the flow controller 215 in a sealed configuration in which the flow controller 215 substantially prevents a flow of a liquid and a gas therethrough.

[0087] After the initial volume of bodily fluid is transferred and/or diverted into the sequestration chamber 214, the control device 200 can be transitioned to its second state or operating mode to sequester, segregate, retain, contain, isolate, etc. the initial volume in the sequestration chamber 214. For example, as described above, the flow controller 215 is placed in the sealed configuration, which fluidically isolates the sequestration chamber 214 from the fluid flow path 254. In addition, the transitioning of the flow controller 215 can be in response to the initial amount of bodily fluid filling the sequestration chamber 214. Accordingly, the initial amount of bodily fluid in the sequestration chamber 214 can limit and/or substantially prevent further amounts of bodily fluid from being transferred into the sequestration chamber 214. Thus, the initial amount and/or portion of bodily fluid is sequestered and/or retained within the sequestration chamber 214. As described above, in some instances, contaminants such as, for example, dermally residing microbes or the like dislodged during the venipuncture event, can be entrained and/or included in the initial volume of the bodily fluid and thus, are sequestered in the sequestration chamber 214 when the initial volume of bodily fluid is sequestered therein.

[0088] With the flow controller 215 in the second state (e.g., an impermeable or sealed state), the negative pressure otherwise exerted on or through the sequestration chamber 214 is now exerted on or through the fluid flow path 254 and thus, on the flow controller 221. In some instances, a magnitude of the negative pressure can build and/or increase within the fluid flow path 254 until the negative pressure becomes sufficient to transition the flow controller 221 from its first state to its second state. More specifically, when the flow controller 221 is a valve, the negative pressure can increase until it becomes sufficient to overcome the cracking pressure of the valve 221. As such, when the valve is placed in its open state (and/or when the flow controller 221 is otherwise in its second state), the inlet 212 is exposed to the negative pressure differential via the fluid flow path 213. With the fluid collection device fluidically

coupled to the outlet 216 and with the control device 200 being in the second state (e.g., the initial volume of bodily fluid is sequestered in or by the sequestration chamber 214), any subsequent volume(s) of the bodily fluid can flow from the inlet 212, through the fluid flow paths 213 and 254, through the flow controller 221 (e.g., valve), through the outlet 216, and into the fluid collection device. Thus, as described above, sequestering the initial volume of bodily fluid in the sequestration chamber 214 prior to collecting or procuring one or more sample volumes of bodily fluid reduces and/or substantially eliminates and amount of contaminants in the one or more sample volumes. Moreover, in some embodiments, the arrangement of the control device 200 can be such that the control device 200 cannot transition to the second state prior to collecting and sequestering the initial volume in the sequestration chamber 214.

[0089] Although not shown in FIG. 2, in some embodiments, the control device 200 can include an actuator and/or the like configured to be moved (e.g., via a force applied by a user) between a first state and a second state. In other embodiments, a control device can include any suitable member, device, mechanism, etc. configured to selectively establish fluid communication between two or more fluid flow paths (e.g., the fluid flow paths 213 and 254).

[0090] In some instances, it may be desirable to modulate and/or control a magnitude of the negative pressure differential to which the sequestration chamber 214 is exposed. Although not shown in FIG. 2, the device 200 can include one or more means for reducing and/or controlling a magnitude of the negative pressure differential. For example, in some embodiments, the device 200 can include a restricted flow path path(s) or portions of flow path(s) having a smaller diameter than the fluid flow paths 213 and/or 254. For example, in some embodiments, the one or more restricted flow paths can have a diameter of about 1.0 micrometers (μm), about 10.0 μm, about 100.0 μm, about 1000.0 μm, about 10,000.0 μm, about 100,000.0 μm, and/or any suitable diameter therebetween. In other embodiments, the restricted flow path(s) can have a diameter smaller than 1.0 μm or larger than 100,000.0 μm. In such embodiments, a restricted flow path having a smaller diameter may result in a lower magnitude of negative pressure being applied through the sequestration chamber 214 than a magnitude of negative pressure when the restricted flow path has a larger diameter. Moreover, in some such embodiments, the one or more restricted flow paths can be, for example, gas flow path(s) configured to receive a flow of gas or air but not a flow of a liquid (e.g., bodily fluid). In some embodiments, the diameter of the restricted flow path can be sufficiently small to limit and/or prevent a flow of a liquid therethrough.

[0091] In some embodiments, the restricted flow path can be, for example, disposed between the junction 218 and the flow controller 215, such that a flow of bodily fluid and/or any other liquid is substantially prevented by the flow controller 215 (e.g., a selectively permeable barrier or seal). More specifically, in some embodiments, the restricted flow path can be disposed between, for example, the flow controller 222 (e.g., valve) and the flow controller 215 (e.g., selectively permeable membrane or member). Accordingly, the flow controller 222 can be exposed to a greater magnitude of negative pressure than the magnitude of negative pressure to which the flow controller 215 is exposed. In such embodiments, the greater magnitude of negative pressure can facilitate the transition of the flow controller 222 from its first state to its second state. For example, in some embodiments, when the flow controller 222 is a valve, this arrangement can allow for the valve to be exposed to a negative pressure differential that is sufficient to overcome the cracking pressure of the valve.

[0092] Although the pressure modulation is described above as being based on a diameter of a restricted flow path, it should be understood that this is presented by way of example only and not limitation. For example, in some embodiments, a control device can include any suitable number of restricted flow paths, each of which can have substantially the same diameter or can have varied diameters. For example, in some embodiments, a control device can include up to 100 restricted flow paths or more. In such embodiments, each of the restricted flow paths can have a diameter of between about 1.0 μm and about 100.0 μm, between about 1.0 μm and about 10.0 μm, or between about 1.0 μm and about 5.0 μm. In some embodiments, multiple restricted flow paths can be configured to (1) selectively provide a flow path between the outlet 216 and the sequestration chamber 214 that exposes the sequestration chamber 214 to the negative pressure differential, and (2) act as a flow controller configured to selectively allow the passage of a gas and/or air while substantially preventing the passage of a liquid (e.g., bodily fluid). Other means of modulating the magnitude of negative pressure to which the sequestration chamber is exposed can include, for example, a porous material, a valve, a membrane, a diaphragm, a specific restriction, a vent, a deformable member or flow path, and/or any other suitable means. In some embodiments, the flow controller 215 can be a selectively permeable membrane or member having a predetermined and/or desired porosity to provide the desired amount of negative pressure modulation.

[0093] In some embodiments, modulating and/or controlling a magnitude of the pressure to which the sequestration chamber 214 is exposed can, in turn, modulate a magnitude of pressure exerted on the bodily fluid and/or within a vein of a patient. In some instances, such

pressure modulation can reduce, for example, hemolysis of a blood sample and/or a likelihood of collapsing a vein. In some instances, the ability to modulate and/or control an amount or magnitude of negative pressure can allow the control device 200 to be used across a large spectrum of patients that may have physiological challenges whereby negative pressure is often needed to facilitate collection of bodily fluid such as, for example, blood (e.g., a pressure differential between atmospheric pressure and a patient's vascular pressure may not be sufficient to facilitate consistent and sufficiently forceful flow) but not so much pressure that a rapid force flattens, collapses, caves-in, and/or otherwise inhibits patency and ability to collect blood.

[0094] FIG. 3 illustrates a fluid control device 300 according to another embodiment. The fluid control device 300 (also referred to herein as "control device" or "device") can be of any suitable shape, size, and/or configuration. For example, in some embodiments, the fluid control device 300 can be similar in at least form and/or function to the fluid control device 100 described above with reference to FIG. 1 and/or the fluid control device 200 described above with reference to FIG. 2. Accordingly, portions of the fluid control device 300 that can be similar to portions of the fluid control devices 100 and/or 200 are not described in further detail herein.

[0095] As described above with reference to the fluid control device 200 shown in FIG. 2, the fluid control device 300 shown in FIG. 3 includes an inlet 312, an outlet 316, and a sequestration chamber 314. The inlet 312 is configured to be placed in fluid communication with a bodily fluid source to receive a flow of bodily fluid therefrom (e.g., via a lumen-containing device such as a needle, IV catheter, PICC line, or the like). The outlet 316 is configured to be fluidically coupled to a fluid collection device, a syringe, an evacuated container, and/or other intermediary bodily fluid transfer device or vessel (not shown in FIG. 3) such as, for example, a transfer device similar to those described in the '510 publication. Furthermore, the control device 300 includes and/or defines one or more fluid flow paths 313 between the inlet 312 and the sequestration chamber 314 and/or one or more fluid flow paths 354 between the inlet 312 and the outlet 316.

[0096] In some embodiments, the device 300 can include a first portion 324 and a second portion 325. As shown in FIG. 3, in some embodiments, the second portion 325 can be, for example, a bypass and/or diversion portion that is physically coupled to and selectively in fluid communication with the first portion 324. Moreover, the device 300 includes and/or forms a first junction 317 at a position where a first end (e.g., an inlet end) of the second portion 325 is

coupled to the first portion 324 and includes and/or forms a second junction 318 at a position where a second end (e.g., an outlet end) of the second portion 325 is coupled to the first portion 324. That is to say, the device 300 can be configured to have and/or form a bifurcation (e.g., the second portion 325) at the first junction 317 which is rejoined at, for example, the second junction 318. In some embodiments, the first portion 324 and/or the second portion 325 of the device 300 can include and/or can be formed by flexible tubing or the like having any suitable shape and/or size and being reconfigurable or movable to be placed in any suitable configuration and/or arrangement.

[0097] As described in further detail herein, the sequestration chamber 314 is configured to (1) receive a flow and/or volume of bodily fluid from the inlet 312 and (2) sequester (e.g., separate, segregate, contain, retain, isolate, etc.) the flow and/or volume of bodily fluid therein. The sequestration chamber 314 can have any suitable shape, size, and/or configuration. For example, in some embodiments, the sequestration chamber 314 can have any suitable size, volume, and/or fluid capacity such as, for example, those described above with reference to the sequestration chamber 114 and/or 214. In some embodiments, at least a portion of the fluid flow path 313 can extend through a portion of the device 300 to form and/or define at least a portion of the sequestration chamber 314. In some embodiments, the sequestration chamber 314 of the device 300 can be substantially similar in form and/or function to one or more of the sequestration chambers 114 and/or 214. Accordingly, portions of the sequestration chamber 314 may not be described in further detail herein.

[0098] As shown in FIG. 3, the sequestration chamber 314 can be formed by and/or included in the second portion 325 of the device 300 and can be selectively placed in fluid communication with (1) the inlet 312 via the fluid flow path 313 and the first junction 317, and (2) the outlet 316 via the fluid flow path 354 and the second junction 318. As such, the sequestration chamber 314 can be configured to (1) selectively receive a flow and/or volume of bodily fluid from the inlet 312 and (2) sequester (e.g., separate, segregate, contain, retain, isolate, etc.) the flow and/or volume of bodily fluid therein.

[0099] In some embodiment, the fluid control device 300 can include and/or define one or more flow controllers. Flow controllers can include for example, valves, membranes, diaphragms, restrictors, vents, selectively permeable members (e.g., a fluid impermeable barrier or seal that allows at least selective passage of gas or air such as, for example, a blood barrier like Porex ®, and/or the like), ports, etc. (collectively referred to herein as a "flow controller") placed suitably and configured to selectively control (at least in part) a flow of

fluids into and/or out of the sequestration chamber 314 and/or any other suitable portion of the device 300. Some embodiments of the device 300, as shown in FIG. 3, can include flow controllers such as a selectively permeable member 315, a check valve 322, and a dissolvable member 323 that are arranged to, under certain states of function and/or under certain conditions, permit, direct, control, and/or obstruct the flow of fluid in one or more specific directions.

[0100] As shown in FIG. 3, the second portion 325 of the device 300 can include the check valve 322 and the selectively permeable member 315. For example, in some embodiments, the check valve 322 and/or the selectively permeable member 315 can be disposed on, at, or near a proximal or second end of the sequestration chamber 314. In other words, the check valve 322 and the selectively permeable member 315 can be positioned at, on, or near an outlet or outlet portion of the sequestration chamber 314. Said another way, the check valve 322 and/or the selectively permeable member can be positioned at, on, or near an end portion of the sequestration chamber 314 that is closer to the second junction 318 than it is to the first junction 317. In some embodiments, the check valve 322 and/or the selectively permeable member 315 can be integrated into at least a portion of the second junction 318. In some embodiments, the check valve 322 can be substantially similar to the valve 222 described above with reference to the device 200. For example, in some embodiments, the check valve 322 can be configured to have a desired cracking pressure such as those described above with reference to the valve 222. Accordingly, the check valve 322 can be configured to selectively control a flow of fluid between, for example, the fluid flow path 354 and the sequestration chamber 314, as described above with reference to the device 200. As such, the check valve 322 is not described in further detail herein. Moreover, in some embodiments, the device 300 need not include a check valve and/or any other suitable valve.

[0101] The selectively permeable member can be any suitable shape, size, and/or configuration. For example, in some embodiments, the selectively permeable member 315 can be, for example, a membrane, a porous material, an absorbent material, a hydrophilic or hydrophobic material, a selectively permeable barrier, etc. In some embodiments, the selectively permeable member 315 can be substantially similar to the flow controller 215 (e.g., selectively permeable member and/or membrane) and thus, aspects of the selectively permeable member 315 are not described in further detail herein. The selectively permeable member 315 can be configured to at least temporarily allow a gas or air to transfer from the second portion 325 of the device 300 and/or the sequestration chamber 314, through the

selectively permeable member 315 and the junction 318, and into the fluid flow path 354 and can be configured to limit and/or substantially prevent a flow of liquid (e.g., bodily fluid) between the second portion 325 and/or the sequestration chamber and the fluid flow path 354 (e.g., via the junction 318). In some embodiments, the selectively permeable member 315 can be in a first or initial state, in which the selectively permeable member 315 allows a flow of air or gas to transfer therethrough, when the device 300 is in its first state and/or configuration. As described in further detail herein, the selectively permeable member 315 can be transitioned to and/or otherwise can be in a second state or configuration, in which the selectively permeable member 315 is substantially impermeable to all fluids (gasses and/or liquids), when the device 300 is in its second state and/or configuration.

[0102] In some embodiments, the dissolvable member 323 can be situated at a suitable position within the first portion of the device 300. For example, in some embodiments, the dissolvable member 323 can be positioned at and/or near the first junction 317, as shown in FIG. 3. In some embodiments, the dissolvable member 323 can be integrated into the junction 317 and/or at least a portion of the junction 317. As such, the dissolvable member 323 can be, for example, upstream of the selectively permeable member 315.

[0103] As described in further detail herein, the dissolvable member 323 can be configured to transition from a first or initial state to a second state in response to contact with a fluid such as, for example, bodily fluid. In some embodiments, for example, the dissolvable member 323 can be disposed within and/or near the first junction 317 to isolate the inlet 312 from the fluid flow path 354 when the device 300 is in the first or initial state. In response to and/or after transferring an initial volume of bodily fluid to the sequestration chamber 314, the device 300 can be transitioned from the first or initial state to the second state. In some embodiments, when the device 300 is in the second state, the dissolvable member 323 can be substantially dissolved, which in turn, can allow fluid communication to be established between the inlet 312 and the fluid flow path 354. In some instances, for example, a portion of the bodily fluid can contact the dissolvable member 323 as the initial volume of bodily fluid flows into the sequestration chamber 314. The contact with the bodily fluid can, in turn, begin to dissolve the dissolvable member 323 such that when the device 300 is transitioned to its second state and/or configuration, the dissolvable member 323 is at least substantially dissolved, thereby placing the inlet 312 in fluid communication with the fluid flow path 354, as described in further detail herein.

[0104] As described above, the device 300 can be used to procure a bodily fluid sample having reduced contamination from microbes such as, for example, dermally residing microbes and/or the like. For example, in some instances, a user such as a doctor, physician, nurse, phlebotomist, technician, etc. can manipulate the device 300 to establish fluid communication between the inlet 312 and the bodily fluid source (e.g., a vein of a patient). Once the inlet 312 is placed in fluid communication with the bodily fluid source (e.g., the portion of the patient), the outlet 316 can be fluidically coupled to the fluid collection device. As described above, in the embodiment shown in FIG. 3, the fluid collection device can be, for example, an evacuated reservoir, a syringe, and/or any container that defines a negative pressure, or is coupled to a downstream source of negative pressure.

[0105] Coupling the outlet 316 to the fluid collection device selectively exposes at least a portion of the fluid flow path 354 to the negative pressure within the fluid collection device. The arrangement of the device 300 when in its first or initial state includes one or more flow controllers in their first state or configuration. For example, the selectively permeable member 315, the check valve 322, and the dissolvable member 323 can each be in their first states and/or configurations when the outlet 316 is coupled to the fluid collection device. In response to the negative pressure, the check valve 322 can be configured to transition from a substantially closed state (e.g., its first configuration or state) to a substantially open state (e.g., its second configuration and/or state). For example, in some instances, establishing fluid communication between the outlet 316 and the fluid collection device can expose the check valve 322 to a negative pressure differential that exceeds, for example, a cracking pressure of the check valve 322. Thus, the check valve 322 can be placed in its second state and/or configuration. In other embodiments, the device 300 need not include a check valve and/or other suitable valve. In such embodiments, the negative pressure differential otherwise operable to transition the check valve 322 would instead be exerted on the selectively permeable member 315, which is substantially similar to when the check valve 322 is in the second or opened state.

[0106] As described above, the selectively permeable member 315 and the dissolvable member 323 are each in their first state or configuration when the outlet 316 is coupled to the fluid collection device. As such, the selectively permeable member 315 can be configured to permit a flow of air, gas, and/or negative pressure therethrough while blocking and/or preventing a flow of liquid therethrough, as described above with reference to the flow controller 215. Furthermore, with the dissolvable member 323 in its first state or configuration, the dissolvable member 323 can be configured to block, isolate, and/or obstruct fluid

communication between, for example, the inlet 312 and the fluid flow path 354 such that it does not permit any flow of fluid (air or liquid or negative pressure) therethrough. Thus, coupling the outlet 316 to the fluid collection device exposes the sequestration chamber 314 to the negative pressure of the fluid collection device, thereby resulting in a negative pressure differential operable in drawing bodily fluid from the bodily fluid source (e.g., the patient), through the inlet 312, and into the sequestration chamber 314.

[0107] As described above with reference to the control devices 100 and 200, the arrangement of the device 300 is such that when a volume of bodily fluid is transferred to and/or through the inlet 312, an initial portion of the volume of bodily fluid (also referred to herein as an "initial volume" or a "first volume") flows from the inlet 312 and into the sequestration chamber 314. That is to say, in some embodiments, the device 300 is in its first or initial state in which the initial portion or volume of bodily fluid can flow from the inlet 312 and into the sequestration chamber 314 in response to the negative pressure differential associated with the fluid collection device. In other words, the negative pressure within the fluid collection device can result in a negative pressure (or negative pressure differential) within at least a portion of the sequestration chamber 314 that is operable in drawing an initial flow of bodily fluid from the inlet 312 into the sequestration chamber 314 when the control device 300 is in the first or initial state. As described in detail above, in some instances, it may be desirable to modulate and/or control a magnitude of the negative pressure differential by any suitable means such as those described herein.

[0108] The initial portion and/or amount of bodily fluid can be any suitable volume of bodily fluid, as described in detail above with reference to the control devices 100 and/or 200. For example, in some instances, the initial volume can be associated with and/or at least partially based on an amount or volume of bodily fluid that is sufficient to fully wet or saturate the membrane 315. In other words, in some embodiments, the initial volume of bodily fluid can be a volume sufficient to transition the selectively permeable member 315 to a second state (e.g., a saturated or fully wetted state). As described above with reference to the flow controller 215, the selectively permeable member 315 is placed in a sealed configuration when transitioned to the second state. Thus, transitioning the selectively permeable member 315 to the second state sequesters, blocks, isolates, separates, segregates, and/or otherwise prevents flow through the selectively permeable member 315.

[0109] After the initial volume of bodily fluid is transferred and/or diverted into the sequestration chamber 314, the control device 300 can be transitioned to its second state or

operating mode to sequester, segregate, retain, contain, isolate, etc. the initial volume in the sequestration chamber 314. As described above, the selectively permeable member 315 is placed in the sealed configuration and thus, substantially prevents a flow of fluid therethrough. In this embodiment, the arrangement of the control device 300 is such that when the selectively permeable member 315 is placed in the sealed configuration, at least a portion of the negative pressure otherwise being exerted through the selectively permeable member 315 is instead exerted on and/or in the fluid flow path 354. The negative pressure, however, can be isolated within the fluid flow path 354 until the dissolvable member 323 is transitioned from its first state and/or configuration to its second state and/or configuration (e.g., until it is at least partially dissolved).

[0110] With the selectively permeable member 315 sealed in its second state and the filling of the sequestration chamber 314 to capacity by the initial volume of bodily fluid drawn, the amount of bodily fluid held at least temporarily at and/or near the junction 317 can place a sufficient amount of bodily fluid in contact with the dissolvable member 323 to transition the dissolvable member 323 from its first state to its second state. In other words, filing the sequestration chamber 314 can place a sufficient volume or amount of bodily fluid into contact with the dissolvable member 323 to substantially dissolve the dissolvable member 323, thereby transitioning it to its second state or configuration. The transition of the dissolvable member 323, in turn, is sufficient to transition the fluid control device 300 from its first state to its second state.

[0111] With the dissolvable member 323 in its second state and/or configuration (e.g., at least partially dissolved), the negative pressure within the fluid flow path 354 can be exerted on the fluid flow path 313 and/or the inlet 312. In some embodiments, the arrangement of the dissolvable member 323 can be such that as the dissolvable member 323 is dissolved, the inlet 312 is exposed to a greater amount and/or magnitude of negative pressure. In other words, the dissolvable member 323 can be configured to dissolve of a predetermined and/or desired period of time, which in turn, can modulate and/or control an amount of negative pressure to which the inlet 312 is exposed. In some embodiments, the dissolvable member 323 can include one or more characteristics that can be tuned, adjusted, and/or the like configured to adjust (e.g., increase or decrease) a rate at which the dissolvable member 323 transitions to its second state (e.g., dissolves). As the dissolvable member 323 is transitioned to its second state and/or configuration, the negative pressure within the fluid flow path 354, urges, draws, and/or induces a flow of bodily fluid from the inlet 312 and the first junction 317, through the fluid

flow path 354 and the outlet 316, and into the fluid collection device. Moreover, the sealed state of the selectively permeable member 315 and the presence of check valves 322 (or other suitable flow controller) can limit and/or substantially prevent flow of bodily fluid from the fluid flow path 354, through the second junction 318, and toward the sequestration chamber 314. In some embodiments, the transitioning of the selectively permeable member 315 and the dissolvable member 323 from their respective first states to their respective second states is operable to sequester and/or retain the initial portion of the bodily fluid in the sequestration chamber 314. As described in further detail herein, in some instances, contaminants such as, for example, dermally residing microbes or the like dislodged during the venipuncture event, can be entrained and/or included in the initial volume of the bodily fluid and thus, are sequestered in the sequestration chamber 314 when the initial volume is sequestered therein.

[0112] With the fluid collection device fluidically coupled to the outlet 316 and with the control device 300 in the second state (e.g., the initial volume of bodily fluid is sequestered in or by the sequestration chamber 314), any subsequent volume(s) of the bodily fluid can flow from the inlet 312, through the fluid flow paths 313 and 354, through the outlet 316, and into the fluid collection device. Thus, as described above, sequestering the initial volume of bodily fluid in the sequestration chamber 314 prior to collecting or procuring one or more sample volumes of bodily fluid reduces and/or substantially eliminates and amount of contaminants in the one or more sample volumes. Moreover, in some embodiments, the arrangement of the fluid control device 300 can be such that the device 300 cannot transition to the second state prior to collecting and sequestering the initial volume in the sequestration chamber 314.

[0113] FIG. 4 illustrates a fluid control device 400 according to an embodiment. The fluid control device 400 can be of any suitable shape, size, and/or configuration. For example, in some embodiments, the fluid control device 400 can be similar in at least form and/or function to one or more of the devices 100, 200, and/or 300 described above with reference to FIG. 1, FIG. 2, and FIG. 3, respectively. Accordingly, portions of the fluid control device 400 that can be similar to portions of the fluid control devices 100, 200, and/or 300 are not described in further detail herein.

[0114] As shown in FIG. 4, the fluid control device 400 (also referred to herein as "control device" or "device") includes an inlet 412, an outlet 416, and a sequestration chamber 414. As described above with reference to the control devices 100, 200, and/or 300, the inlet 412 is configured to be placed in fluid communication with a bodily fluid source to receive a flow of bodily fluid therefrom (e.g., via a lumen-containing device such as a needle, IV catheter, PICC

line, and/or the like). The outlet 416 is configured to be fluidically coupled to fluid collection device, a syringe, a transfer adapter, and/or the like (not shown in FIG. 4). Furthermore, the control device 400 includes and/or defines one or more fluid flow paths 413 between the inlet 412 and at least the sequestration chamber 414 and/or one or more fluid flow paths 454 between the inlet 412 and the outlet 416.

[0115] In some embodiments, the device 400 can include a first portion 424 and a second portion 425. As shown in FIG. 4, in some embodiments, the second portion 425 can be, for example, a bypass and/or diversion portion that is physically coupled to and selectively in fluid communication with the first portion 424. Moreover, the device 400 includes and/or forms a first junction 417 at a position where a first end (e.g., an inlet end) of the second portion 425 is coupled to the first portion 424 and includes and/or forms a second junction 418 at a position where a second end (e.g., an outlet end) of the second portion 425 is coupled to the first portion 424. That is to say, the device 400 can be configured to have and/or form a bifurcation (e.g., the second portion 425) at the first junction 417 which is rejoined at, for example, the second junction 418. In some embodiments, the first portion 424 and/or the second portion 425 of the device 400 can include and/or can be formed by flexible tubing or the like having any suitable shape and/or size and being reconfigurable or movable to be placed in any suitable configuration and/or arrangement.

[0116] The sequestration chamber 414 can have any suitable shape, size, and/or configuration. For example, in some embodiments, the sequestration chamber 414 can have any suitable size, volume, and/or fluid capacity such as, for example, those described above with reference to the sequestration chamber 114. In some embodiments, the sequestration chamber 414 of the device 400 can be substantially similar in form and/or function to one or more of the sequestration chambers 114, 214, and/or 314. Accordingly, portions of the sequestration chamber 414 may not be described in further detail herein.

[0117] As shown in FIG. 4, the sequestration chamber 414 can be formed by and/or included in the second portion 425 of the device 400 and can be selectively placed in fluid communication with (1) the inlet 412 via the fluid flow path 413 and the first junction 417, and (2) the outlet 416 via the fluid flow path 454 and the second junction 418. As such, the sequestration chamber 414 can be configured to (1) selectively receive a flow and/or volume of bodily fluid from the inlet 412 and (2) sequester (e.g., separate, segregate, contain, retain, isolate, etc.) the flow and/or volume of bodily fluid therein.

[0118] The second portion 425 of the device 400 and/or the sequestration chamber 414 specifically, can include, form, and/or define a flow controller 415 disposed on, at, or near a proximal or second end of the sequestration chamber 414. In other words, the flow controller 415 can be positioned at, on, or near an outlet or outlet portion of the sequestration chamber 414. Said another way, the flow controller can be positioned at, on, or near an end portion of the sequestration chamber 414 that is closer to the second junction 418 than it is to the first junction 417. In some embodiments, the flow controller 415 can be, for example, a membrane, a porous material, an absorbent material, a hydrophilic or hydrophobic material, a selectively permeable barrier, etc. The flow controller 415 can be any suitable shape, size, and/or configuration. In some embodiments, the flow controller 415 can be substantially similar to the flow controller 215 and/or the flow controller 315 and thus, is not described in further detail herein.

[0119] As described in detail above, the flow controller 415 is positioned within the second portion 425 of the device to selectively establish fluid communication between the second portion 425 and/or the sequestration chamber 414 and the outlet 416 via the junction 418. Thus, with the flow controller 415 configured to selectively control fluid flow therethrough (e.g., configured as a semi-permeable member), the flow controller 415 can be configured to at least temporarily allow a gas or air to transfer from the second portion 425 of the device 400 and/or the sequestration chamber 414, through the flow controller 415 and the junction 418, and into the fluid flow path 454 and can be configured to limit and/or substantially prevent a flow of liquid (e.g., bodily fluid) between the second portion 425 and/or the sequestration chamber and the fluid flow path 454 (e.g., via the junction 418), as described in further detail herein.

[0120] As described above with reference to the devices 100, 200, and/or 300, the device 400 can include one or more flow controllers that is/are configured to selectively control a flow of gas or liquid (e.g., air or bodily fluid, respectively) through the device 400. For example, in the embodiment illustrated in FIG. 4, the device 400 includes a first flow restrictor 431 and a second flow restrictor 432. The flow restrictors 431 and 432 (and/or any other suitable flow controllers that may be included but not illustrated in FIG. 4) can be included at predetermined and/or desired positions along the first portion 424 and/or the second portion 425 of the device 400 to control, manipulate, divert, and/or direct the flow of air, liquid (e.g., bodily fluid), and/or negative pressure. The flow restrictors 431 and 432 can be configured with varying flow permitting or flow obstructing properties. For example, in some embodiments, the flow restrictor 431 and/or the flow restrictor 432 can have and/or can define any suitable inner cross-

sectional shape, size, and/or configuration to selectively allow fluid flow therethrough, as described in further detail herein.

[0121] In the embodiment shown in FIG. 4, the flow restrictors 431 and 432 each can be a flow restrictor configured to define a flow path therethrough having one or more specific, desired, and/or predetermined characteristics. Moreover, in some embodiments, the second flow restrictor 432 (e.g., the flow restrictor positioned between the second junction 418 and the sequestration chamber 414) can have a flow path that is less restrictive than the flow path of the first flow restrictor 431 (e.g., the flow restrictor positioned between the outlet 416 and the first junction 417). In other words, a pressure differential sufficient to allow fluid (e.g., a gas or liquid) to pass through the second flow restrictor 432 can be less than a pressure differential sufficient to allow fluid (e.g., gas or liquid) to pass through the first flow restrictor 431. Accordingly, the first flow restrictor 431 and the second flow restrictor 431 can be similar to the first valve 221 and second valve 222 described above with reference to FIG. 2.

[0122] As described in further detail herein, the arrangement of the flow restrictors 431 and 432 can be such that when a source of negative pressure (e.g., a fluid collection device and/or the like) is coupled to the outlet 416, the negative pressure differential can result in a flow through the second flow restrictor 432 prior to a flow through the first flow restrictor 431. In some instances, this sequential opening of the flow restrictors (e.g., the flow restrictor 432 before the flow restrictor 431), can be operable to direct a flow of fluid (e.g., a first flow) towards the sequestration chamber 414 and then direct the flow of fluid (e.g., a second flow) towards the fluid collection device and/or negative pressure source coupled to the outlet 416. Said another way, in some embodiments, the device 400 can be configured to transition between a first state in which (1) the inlet 412 is placed in fluid communication with the second portion 425 of the device 400 (e.g., the sequestration chamber 414) and (2) the second flow restrictor 432 establishes selective fluid communication between the sequestration chamber 414 and the outlet 416, and a second state in which (1) the second flow restrictor 432 isolates the sequestration chamber 414 from the outlet 416 and (2) the first flow restrictor 431 establishes selective fluid communication between the inlet 412 and the first portion 424 of the device 400 and/or the outlet 416.

[0123] As described above, with respect to devices 100, 200, and 300, the device 400 can be used to procure a bodily fluid sample having reduced contamination. In some instances, a user such as a doctor, physician, nurse, phlebotomist, technician, etc. can manipulate the device 400 to establish fluid communication between the inlet 412 and the bodily fluid source (e.g., a

vein of a patient). For example, in some embodiments, the user can couple the inlet 412 to an inlet device, a needle, an indwelling catheter or IV, and/or any other suitable lumen-containing device. Once the inlet 412 is placed in fluid communication with the bodily fluid source (e.g., the portion of the patient), the outlet 416 can be fluidically coupled to the fluid collection device. As described herein, the fluid collection device can be any suitable reservoir, syringe, pump, and/or device configured to define and/or produce a negative pressure. In other embodiments, the outlet 416 can be coupled to the fluid collection device, which in turn, is coupled to a downstream source of negative pressure.

[0124] The control device 400 can be in a first or initial state prior to coupling the outlet 416 to the fluid collection device. Coupling the outlet 416 to the fluid collection device selectively exposes at least a portion of the fluid flow path 454 to the negative pressure within the fluid collection device. For example, with the device 400 in its initial or first state, the flow controller 415 can be in its first state or configuration such that the flow controller 415 is permeable to a flow of air or gas but impermeable to a flow of liquid (e.g., bodily fluid). Moreover, the arrangement of the flow restrictors 431 and 432 is such that the first flow restrictor 431 is more restrictive toward a flow of liquid or air therethrough than is the second flow restrictor 432.

[0125] The negative pressure differential defined and/or produced by the fluid collection device results in a suction or drawing of fluid (e.g., air or gas) from the fluid flow path 454. In other words, the negative pressure within and/or produced by the fluid collection device results in a negative pressure differential within the fluid flow path 454. The arrangement of the flow restrictors 431 and 432, and the flow controller 415 can be such that the negative pressure differential within the fluid flow path 454, results in a negative pressure differential through and/or across the outlet 416, the second junction 418, the second flow restrictor 432, the flow controller 415, and the sequestration chamber 414. Moreover, with the first flow restrictor 431 configured to be more restrictive than the second flow restrictor 432, the flow through the second flow restrictor 432 can at least partially maintain a magnitude of the negative pressure within the fluid flow path 454 below a threshold magnitude of negative pressure otherwise operable to induce a flow of fluid through the first flow restrictor 431. That is to say, when the device 400 is in the first state, the negative pressure within the fluid flow path 454 is sufficient to result in a flow through the second flow restrictor 432 but is insufficient to result in a flow through the first flow restrictor 431. Accordingly, the negative pressure within and/or produced by the fluid collection device (coupled to the outlet 416) can draw air and/or gas through the

flow controller 415 and the second flow restrictor 432 and into the fluid flow path 454. Although not shown in FIG. 4, in some embodiments, the device 400 can include a vent or one-way valve configured to allow the air or gas withdrawn from the sequestration chamber 414 to be vented to the atmosphere. In other embodiments, the air and/or gas can be transferred to the fluid collection device, which in turn, can directly or indirectly allow the air or gas to be vented. Thus, the negative pressure within and/or produced by the fluid collection device can result in a negative pressure (or negative pressure differential) within at least a portion of the sequestration chamber 414.

[0126] The negative pressure within the sequestration chamber 414 can be operable in drawing an initial flow of bodily fluid from the inlet 412, through the fluid flow path 413 and the first junction 417, and into the sequestration chamber 414 when the control device 400 is in the first or initial state. In some instances, it may be desirable to modulate and/or control a magnitude of the negative pressure differential by any suitable means such as those described herein, including manipulating the permissibility and/or permeability of flow restrictors 431 and/or 432 and/or the flow controller 415. In some embodiments, the flow restrictors 431 and/or 432 can be configured to have one or more external actuators, controllers, and/or adjusters configured to control the amount of flow through the flow restrictors 431 and/or 432 (e.g., by altering or adjusting an inner diameter of the flow restrictors 431 and/or 432). In some other embodiments, the flow restrictors 431 and/or 432 can be configured to adjust and/or alter their properties of permitting fluid flow therethrough based on time, interaction with one or more fluids, and/or any other suitable parameter. In some embodiments, the structure of the flow restrictors 431 and/or 432 can be manipulated (e.g., squeezed, squished, pinched, compressed, etc.) to modulate the degree of negative pressure.

[0127] In some embodiments, modulating and/or controlling a magnitude of the pressure to which the sequestration chamber 414 is exposed can, in turn, modulate a magnitude of pressure (i.e., negative pressure) exerted on the bodily fluid and/or within a vein of a patient. In some instances, such pressure modulation can reduce, for example, hemolysis of a blood sample and/or a likelihood of collapsing a vein. In some instances, the ability to modulate and/or control an amount or magnitude of negative pressure can allow the control device 400 to be used across a large spectrum of patients that may have physiological challenges whereby negative pressure is often needed to facilitate collection of bodily fluid such as, for example, blood but not so much pressure that a rapid force flattens, collapses, caves-in, and/or otherwise inhibits patency and ability to collect blood, as described above.

[0128] The initial portion and/or amount of bodily fluid can be any suitable volume of bodily fluid, as described in detail above with reference to the control devices 100, 200, and/or 300. For example, in some instances, the initial volume can be associated with and/or at least partially based on an amount or volume of bodily fluid that is sufficient to fully wet or saturate the flow controller 415. In other words, in some embodiments, the initial volume of bodily fluid can be a volume sufficient to transition the flow controller 415 to a second state (e.g., a saturated or fully wetted state or a sealed state), in which the flow controller 415 is placed in a sealed state and/or configuration. In some embodiments, transitioning the flow controller 415 to the second state sequesters, blocks, isolates, separates, segregates, and/or otherwise prevents a flow of air, gas, and/or liquid (e.g., bodily fluid) through the flow controller 415.

[0129] After the initial volume of bodily fluid is transferred and/or diverted into the sequestration chamber 414, the control device 400 can be in and/or can be placed in its second state or operating mode to sequester, segregate, retain, contain, isolate, etc. the initial volume in the sequestration chamber 414. As described above, the flow controller 415 in its second state or sealed state substantially prevents a flow of fluid including air and liquid therethrough (e.g., and into the second flow restrictor 432 and/or fluid flow path 454). Therefore, the sequestration chamber 414 is fluidically isolated from the fluid collection device and/or source of negative pressure, which in turn, can allow a pressure differential between the sequestration chamber 414 and, for example, the inlet 412 to equalize such that the flow of bodily fluid to the sequestration chamber 414 is limited and/or substantially stops.

[0130] As described previously, an amount of negative pressure sufficient to induce and/or allow a flow of fluid through the first flow restrictor 431 can be greater than an amount of negative pressure sufficient to induce and/or allow a flow of fluid through the second flow restrictor 432. In this embodiment, the arrangement of the control device 400 is such that when the flow controller 415 is placed in the second or sealed configuration, at least a portion of the negative pressure otherwise being exerted through the flow controller 415 builds and/or increases within the fluid flow path 454 to an extent sufficient to induce and/or allow a flow of fluid through the first flow restrictor 431. Thus, with the device 400 in its second state, the negative pressure exerted by the fluid collection device and/or negative pressure source can result in negative pressure within the fluid flow path 454 sufficient to allow bodily fluid to flow from the inlet 412, through the first flow restrictor 431, the fluid flow path 454, and the outlet 416, and into the fluid collection device. As described above, in some instances, contaminants such as, for example, dermally residing microbes or the like dislodged during the venipuncture

event, can be entrained and/or included in the initial volume of the bodily fluid and thus, are sequestered in the sequestration chamber 414. Moreover, as described for devices 100, 200, 300, in some embodiments, the arrangement of the fluid control device 400 can be such that the device cannot transition to the second state prior to collecting and sequestering the initial volume in the sequestration chamber 414.

[0131] While the flow restrictors 431 and 432 are particularly described above with reference to FIG. 4, in other embodiments, a fluid control device can include other forms of flow controllers and/or restrictors in addition to and/or instead of those described in association with device 400. In some embodiments, a fluid control device can include any other suitable means or combination of means for controlling fluid flow therethrough. For example, FIGS. 5-7 illustrate three different embodiments of flow controllers and/or flow restrictors, each according to a different embodiment. FIG. 5 shows a flow restrictor 433 defining an orifice or channel for the passage of air and/or fluid. In this embodiment, the fluid restrictor 433 can have a relatively large inner diameter and a relatively long length. FIG. 6, on the other hand, shows a flow restrictor 434 defining an orifice or channel having a relatively small inner diameter (e.g., smaller than the inner diameter of the flow restrictor 433) and a relatively short length (e.g., shorter than the length of the flow restrictor 433).

[0132] As will be understood, adjusting a length and/or diameter of an orifice or channel of a flow restrictor can allow for an adjusting of a magnitude of a pressure differential sufficient to induce and/or result in a flow of fluid (e.g., bodily fluid) through the orifice or channel. For example, in some embodiments, a flow restriction and/or a restricted flow path can have a diameter of about 1.0 micrometers (μm), about 10.0 μm, about 100.0 μm, about 1000.0 μm, about 10,000.0 μm, about 100,000.0 μm, and/or any suitable diameter therebetween. In other embodiments, the restricted flow path can have a diameter smaller than 1.0 μm or larger than 100,000.0 μm. In such embodiments, a restricted flow path having a smaller diameter may be designed such that a magnitude of a pressure (e.g., negative pressure) sufficient to induce or draw a flow of fluid through the restricted flow path is greater than a magnitude of a pressure sufficient to induce or draw a flow of fluid through a restricted flow path having a larger diameter. Similarly, a longer restricted flow path may be designed such that a magnitude of a pressure (e.g., negative pressure) sufficient to induce or draw a flow of fluid through the restricted flow path is greater than a magnitude of a pressure sufficient to induce or draw a flow of fluid through a restricted flow path having a shorter length.

[0133] FIG. 7 shows a flow controller 435 including a porous material 436 disposed within the flow controller 435. In such embodiments, a porosity and/or permeability of the porous material 436 can be adjusted to adjust a magnitude of a pressure differential sufficient to induce and/or result in a flow of fluid (e.g., bodily fluid) through the orifice or channel. Other examples of flow restrictors and/or flow controllers can include but are not limited to, flow controllers where the restricted or restrictive regions include regions with varying diameter of the cross-section permitting fluid flow or include structures (e.g., porous material) designed to selectively allow or deter fluid flow or air flow as desired. Other embodiments can include, for example, valves, actuators, selectively permeable membranes and/or materials, and/or the like.

[0134] FIGS. 8-10 illustrate a fluid control device 500 according to an embodiment. FIG. 8 shows, for example, a top view of the device 500 and FIGS. 9 and 10 each show a cross-sectional view of the device 500, in a first state and a second state, respectively. The fluid control device 500 can be similar in at least form and/or function to any of the fluid control devices 100, 200, 300, and/or 400. Accordingly, portions of the fluid control device 500 that can be similar to portions of the fluid control devices 100, 200, 300, and/or 400 are not described in further detail herein.

[0135] As shown in FIGS. 8-10, the fluid control device 500 (also referred to herein as "control device" or "device") includes an inlet 512 and an outlet 516, and a sequestration chamber 514. As described above with reference to the control devices 100, 200, 300, and/or 400, the inlet 512 is configured to be placed in fluid communication with a bodily fluid source to receive a fluid of bodily fluid therefrom (e.g., via a lumen-containing device such as a needle or the like). The outlet 516 is configured to be fluidically coupled to a fluid collection device (not illustrated). The inlet 512, the outlet 516, and the fluid collection device can be substantially similar to those described above and thus, are not described in further detail herein.

[0136] As described above, the control device 500 is configured to (1) receive an initial flow and/or volume of bodily fluid via the inlet 512 and (2) sequester (e.g., separate, segregate, contain, retain, isolate, etc.) the flow and/or volume of bodily fluid within the sequestration chamber 514. The device 500 can be any suitable shape, size, and/or configuration. In some embodiments, the device 500 can have a size that is at least partially based on a volume of bodily fluid at least temporarily stored, for example, in the sequestration chamber 514. For example, in the embodiment shown in FIGS. 8-10, the device 500 can be arranged in and/or

can have a substantially "inline" configuration in which portions of the device 500 are at least partially aligned.

[0137] The device 500 includes and/or defines one or more fluid flow paths 513 between the inlet 512 and at least the sequestration chamber 514 and/or one or more fluid flow paths 554 between the inlet 512 and the outlet 516. In some embodiments, the device 500 can include a first portion 524 and a second portion 525. As shown in FIGS. 9 and 10, in some embodiments, the second portion 525 can be, for example, a bypass and/or diversion portion that is physically coupled to and selectively in fluid communication with the first portion 524. Moreover, the device 500 includes and/or forms a junction 517 at a position where each of a first end (e.g., an inlet end) of the first portion 524 and a first end (e.g., an inlet end) of the second portion 525 couple to the inlet 512. In some embodiments, the first portion 524 and the second portion 525 can be collectively disposed in a housing or otherwise at least partially enclosed by a common structure. In other embodiments, the first portion 524 and/or the second portion 525 of the device 500 can include and/or can be formed by flexible tubing or the like having any suitable shape and/or size and being reconfigurable or movable to be placed in any suitable configuration and/or arrangement.

[0138] The sequestration chamber 514 can have any suitable shape, size, and/or configuration. For example, in some embodiments, the sequestration chamber 514 can have any suitable size, volume, and/or fluid capacity such as, for example, those described above with reference to the sequestration chamber 114. The sequestration chamber 514 can be formed by and/or included in the second portion 525 of the device 500 and can be selectively placed in fluid communication with (1) the inlet 512 via the fluid flow path 513 and the first junction 517, and (2) the outlet 516 via the fluid flow path 554 and a flow controller 515 (described in further detail herein). In some embodiments, the sequestration chamber 514 of the device 500 can be substantially similar in form and/or function to one or more of the sequestration chambers 114, 214, 314, and/or 414. Accordingly, portions of the sequestration chamber 514 may not be described in further detail herein.

[0139] As shown in FIGS. 9 and 10, the second portion 525 of the device 500 and/or the sequestration chamber 514 specifically, can include, form, and/or define the flow controller 515 disposed on, at, or near a proximal or second end of the sequestration chamber 514. In other words, the flow controller 515 can be positioned at, on, or near an outlet or outlet portion of the sequestration chamber 514 to establish selective fluid communication between the sequestration chamber 514 and the fluid flow path 554. The flow controller 515 can be any

suitable shape, size, and/or configuration. In some embodiments, the flow controller 515 can be, for example, a membrane, a porous material, an absorbent material, a hydrophilic or hydrophobic material, a selectively permeable barrier, etc. In some embodiments, the flow controller 515 can be configured to at least temporarily allow a gas or air to transfer from the second portion 525 of the device 500 and/or the sequestration chamber 514, through the flow controller 515, and into the fluid flow path 554 and can be configured to limit and/or substantially prevent a flow of liquid (e.g., bodily fluid) between the second portion 525 and/or the sequestration chamber 514 and the fluid flow path 554. In some embodiments, the flow controller 515 can be substantially similar in at least form and/or function to the flow controllers 215, 315, and/or 415 and thus, aspects of the flow controller 515 are not described in further detail herein.

[0140] In some embodiments, the device 500 can include one or more flow controllers in addition to the flow controller 515 configured to selectively control, direct, divert, and/or manipulate fluid flow through at least a portion of the flow paths 513 and/or 554. In some embodiments, such flow controllers can be configured to selectively control a flow of fluid through the device 500 in response to, for example, an external force or actuation (e.g., manual intervention by the user), or automatically (e.g., after a period of time and/or in response to a predetermined force, pressure, flow rate, volume of fluid, saturation level, etc. For example, in this embodiment, the device 500 includes a diaphragm 576 movably disposed within the body of the device 500 and configured to at least partially define the sequestration chamber 514. In some embodiments, the diaphragm 576 can be configured to transition, flip, move, switch, deform, etc., from a first configuration or state (FIG. 9) to a second configuration or state (FIG. 10) in response to a negative pressure differential within and/or across at least a portion of the device 500 (e.g., a negative pressure differential associated with and/or resulting from the coupling of the fluid collection device to the outlet 516).

[0141] In some embodiments, the diaphragm 576 can be coupled to a piercing member 578 and configured to move through at least a portion of the device 500 in response to movement of the diaphragm 576. As shown in FIGS. 9 and 10, the device 500 includes a film, barrier, and/or frangible member 574 (referred to herein as "barrier") configured to at least temporarily isolate, separate, and/or sequester the fluid flow path 513 (e.g., an inlet fluid flow path) from the fluid flow path 554 (e.g., an outlet fluid flow path). In some embodiments, the arrangement of the diaphragm 576 and/or the piercing member 578 can be such that as the diaphragm 576 is transitioned from its first state, configuration, and/or position to its second state,

configuration, and/or position, the piercing member 578 is transitioned and/or moved through a portion of the device 500 to pierce, puncture, rupture, break, and/or otherwise reconfigure the barrier 574.

[0142] More specifically, as shown in FIG. 9, the diaphragm 576 can have, for example, a concave shape relative to the barrier 574 when in its first or initial state and the piercing member 578 coupled to the diaphragm 576 is disengaged with and/or separated from the barrier 574. As such, the barrier 574 can be in a first or initial state in which the barrier 574 is sealed, unbroken, not punctured, and/or otherwise acting to fluidically isolate the fluid flow path 513 from the fluid flow path 554. As shown in FIG. 10, the diaphragm 576 can have, for example, a convex shape relative to the barrier 574 when in its second or subsequent state and the piercing member 578 coupled to the diaphragm 576 is engaged with, in contact with, and/or otherwise reconfiguring the barrier 574, thereby piercing through and/or defining an opening through the barrier 574. In other words, as illustrated in FIGS. 9 and 10 respectively, the device 500 and/or the diaphragm 576 is configured to move between a first or initial state in which the fluid flow path 513 is fluidically isolated and/or sequestered from the fluid flow path 554 such that a flow of fluid (e.g., bodily fluid) can flow from the inlet 512, through at least a portion of the fluid flow path 513, and into the sequestration chamber 514, and a second or subsequent state in which the fluid flow path 513 is in fluid communication with the fluid flow path 554 such that a flow of fluid (e.g., bodily fluid) can flow from the inlet 512, through the barrier 574 and the fluid flow path 554, and to the outlet 516. In some embodiments, the transitioning of the device 500 and/or diaphragm 576 from the first state to the second state can be such that a volume of the device 500 defined between the diaphragm 576, the flow controller 515, and the one or more walls of the sequestration chamber 514 is increased (i.e., a volume of the sequestration chamber 514 is increased), which in turn, results in a negative pressure therein that can be operable in drawing at least a portion of the initial volume of bodily fluid through the inlet 512 and into the sequestration chamber 514, as described further below.

[0143] As described above, with respect to devices 100, 200, 300, and/or 400, the device 500 can be used to procure a bodily fluid sample having reduced contamination. For example, in some instances, the control device 500 can be in the first or initial state and a user can manipulate the device 500 to establish fluid communication between the inlet 512 and the bodily fluid source (e.g., a vein of a patient) and to establish fluid communication between the outlet 516 and the fluid collection device (e.g., a sample vessel, syringe, reservoir, etc.). With the device 500 in its initial or first state, coupling the outlet 516 to the fluid collection device

selectively exposes at least a portion of the fluid flow path 554 to the negative pressure within the fluid collection device. Moreover, when the device 500 is in its initial or first state, the flow controller 515 can be in its first state or configuration such that the flow controller 515 is permeable to a flow of air or gas but impermeable to a flow of liquid (e.g., bodily fluid). The barrier 574 is also in its first or initial state such that the barrier 574 fluidically isolates the fluid flow path 513 from the fluid flow path 554. As such, the negative pressure differential defined and/or produced by the fluid collection device results in a suction force within the fluid flow path 554, which in turn, is exerted on or through the flow controller 515. Thus, coupling the outlet 516 to the fluid collection device exposes the sequestration chamber 514 to the negative pressure defined and/or produced by the fluid collection device, thereby resulting in a negative pressure differential operable in drawing the initial volume and/or amount of bodily fluid from the bodily fluid source (e.g., the patient's vasculature), through the inlet 512, at least a portion of the fluid flow path 513, and the junction 517, and into the sequestration chamber 514. Although not shown in FIGS. 8-10, in some embodiments, the device 500 can include any suitable device and/or mechanism configured to modulate the negative pressure to which the sequestration chamber 514 is exposed, as described in detail above.

[0144] The initial portion and/or amount of bodily fluid can be any suitable volume of bodily fluid, as described in detail above with reference to the control devices 100, 200, 300, and/or 400. For example, in some instances, the initial volume can be associated with and/or at least partially based on an amount or volume of bodily fluid that is sufficient to fully wet or saturate the flow controller 515 (e.g., transition the flow controller 515 from its first or selectively open state to its second or sealed state). With the flow controller 515 in its second state or sealed state, the flow controller 515 substantially prevents a flow of fluid including air and liquid therethrough, thereby sequestering and/or fluidically isolating the sequestration chamber 514 from the fluid flow path 554. As a result, in some instances, a pressure differential between, for example, the sequestration chamber 514 and the inlet 512 can equalize such that the flow of bodily fluid to the sequestration chamber 514 is limited and/or substantially stops.

[0145] In this embodiment, the arrangement of the control device 500 is such that when the flow controller 515 is placed in the second or sealed configuration, at least a portion of the negative pressure otherwise being exerted through the flow controller 515 builds and/or increases within the fluid flow path 554 to an extent sufficient to transition the diaphragm 576 from its first state or configuration (FIG. 9) to its second state or configuration (FIG. 10). In some embodiments, for example, the diaphragm 576 can flip and/or can be moved from a

concave configuration relative to the barrier 574 to a convex configuration relative to the barrier 574. Moreover, as described above, the transitioning of the diaphragm 576, in turn, moves the piercing member 578 such that the piercing member 578 engages, pierces, punctures, opens, breaks, and/or otherwise reconfigures the barrier 574, thereby placing the fluid flow path 513 in fluid communication with the fluid flow path 554. Thus, with the device 500 in its second state, the negative pressure exerted by the fluid collection device and/or negative pressure source can result in negative pressure within the fluid flow path 554 sufficient to allow bodily fluid to flow from the inlet 512, through the fluid flow path 513, barrier 574, fluid flow path 554, and outlet 516, and into the fluid collection device.

[0146] As described above, in some instances, contaminants such as, for example, dermally residing microbes or the like dislodged during the venipuncture event, can be entrained and/or included in the initial volume of the bodily fluid and thus, are sequestered in the sequestration chamber 514. Moreover, as described for devices 100, 200, 300, and/or 400, in some embodiments, the arrangement of the fluid control device 500 can be such that the device cannot transition to the second state prior to collecting and sequestering the initial volume in the sequestration chamber 514.

[0147] While the flow controller 515 is shown in FIGS. 8-10 as being in fluid communication with the fluid flow path 554 without a feature, device, mechanism, and/or means to modulate an amount of negative pressure disposed therebetween, in other embodiments, a fluid control device can include any suitable feature, device, mechanism, and/or means configured to modulate an amount or magnitude of negative pressure to which a flow controller is exposed. For example, FIGS. 11 and 12 are schematic illustrations of a fluid control device 600 in a first state and a second state, respectively, according to another embodiment. The fluid control device 600 (also referred to herein as "control device" or "device") can be any suitable shape, size, and/or configuration. For example, in some embodiments, the device 600 can be substantially similar in at least form and/or function to any of the devices 100, 200, 300, 400, and/or 500 described herein. More particularly, the device 600 can be substantially similar in at least form and/or function to the device 500 described above with reference to FIGS. 8-10. Accordingly, portions and/or aspects of the fluid control device 600 are not described in further detail herein.

[0148] As shown in FIGS. 11 and 12, the device 600 includes an inlet 612, an outlet 616, and a sequestration chamber 614. In addition, the device 600 includes and/or defines one or more fluid flow paths 613 between the inlet 612 and at least the sequestration chamber 614

and/or one or more fluid flow paths 654 between the inlet 612 and the outlet 616. The inlet 612 is configured to be placed in fluid communication with a bodily fluid source to receive a fluid of bodily fluid therefrom. The outlet 616 is configured to be fluidically coupled to a fluid collection device substantially similar to those described above. The sequestration chamber 614 can be included in and/or formed by a portion of the device 600 and can be selectively placed in fluid communication with (1) the inlet 612 via the fluid flow path 613, and (2) the outlet 616 via the fluid flow path 654 and a flow controller 615. The flow controller 615 can be any suitable shape, size, and/or configuration and can be configured to selectively control, permit, allow, and/or transfer a flow of fluid therethrough. For example, as described above, the flow controller 615 can be a selectively permeable member configured to be selectively permeable to a gas (e.g., air) and substantially impermeable to a liquid (e.g., bodily fluid). In some embodiments, the inlet 612, the outlet 616, the sequestration chamber 614, and the flow controller 615 can be substantially similar to the inlet 512, the outlet 516, the sequestration chamber 514, and the flow controller 515, respectively, described above with reference to the device 500 shown in FIGS. 8-10. Accordingly, portions and/or aspects of the inlet 612, the outlet 616, the sequestration chamber 614, and/or the flow controller 615 are not described in further detail herein.

[0149] In some embodiments, the device 600 can include a first portion 624 and a second portion 625. As shown in FIGS. 11 and 12, in some embodiments, the second portion 625 can be, for example, a bypass and/or diversion portion that (1) is physically coupled to and selectively in fluid communication with the first portion 624 and (2) includes and/or forms the sequestration chamber 614. Moreover, the device 600 includes and/or forms a junction 617 at a position where each of a first end (e.g., an inlet end) of the first portion 624 and a first end (e.g., an inlet end) of the second portion 625 couple to the inlet 612. In some embodiments, the first portion 624 and the second portion 625 can be collectively disposed in a housing or otherwise at least partially enclosed by a common structure. In other embodiments, the first portion 624 and/or the second portion 625 of the device 600 can include and/or can be formed by flexible tubing or the like having any suitable shape and/or size and being reconfigurable or movable to be placed in any suitable configuration and/or arrangement.

[0150] As described above with reference to the device 500, the device 600 includes a diaphragm 676 movably disposed within at least a portion of the device 600 and a piercing member 678 coupled to the diaphragm 676. In some embodiments, the diaphragm 676 can define at least a portion of the sequestration chamber 614. In some embodiments, the

diaphragm 676 and the piercing member 678 can be substantially similar in at least form and/or function to the diaphragm 576 and piercing member 578, respectively, of the device 500. For example, as described above with reference to the diaphragm 576 of the device 500, the diaphragm 676 is configured to transition between a first state, in which the fluid flow path 613 is fluidically isolated from the fluid flow path 654, and a second state, in which the fluid flow path 613 is in fluid communication with the fluid flow path 654, as described in further detail herein.

[0151] While the device 500 is shown and described above as including a single barrier 574 configured to selectively isolate and/or otherwise selectively prevent fluid communication between the fluid flow paths 513 and 554, in the embodiment shown in FIGS. 11 and 12, the device 600 includes a set of barriers configured to selectively prevent or selectively allow fluid flow through the device 600. For example, in some embodiments, the device 600 can include two barriers 674 and 675. Each of the barriers 674 and 675 can be substantially similar in at least form and/or function to the barrier 574 of the device 500 described above with reference to FIGS. 9 and 10. Accordingly, the arrangement of the device 600 can be such that when the diaphragm 676 is in its first state, the piercing member 678 can be disengaged and/or separated from the barriers 674 and 675, which in turn, remain in a sealed, closed, and/or substantially undeformed state (FIG. 11). As the diaphragm 676 is transitioned to its state, however, the piercing member 678 can be moved within the device 600 such that the piercing member 678 engages, contacts, pierces, punctures, and/or otherwise reconfigures each of the barriers 674 and 675, thereby transitioning the barriers 674 and 675 to an unsealed, opened, pierced, and/or deformed state (FIG. 12), as described in further detail herein.

[0152] As described above, the device 600 can include one or more features, mechanisms, devices, and/or means of modulating a negative pressure exerted through one or more portions of the device 600. For example, as shown in FIGS. 11 and 12, the device 600 includes and/or defines a restricted flow path 631 (also referred to herein as a "flow restrictor") configured to establish fluid communication between, for example, the flow controller 615 and the fluid flow path 654. As described above with reference to the flow restrictors 431 and 432 of the device 400 shown in FIG. 4, the flow restrictor 631 can be configured to define a restricted and/or limited flow path therethrough having one or more specific, desired, and/or predetermined characteristics. As described in further detail herein, the arrangement of the flow restrictor 631 can be such that when a source of negative pressure (e.g., a fluid collection device and/or the like) is coupled to the outlet 616, a negative pressure differential can result in a restricted and/or

modulated flow or suction force through the flow restrictor 631, which in turn, results in a restricted and/or modulated negative pressure being exerted on the flow controller 615. Accordingly, the flow restrictor 631 can be substantially similar in at least form and/or function to the flow restrictor 432 described above with reference to FIG. 4.

[0153] As described above with respect to devices 100, 200, 300, 400, and/or 500, the device 600 can be used to procure a bodily fluid sample having reduced contamination. For example, in some instances, the control device 600 can be in the first or initial state (see e.g., FIG. 11) and a user can manipulate the device 600 to establish fluid communication between the inlet 612 and the bodily fluid source (e.g., a vein of a patient) and to establish fluid communication between the outlet 616 and the fluid collection device (e.g., a sample vessel, syringe, reservoir, etc.). With the control device 600 in its first or initial state, coupling the outlet 616 to the fluid collection device selectively exposes at least a portion of the fluid flow path 654 to the negative pressure within the fluid collection device. When the control device 600 is in the first state, the diaphragm 676, the flow controller 615, and the barriers 674 and 675 each can be in their respective first states. Accordingly, the diaphragm 676 can be disposed in a position and/or state such that the piercing member 678 is separated and/or disengaged from the barriers 674 and 675. As such, the barriers 674 and 675 are in their first or sealed state such that the barrier 674 (e.g., a first barrier) fluidically isolates and/or sequesters the fluid flow path 613 from the flow restrictor 631 (e.g., restricted flow path) and such that the barrier 675 (e.g., a second barrier) fluidically isolates and/or sequesters the fluid flow path 613 (e.g., an inlet flow path) from the fluid flow path 654 (e.g., an outlet flow path), as shown in FIG. 11.

[0154] With the fluid collection device coupled to the outlet 616, the negative pressure within the fluid collection device can result in a negative pressure (or negative pressure differential) within at least a portion of the fluid flow path 654. As shown in FIG. 11, however, the barrier 675 fluidically isolates at least a portion of the fluid flow path 654 from other portions of the device 600 and thus, the negative pressure within the fluid flow path 654 is transferred and/or exerted through the flow restrictor 631. Accordingly, a modulated and/or desired portion of the negative pressure within and/or produced by the fluid collection device (coupled to the outlet 616) is transferred through the flow restrictor 631 and in turn, exerted on the flow controller 615. Moreover, with the flow controller 615 in its first state (e.g., a selectively permeable state), the modulated and/or desired portion of the negative pressure within and/or produced by the fluid collection device can result in a negative pressure (or

negative pressure differential) within at least a portion of the sequestration chamber 614 that is operable in drawing an initial flow of bodily fluid from the inlet 612, through at least a portion of the fluid flow path 613, and into the sequestration chamber 614, as described above with reference to, for example, the devices 100, 200, 300, 400, and/or 500.

[0155] The initial portion and/or amount of bodily fluid can be any suitable volume of bodily fluid, as described in detail above with reference to the control devices 100, 200, 300, 400, and/or 500. For example, in some instances, the initial volume can be associated with and/or at least partially based on an amount or volume of bodily fluid that is sufficient to fully wet or saturate the flow controller 615 (e.g., transition the flow controller 615 from its first or selectively open state to its second or sealed state). With the flow controller 615 in its second or sealed state, the flow controller 615 substantially sequesters, blocks, isolates, separates, segregates, and/or otherwise prevents a flow of fluid (e.g., gas and liquid) through the flow controller 615, thereby sequestering and/or fluidically isolating the sequestration chamber 614 from the fluid flow path 654. As a result, in some instances, a pressure differential between, for example, the sequestration chamber 614 and the inlet 612 can equalize such that the flow of bodily fluid to the sequestration chamber 614 is limited and/or substantially stops.

[0156] As described above with reference to the device 500, the arrangement of the control device 600 is such that when the flow controller 615 is placed in its second or sealed state, at least a portion of the negative pressure otherwise being exerted through the flow controller 615 is instead exerted on a concave side or surface of the diaphragm 676. The increased negative pressure on the concave side and/or surface of the diaphragm 676 can be operable to flip, switch, and/or transition the diaphragm 676 from its first state (e.g., a concave state relative to the barrier 674) to its second state (e.g., a convex state relative to the barrier 674). In some embodiments, the flow restrictor 631 can be configured to modulate and/or regulate a magnitude or change in magnitude of the negative pressure being exerted on the diaphragm 676 in substantially the same manner as the modulation and/or regulation of the negative pressure being exerted on or through the flow controller 615. In some instances, modulating the negative pressure exerted on the diaphragm 676 can in turn, modulate, reduce, and/or control a rate at which the diaphragm 676 is transitioned from its first state to its second state.

[0157] As described above, the transitioning of the diaphragm 676, in turn, moves the piercing member 678 coupled thereto such that the piercing member 678 engages, pierces, punctures, opens, breaks, and/or otherwise reconfigures each of the barriers 674 and 675 such that each barrier 674 and 675 is placed in an open state and/or otherwise defines an opening

through which fluid can flow. In other embodiments, the barrier 674 can be configured to form a substantially fluid tight seal with an outer surface of the piercing member 678 as the piercing member 678 extends therethrough. Moreover, as described above with reference to the device 500, the opening of the barrier 675 places the fluid flow path 613 in fluid communication with the fluid flow path 654. As such, the device 600 can be in and/or can be placed in its second state, and the negative pressure exerted by the fluid collection device and/or negative pressure source can result in negative pressure within the fluid flow path 654 sufficient to allow bodily fluid to flow from the inlet 612, through the fluid flow path 613, barrier 675, fluid flow path 654, and outlet 616, and into the fluid collection device (not shown). As described above, in some instances, contaminants such as, for example, dermally residing microbes or the like dislodged during the venipuncture event, can be entrained and/or included in the initial volume of the bodily fluid and thus, are sequestered in the sequestration chamber 614. Moreover, as described for devices 100, 200, 300, 400, and/or 500, in some embodiments, the arrangement of the fluid control device 600 can be such that the device cannot transition to the second state prior to collecting and sequestering the initial volume in the sequestration chamber 614.

[0158] While the device 600 is described above as including the piercing member 678 that pierces the barrier 675 to place the device 600 in the second state, in other embodiments, a device can include any suitable member configured to transition any suitable barrier. For example, FIGS. 13 and 14 illustrate a device 700 according to an embodiment. The device 700 can be substantially similar to the device 600 and thus, similar portions are not described in further detail herein. The device 700 (FIGS. 13 and 14) can differ from the device 600 (FIGS. 11 and 12), however, by including a diaphragm 776 that includes and/or that is coupled to a rod, a pusher, a plunger, an actuator, and/or the like (referred to herein for simplicity as an "actuator"). Moreover, rather than including the barriers 674 and 675 that are configured to be pierced, as described above with reference to the device 600), the device 700 includes barriers 774 and 775 that can have any suitable shape, size, and/or configuration and that can be transitioned, in some instances, in any suitable manner. For example, the barrier 774 can be configured and/or otherwise disposed to form a substantially fluid tight seal with one or more inner surfaces of the device 700 and with one or more outer surfaces of the actuator 778. In this manner, the barrier 774 can limit and/or substantially prevent bodily fluid from undesirably flowing out of a fluid flow path 754 and into other portions of the device 700 (e.g., in a manner similar to that described above with reference to the barrier 674).

[0159] As shown in FIG. 13, when the device 700 is in a first state, the diaphragm 776 can be in a first state (e.g., a non-flipped, unactuated, and/or initial state). Similarly, the actuator 778 coupled to the diaphragm 776 and the barrier 775 can be in a first or initial state. As described in detail above with reference to the device 600, when the barrier 775 is in the first state, a flow path 713 of the device 700 (e.g., an inlet flow path or the like) can be sequestered from the flow path 754 (e.g., an outlet flow path or the like). In other words, the barrier 775 (e.g., a flow controller) can be configured to sequester the flow path 713 from the flow path 754. Thus, when a negative pressure is generated within a portion of the device 700 (e.g., in response to coupling a fluid collection device to an outlet of the device 700), an initial volume of bodily fluid can flow into a sequestration chamber of the device 700 (e.g., a sequestration portion of the device 700, a sequestration flow path, a sequestration reservoir or container, etc.), as described in detail above with reference to the device 600.

[0160] After the initial volume of bodily fluid is received in the sequestration chamber, the arrangement of the device 700 can be such that the diaphragm 776 flips, actuates, moves, and/or otherwise transitions from the first state (FIG. 13) to a second state (FIG. 14). As described in detail above, the movement of the diaphragm can result in a similar movement of the actuator 778 such that the actuator 778 is placed in contact with and moves and/or otherwise transitions the barrier 775 within the device 700. For example, as shown in FIG. 14, the actuator 778 can move the barrier 775 in a substantially linear motion from a first position to a second position, which in turn, can be a position in which the barrier 775 no longer sequesters the flow path 713 from the flow path 754. Thus, a subsequent volume of bodily fluid that is substantially free of contaminants can flow through the device 700 and into the fluid collection device coupled thereto. In this manner, the device 700 can be substantially similar in at least form and/or function to the device 600 and thus, is not described in further detail herein.

[0161] Referring now to FIG. 15, a flowchart is shown illustrating a method 10 of using a fluid control device, such as those described herein, to divert an initial volume of bodily fluid to procure bodily fluid samples with reduced contamination, according to an embodiment. The fluid control device (also referred to herein as "control device") can be similar to and/or substantially the same as any of the control devices 100, 200, 300, 400, 500, 600, and/or 700 described herein.

[0162] The method 10 includes establishing fluid communication between a bodily fluid source and an inlet of the control device, at 11. In some instances, for example, the bodily fluid source can be a fluid source within a patient's body. More specifically, in some instances, the

bodily fluid source can be a vein and/or vascular structure in the patient's body. As described above, the control device can be configured to couple to and/or include an inlet device such as, for example, an intravenous catheter, a butterfly needle, and/or the like. In other embodiments, the inlet device can be any suitable coupler, port, etc. configured to fluidically couple to the bodily fluid source. As such, the inlet device can be manipulated to establish fluid communication between the bodily fluid source and the fluid control device, as described in detail above.

[0163] Having established fluid communication with the bodily fluid source, an initial volume of bodily fluid is transferred from the bodily fluid source to a sequestration chamber included in and/or defined by the control device when the control device is in a first state, at 12. In some embodiments, the control device or a portion thereof (e.g., the sequestration chamber, a junction, an actuator, a flow controller, etc.) is in a first state and/or configuration prior to use. As such, establishing fluid communication with the bodily fluid source automatically establishes fluid communication with the sequestration chamber. More particularly, in some embodiments, a flow controller such as, for example, a valve, a flow restrictor, a selectively permeable member, and/or the like can be in a first state and/or configuration such a flow of at least a gas can pass and/or can be conveyed therethrough.

[0164] As described in detail herein, the initial volume can be any suitable volume of bodily fluid. For example, in some instances, the initial volume can be as small as one drop of bodily fluid (or a relatively few drops of bodily fluid). In other instances, the initial volume can be, for example, up to about 30 mL, 40 mL, 50 mL, or more. Moreover, as described in detail above with reference to specific embodiments, the initial volume can be at least partially based on and/or can be associated with an amount of bodily fluid that can be contained and/or sequestered in the sequestration chamber. In some instances, the initial volume can be at least partially based on and/or associated with a desired amount of fluid sufficient to transition the control device from an initial or first state to a subsequent or second state, using a negative pressure differential defined and/or produced by a negative pressure source coupled to the outlet of the fluid control device. In some instances, the initial volume can be at least partially based on and/or associated with a desired amount of fluid sufficient to transition one or more flow controllers included in the fluid control device from its/their first state to its/their second state. For example, in some instances one or more flow controllers can be driven and/or transitioned by a pressure differential, a predetermined and/or desired fluid volume, a fluid contact, the passage of predetermined and/or desired time, and/or the like, as described herein.

In some instances, the initial volume can be a volume that is sufficient to entrain and/or contain substantially all the undesired microbes that may have been dislodged and/or the like as the fluid communication was being established between the bodily fluid source and the inlet device.

[0165] In response to the initial volume of bodily fluid being disposed in the sequestration chamber, the control device is transitioned (e.g., automatically, passively, or in response to an actuation) from the first state to the second state to sequester the initial volume of bodily fluid in the sequestration chamber, at 13. In some embodiments, for example, the initial volume of bodily fluid can fill the sequestration chamber such that any additional volume of bodily fluid is substantially prevented from entering and/or being contained in the sequestration chamber. In such embodiments, the filled sequestration chamber can form, for example, a fluid lock or the like that substantially prevents additional amounts of bodily fluid from entering the sequestration chamber and/or that substantially prevents bodily fluid from exiting the sequestration chamber. In some embodiments, the sequestration chamber can include a membrane or material interacting with the bodily fluid (e.g., a semi-permeable membrane or the like such as described above with reference to the control devices 100, 200, 300, 400, 500, 600, and/or 700). In some embodiments, the sequestration chamber and/or device can include one or more flow controllers that can be activated (e.g., diaphragms as described with reference to control device 500, 600, and/or 700, and/or any other suitable flow controller) that are activated using any suitable mechanism to draw, divert, and/or sequester bodily fluid. For example, such flow controllers can use a change in a pressure differential (e.g., a pressure differential that can occur when portions of the flow path are sealed and/or closed off from interacting with bodily fluid), as described with reference to control device 500, 600, and/or 700, or can be user activated or activated on the basis of other variables like time, gravity, or the like.

[0166] In some instances, two or more of these mechanisms can be used in combination. For example, in some embodiments, the diversion and/or sequestration of bodily fluid can be carried out using passive mechanisms (e.g., based on one or more pressure differentials and/or filling of the sequestration chamber). In other embodiments, the diversion and sequestration or fluid can also result from one or more active methods such as, for example, one or more actuators operated with or without user intervention. In some embodiments, one or more user mediated mechanisms, actuators, controllers, etc. can be included to provide additional control functions such as, for example, a supervisory or safety override function that may be used in

certain settings such as, for example, during training of personnel on the use of the control devices. In other embodiments, the sequestration chamber can retain and/or sequester the initial volume of bodily fluid in any suitable manner such as those described herein and/or any suitable combination(s) thereof.

[0167] With the control device being transitioned to the second state (e.g., passively or through user intervention), a subsequent volume of bodily fluid is transferred from the bodily fluid source to a fluid collection device (e.g., any of those described herein) in fluid communication with the control device, at 14. As described in detail above, the sequestering of the initial volume of bodily fluid in the sequestration chamber can be operable to sequester any contaminants contained in the initial volume of bodily fluid in the sequestration chamber. Accordingly, the subsequent volume of bodily fluid transferred to the fluid collection device is substantially free of contaminants.

[0168] Referring now to FIG. 16, a flowchart is shown illustrating a method 20 of using a fluid control device, such as those described herein, to divert an initial volume of bodily fluid to procure bodily fluid samples with reduced contamination, according to an embodiment. The fluid control device (also referred to herein as "control device") can be similar to and/or substantially the same as any of the control devices 100, 200, 300, 400, 500, 600, and/or 700 described herein. In some embodiments, for example, the fluid control device can include an inlet configured to be placed in fluid communication with a bodily fluid source and an outlet configured to be coupled to a fluid collection device. Moreover, the fluid control device can include a sequestration portion that is in fluid communication with the inlet and a sampling portion that is in fluid communication with the outlet.

[0169] The method 20 includes coupling a fluid collection device to the outlet of the fluid control device, at 21. The fluid collection device can be any of those described herein. For example, in some embodiments, the fluid collection device can be an evacuated container, sample bottle, syringe, and/or the like. Moreover, the coupling of the fluid collection device to the outlet can be such that a negative pressure differential is produced and/or generated within at least a portion of the fluid control device, as described in detail above.

[0170] A first flow controller of the fluid control device is transitioned from a first state to a second state when the negative pressure differential within the fluid control device has a first magnitude, at 22. As described above, the first flow controller can be a valve, selectively permeable material, restricted flow path, and/or the like configured to sequester the

sequestration portion of the fluid control device from the outlet when in the first state and to establish fluid communication between the sequestration portion and the outlet when in the second state, as described in detail above.

[0171] An initial volume of bodily fluid is received from the inlet of the fluid control device and into the sequestration portion of the fluid control device in response to the negative pressure differential when the first flow controller is in the second state, at 23. In some instances, for example, the inlet can be in fluid communication with a bodily fluid source such as a bodily fluid source within a patient's body (e.g., a vein and/or vascular structure in the patient's body). In some embodiments, for example, the inlet can be coupled to an inlet device such as, for example, an intravenous catheter, a butterfly needle, and/or the like, which in turn, is inserted into a portion of the patient. Thus, bodily fluid can flow from the bodily fluid source, through the inlet of the fluid control device, and into the sequestration portion.

[0172] The first flow controller is transitioned from the second state to a third state in response to the sequestration portion receiving the initial volume of bodily fluid, at 24. As described in detail herein, the initial volume can be any suitable volume such as, for example, a volume as small as one drop of bodily fluid (or a relatively few drops of bodily fluid) up to, for example, 50.0 mL or more. In some instances, the initial volume can be at least partially based on and/or associated with a desired amount of fluid sufficient to transition the first flow controller from the second state to the third state. In some instances, the initial volume can be a volume of bodily fluid that is transferred into the sequestration portion until a negative pressure differential (e.g., between the first flow controller and the inlet) is in substantial equilibrium or the like. In such instances, the first flow controller can automatically transitioned from the second state to the third state when the negative pressure differential operable to draw the initial volume of bodily fluid is in substantial equilibrium. In some embodiments, the first flow controller can include, for example, a selectively permeable material that can be saturated by at least a portion of the initial volume of bodily fluid to transition the first flow controller from the second state to the third state, as described in detail above. As such, the first flow controller can sequester the sequestration portion from the outlet when in the third state.

[0173] With the first flow controller in the third state, the negative pressure differential within a portion of the fluid control device can increase from the first magnitude to a second magnitude. When the negative pressure differential has the second magnitude, a second flow controller is transitioned from a first state to a second state, at 25. The second flow controller

can be configured to, for example, sequester the sampling portion of the fluid control device from the inlet when in the first state and is configured to establish fluid communication between the sampling portion and the inlet when in the second state. As described above with reference to specific embodiments, the second flow controller can be any suitable control device or mechanism such as, for example, a valve, a selectively permeable material, a restricted flow path, a dissolvable material, a frangible barrier, a movable barrier, and/or the like.

[0174] As described above, a pressure differential sufficient to transition the second flow controller from the first state (e.g., a non-flow state) to the second state (e.g., a flow state) is greater than a pressure differential sufficient to transition the first flow controller from the first state (e.g., a non-flow state) to the second state (e.g., a flow state). As such, the second flow controller can be configured to transition to the second state after the first flow controller has transitioned between its first, second, and third states. Thus, a subsequent volume of bodily fluid is transferred from the inlet to the fluid collection device via the sampling portion and the outlet, at 26. As described in detail above, receiving the initial volume of bodily fluid in the sequestration portion and sequestering the sequestration portion from the outlet can be operable to sequester any contaminants contained in the initial volume of bodily fluid in the sequestration portion of the fluid control device. Accordingly, the subsequent volume of bodily fluid transferred to the fluid collection device can have reduced contamination and/or can be substantially free of contaminants.

[0175] While various embodiments have been described above, it should be understood that they have been presented by way of example only, and not limitation. Where schematics and/or embodiments described above indicate certain components arranged in certain orientations or positions, the arrangement of components may be modified. While the embodiments have been particularly shown and described, it will be understood that various changes in form and details may be made. For example, while the control devices 100, 200, 300, 400, 500, 600, and/or 700, are described as transferring a bodily fluid into the device as a result of a negative pressure within a fluid collection device, in other embodiments, the devices described herein can be used with any suitable device configured to establish a pressure differential (e.g., a negative pressure differential). For example, in some embodiments, an outlet of a control device can be coupled to a syringe or pump. In other embodiments, a control device can include a pre-charged sequestration chamber, a vented sequestration chamber, a manually activated device configured to produce a negative pressure, an energy source, and/or

any other suitable means of defining and/or forming a pressure differential within a portion of the control device.

[0176] In some other embodiments, the source of negative pressure can be associated with but independent of the fluid collection device. For example, a source of negative pressure such as a syringe, a pump, a passive source like a gravity aided or structurally aided container, etc., can be placed downstream of the outlet of the fluid control device such that the negative pressure imparted is communicated to the fluid collection device and the outlet. For example the source of negative pressure may be in fluid communication with the outlet via the fluid collection device. In other embodiments, under some circumstances, the source of negative pressure may be placed in fluid communication with the outlet to impart the pressure differential and the outlet may then be placed in fluid communication with the collection device to collect the fluid drawn by the pressure differential imparted, as described in further detail herein.

[0177] In some embodiments, any of the fluid control devices described herein can be formed from any suitable components that can be manufactured, sterilized, and packaged as individual parts or components. In such embodiments, a user can, for example, open one or more packages containing one or more components, can assemble the components to form the fluid control device, and can use the fluid control device as described above. In other embodiments, any of the fluid control devices described herein can be formed from any suitable components that can be manufactured, sterilized, assembled, and packaged as an assembly or integrated device. In such embodiments, a user can, for example, open a packaging containing such an assembly or integrated device and can use the device as described above without further assembly of components. In some embodiments, any of the control devices can be monolithically formed in whole or at least in part.

[0178] In some embodiments, any of the control devices can be physically and/or fluidically coupled to a collection device (e.g., a sample reservoir, a syringe, a blood culture bottle, a collection vial, a fluid transfer container, and/or any other suitable reservoir, collection device, and/or transfer device) by a user prior to or during use, as described in detail above. In other embodiments, any of the control devices can be physically coupled, attached, formed, and/or otherwise mated to a fluid collection device during a manufacturing process. This can be done prior to sterilization so the collection pathway(s) and connection interface(s) (e.g., where the control device couples to the fluid collection device) maintain a closed-system,

mechanical diversion device within a sterile environment that is not subject to touch-point contamination from external sources.

[0179] In some embodiments, the pre-assembly of the control device and the collection device can be such that the user is forced first to sequester, segregate, and/or isolate at least a portion of the initial bodily fluid volume or flow prior to transferring a sample volume to the pre-assembled fluid collection device. For example, the control device can include an actuator that is configured to isolate an outlet from other portions of the control device, thereby isolating the collection device from such portions of the control device. Moreover, after transferring the initial volume of bodily fluid, the actuation of the actuator can result in sequestration of the initial volume of bodily fluid and the fluidic coupling of the outlet to additional portions of the control device (e.g., an inlet). In some embodiments, pre-assembling the control device and the collection device (e.g., during manufacturing) can, for example, force compliance with a sample procurement protocol that calls for the sequestration of an initial amount of bodily fluid prior to collecting a sample volume of bodily fluid.

[0180] In some embodiments, the coupling, mating, and/or attachment of the fluid control device to the fluid collection device (e.g., during manufacturing) can be executed such that the control device can be removed (physically decoupled, removed with a specific "key," and/or any other approach used to separate the control device from the fluid collection device) after use to allow access to the fluid collection device. After decoupling, the collection device can be placed in an incubator and/or any other type of analytical machine, and accessed for analysis and/or otherwise further processed. In some embodiments, such decoupling may be blocked, limited, and/or substantially prevented prior to use and unblocked or allowed after use. In other embodiments, the fluid control device and the fluid collection device can be permanently coupled and/or monolithically formed (at least in part) to prevent such decoupling.

[0181] Any of the embodiments described herein can be used in conjunction with any suitable fluid transfer, fluid collection, and/or fluid storage device such as, for example, the fluid reservoirs described in the '420 patent, the transfer devices described in the '510 publication, and/or the transfer adapters described in the '352 publication. In some embodiments, any of the embodiments described herein can be used in conjunction with fluid transfer, fluid collection, and/or fluid storage devices such as, for example, the devices described in U.S. Patent No. 8,535,241 entitled, "Fluid Diversion Mechanism for Bodily-Fluid Sampling," filed October 12, 2012; U.S. Patent No. 9,060,724 entitled, "Fluid Diversion Mechanism for Bodily-Fluid Sampling," filed May 29, 2013; U.S. Patent No. 9,155,495

entitled, "Syringe-Based Fluid Diversion Mechanism for Bodily-Fluid Sampling," filed December 2, 2013; U.S. Patent Publication No. 2016/0361006 entitled, "Devices and Methods for Syringe Based Fluid Transfer for Bodily-Fluid Sampling," filed June 13, 2016; U.S. Patent Publication No. 2018/0140240 entitled, "Systems and Methods for Sample Collection with Reduced Hemolysis," filed November 20, 2017; and/or U.S. Patent Publication No. 2017/0065733 entitled, "Apparatus and Methods for Maintaining Sterility of a Specimen Container," filed September 6, 2016, the disclosures of each of which are incorporated herein by reference in their entireties.

[0182] While some of the embodiments described above include a flow controller that selectively establishes fluid communication between a sequestration chamber and a fluid collection device (or other source of negative pressure) in other embodiments, a control device can be arranged to transfer a flow of bodily fluid in response to negative pressure differentials resulting from any suitable portion(s) of the device. For example, while the control device 200 is described above as including the flow controllers (e.g., the membrane 215, and/or the like) that place the sequestration chamber 214 in selective fluid communication with the fluid collection device (e.g., a sample reservoir or syringe) until the membrane 215 is transitioned to a sealed or closed state (e.g., until the membrane 215 is sufficiently wetted), in other embodiments, a control device can include a sequestration chamber that is a pre-sealed, evacuated, and/or pre-charged chamber such that establishing fluid communication between an inlet and the sequestration chamber results in a negative pressure differential that is sufficient to draw an initial volume of bodily fluid into the sequestration chamber. In such embodiments, the control device can be configured to transfer bodily fluid to the sequestration chamber until the pressure differential is sufficiently reduced and/or until pressures otherwise substantially equalize. Moreover, in some such embodiments, the sequestration chamber and/or the inlet can include a coupler, an actuator, a needle, a septum, a port, and/or any other suitable member that can establish fluid communication therebetween (e.g., that can transition the sequestration chamber from a sealed to an unsealed configuration).

[0183] While the embodiments have been described above as including particular means for modulating and/or controlling a magnitude of negative pressure applied on or through at least a portion of the device(s), in other embodiments, a control device can include any suitable feature, mechanism, and/or device configured to modulate, create, and/or otherwise control one or more pressure differentials through at least a portion of the control device. For example, in some embodiments, a user can transition and/or move an actuator to change (e.g., reduce or

increase) the size of one or more portions of a fluid flow path or fluid flow interface within a portion of the control device to manually modulate and/or otherwise control an amount or magnitude of negative pressure within one or more portions of a control device.

[0184] By way of another example, any of the embodiments described herein can include any suitable actuator and/or flow controller configured to selectively control fluid flow through at least a portion of the device. Specifically, a flow controller or the like can be one or more of a selectively permeable material or membrane, a valve, a diaphragm, and/or any other suitable flow controller. While some of the embodiments have been described as including an actuator rod configured to be transitioned from a first configuration or position to a second configuration or position, in other embodiments, any actuator described herein can include an actuator rod configured to transition from between a first position and second position to at least temporarily isolate an outlet from of the device from one or more other portions of the device. In some embodiments, such an actuator can be configured for use with a given and/or predetermined collection device such as, for example, a syringe. In other embodiments, such an actuator can be used with any suitable collection device.

[0185] While the embodiments have been described above as including or coupling to an inlet device such as a needle or the like that is configured to puncture the skin of a patient to place the lumen of the needle in fluid communication with a vein in the patient, in other embodiments, a fluid control device can include and/or can couple to any suitable inlet device. For example, in some embodiments, an inlet device can include a trocar or the like and a catheter. The trocar is configured to puncture the skin of a patient and then configured to be withdrawn from the patient, leaving the catheter of the inlet device placed within the patient. In other embodiments, the inlet device need not puncture the skin of a patient. For example, in some embodiments, the inlet device can include a needle or catheter that can be placed in a dish, well, sample volume, container, reservoir, etc. In still other embodiments, the inlet device can be and/or can include a coupler or port configured to couple to an indwelling needle or intravenous catheter. In other embodiments, such a coupler or port can be configured to couple to any suitable bodily fluid source (or port thereof) such as, for example, a syringe, a reservoir, a container, etc.

[0186] Accordingly, while the embodiments are described above as withdrawing and sequestering an initial volume of bodily fluid to sequester contaminants such as, for example, dermally-residing microbes, in other embodiments, the inlet device can be coupled to any suitable bodily fluid source and the control device can be configured to sequester an initial

volume of bodily fluid withdrawn from that bodily fluid source to sequester contaminants that may be present within the source and/or any an interface of the container or reservoir containing the bodily fluid. For example, in some embodiments, a needle of an inlet device can be configured to puncture a port or surface of a reservoir to place the needle in fluid communication with an interior volume of the container or device. In such embodiments, the devices described herein can be used to sequester an initial volume of bodily fluid from the bodily fluid source, which in turn, can sequester contaminants or the like that may have been present on the interface, port, or surface that was punctured. Thus, the devices and methods described herein can be used to procure bodily fluid samples having reduced contamination from any suitable bodily fluid source. Moreover, while some such contaminants are described herein as being dermally residing microbes, it should be understood that the contaminants can be any contaminant that is, for example, exterior to the bodily fluid source and/or otherwise that is or that includes any constituent component (e.g., microbe, virus, molecule, particle, element, etc.) that is otherwise foreign to the bodily fluid.

[0187] Although various embodiments have been described as having particular features, concepts, and/or combinations of components, other embodiments are possible having any combination or sub-combination of any features, concepts, and/or components from any of the embodiments described herein. For example, as described above, the device 700 includes concepts, features, and/or elements of the device 600, the device 600 includes concepts, features, and/or elements of the device 500, and the device 400 includes concepts, features, and/or elements of the devices 200 and 300. The specific configurations of the various components can also be varied. For example, the size and specific shape of the various components can be different from the embodiments shown, while still providing the functions as described herein. More specifically, the size and shape of the various components can be specifically selected for a desired rate and/or volume of bodily fluid flow into a fluid reservoir. Likewise, the size and/or shape of the various components can be specifically selected for a desired or intended usage. Thus, it should be understood that the size, shape, and/or arrangement of the embodiments and/or components thereof can be adapter for a given use unless the context explicitly states otherwise.

[0188] In some embodiments, the specific configurations of the various components can also be varied. For example, the size and specific shape of the various components can be different from the embodiments shown, while still providing the functions as described herein. More specifically, the size and shape of the various components can be specifically selected

for a desired rate and/or volume of bodily fluid flow into a fluid reservoir. Likewise, the size and/or shape of the various components can be specifically selected for a desired or intended usage. For example, in some embodiments, a device such as those described herein can be configured for use with or on seemingly healthy adult patients. In such embodiments, the device can include a sequestration chamber that has a first volume (e.g., about 0.5 ml to about 5.0 ml). In other embodiments, a device such as those described herein can be configured for use with or on, for example, very sick patients and/or pediatric patients. In such embodiments, the device can include a sequestration chamber that has a second volume that is less than the first volume (e.g., less than about 0.5 ml). Thus, it should be understood that the size, shape, and/or arrangement of the embodiments and/or components thereof can be adapted for a given use unless the context explicitly states otherwise.

[0189] Although not shown, any of the devices described herein can include an opening, port, coupler, septum, Luer-Lok, gasket, valve, threaded connecter, standard fluidic interface, etc. (referred to for simplicity as a "port") in fluid communication with the sequestration chamber. In some such embodiments, the port can be configured to couple to any suitable device, reservoir, pressure source, etc. For example, in some embodiments, the port can be configured to couple to a reservoir, which in turn, can allow a greater volume of bodily fluid to be diverted and/or transferred into the sequestration chamber. In other embodiments, the port can be coupled to a negative pressure source such as an evacuated container, a pump, a syringe, and/or the like to collect a portion of or the full volume of bodily fluid in the sequestration chamber, channel, reservoir, etc. and use that volume of bodily fluid (e.g., the pre-sample volume) for additional clinical and/or in vitro diagnostic testing purposes. In other embodiments, the port can be coupled to any suitable pressure source or infusion device configured to infuse the initial volume of bodily fluid sequestered in the sequestration chamber back into the patient and/or bodily fluid source (e.g., in the case of pediatric patients, very sick patients, patients having a low blood volume, and/or the like).

[0190] In some embodiments, the port can be configured to receive a probe, sampling tool, testing device, and/or the like that can be used to perform one or more tests (e.g., tests not sensitive to potential contamination) on the initial volume while the initial volume is disposed or sequestered in the sequestration chamber. In other embodiments, the sequestration channel, chamber, and/or reservoir can be configured with the addition of other diagnostic testing components integrated into the chamber (e.g., a paper test) such that the initial bodily fluid is used for that test. In still other embodiments, the sequestration chamber, channel, and/or

reservoir can be designed, sized and configured to be removable and compatible with testing equipment and/or specifically accessible for other types of bodily fluid tests commonly performed on patients with suspected conditions. By way of example, a patient with suspected sepsis commonly has blood samples collected for lactate testing, procalcitonin testing, and blood culture testing. All of the fluid control devices described herein can be configured such that the sequestration chamber, channel, reservoir, etc. can be removed (e.g., after receiving the initial volume of bodily fluid) and the bodily fluid contained therein can be used for these additional testing purposes before or after the subsequent sample is collected for microbial testing.

[0191] Although not shown, in some embodiments, a fluid control device can include one or more lumen, channels, flow paths, etc. configured to selectively allow for a "bypass" flow of bodily fluid, where an initial amount or volume of bodily fluid can flow from the inlet, through the lumen, cannel, flow path, etc. to bypass the sequestration chamber, and into the collection device. In some embodiments, the fluid control device can include an actuator having, for example, at least three states – a first in which bodily fluid can flow from the inlet to the sequestration chamber, a second in which bodily fluid can flow from the inlet to the outlet after the initial volume is sequestered in the sequestration chamber, and a third in which bodily fluid can flow from the inlet, through the bypass flow path, and to the outlet. In other embodiments, the control device can include a first actuator configured to transition the device between a first and second state, as described in detail above with reference to specific embodiments, and can include a second actuator configured to transition the device to a bypass configuration or the like. In still other embodiments, the control device can include any suitable device, feature, component, mechanism, actuator, controller, etc. configured to selectively place the fluid control device in a bypass configuration or state.

[0192] In some embodiments, a method of using a fluid control device employing an external negative pressure source can include the ordered steps of establishing fluid communication between a bodily fluid source (e.g., a vein of a patient or the like) and an inlet of the fluid control device. An outlet of the fluid control device is then placed in fluid communication with and/or otherwise engages a negative pressure source. Such a negative pressure source can be a sample reservoir, a syringe, an evacuated container, an intermediate transfer device, and/or the like. The fluid control device can be in a first state or operating mode when the outlet is coupled to the negative pressure source and, as such, a negative pressure differential is applied through at least a portion of the fluid control device that can be

operable to draw an initial volume of bodily fluid into a sequestration chamber of the fluid control device. Once the initial volume of bodily fluid is disposed in the sequestration chamber, the fluid control device is transitioned, either automatically or via user intervention, from the first state or operating mode to a second state or operating mode such that (1) the initial volume is sequestered in the sequestration chamber and (2) fluid communication is established between the inlet and the outlet. The sequestration of the initial volume can be such that contaminants entrained in the flow of the initial volume are likewise sequestered within the sequestration chamber. With the initial volume of bodily fluid sequestered in the sequestration chamber and with fluid communication established between the inlet and the outlet, subsequent volumes of bodily fluid that are substantially free of contamination can be collected in one or more sample reservoirs.

[0193] While the method of using the fluid control device is explicitly described as including the recited ordered steps, in other embodiments, the ordering of certain events and/or procedures in any of the methods or processes described herein may be modified and such modifications are in accordance with the variations of the invention. Additionally, certain events and/or procedures may be performed concurrently in a parallel process when possible, as well as performed sequentially as described above. Certain steps may be partially completed or may be omitted before proceeding to subsequent steps.

[0194] For example, while the devices are described herein as transitioning from a first state to a second state in a discrete operation or the like, it should be understood that the devices described herein can be configured to automatically and/or passively transition from the first state to the second state and that such a transitioning may occur over a period of time. In other words, the transitioning from the first state to the second state may, in some instances, be relatively gradual such that as a last portion of the initial volume of bodily fluid is being transferred into the sequestration chamber, the housing begins to transition from the first state to the second state. In some instances, the rate of change when transitioning from the first state to the second state can be selectively controlled to achieve one or more desired characteristics associated with the transition. Moreover, in some such instances, the inflow of the last portion of the initial volume can limit and/or substantially prevent bodily fluid already disposed in the sequestration chamber from escaping therefrom. Accordingly, while the transitioning from the first state to the second state may occur over a given amount of time, the sequestration chamber can nonetheless sequester the volume of bodily fluid disposed therein.

What is claimed:

1. A fluid control device, comprising:

an inlet configured to be placed in fluid communication with a bodily fluid source;

an outlet configured to be placed in fluid communication with a fluid collection device, a negative pressure differential being produced between the outlet and the inlet when the outlet is placed in fluid communication with the fluid collection device;

a sequestration portion in fluid communication with the inlet, the sequestration portion including a first flow controller configured to transition from a first state in which the sequestration portion is sequestered from the outlet to a second state in which the sequestration portion is in fluid communication with the outlet when the negative pressure differential has a first magnitude; and

a sampling portion in fluid communication with the outlet, the sampling portion including a second flow controller configured to transition from a first state in which the sampling portion is sequestered from the inlet to a second state in which the sampling portion is in fluid communication with the inlet when the negative pressure differential has a second magnitude greater than the first magnitude.

2. The system of claim 1, wherein the fluid collection device is a sample bottle, the sample bottle being at least partially evacuated such that coupling the outlet to the sample bottle generates the negative pressure differential.

3. The system of claim 1, wherein the fluid collection device is a syringe that is configured to be manipulated after the outlet is coupled to the syringe to generate the negative pressure differential.

4. The system of claim 1, wherein the first flow controller is configured to transition from the first state to the second state automatically.

5. The system of claim 1, wherein the second flow controller is configured to transition from the first state to the second state automatically.

6. The system of claim 1, wherein the sequestration portion is configured to receive an initial volume of bodily fluid withdrawn from the bodily fluid source in response to the first flow controller transitioning to the second state.

7. The system of claim 6, wherein the first flow controller has a third state in which the sequestration portion is sequestered from the outlet, the first flow controller configured to transition from the second state to the third state as a result of the sequestration portion receiving the initial volume of bodily fluid.

8. The system of claim 7, wherein the first flow controller being placed in the third state results in an increase in a magnitude of the negative pressure differential within the sampling portion from the first magnitude to the second magnitude.

9. The system of claim 7, wherein the first flow controller includes a selectively permeable material, the selectively permeable material configured to (1) allow a flow of a gas and prevent a flow of bodily fluid through the selectively permeable material when in a first state and (2) prevent a flow of gas and bodily fluid through the selectively permeable material when in a second state.

10. The system of claim 9, wherein the selectively permeable material is configured to transition from the first state to the second state as a result the initial volume of bodily fluid being received in the sequestration portion, thereby placing the first flow controller in the third state.

11. A fluid control device, comprising:

a housing having an inlet configured to establish fluid communication with a bodily fluid source and an outlet configured to be coupled to a fluid collection device, the coupling of the outlet to the fluid collection device resulting in a negative pressure differential within at least a portion of the housing, the housing defining a sequestration flow path in fluid communication with the inlet and a sampling flow path in fluid communication with the outlet;

a first flow controller having a flow state in which fluid communication is established between the sequestration flow path and the outlet and a non-flow state in which the sequestration flow path is sequestered from the outlet; and

a second flow controller having a flow state in which fluid communication is established between the sampling flow path and the inlet and a non-flow state in which the sampling flow path is sequestered from the inlet,

the first flow controller configured to be in the flow state when the negative pressure differential generated by coupling the outlet to the fluid collection device has a first magnitude

such that an initial volume of bodily fluid flows through the sequestration flow path toward the first flow controller, and

the first flow controller configured to transition to the non-flow state when the initial volume of bodily fluid is received in the sequestration flow path such that (1) the sequestration flow path is sequestered from the outlet and (2) the negative pressure differential is increased to a second magnitude operable to transition the second flow controller from the non-flow state to the flow state.

12. The system of claim 11, wherein the fluid collection device is a sample bottle, the sample bottle being at least partially evacuated such that coupling the outlet to the sample bottle generates the negative pressure differential.

13. The system of claim 11, wherein the fluid collection device is a syringe that is configured to be manipulated after the outlet is coupled to the syringe to generate the negative pressure differential.

14. The system of claim 11, wherein the first flow controller is configured to transition from the first state to the second state automatically.

15. The system of claim 11, wherein the second flow controller is configured to transition from the first state to the second state automatically.

16. The system of claim 11, wherein the first flow controller is at least one of a valve, a selectively permeable material, or a restricted flow path.

17. The system of claim 16, wherein the second flow controller is at least one of a valve, a selectively permeable material, a dissolvable material, a frangible barrier, a movable barrier, or a restricted flow path.

18. The system of claim 11, wherein the first flow controller includes a selectively permeable material configured to (1) allow a flow of a gas and prevent a flow of bodily fluid through the selectively permeable material when in a first state and (2) prevent a flow of gas and bodily fluid through the selectively permeable material when in a second state.

19. The system of claim 18, wherein the selectively permeable material is configured to transition from the first state to the second state as a result of the sequestration flow path receiving the initial volume of bodily fluid, the transitioning of the selectively permeable material from the first state to the second state places the first flow controller in the non-flow state.

20. The system of claim 19, wherein the first state of the selectively permeable material is an unsaturated state and the second state of the selectively permeable material is a saturated state.

21. A method of using a fluid control device to obtain a bodily fluid sample with reduced contamination, the method comprising:

coupling a fluid collection device to an outlet of the fluid control device, the coupling of the fluid collection device to the outlet configured to produce a negative pressure differential within at least a portion of the fluid control device;

transitioning a first flow controller from a first state to a second state when the negative pressure differential has a first magnitude, the first flow controller sequestering a sequestration portion of the fluid control device from the outlet when in the first state and establishing fluid communication between the sequestration portion and the outlet when in the second state;

receiving an initial volume of bodily fluid from an inlet of the fluid control device and into the sequestration portion in response to the negative pressure differential when the first flow controller is in the second state;

transitioning the first flow controller from the second state to a third state in response to the receiving, the first flow controller sequestering the sequestration portion from the outlet when in the third state, the negative pressure differential being increased from the first magnitude to a second magnitude when the first flow controller is in the third state;

transitioning a second flow controller from a first state to a second state when the negative pressure differential has the second magnitude, the second flow controller sequestering a sampling portion of the fluid control device from the inlet when in the first state and establishing fluid communication between the sampling portion and the inlet when in the second state; and

transferring a subsequent volume of bodily fluid from the inlet to the fluid collection device via the sampling portion and the outlet.

22. The method of claim 21, wherein the transitioning of the first flow controller from the first state to the second state includes automatically transitioning the first flow controller from the first state to the second state without manual intervention.

23. The method of claim 22, wherein the transitioning of the first flow controller from the second state to the third state includes automatically transitioning the first flow controller from the first state to the second state without manual intervention.

24. The method of claim 21, wherein the transitioning of the second flow controller from the first state to the second state includes automatically transitioning the second flow controller from the first state to the second state without manual intervention.

25. The method of claim 21, wherein the first flow controller includes a selectively permeable material configured to (1) allow a flow of a gas and prevent a flow of bodily fluid through the selectively permeable material when in a first state and (2) prevent a flow of gas and bodily fluid through the selectively permeable material when in a second state,

the transitioning of the first flow controller from the second state to the third state includes the selectively permeable material being placed in its second state.

26. The method of claim 21, further comprising:

establishing fluid communication between the inlet and a bodily fluid source, wherein the initial volume of bodily fluid contains contaminants associated with the establishing of fluid communication between the inlet and the bodily fluid source.

27. The method of claim 26, wherein the initial volume of bodily fluid and the contaminants are sequestered within the sequestration portion when the first flow controller is in the third state such that the subsequent volume of bodily fluid is substantially free of contaminants.

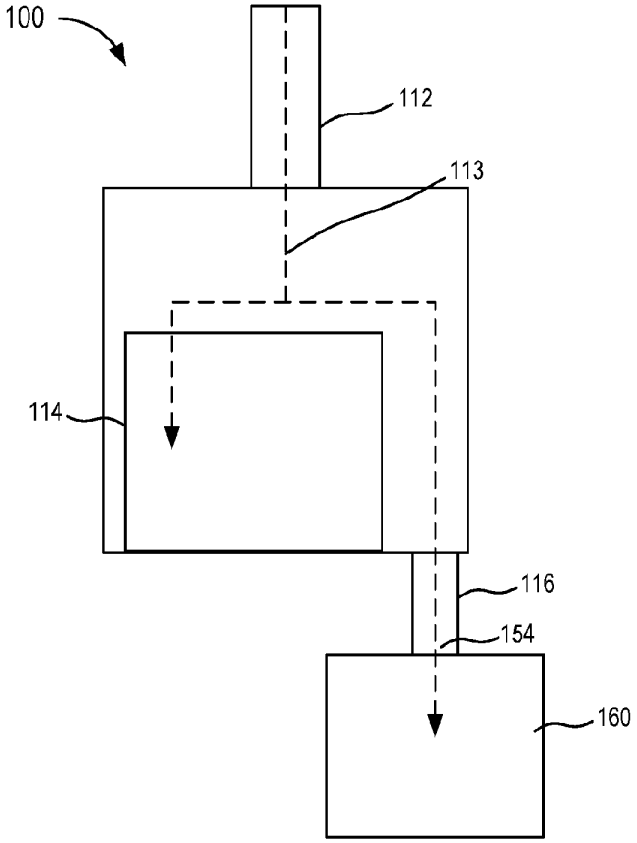


FIG. 1

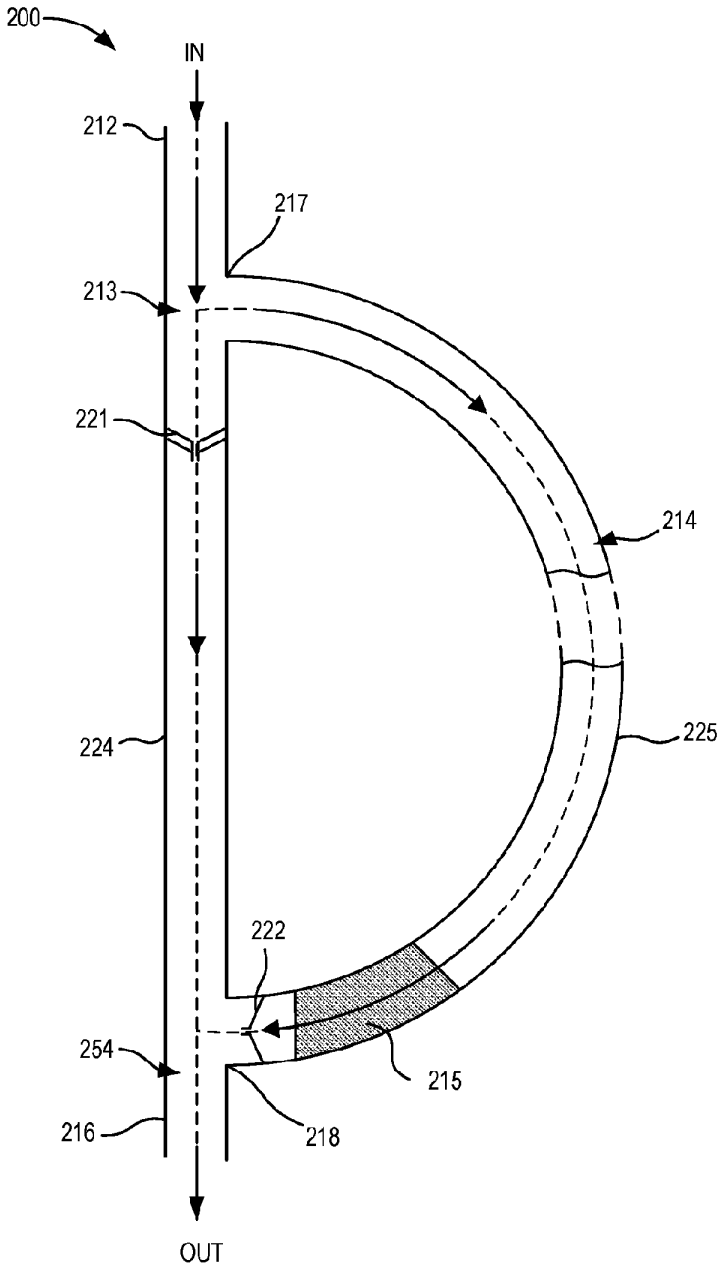


FIG. 2

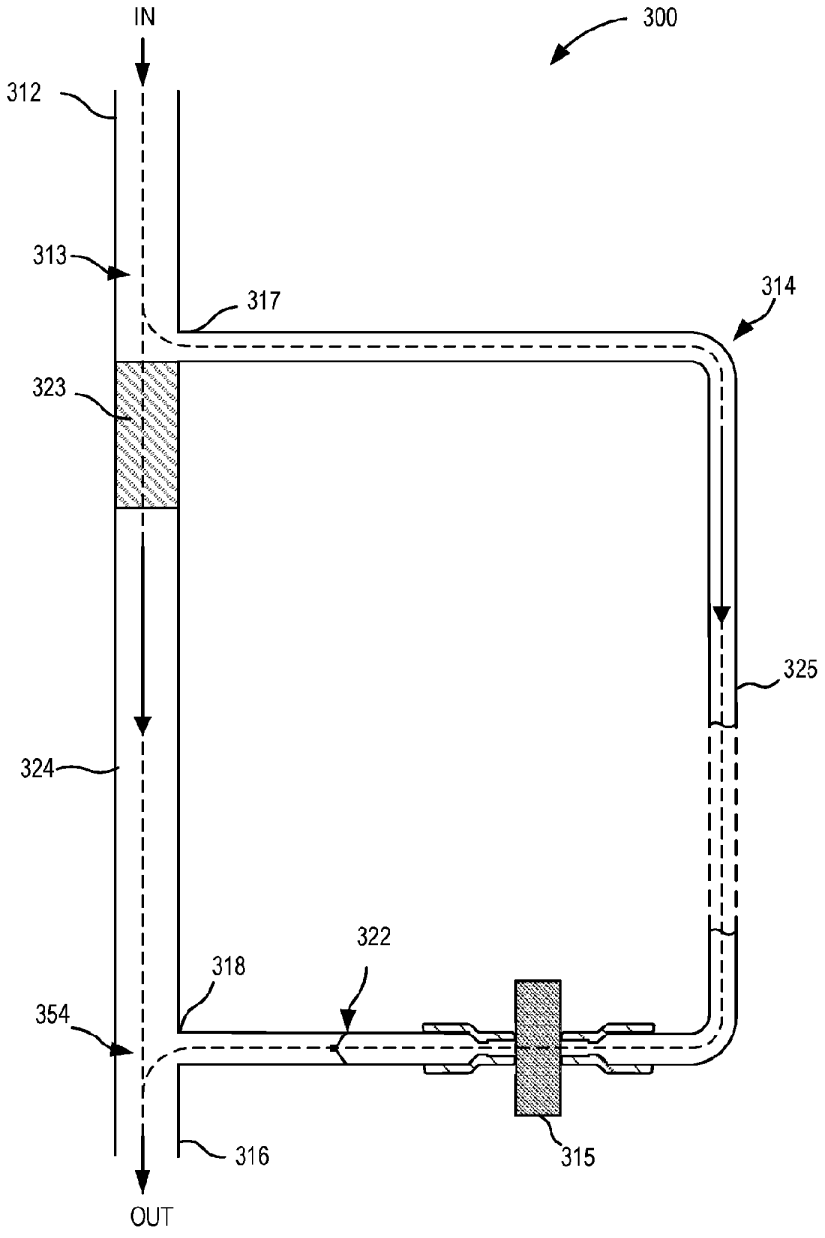


FIG. 3

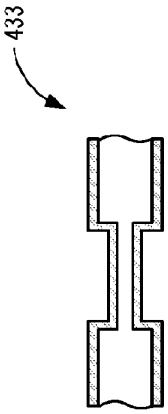


FIG. 5

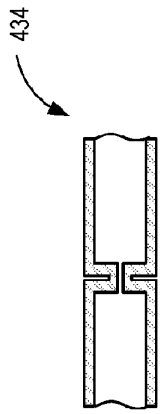


FIG. 6

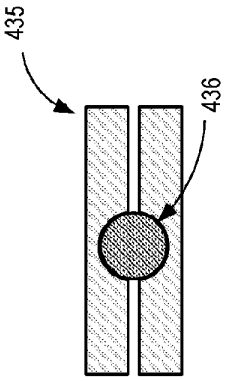


FIG. 7

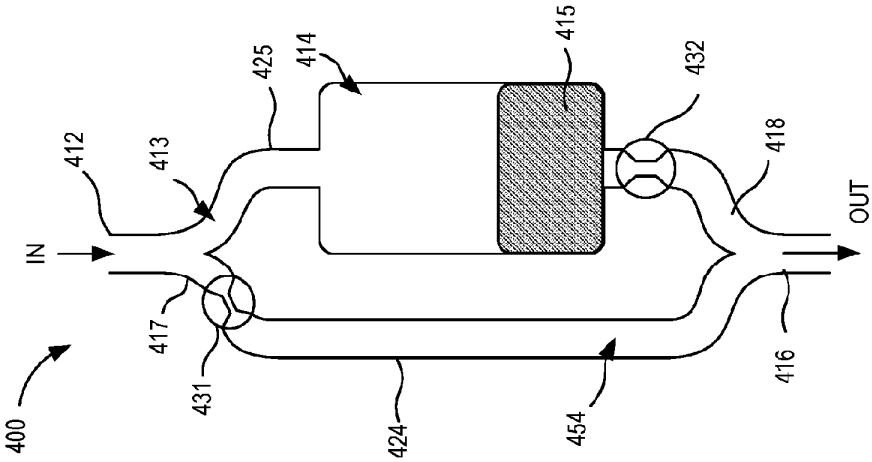


FIG. 4

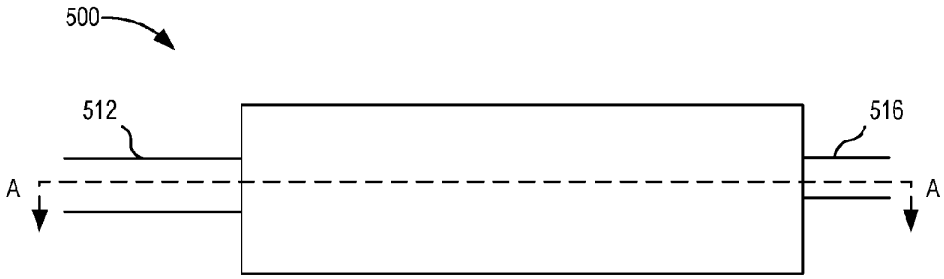


FIG. 8

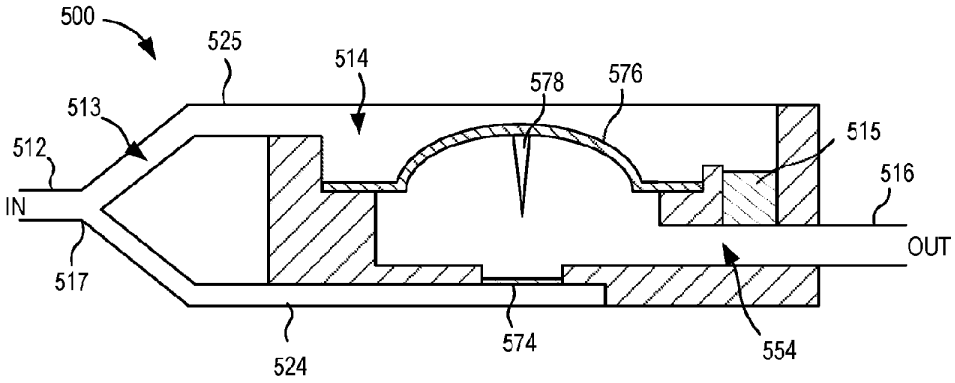


FIG. 9

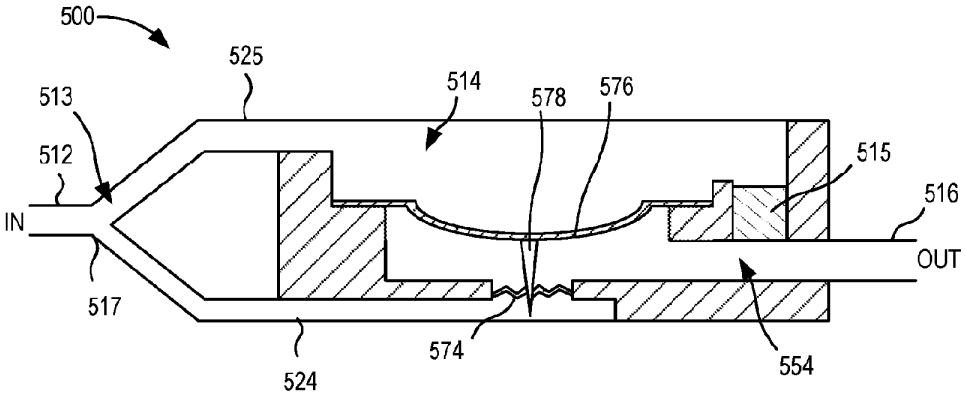


FIG. 10

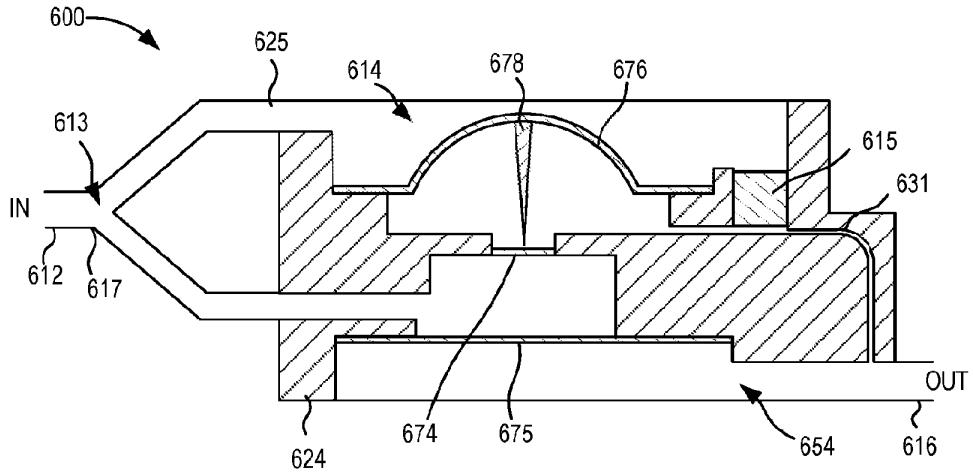

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FIG. 11

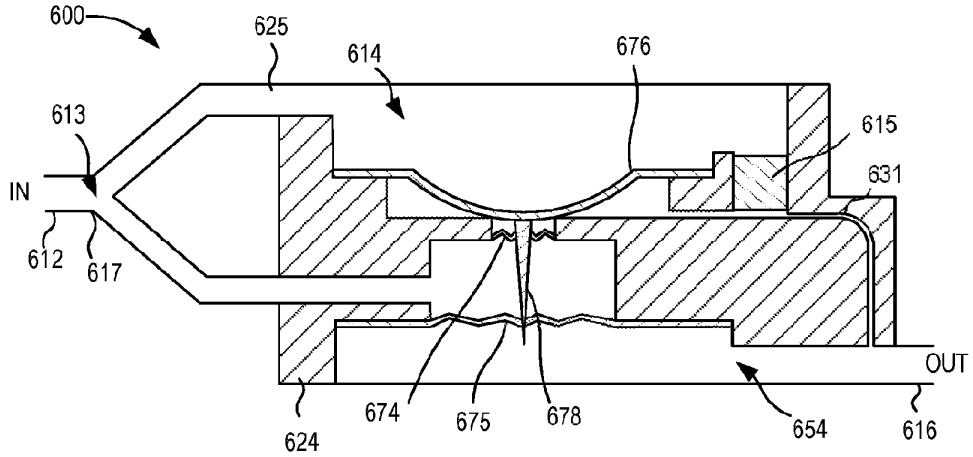

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FIG. 12

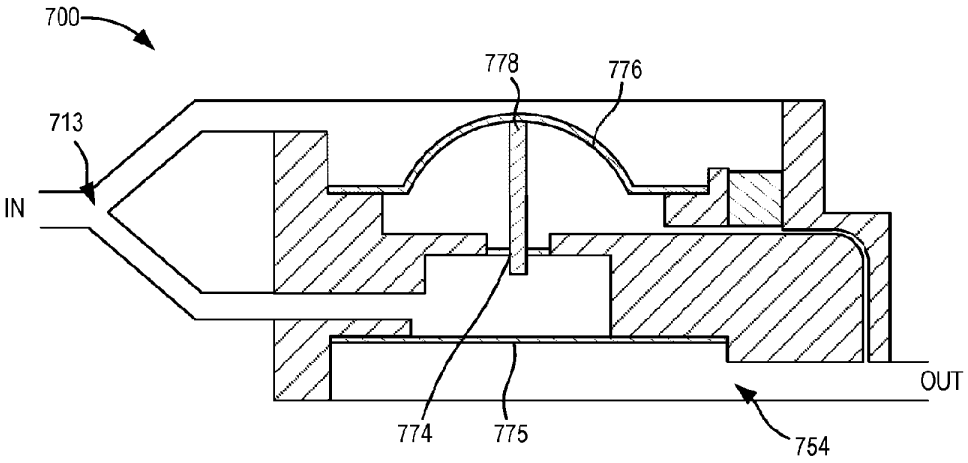

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FIG. 13

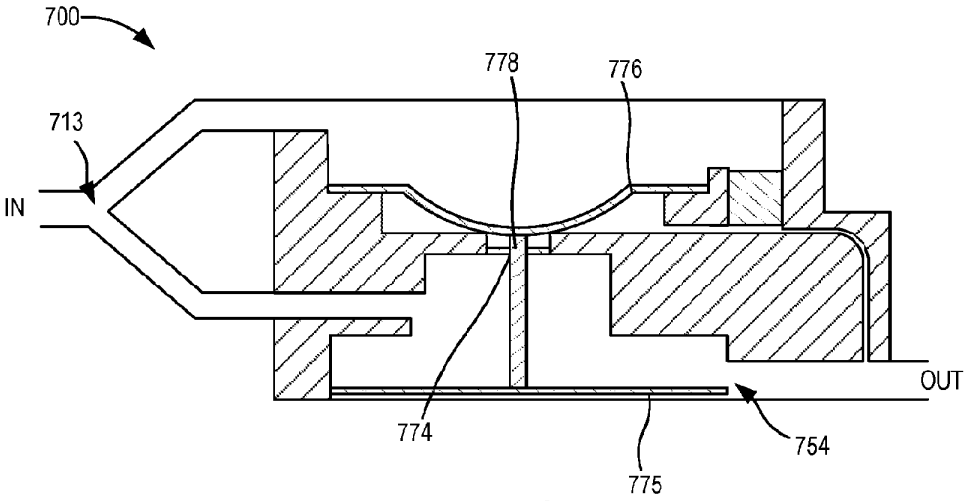

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FIG. 14

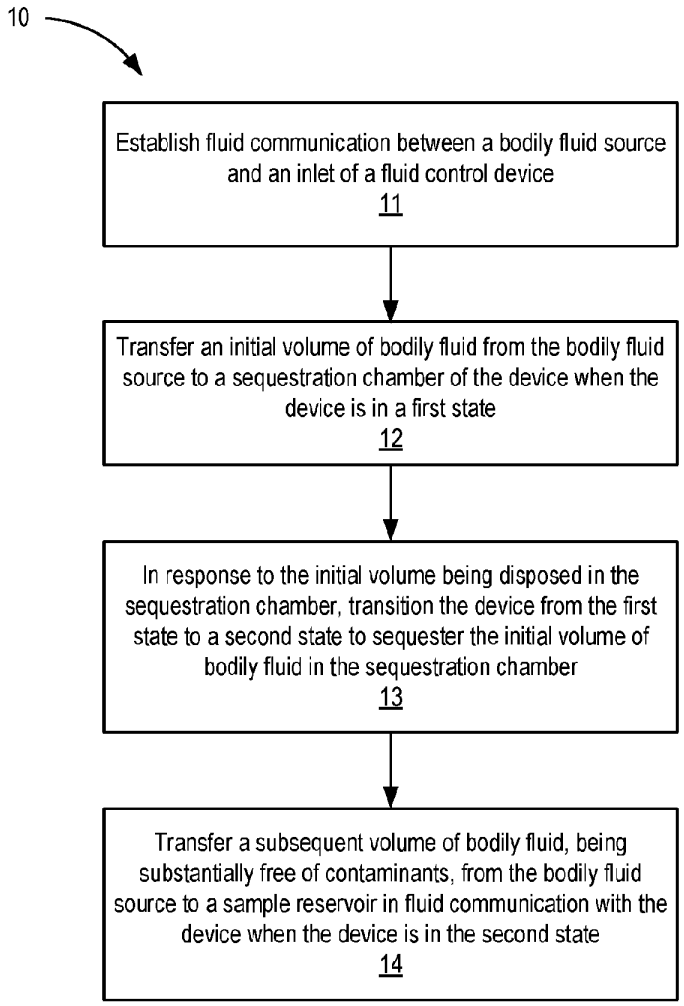

10
Establish fluid communication between a bodily fluid source and an inlet of a fluid control device
11
Transfer an initial volume of bodily fluid from the bodily fluid source to a sequestration chamber of the device when the device is in a first state
12
In response to the initial volume being disposed in the sequestration chamber, transition the device from the first state to a second state to sequester the initial volume of bodily fluid in the sequestration chamber
13
Transfer a subsequent volume of bodily fluid, being substantially free of contaminants, from the bodily fluid source to a sample reservoir in fluid communication with the device when the device is in the second state
14

FIG. 15

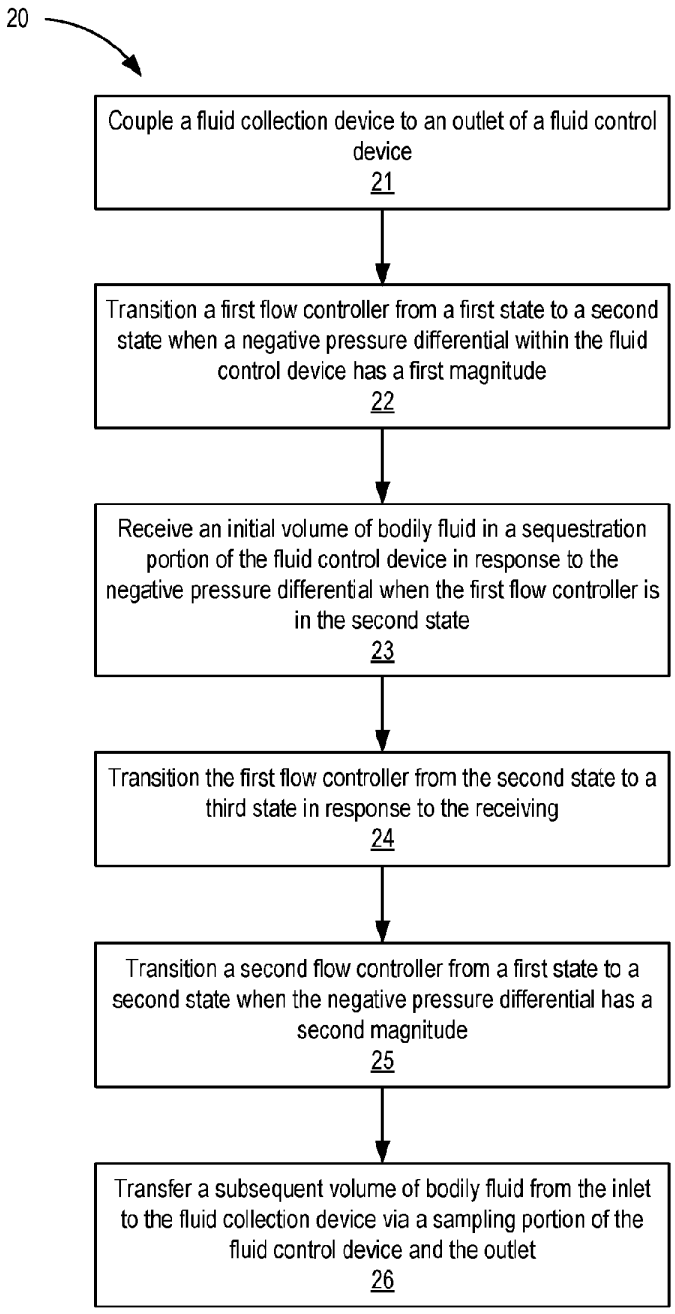

20
Couple a fluid collection device to an outlet of a fluid control device
21
Transition a first flow controller from a first state to a second state when a negative pressure differential within the fluid control device has a first magnitude
22
Receive an initial volume of bodily fluid in a sequestration portion of the fluid control device in response to the negative pressure differential when the first flow controller is in the second state
23
Transition the first flow controller from the second state to a third state in response to the receiving
24
Transition a second flow controller from a first state to a second state when the negative pressure differential has a second magnitude
25
Transfer a subsequent volume of bodily fluid from the inlet to the fluid collection device via a sampling portion of the fluid control device and the outlet
26

FIG. 16

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2019/034626

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61B5/15 A61B5/153 A61B5/154
ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 2017/020427 A1 (ROGERS BOBBY E [US] ET AL) 26 January 2017 (2017-01-26) paragraphs [0125], [0126] figures 23A, 23B	1-27
A	US 2016/361006 A1 (BULLINGTON GREGORY J [US] ET AL) 15 December 2016 (2016-12-15) cited in the application paragraphs [0040] - [0073] figures 1-7	1-27
A	US 2015/011910 A1 (BULLINGTON GREGORY [US] ET AL) 8 January 2015 (2015-01-08) paragraphs [0078] - [0104] figures 2-12	1-27

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[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

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"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
6 August 2019	22/08/2019

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Schultz, Ottmar

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INTERNATIONAL SEARCH REPORT

International application No
PCT/US2019/034626

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 2014/163419 A1 (BULLINGTON GREGORY J [US] ET AL) 12 June 2014 (2014-06-12) the whole document	1-27
A	US 8 535 241 B2 (BULLINGTON GREGORY [US]; PATTON RICHARD G [US] ET AL.) 17 September 2013 (2013-09-17) cited in the application the whole document	1-27

1

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2019/034626

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Form PCT/ISA/210 (patent family annex) (April 2005)

Espacenet

Bibliographic data: WO2019055487 (A1) — 2019-03-21

FLUID CONTROL DEVICES AND METHODS OF USING THE SAME

Inventor(s): BULLINGTON GREGORY J [US]; MIAZGA JAY M [US]; GAW SHAN E [US]; RAMSEY TIMOTHY F [US] ± (BULLINGTON, Gregory J, ; MIAZGA, Jay M, ; GAW, Shan E, ; RAMSEY, Timothy F)

Applicant(s): MAGNOLIA MEDICAL TECHNOLOGIES INC [US] ± (MAGNOLIA MEDICAL TECHNOLOGIES, INC)

Classification: **- international:** ***A61B17/00; A61B5/00; A61M1/00; A61M39/00***
- cooperative: **A61B5/15003 (EP, US); A61B5/150099 (US); A61B5/150213 (US); A61B5/150221 (EP, US); A61B5/150251 (EP, US); A61B5/150946 (US); A61B5/150992 (EP, US); B01L3/502 (US);** B01L2200/026 (US); B01L2200/027 (US); B01L2200/0684 (US); B01L2200/0689 (US); B01L2200/141 (US); B01L2300/0681 (US); B01L2300/14 (US); B01L2400/0478 (US); B01L2400/0487 (US)

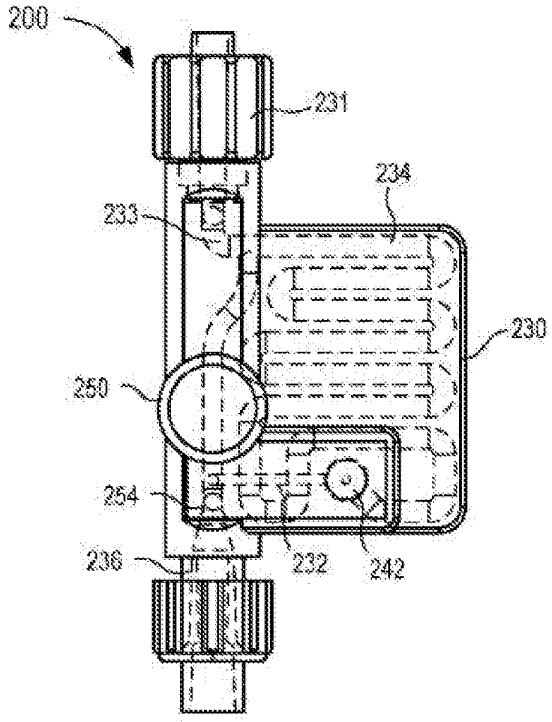
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A fluid control device includes an inlet configured to be placed directly or indirectly in fluid communication with a bodily fluid source and an outlet configured to be placed in fluid communication with a fluid collection device. The fluid control device has a first state in which a negative pressure differential produced from an external source such as the fluid collection device is applied to the fluid control device to draw an initial volume of bodily fluid from the bodily fluid source, through the inlet, and into a sequestration portion of the fluid control device. The fluid control device has a second state in which (1) the sequestration portion sequesters the initial volume, and (2) the negative pressure differential draws a subsequent volume of bodily fluid, being substantially free of contaminants, from the bodily fluid source, through the fluid control device, and into the fluid collection device.


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(54) Title: FLUID CONTROL DEVICES AND METHODS OF USING THE SAME

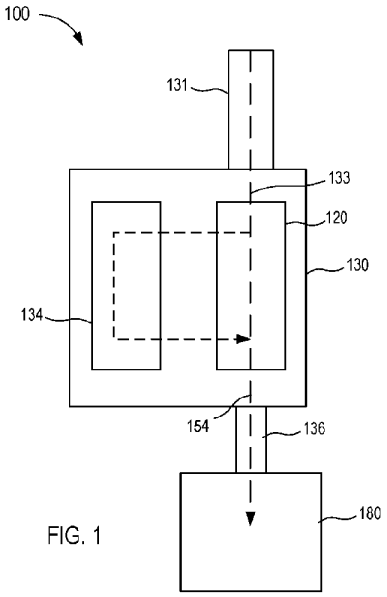


FIG. 1

(57) Abstract: A fluid control device includes an inlet configured to be placed directly or indirectly in fluid communication with a bodily fluid source and an outlet configured to be placed in fluid communication with a fluid collection device. The fluid control device has a first state in which a negative pressure differential produced from an external source such as the fluid collection device is applied to the fluid control device to draw an initial volume of bodily fluid from the bodily fluid source, through the inlet, and into a sequestration portion of the fluid control device. The fluid control device has a second state in which (1) the sequestration portion sequesters the initial volume, and (2) the negative pressure differential draws a subsequent volume of bodily fluid, being substantially free of contaminants, from the bodily fluid source, through the fluid control device, and into the fluid collection device.

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FLUID CONTROL DEVICES AND METHODS OF USING THE SAME

Cross-Reference to Related Applications

[1001] This application claims priority to and the benefit of U.S. Provisional Patent Application Serial No. 62/557,530 entitled, "Fluid Control Devices and Methods of Using the Same," filed September 12, 2017, the disclosure of which is incorporated herein by reference in its entirety.

[1002] This application also claims priority to and the benefit of U.S. Provisional Patent Application Serial No. 62/634,569 entitled, "Fluid Control Devices and Methods of Using the Same," filed February 23, 2018, the disclosure of which is incorporated herein by reference in its entirety.

[1003] This application also claims priority to and the benefit of U.S. Provisional Patent Application Serial No. 62/678,632 entitled, "Fluid Control Devices and Methods of Using the Same," filed May 31, 2018, the disclosure of which is incorporated herein by reference in its entirety.

Background

[1004] The invention relates generally to the parenteral procurement of bodily fluid samples, and more particularly to fluid diversion, sequestration, and/or isolation devices and methods for procuring bodily fluid samples with reduced contaminants such as dermally residing microbes and/or other contaminants exterior to the bodily fluid source.

[1005] Health care practitioners routinely perform various types of microbial as well as other broad diagnostic tests on patients using parenterally obtained bodily fluids. As advanced diagnostic technologies evolve and improve, the speed, accuracy (both sensitivity and specificity), and value of information that can be provided to clinicians continues to improve. Maintaining the integrity of the bodily fluid sample during and/or after collection also ensures that analytical diagnostic results are representative of the in vivo conditions of a patient. Examples of diagnostic technologies that are reliant on high quality, non-contaminated, and/or unadulterated bodily fluid samples include but are not limited to microbial detection, molecular diagnostics, genetic sequencing (e.g., deoxyribonucleic acid (DNA), ribonucleic acid (RNA), next-generation sequencing (NGS), etc.), biomarker identification, and the like. When biological matter, which can include cells external to the intended source for sample procurement, and/or other external contaminants are inadvertently included in the bodily fluid

sample that is to be analyzed, there is an opportunity for inaccurate test results to be derived. In short, when the purity of the sample intended to be derived or collected from a specific bodily fluid source is compromised during the specimen procurement process, resultant analytical test results may be inaccurate, distorted, adulterated, falsely positive, falsely negative, and/or otherwise not representative of the actual condition of the patient, which in turn, can inform faulty, inaccurate, confused, unsure, low-confidence, and/or otherwise undesired clinical decision making.

[1006] In some instances, patient samples (e.g., bodily fluids) are tested for the presence of one or more potentially undesirable microbes, such as bacteria, fungi, or yeast (e.g., Candida). In some instances, microbial testing may include incubating patient samples in one or more sterile and/or non-sterile vessels that may contain culture media, common additives, and/or other types of solutions that are conducive to microbial growth. In other instances, the sample in the vessel may be analyzed directly (i.e., not incubated) and may not contain culture media or additives associated with incubating the specimen. In still other instances, various technologies can be employed to assist in the detection of the presence of microbes as well as other types of biological matter, specific types of cells, biomarkers, proteins, antigens, enzymes, blood components, and/or the like during diagnostic testing. Examples include but are not limited to molecular polymerase chain reaction (PCR), magnetic resonance and other magnetic analytical platforms, automated microscopy, spatial clone isolation, flow cytometry, whole blood ("culture free") specimen analysis (e.g. NGS) and associated technologies, morphokinetic cellular analysis, and/or other common or evolving and advanced technologies utilized in the clinical laboratory environment to characterize patient specimens and/or to detect, identify, type, categorize, and/or characterize specific organisms, antibiotic susceptibilities, and/or the like.

[1007] In some instances, the detection of the presence of microbes includes allowing the microbes and/or organisms to grow for an amount of time (e.g., a variable amount of time from less than an hour to a few hours to several days – which can be longer or shorter depending on the diagnostic technology employed). The microbe and/or organism growth can then be detected by automated, continuous monitoring, and/or other methods specific to the analytical platform and technology used for detection, identification, and/or the like.

[1008] In culture testing, for example, when microbes are present in the patient sample, the microbes flourish over time in the culture medium and, in some instances, automated monitoring technologies can detect carbon dioxide produced by organism growth. The presence of microbes in the culture medium (as indicated by observation of carbon dioxide

and/or via other detection methods) suggests the presence of the same microbes in the patient sample which, in turn, suggests the presence of the same microbes in the bodily fluid of the patient from whom the sample was obtained. Accordingly, when microbes are determined to be present in the culture medium (or more generally in the sample used for testing), the patient may be diagnosed and prescribed one or more antibiotics or other treatments specifically designed to treat or otherwise remove the undesired microbes from the patient.

[1009] Patient samples, however, can become contaminated during procurement and/or otherwise can be susceptible to false positive or false negative results. For example, microbes from a bodily surface (e.g., dermally residing microbes) that are dislodged during the specimen procurement process (which can include needle insertion into a patient, specimen procurement via a lumen-containing device such as a peripheral IV catheter (PIV), a central line (PICC) and/or other indwelling catheter(s), collection with a syringe or any other suitable means employed to collect a patient specimen), either directly or indirectly via tissue fragments, hair follicles, sweat glands, and other skin adnexal structures, can be subsequently transferred to a culture medium, test vial, or other suitable specimen collection or transfer vessel with the patient sample and/or included in the specimen that is to be analyzed for non-culture based testing. Another possible source of contamination is from the person drawing the patient sample (e.g., a doctor, phlebotomist, nurse, technician, etc.). Specifically, equipment, supplies, and/or devices used during a patient sample procurement process often include multiple fluidic interfaces (by way of example, but not limited to, patient to needle, needle to transfer adapter, transfer adapter to sample vessel, catheter hub to syringe, syringe to transfer adapter, needle/tubing to sample vessels, and/or any other fluidic interface or any combination thereof) that can each introduce points of potential contamination. In some instances, such contaminants may thrive in a culture medium and/or may be identified by another non-culture based diagnostic technology and eventually may yield a false positive and/or a false negative microbial test result, which may inaccurately reflect the presence or lack of such microbes within the patient (i.e., in vivo).

[1010] Such inaccurate results because of contamination and/or other sources of adulteration that compromise the purity of the sample are a concern when attempting to diagnose or treat a wide range of suspected illnesses, diseases, infections, patient conditions or other maladies of concern. For example, false negative results from microbial tests may result in a misdiagnosis and/or delayed treatment of a patient illness, which, in some cases, could result in the death of the patient. Conversely, false positive results from microbial tests may result in the patient being unnecessarily subjected to one or more anti-microbial therapies,

which may cause serious side effects to the patient including, for example, death, as well as produce an unnecessary burden and expense to the health care system due to extended length of patient stay and/or other complications associated with erroneous treatments. The use of diagnostic imaging equipment attributable to these false positive results is also a concern from both a cost as well as patient safety perspective as unnecessary exposure to concentrated radiation associated with a variety of imaging procedures (e.g., CT scans) has many known adverse impacts on long-term patient health.

[1011] In some instances, devices and/or systems can be used to reduce the likelihood of contamination, adulteration, and/or the like of bodily fluid samples for testing. For example, some known devices can be configured to collect, divert, separate, and/or isolate or sequester an initial volume of bodily fluid that may be more likely to contain contaminants such as dermally residing microbes or the like. Some such devices, however, can be cumbersome, non-intuitive, perceived as difficult to use, inappropriate or unusable as intended for the target patient population, etc. In addition, some such devices can require training, user observation, intervention by more than one user, and/or can otherwise present challenges that can lead to limited efficacy based on variables including environmental, educational, clinician skill, patient condition, and/or the like. In some instances, such challenges can complicate the collection of consistently high quality samples that are non-contaminated, sterile, unadulterated, etc., which in turn, can impact the validity of test result outcomes.

[1012] On the other hand, some known passive diversion devices and/or systems (e.g., systems that do not specifically utilize or rely on direct user intervention, interaction, manipulation, and/or the like) may fail to adequately divert, sequester, and/or isolate a clinically desired and efficacious pre-sample volume of bodily fluid due to clinical realities such as, for example, the time required to fill a sequestration reservoir with a meaningful volume of fluid. In some instances, the operation of some known passive devices is dependent on a positive pressure applied by a bodily fluid source (e.g., a patient's blood pressure). The positive pressure applied by the bodily fluid source, however, may be insufficient to result in flow dynamics and/or flow rates that makes use of such devices practical in various clinical settings (including emergency rooms and other intensive settings). For example, the patient population with symptoms requiring diagnostic testing noted above commonly are in such physical condition that attaining vascular access and/or collection of bodily fluid samples can be difficult due to a hypotensive state (i.e., low blood pressure), hypovolemic state (i.e., low blood volume), and/or other physical challenges (e.g., severe dehydration, obesity, difficult and/or inaccessible vasculature, etc.). Such states or physical conditions can result in difficulty

in providing sufficient blood flow and/or pressure to achieve passive filling of a sequestration chamber, channel, reservoir, container (or other diversion volume) consistently with sufficient volume to meet clinically validated, evidence-based efficacy and results in diverting, sequestering, and/or isolating contaminants which otherwise can lead to distorted, inaccurate, falsely positive, falsely negative, and/or otherwise adulterated diagnostic test results. The challenges associated with this approach (e.g., relying on a positive pressure differential applied by the bodily fluid source without utilizing a specific external energy source and/or negative pressure to facilitate collection of an appropriate and clinically efficacious initial volume of bodily fluid) can render it impractical as failure rates can be unacceptably high for the fragile patient population from whom these samples are collected.

[1013] As such, a need exists for fluid diversion devices and methods for procuring bodily fluid samples with reduced contaminants such as dermally residing microbes and/or other contaminants exterior to the bodily fluid source that result in consistent bodily fluid collection (e.g., from a general patient population and/or a challenging patient population). Some such devices and methods can include, for example, bodily fluid collection with the assistance of various sources of external energy and/or negative pressure. Furthermore, a need exists for such devices that are user-friendly, demonstrate consistent efficacy, and address the challenges associated with collecting samples from patients with challenging health circumstances and/or physical characteristics that impact the ability to collect bodily fluid samples.

Summary

[1014] Devices and methods for procuring bodily fluid samples with reduced contaminants such as dermally residing microbes and/or other contaminants exterior to the bodily fluid source are described herein. In some embodiments, a system includes a housing, a flow controller, and a fluid collection device. The housing has an inlet and an outlet, and forms a sequestration portion. The inlet is configured to be placed in fluid communication with a bodily fluid source. The sequestration portion is configured to receive an initial volume of bodily fluid from the bodily fluid source. The flow controller is at least partially disposed in the sequestration portion of the housing and is configured to transition from a first state to a second state. The fluid collection device is configured to be fluidically coupled to the outlet to produce a negative pressure differential within at least a portion of the housing. The negative pressure differential is operable to draw the initial volume of bodily fluid into the sequestration portion when the flow controller is in the first state and is operable to draw the sample volume of bodily

fluid through the outlet and into the fluid collection device when the flow controller is in the second state.

Brief Description of the Drawings

[1015] FIG. 1 is a schematic illustration of a fluid control device according to an embodiment.

[1016] FIGS. 2-5 are various views of a fluid control device according to an embodiment.

[1017] FIGS. 6-8 are various views of a fluid control device according to an embodiment.

[1018] FIGS. 9 and 10 are front view illustrations of a fluid control device in a first operating mode and a second operating mode, respectively, according to an embodiment.

[1019] FIGS. 11 and 12 are front view illustrations of a fluid control device in a first operating mode and a second operating mode, respectively, according to an embodiment.

[1020] FIGS. 13-15B are various views of a fluid control device according to an embodiment.

[1021] FIGS. 16-18 are various views of a fluid control device according to an embodiment.

[1022] FIGS. 19-25 are various views of a fluid control device according to an embodiment.

[1023] FIGS. 26-28 are each a perspective view of a fluid control device according to different embodiments.

[1024] FIGS. 29-34 are various views of a fluid control device according to an embodiment.

[1025] FIGS. 35-40 are various views of a fluid control device according to an embodiment.

[1026] FIGS. 41-44 are various views of a fluid control device according to an embodiment.

[1027] FIGS. 45-50 are various views of a fluid control device according to an embodiment.

[1028] FIGS. 51 and 52 are cross-sectional views of a fluid control device according to an embodiment.

[1029] FIG. 53 is a flowchart illustrating a method of using a fluid control device according to an embodiment.

Detailed Description

[1030] Devices and methods for collecting, diverting, sequestering, isolating, etc. an initial volume of bodily fluid to reduce contamination in subsequently procured bodily fluid samples are described herein. Any of the fluid control devices described herein can be configured to receive, procure, and/or transfer a flow, bolus, volume, etc., of bodily fluid. A first reservoir, channel, flow path, or portion of the device can receive an initial amount of the bodily fluid flow, which then can be substantially or fully sequestered (e.g., contained or retained, circumvented, isolated, segregated, vapor-locked, separated, and/or the like) in or by the first reservoir or first portion of the device. In some instances, contaminants such as dermally residing microbes or the like can be included and/or entrained in the initial amount of the bodily fluid and likewise are sequestered in or by the first reservoir or first portion of the device. Once the initial amount is sequestered, any subsequent amount of the bodily fluid flow can be diverted, channeled, directed, flow controlled (e.g., manually, automatically, and/or semi-automatically) to a second reservoir, second portion of the device, and/or any additional flow path(s). Thus, with the initial amount sequestered, any additional and/or subsequent amount(s) of bodily fluid flow are substantially free from contaminants that may otherwise produce inaccurate, distorted, adulterated, falsely positive, falsely negative, etc., results in some diagnostics and/or testing. In some instances, the initial amount of bodily fluid also can be used, for example, in other testing such as those less affected by the presence of contaminants, can be discarded as a waste volume, can be infused back into the patient, and/or can be used for any other suitable clinical application.

[1031] In some embodiments, a feature of the fluid control devices and/or methods described herein is the use of an external negative pressure source (e.g., provided by a fluid collection device or any other suitable means) to (1) overcome physical patient challenges which can limit and/or prevent a sufficient pressure differential (e.g., a differential in blood pressure to ambient air pressure) to fully engage the sequestration chamber and/or to transition fluid flow to the fluid collection device; (2) result in proper filling of the sequestration chamber with a clinically validated and/or desirable volume of bodily fluid; (3) result in efficient, timely, and/or user-accepted consistency with bodily fluid collection process; and/or (4) provide a means of manipulating and/or automatically transitioning fluid flow (e.g., movement of physical components of the system or changing, switching, engaging, and/or otherwise employing or achieving desired fluid flow dynamics) to enable sequestration and/or isolation of the initial sample and collection of a subsequent sample.

[1032] In some embodiments, a fluid control device includes an inlet and an outlet. The inlet is configured to be placed in fluid communication with a bodily fluid source or an intermediary bodily fluid transfer device and the outlet is configured to be placed in fluid communication with a fluid collection device such as, for example, a sample reservoir, a syringe, a lumen-containing device, and/or any other suitable bodily fluid collection and/or transfer device. The fluid control device has a first state in which a negative pressure differential produced from an external source (e.g., the fluid collection device such as a sample reservoir, a syringe, a vessel, and/or any suitable intermediary fluid reservoir) is applied to the fluid control device to draw an initial volume of bodily fluid from the bodily fluid source, through the inlet, and into a sequestration and/or diversion portion of the fluid control device (which can be formed by or in the fluid control device or coupled thereto). The fluid control device has a second state in which (1) the sequestration chamber sequesters the initial volume, and (2) the negative pressure differential draws a subsequent volume of bodily fluid, being substantially free of contaminants, from the bodily fluid source, through the fluid control device, and into the fluid collection device.

[1033] In some embodiments, a system includes a housing, a flow controller, and a fluid collection device. The housing has an inlet and an outlet, and forms a sequestration portion. The inlet is configured to be placed in fluid communication with a bodily fluid source. The sequestration portion is configured to receive an initial volume of bodily fluid from the bodily fluid source. The flow controller is at least partially disposed in the sequestration portion of the housing and is configured to transition from a first state to a second state. The fluid collection device is configured to be fluidically coupled to the outlet to produce a negative pressure differential within at least a portion of the housing. The negative pressure differential is operable to draw the initial volume of bodily fluid into the sequestration portion when the flow controller is in the first state and is operable to draw the sample volume of bodily fluid through the outlet and into the fluid collection device when the flow controller is in the second state.

[1034] In some embodiments, an apparatus includes a housing and an actuator coupled to the housing. The housing has an inlet configured to be placed in fluid communication with a bodily fluid source and an outlet configured be placed in fluid communication with a fluid collection device. The housing forms a sequestration portion that is configured to receive an initial volume of bodily fluid from the bodily fluid source. The actuator has a first configuration in which a first fluid flow path places the inlet in fluid communication with the sequestration portion and a second configuration in which a second fluid flow path places the

inlet in fluid communication with the outlet. The fluid collection device is configured to be placed in fluid communication with the outlet to produce a negative pressure differential (1) within the first fluid flow path that is operable to draw the initial volume of bodily fluid into the sequestration portion when the actuator is in the first configuration, and (2) within the second fluid flow path that is operable to draw a sample volume of bodily fluid into the fluid collection device when the actuator is in the second configuration.

[1035] In some embodiments, a method of using a fluid control device to obtain a bodily fluid sample with reduced contamination includes establishing fluid communication between a bodily fluid source and an inlet of the fluid control device. A fluid collection device is coupled to an outlet of the fluid control device and is configured to produce a negative pressure differential within at least a portion of the fluid control device. An initial volume of bodily fluid is received from the inlet and into a sequestration portion of the fluid control device in response to the negative pressure differential. In response to contact with a portion of the initial volume of bodily fluid, a flow controller disposed in the sequestration portion is transitioned from a first state in which the flow controller allows a flow of a gas through the flow controller and prevents a flow of bodily fluid through the flow controller, to a second state in which the flow controller prevents a flow of gas and bodily fluid through the flow controller. The initial volume of bodily fluid is sequestered in the sequestration portion after the flow controller is transitioned to the second state and a subsequent volume of bodily fluid is transferred from the inlet to an outlet in fluid communication with a fluid collection device.

[1036] As used in this specification and the claims, the singular forms "a," "an" and "the" include plural referents unless the context clearly dictates otherwise. Thus, for example, the term "a member" is intended to mean a single member or a combination of members, "a material" is intended to mean one or more materials, or a combination thereof.

[1037] As used herein, the terms "about," "approximate," and/or "substantially" when used in connection with stated value and/or other geometric relationships is intended to convey that the structure so defined is nominally the value stated and/or the geometric relationship described. In some instances, the terms "about," "approximately," and/or "substantially" can generally mean and/or can generally contemplate plus or minus 10% of the value or relationship stated. For example, about 0.01 would include 0.009 and 0.011, about 0.5 would include 0.45 and 0.55, about 10 would include 9 to 11, and about 1000 would include 900 to 1100. While a value stated may be desirable, it should be understood that some variance may occur as a result of, for example, manufacturing tolerances or other practical considerations (such as, for example, the pressure or force applied through a portion of a device, conduit,

lumen, etc.). Accordingly, the terms "about," "approximately," and/or "substantially" can be used herein to account for such tolerances and/or considerations.

[1038] As used herein, "bodily fluid" can include any fluid obtained directly or indirectly from a body of a patient. For example, "bodily fluid" includes, but is not limited to, blood, cerebrospinal fluid, urine, bile, lymph, saliva, synovial fluid, serous fluid, pleural fluid, amniotic fluid, mucus, sputum, vitreous, air, and the like, or any combination thereof.

[1039] As used herein, the words "proximal" and "distal" refer to the direction closer to and away from, respectively, a user who would place the device into contact with a patient. Thus, for example, the end of a device first touching the body of the patient would be the distal end, while the opposite end of the device (e.g., the end of the device being manipulated by the user) would be the proximal end of the device.

[1040] As described in further detail herein, any of the devices and methods can be used to procure bodily fluid samples with reduced contamination by, for example, diverting a "pre-sample" volume of bodily fluid prior to collecting a "sample" volume of bodily fluid. Each of the terms "pre-sample," "first," and/or "initial," can be used interchangeably to describe and/or refer to an amount, portion, or volume of bodily fluid that is transferred, diverted, and/or sequestered prior to procuring the "sample" volume. In some embodiments, the terms "pre-sample," "first," and/or "initial" can refer to a predetermined, defined, desired, or given volume, portion, or amount of bodily fluid. For example, in some embodiments, a predetermined and/or desired pre-sample volume of bodily fluid can be about 0.1 milliliter (mL), about 0.2 mL, about 0.3 mL, about 0.4 mL, about 0.5 mL, about 1.0 mL, about 2.0 mL, about 3.0 mL, about 4.0 mL, about 5.0 mL, about 10.0 mL, about 20 mL, about 50 mL, and/or any volume or fraction of a volume therebetween. In other embodiments, the pre-sample volume can be greater than 50 mL or less than 0.1 mL. In some specific embodiments, a predetermined and/or desired pre-sample volume can be between about 0.1 mL and about 5.0 mL. In other embodiments, the pre-sample volume can be, for example, a drop of bodily fluid, a few drops of bodily fluid, a combined volume of any number of lumen that form, for example, a flow path (or portion thereof) from the bodily fluid source to an initial collection chamber, portion, reservoir, etc. (e.g., a sequestration chamber).

[1041] On the other hand, the terms "sample," "second," and/or "subsequent" when used in the context of a volume of bodily fluid can refer to a volume, portion, or amount of bodily fluid that is either a random volume or a predetermined or desired volume of bodily fluid collected after transferring, diverting, sequestering, and/or isolating the pre-sample volume of bodily fluid. For example, in some embodiments, a desired sample volume of bodily fluid can

be about 10 mL to about 60 mL. In other embodiments, a desired sample volume of bodily fluid can be less than 10 mL or greater than 60 mL. In some embodiments, for example, a sample volume can be at least partially based on one or more tests, assays, analyses, and/or processes to be performed on the sample volume.

[1042] The embodiments described herein can be configured to selectively transfer bodily fluid to one or more fluid collection device(s). In some embodiments, a fluid collection device can include, but is not limited to, any suitable vessel, container, reservoir, bottle, adapter, dish, vial, syringe, device, diagnostic and/or testing machine, and/or the like. By way of specific example, in some instances, any of the embodiments and/or methods described herein can be used to transfer a sample volume into a sample reservoir such as any of those described in detail in U.S. Patent No. 8,197,420 entitled, "Systems and Methods for Parenterally Procuring Bodily-Fluid Samples with Reduced Contamination," filed December 13, 2007 ("the '420 Patent"), the disclosure of which is incorporated herein by reference in its entirety.

[1043] In some embodiments, a sample reservoir can be a sample or culture bottle such as, for example, an aerobic culture bottle or an anaerobic culture bottle. In this manner, the culture bottle can receive a bodily fluid sample, which can then be tested (e.g., via in vitro diagnostic (IVD) tests, and/or any other suitable test) for the presence of, for example, Gram-Positive bacteria, Gram-Negative bacteria, yeast, fungi, and/or any other organism. In some instances, the culture bottle can receive a bodily fluid sample and the culture medium (disposed therein) can be tested for the presence of any suitable organism. If such a test of the culture medium yields a positive result, the culture medium can be subsequently tested using a PCR-based system to identify a specific organism. Moreover, as described in further detail herein, in some instances, diverting a pre-sample or initial volume of bodily fluid can reduce and/or substantially eliminate contaminants in the bodily fluid sample that may otherwise lead to inaccurate test results.

[1044] Any of the sample containers, reservoirs, bottles, dishes, vials, etc., described herein can be devoid of contents prior to receiving a sample volume of bodily fluid or can include, for example, any suitable additive, culture medium, substances, enzymes, oils, fluids, and/or the like. For example, in some embodiments, a sample reservoir can include an aerobic or anaerobic culture medium (e.g., a nutrient rich and/or environmentally controlled medium to promote growth, and/or other suitable medium(s)), which occupies at least a portion of the inner volume defined by the sample reservoir. In some embodiments, a sample reservoir can include, for example, any suitable additive or the like such as, heparin, citrate, ethylenediaminetetraacetic acid (EDTA), oxalate, SPS, and/or the like, which similarly

occupies at least a portion of the inner volume defined by the sample reservoir. In other embodiments, a sample reservoir can be any suitable container used to collect a specimen.

[1045] While the term "culture medium" can be used to describe a substance configured to react with organisms in a bodily fluid (e.g., microorganisms such as bacteria) and the term "additive" can be used to describe a substance configured to react with portions of the bodily fluid (e.g., constituent cells of blood, serum, synovial fluid, etc.), it should be understood that a sample reservoir can include any suitable substance, liquid, solid, powder, lyophilized compound, gas, etc. Moreover, when referring to an "additive" within a sample reservoir, it should be understood that the additive could be a culture medium, such as an aerobic culture medium and/or an anaerobic culture medium contained in a culture bottle, an additive and/or any other suitable substance or combination of substances contained in a culture bottle and/or any other suitable reservoir such as those described above. That is to say, the embodiments described herein can be used with any suitable fluid reservoir or the like containing any suitable substance. Furthermore, any of the embodiments and/or methods described herein can be used to transfer a volume of bodily fluid to a reservoir (or the like) that does not contain a culture medium, additive, and/or any other substance prior to receiving a flow of bodily fluid.

[1046] While some of the embodiments are described herein as being used for procuring bodily fluid for one or more culture sample testing, it should be understood that the embodiments are not limited to such a use. Any of the embodiments and/or methods described herein can be used to transfer a flow of bodily fluid to any suitable device that is placed in fluid communication therewith. Thus, while specific examples are described herein, the devices, methods, and/or concepts are not intended to be limited to such specific examples.

[1047] The embodiments described herein and/or portions thereof can be formed or constructed of one or more biocompatible materials. In some embodiments, the biocompatible materials can be selected based on one or more properties of the constituent material such as, for example, stiffness, toughness, durometer, bioreactivity, etc. Examples of suitable biocompatible materials include metals, glasses, ceramics, or polymers. Examples of suitable metals include pharmaceutical grade stainless steel, gold, titanium, nickel, iron, platinum, tin, chromium, copper, and/or alloys thereof. A polymer material may be biodegradable or non-biodegradable. Examples of suitable biodegradable polymers include polylactides, polyglycolides, polylactide-co-glycolides (PLGA), polyanhydrides, polyorthoesters, polyetheresters, polycaprolactones, polyesteramides, poly(butyric acid), poly(valeric acid), polyurethanes, and/or blends and copolymers thereof. Examples of non-biodegradable polymers include nylons, polyesters, polycarbonates, polyacrylates, polymers of ethylene-vinyl

acetates and other acyl substituted cellulose acetates, non-degradable polyurethanes, polystyrenes, polyvinyl chloride, polyvinyl fluoride, poly(vinyl imidazole), chlorosulphonate polyolefins, polyethylene oxide, and/or blends and copolymers thereof.

[1048] The embodiments described herein and/or portions thereof can include components formed of one or more parts, features, structures, etc. When referring to such components it should be understood that the components can be formed by a singular part having any number of sections, regions, portions, and/or characteristics, or can be formed by multiple parts or features. For example, when referring to a structure such as a wall or chamber, the structure can be considered as a single structure with multiple portions, or multiple, distinct substructures or the like coupled to form the structure. Thus, a monolithically constructed structure can include, for example, a set of substructures. Such a set of substructures may include multiple portions that are either continuous or discontinuous from each other. A set of substructures can also be fabricated from multiple items or components that are produced separately and are later joined together (e.g., via a weld, an adhesive, or any suitable method).

[1049] Referring now to the drawings, FIG. 1 is a schematic illustration of a fluid control device 100 according to an embodiment. Generally, the fluid control device 100 (also referred to herein as "control device" or "device") is configured to withdraw bodily fluid from a patient. A first portion or amount (e.g., an initial amount) of the withdrawn bodily fluid is sequestered from a second portion or amount (e.g., a subsequent amount) of the withdrawn bodily fluid which can be subsequently used for additional testing, discarded, and/or reinfused into the patient. In this manner, contaminants or the like can be sequestered within the first portion or amount, leaving the second portion or amount substantially free of contaminants. The second portion or amount of bodily fluid can then be used as a biological sample in one or more tests for the purpose of medical diagnosis and/or treatment (e.g., a blood culture test or the like), as described in more detail herein. The first portion or amount of bodily fluid can be discarded as waste or can be used in any suitable test that is less likely to produce false, inaccurate, distorted, inconsistent, and unreliable results as a result of potential contaminants contained therein. In other instances, the first portion or amount of bodily fluid can be infused back into the patient.

[1050] The control device 100 includes a housing 130 that has and/or forms an inlet 131, at least one outlet 136, and a sequestration chamber 134. The inlet 131 is configured to fluidically couple to a lumen-containing device, which in turn, can place the housing 130 in fluid communication with a bodily fluid source. For example, the housing 130 can be coupled to and/or can include a lumen-containing device that is in fluid communication with the inlet

131 and that is configured to be percutaneously disposed in a patient (e.g., a butterfly needle, intravenous (IV) catheter, peripherally inserted central catheter (PICC), syringe, sterile tubing, intermediary lumen-containing device, and/or bodily-fluid transfer device or the like). Thus, bodily fluid can be transferred from the patient and/or other bodily fluid source to the housing 130 via the inlet 131, as described in further detail herein. The outlet(s) 136 can be placed in fluid communication with a fluid collection device 180 (e.g., a fluid or sample reservoir, syringe, evacuated container, etc.). As such, the control device 100 can be used and/or manipulated to selectively transfer a volume of bodily fluid from a bodily fluid source, through the inlet 131, the housing 130, and the outlet(s) 136 to the fluid collection device 180, as described in further detail herein.

[1051] The housing 130 defines one or more fluid flow paths 133 between the inlet 131 and the sequestration chamber 134 and/or one or more fluid flow paths 154 between the inlet 131 and the outlet 136. The housing 130 of the device 100 can be any suitable shape, size, and/or configuration. For example, in some embodiments, the housing 130 can have a size that is at least partially based on a volume of bodily fluid at least temporarily stored, for example, in the sequestration chamber 134. As described in further detail herein, the control device 100 and/or the housing 130 can be configured to transition between operating modes such that bodily fluid flows through at least one of the fluid flow paths 133 and/or 154. Moreover, the control device 100 and/or the housing 130 can be configured to transition automatically (e.g., based on pressure differential, time, electronically, saturation of a membrane, an absorbent and/or barrier material, etc.) or via intervention (e.g., user intervention, mechanical intervention, or the like).

[1052] The sequestration chamber 134 is at least temporarily placed in fluid communication with the inlet 131 via the fluid flow path(s) 133. As described in further detail herein, the sequestration chamber 134 is configured to (1) receive a flow and/or volume of bodily fluid from the inlet 131 and (2) sequester (e.g., separate, segregate, contain, retain, isolate, etc.) the flow and/or volume of bodily fluid therein. The sequestration chamber 134 can have any suitable arrangement such as, for example, those described herein with respect to specific embodiments. It should be understood, however, that the control device 100 and/or the housing 130 can have a sequestration chamber 134 in any suitable arrangement and is not intended to be limited to those shown and described herein. For example, in some embodiments, the sequestration chamber 134 can be at least partially formed by the housing 130. In other embodiments, the sequestration chamber 134 can be a reservoir placed and/or disposed within a portion of the housing 130. In other embodiments, the sequestration chamber

134 can be formed and/or defined by a portion of the fluid flow path 133. That is to say, the housing 130 can define one or more lumens and/or can include one or more lumen defining device(s) configured to receive a flow of bodily fluid from the inlet 131, thereby defining the fluid flow path 133. In such embodiments, at least a portion of the lumen and/or a portion of the lumen defining device(s) can form and/or can define the sequestration chamber 134.

[1053] The sequestration chamber 134 can have any suitable volume and/or fluid capacity. For example, in some embodiments, the sequestration chamber 134 can have a volume and/or fluid capacity between about 0.25 mL and about 5.0 mL. In some embodiments, the sequestration chamber 134 can have a volume measured in terms of an amount of bodily fluid (e.g., the initial or first amount of bodily fluid) configured to be transferred in the sequestration chamber 134. For example, in some embodiments, the sequestration chamber 134 can have a volume sufficient to receive an initial volume of bodily fluid as small as a microliter or less of bodily fluid (e.g., a volume as small as 20 drops of bodily fluid, 10 drops of bodily fluid, 5 drops of bodily fluid, a single drop of bodily fluid, or any suitable volume therebetween). In other embodiments, the sequestration chamber 134 can have a volume sufficient to receive an initial volume of bodily fluid up to, for example, about 5.0 mL, 10.0 mL, 15 mL, 20 mL, 30 mL, 40 mL, 50 mL, or more. In some embodiments, the sequestration chamber 134 can have a volume that is equal to a fraction of and/or a multiple of at least some of the volumes of one or more lumen(s) placing the sequestration chamber 134 in fluid communication with the bodily fluid source.

[1054] Although not shown in FIG. 1, in some embodiments, the sequestration chamber 134 can include any suitable arrangement, configuration, and/or feature, and/or can be formed of one or more materials configured to interact with a portion of the bodily fluid transferred into the sequestration chamber 134. For example, in some embodiments, the housing 130 can include an absorbent and/or hydrophilic material disposed within the sequestration chamber 134. Accordingly, when bodily fluid is transferred into the sequestration chamber 134, the absorbent and/or hydrophilic material can absorb, attract, retain, expand, and/or otherwise interact with at least a portion of the bodily fluid, which in turn, can sequester and/or retain at least an initial portion of the bodily fluid within the sequestration chamber 134, as described in further detail herein. In other embodiments, the sequestration chamber 134 can include and/or can be formed of an expandable or collapsible material configured to transition between a first state (e.g., while an initial portion of the bodily fluid is being transferred into the sequestration chamber 134) to a second state (e.g., after the initial portion of the bodily fluid is transferred into the sequestration chamber 134). In some embodiments, a force associated with and/or

resulting from such a material expanding or collapsing can be operable to transition the housing 130 and/or the device 100 from a first state, position, configuration, etc. to a second state, position, configuration, etc. In some embodiments, the sequestration chamber 134 and/or any other suitable portion of the housing 130 can include one or more chemicals, compounds, and/or the like configured to chemically interact with bodily fluid transferred through a portion of the housing 130, which can be operable to transition the control device 100 and/or the housing 130 between the first state and the second state (e.g., via a force or any other suitable means).

[1055] In some embodiments, the control device 100 and/or the housing 130 can include and/or define a flow controller 120 configured to selectively control a flow of fluids (e.g., gas or liquids) through a portion of the control device 100. For example, in some embodiments, the flow controller 120 can control a flow of bodily fluid through the control device 100 (or housing 130) and/or otherwise selectively control a flow of bodily fluid through at least one of the fluid flow paths 133 and/or 154. The flow controller 120 can be, for example, a valve, a membrane, a diaphragm, a restrictor, a vent, a selectively permeable member (e.g., a fluid impermeable barrier or seal that at least selectively allows the passage of air or gas therethrough), a port, a junction, an actuator, and/or the like, or any suitable combination thereof. In some embodiments, the flow controller 120 can be configured to selectively control (at least in part) a flow of fluids into and/or out of the sequestration chamber 134 and/or any other suitable portion of the housing 130. In this context, the flow of fluids, for example, can be a liquid such as water, oil, dampening fluid, bodily fluid, and/or any other suitable liquid, and/or can be a gas such as air, oxygen, carbon dioxide, helium, nitrogen, ethylene oxide, and/or any other suitable gas. For example, in some embodiments, a wall or structure of the housing 130 can define an opening, aperture, port, orifice, and/or the like that is in fluid communication with the sequestration chamber 134. In such embodiments, the flow controller 120 can be, for example, a semi-permeable member or membrane disposed in or about the opening to selectively allow a flow of air or gas through the opening while limiting or substantially preventing a flow of fluid (e.g., bodily fluid such as blood) through the opening.

[1056] In some embodiments, one or more flow controllers 120 or the like can be configured to facilitate air (or other fluid) displacement through one or more portions of the control device 100, which in some instances, can result in a pressure differential across one or more portions of the control device 100 or can result in and/or allow for a pressure equalization across one or more portions of the housing 130. In some embodiments, the control device 100 can be configured to selectively transfer a volume of bodily fluid to the sequestration chamber

134 or to the outlet 136 based at least in part on a pressure differential between two or more portions of the control device 100. In some embodiments, the pressure differential can result from fluidically coupling the outlet 136 to the fluid collection device 180, which can define and/or can be configured to produce a negative pressure (e.g., an evacuated reservoir, a syringe, a pressure charged canister, and/or other source or potential energy to create a vacuum or pressure differential). In other embodiments, the pressure differential can result from a change in volume and/or temperature. In still other embodiments, the pressure differential can result from at least a portion of the control device 100, the housing 130, and/or other portions of the flow path being evacuated and/or charged (e.g., the sequestration chamber 134 and/or any other suitable portion). In some embodiments, the pressure differential can be established automatically or via direct or indirect intervention (e.g., by the user).

[1057] Moreover, a flow of a fluid (e.g., gas and/or liquid) resulting from a pressure differential can be selectively controlled via one or more flow controllers 120 that can, for example, transition between one or more operating conditions to control the fluid flow. In some embodiments, for example, the flow controller 120 can be an actuator or the like configured to transition between one or more operating conditions or states to establish fluid communication between one or more portions of the control device 100 and/or configured to sequester one or more portions of the control device 100 (e.g., the sequestration chamber 134). In some embodiments, the flow controller 120 can be member or device formed of an absorbent material configured to selectively allow fluid flow therethrough. For example, such an absorbent material can be transitioned from a first state in which the material allows a flow of gas (e.g., air) therethrough but prevents a flow of liquid (e.g., bodily fluid) therethrough, to a second state in which the material substantially prevents a flow of gas and liquid therethrough. In other embodiments, the flow controller 120 can include one or more valves, membranes, diaphragms, and/or the like. In some embodiments, the flow controller 120 can include any suitable combination of devices, members, and/or features. It should be understood that the flow controllers included in the embodiments described herein are presented by way of example and not limitation. Thus, while specific flow controllers are described herein, it should be understood that fluid flow can be controlled through the control device 100 by any suitable means.

[1058] The outlet(s) 136 is/are in fluid communication with and/or is/are configured to be placed in fluid communication with the fluid flow paths 133 and/or 154. As shown in FIG. 1, the outlet 136 can be any suitable outlet, opening, port, stopcock, lock, seal, coupler, valve (e.g. one-way, check valve, duckbill valve, umbrella valve, and/or the like), etc. and is configured

to be fluidically coupled to the fluid collection device 180 (e.g., a fluid reservoir, culture sample bottle, syringe, container, vial, dish, receptacle, pump, adapter, and/or any other suitable collection or transfer device). In some embodiments, the outlet 136 can be monolithically formed with the fluid collection device 180. In other embodiments, the outlet 136 can be at least temporarily coupled to the fluid collection device 180 via an adhesive, a resistance fit, a mechanical fastener, a threaded coupling, a piercing or puncturing arrangement, any number of mating recesses, and/or any other suitable coupling or combination thereof. Similarly stated, the outlet 136 can be physically (e.g., mechanically) and/or fluidically coupled to the fluid collection device 180 such that an interior volume defined by the fluid collection device 180 is in fluid communication with the outlet 136. In still other embodiments, the outlet 136 can be operably coupled to the fluid collection device 180 via an intervening structure (not shown in FIG. 1), such as a flexible sterile tubing. In some embodiments, the arrangement of the outlet 136 can be such that the outlet 136 is physically and/or fluidically sealed prior to coupling to the fluid collection device 180. In some embodiments, the outlet 136 can be transitioned from a sealed configuration to an unsealed configuration in response to being coupled to the fluid collection device 180 and/or in response to a negative pressure differential between an environment within the outlet 136 and/or housing 130 and an environment within the fluid collection device 180.

[1059] The fluid collection device 180 can be any suitable device for at least temporarily containing a bodily fluid, such as, for example, any of those described in detail above. For example, in some embodiments, the fluid collection device 180 can be a single-use disposable collection tube(s), a syringe, a vacuum-based collection tube(s), an intermediary bodily-fluid transfer device, and/or the like. In some embodiments, the fluid collection device 180 can be substantially similar to or the same as known sample containers such as, for example, a Vacutainer® (manufactured by BD), a BacT/ALERT ® SN or BacT/ALERT ® FA (manufactured by Biomerieux, Inc.), and/or any suitable reservoir, vial, microvial, microliter vial, nanoliter vial, container, microcontainer, nanocontainer, and/or the like. In some embodiments, the fluid collection device 180 can be a sample reservoir that includes a vacuum seal that maintains negative pressure conditions (vacuum conditions) inside the sample reservoir, which in turn, can facilitate withdrawal of bodily fluid from the patient, through the control device 100, and into the sample reservoir, via a vacuum or suction force, as described in further detail herein. In embodiments in which the fluid collection device 180 is an evacuated container or the like, the user can couple the fluid collection device 180 to the outlet 136 to initiate a flow of bodily fluid from the patient such that a first or initial portion of the

bodily fluid is transferred into and sequestered by the sequestration chamber 134 and such that any subsequent portion or volume of bodily fluid bypasses and/or is otherwise diverted away from the sequestration chamber 134 and flows into the fluid collection device 180, as described in further detail herein.

[1060] Although the outlet 136 of the control device 100 and/or the housing 130 is described above as being fluidically coupled to and/or otherwise placed in fluid communication with the fluid collection device 180, in other embodiments, the control device 100 can be used in conjunction with any suitable bodily fluid collection device and/or system. For example, in some embodiments, the control device 100 described herein can be used in any suitable fluid transfer device such as those described in U.S. Patent Publication No. 2015/0342510 entitled, "Sterile Bodily-Fluid Collection Device and Methods," filed June 2, 2015 (referred to herein as the "'510 publication"), the disclosure of which is incorporated herein by reference in its entirety. More particularly, the control device 100 can be used in an "all-in-one" or pre-assembled device (e.g., such as those described in the '510 publication) to receive and sequester an initial volume of bodily fluid such that contaminants in subsequent volumes of bodily fluid are reduced and/or eliminated.

[1061] As described above, the device 100 can be used to procure a bodily fluid sample having reduced contamination from microbes such as, for example, dermally residing microbes, and/or the like. For example, in some instances, a user such as a doctor, physician, nurse, phlebotomist, technician, etc. can manipulate the device 100 to establish fluid communication between the inlet 131 and the bodily fluid source (e.g., a vein of a patient, cerebral spinal fluid (CSF) from the spinal cavity, urine collection, and/or the like). As a specific example, in some instances, the inlet 131 can be coupled to and/or can include a needle or the like that can be manipulated to puncture the skin of the patient and to insert at least a portion of the needle in the vein of the patient, thereby placing the inlet 131 in fluid communication with the bodily fluid source (e.g., the vein, an IV catheter, a PICC, etc.).

[1062] In some embodiments, once the inlet 131 is placed in fluid communication with the bodily fluid source (e.g., the portion of the patient), the outlet 136 can be fluidically coupled to the fluid collection device 180. As described above, in some embodiments, the fluid collection device 180 can be any suitable reservoir, container, and/or device configured to receive a volume of bodily fluid. For example, the fluid collection device 180 can be an evacuated reservoir or container that defines a negative pressure and/or can be a syringe that can be manipulated to produce a negative pressure. In some instances, coupling the outlet 136 to the fluid collection device 180 selectively exposes at least a portion of the fluid flow paths 133

and/or 154 to the negative pressure, thereby resulting in a negative pressure differential operable in drawing bodily fluid from the bodily fluid source (e.g., the patient), through the inlet 131, and into the housing 130.

[1063] In some embodiments, the arrangement of the housing 130 is such that when a volume of bodily fluid is transferred to and/or through the inlet 131, an initial portion of the volume of bodily fluid (also referred to herein as an "initial volume" or a "first volume") flows from the inlet 131, through at least a portion of the fluid flow path 133, and into the sequestration chamber 134. That is to say, in some embodiments, the control device 100 and/or the housing 130 can be in first or initial state in which the initial portion or volume of bodily fluid can flow in or through at least a portion the fluid flow path 133 and into the sequestration chamber 134. For example, in some embodiments, the initial state of the control device 100 and/or the housing 130 can be one in which one or more flow controllers 120 (e.g., valves, membranes, diaphragms, restrictors, vents, air permeable and fluid impermeable barriers, ports, actuators, and/or the like, or a combination thereof) are in a first state in which the fluid flow path 133 is exposed to the negative pressure differential via the sequestration chamber 134. In other words, the negative pressure within or created by the fluid collection device 180 can result in a negative pressure (or negative pressure differential) within at least a portion of the sequestration chamber 134 that is operable in drawing an initial flow of bodily fluid into the sequestration chamber 134 when one or more flow controllers 120 is/are in a first or initial state.

[1064] For example, in some embodiments, the flow controller 120 can be an actuator or the like that includes a valve (e.g. one-way valve, check valve, duckbill valve, umbrella valve, and/or the like), a selectively permeable member (e.g., a fluid impermeable barrier or seal that allows at least selective passage of gas or air), a selectively permeable membrane, a diaphragm, and/or the like that is at least temporarily fluidically coupled to a flow path between the fluid collection device 180 and the sequestration chamber 134 (e.g., at least a portion of the fluid flow path 154). While in some embodiments the flow controller 120 examples noted above can be, for example, known off-the-shelf components that are used in medical devices to control the flow of fluids and air, in other embodiments, the flow controller 120 can be a custom, proprietary, and/or specifically tailored component integrated into the device 100. When the flow controller 120 is in the first or initial state, the flow controller 120 can allow a flow of fluid therethrough in response to the negative pressure of the fluid collection device 180. In some embodiments, the flow controller 120 or a portion or component thereof is configured to allow only a flow of air or gas through the flow controller 120 and is configured

to limit and/or substantially prevent a flow of liquid (e.g., bodily fluid) through the flow controller 120. As such, the fluid collection device 180 can produce a negative pressure differential within the sequestration chamber 134 that is operable to draw an initial portion and/or amount of bodily fluid into the sequestration chamber 134 when the flow controller 120 is in a first or initial state without allowing the initial portion of bodily fluid to flow into the fluid flow path 154 and/or otherwise out of the sequestration chamber 134.

[1065] Although not shown in FIG. 1, in some embodiments, the control device 100 and/or the housing 130 can include a member, device, mechanism, feature, etc. configured to modulate a magnitude of the negative pressure to which the sequestration chamber 134 is exposed. For example, in some embodiments, a housing can include a valve, a membrane, a porous material, a restrictor, an orifice, and/or any other suitable member, device, and/or feature configured to modulate pressure. In some embodiments, modulating and/or controlling a magnitude of the pressure to which the sequestration chamber 134 is exposed can, in turn, modulate a magnitude of pressure exerted on the bodily fluid and/or within a vein of a patient. In some instances, such pressure modulation can reduce, for example, hemolysis of a blood sample and/or a likelihood of collapsing a vein (e.g., which is particularly important in fragile patients needing microbial and/or other diagnostic testing associated with use of the control device 100). In addition, the modulation of the negative pressure can, for example, at least partially control a rate at which the control device 100 transitions between a first configuration or state and a second configuration or state. In some embodiments, modulating the negative pressure can act like a timer. For example, a time between the introduction of the negative pressure differential and the transitioning of the control device 100 from the first state to the second state can be known, predetermined, calculated, and/or controlled. As such, in some instances, modulating the negative pressure can at least partially control an amount or volume of bodily fluid transferred into the sequestration chamber 134 (i.e., can control a volume of the initial amount of bodily fluid).

[1066] The initial portion and/or amount of bodily fluid can be any suitable volume of bodily fluid, as described above. For example, in some instances, the control device 100 and/or the housing 130 can remain in the first state until a predetermined and/or desired volume (e.g., the initial volume) of bodily fluid is transferred to the sequestration chamber 134. In some embodiments, the initial volume can be associated with and/or at least partially based on a volume of the sequestration chamber 134. In other embodiments, the initial volume can be associated with and/or at least partially based on an amount or volume of bodily fluid that can be absorbed by an absorbent material, an expandable material, a hydrophilic material, a

wicking material, and/or other suitable material disposed in the sequestration chamber 134. In other embodiments, the initial volume of bodily fluid can be associated with and/or at least partially based on an amount or volume of bodily fluid that can be transferred into the sequestration chamber 134 in a predetermined time. In still other embodiments, the initial volume can be associated with and/or at least partially based on an amount or volume of bodily fluid that is sufficient to fully wet or saturate a semi-permeable member or membrane otherwise configured to selectively expose the sequestration chamber 134 to the negative pressure of the fluid collection device 180 (i.e., the flow controller 120 such as an air permeable and liquid impermeable member or membrane). In other words, in some embodiments, the initial volume of bodily fluid can be a volume sufficient to transition one or more flow controllers 120 to a second state (e.g., a saturated or fully wetted state). In still other embodiments, the control device 100 and/or the housing 130 can be configured to transfer a volume of bodily fluid (e.g., the initial volume) into the sequestration chamber 134 until a pressure differential between the sequestration chamber 134 and the fluid flow path 133 and/or the bodily fluid source is brought into substantial equilibrium and/or is otherwise reduced below a desired threshold.

[1067] After the initial volume of bodily fluid is transferred and/or diverted into the sequestration chamber 134, the initial volume is sequestered, segregated, retained, contained, isolated, etc. in the sequestration chamber 134. For example, in some embodiments, the transitioning of the one or more flow controllers 120 from a first state to a second state can be operable to sequester and/or retain the initial portion of the bodily fluid in the sequestration chamber 134. As described in further detail herein, in some instances, contaminants such as, for example, dermally residing microbes or the like dislodged during the venipuncture event, other external sources of contamination, colonization of catheters and PICC lines that are used to collect samples, and/or the like can be entrained and/or included in the initial volume of the bodily fluid and thus, are sequestered in the sequestration chamber 134 when the initial volume is sequestered therein.

[1068] With the initial volume transferred and/or diverted into the sequestration chamber 134, the device 100 can transition to the second state in which a subsequent volume(s) of bodily fluid can flow through at least a portion the fluid flow paths 133 and/or 154 from the inlet 131 to the outlet 136. In some embodiments, the control device 100 and/or the housing 130 can passively and/or automatically transition (e.g., without user intervention) from the first state to the second state once the initial volume of bodily fluid is sequestered in the sequestration chamber 134. For example, in some embodiments, filling the sequestration chamber 134 to capacity and/or fully saturating, wetting, and/or impregnating an absorbent or similar material

disposed between the sequestration chamber 134 and the fluid collection device 180 can be such that further transfer of bodily fluid into the sequestration chamber 134 is limited and/or substantially prevented due to a removal or diversion of the negative pressure. In other embodiments, the control device 100 and/or the housing 130 can be manually transitioned or transitioned in response to at least an indirect interaction by a user. For example, in some embodiments, a user can transition the control device 100 and/or the housing 130 from the first state to the second state by actuating an actuator or the like (e.g., actuating the flow controller 120 or a portion thereof). In still other embodiments, at least a portion of the initial volume of bodily fluid can transition the control device 100 and/or the housing 130 from the first state to the second state. For example, the control device 100 can include a flow controller 120 that is and/or that includes a bodily fluid activated switch, valve, port, and/or the like. In other embodiments, a volume of bodily fluid can move and/or displace one or more flow controller 120 (e.g., actuators or the like) that can, for example, open a port, flow path, and/or outlet. In still other embodiments, a user can manipulate such a flow controller 120 (e.g., switch, valve, port, actuator, etc.) to transition the control device 100 and/or the housing 130 from the first state to the second state.

[1069] With the fluid collection device 180 fluidically coupled to the outlet 136 and with the control device 100 and/or the housing 130 being in the second state (e.g., the initial volume of bodily fluid is sequestered in or by the sequestration chamber 134), any subsequent volume(s) of the bodily fluid can flow from the inlet 131, through at least one of the fluid flow paths 133 and/or 154, through the outlet 136, and into the fluid collection device 180. Thus, as described above, sequestering the initial volume of bodily fluid in the sequestration chamber 134 prior to collecting or procuring one or more sample volumes of bodily fluid reduces and/or substantially eliminates an amount of contaminants in the one or more sample volumes. Moreover, in some embodiments, the arrangement of the control device 100 and/or the housing 130 can be such that the control device 100 and/or the housing 130 cannot transition to the second state prior to collecting and sequestering the initial volume in the sequestration chamber 134.

[1070] FIGS. 2-5 illustrate a fluid control device 200 according to an embodiment. The fluid control device 200 can be similar in at least form and/or function to the fluid control device 100 described above with reference to FIG. 1. Accordingly, portions of the fluid control device 200 that can be similar to portions of the fluid control device 100 are not described in further detail herein.

[1071] As shown in FIGS. 2-5, the fluid control device 200 (also referred to herein as "control device" or "device") includes a housing 230 having an inlet 231, an outlet 236, and an actuator 250. As described above with reference to the control device 100, the inlet 231 is configured to be placed in fluid communication with a bodily fluid source to receive a flow of bodily fluid therefrom (e.g., via a lumen-containing device such as a needle, IV catheter, PICC line, or the like). The outlet 236 is configured to be fluidically coupled to a fluid collection device such as, for example, a sample reservoir, a syringe, and/or other intermediary bodily fluid transfer device or vessel (e.g., a transfer device similar to those described in the '510 publication), and/or the like.

[1072] As described above with reference to the housing 130, the housing 230 defines one or more fluid flow paths 233 between the inlet 231 and a sequestration chamber 234 and/or one or more fluid flow paths 254 between the inlet 231 and the outlet 236. The housing 230 of the device 200 can be any suitable shape, size, and/or configuration. For example, in some embodiments, the housing 230 can be substantially similar in at least form and/or function to the housing 130 described above with reference to FIG. 1. The sequestration chamber 234 of the housing 230 is at least temporarily placed in fluid communication with the inlet 231 via the fluid flow path(s) 233. Moreover, the sequestration chamber 234 can be selectively placed in fluid communication with the fluid flow path 254 such that at least air or gas can be transferred therebetween, as described in further detail herein.

[1073] As described in further detail herein, the sequestration chamber 234 is configured to (1) receive a flow and/or volume of bodily fluid from the inlet 231 and (2) sequester (e.g., separate, segregate, contain, retain, isolate, etc.) the flow and/or volume of bodily fluid therein. The sequestration chamber 234 can have any suitable shape, size, and/or configuration. For example, in some embodiments, the sequestration chamber 234 can have any suitable size, volume, and/or fluid capacity such as, for example, those described above with reference to the sequestration chamber 134. In the embodiment shown in FIGS. 2-5, the sequestration chamber 234 can be at least partially formed by the housing 230 that defines a lumen or flow path. In some embodiments, at least a portion of the fluid flow path 233 can extend through a portion of the housing 230 to form and/or define at least a portion of the sequestration chamber 234. As shown in FIGS. 2-5, the sequestration chamber 234 and/or a portion of the fluid flow path 233 forming the sequestration chamber 234 can have a serpentine configuration or the like. In other embodiments, the sequestration chamber 234 can have any suitable arrangement. For example, in some embodiments, a housing can include a sequestration chamber that is formed by a flexible tubing or the like that can be arranged in any suitable shape and/or configuration.

[1074] In some embodiments, the housing 230 and/or the sequestration chamber 234 can include, form, and/or define a flow controller 242. The flow controller 242 can be, for example, a valve, membrane, diaphragm, restrictor, vent, a selectively permeable member (e.g., a fluid impermeable barrier or seal that allows at least selective passage of gas or air such as, for example, a blood barrier and/or the like), port, etc. (collectively referred to herein as a "flow controller") configured to selectively control (at least in part) a flow of fluids into and/or out of the sequestration chamber 234 and/or any other suitable portion of the housing 230. More particularly, in the embodiment shown in FIGS. 2-5, the flow controller 242 is a selectively permeable fluid barrier (e.g., a blood barrier) that includes and/or is formed of a porous material configured to selectively allow a flow of gas therethrough but to prevent a flow of a liquid therethrough.

[1075] As shown, the flow controller 242 is positioned within the housing 230 to selectively establish fluid communication between the sequestration chamber 234 and the fluid flow path 254. Thus, with the flow controller 242 being configured as a semi-permeable member, the flow controller 242 can be configured to at least temporarily allow a gas or air to transfer between the fluid flow path 254 and the sequestration chamber 234 and can be configured to substantially prevent a flow of liquid between the fluid flow path 254 and the sequestration chamber 234, as described in further detail herein.

[1076] The outlet 236 of the housing 230 is in fluid communication with and/or is configured to be placed in fluid communication with the fluid flow paths 233 and/or 254. As shown in FIGS. 2-5, the outlet 236 can be any suitable outlet, opening, port, lock, seal, coupler, etc. and is configured to be fluidically coupled to a fluid collection device such as a sample reservoir, a syringe, container, and/or other sample vessel. In some embodiments, the outlet 236 can be monolithically formed with the fluid collection device or can be at least temporarily coupled to the fluid collection device, as described above with reference to the outlet 136 of the housing 130. The fluid collection device can be any suitable reservoir, container, and/or device for containing a bodily fluid, such as, for example, any of those described in detail above with reference to the fluid collection device 180. More particularly, in some embodiments, the outlet 236 can be configured to couple to an evacuated sample reservoir. As such, the user can couple the sample reservoir to the outlet 236 to initiate a flow of bodily fluid from the patient such that a first or initial portion of the bodily fluid is transferred into and sequestered by the sequestration chamber 234 and such that any subsequent portion or volume of bodily fluid bypasses and/or is otherwise diverted away from the sequestration chamber 234 and flows into the sample reservoir.

[1077] As shown in FIGS. 3-5, the housing 230 includes and/or is coupled to the actuator 250 configured to selectively control a flow of bodily fluid through the housing 230. More particularly, the actuator 250 is disposed, for example, between a portion of the fluid flow path 233 and a portion of the fluid flow path 254. While the actuator 250 is shown in FIGS. 3-5 as being positioned apart from, away from, and/or downstream of a junction between the fluid flow path 233 and the sequestration chamber 234, in other embodiments, the actuator 250 can be disposed at any suitable position within the housing 230. For example, in some embodiments, the actuator 250 can be positioned at and/or can form at least a portion of a junction between the fluid flow path 233, the sequestration chamber 234, and the fluid flow path 254.

[1078] The actuator 250 can be any suitable shape, size, and/or configuration. For example, in some embodiments, the actuator 250 can be any suitable member or device configured to transition between a first state and a second state. In the embodiment shown in FIGS. 2-5, the actuator 250 is configured to isolate, sequester, separate, and/or otherwise prevent fluid communication between the fluid flow path 233 and the fluid flow path 254 when in the first state and is configured to place the fluid flow path 233 in fluid communication with the fluid flow path 254 when in the second state. In some embodiments, for example, the actuator 250 can be a valve, plunger, seal, membrane, flap, plate, and/or the like. As shown, for example, in FIG. 5, the actuator 250 can include one or more seals 265 configured to selectively establish fluid communication between the fluid flow channels 233 and 254 when the actuator 250 is transitioned from a first state to a second state (e.g., pressed, rotated, moved, activated, switched, slid, etc.).

[1079] Although the actuator 250 is particularly shown in FIGS. 2-5 and described above, in other embodiments, the control device 200 can include any suitable actuator or device configured to selectively establish fluid communication between the fluid flow path 233 and 254. Thus, while particularly shown in FIGS. 2-5, it should be understood that the control device 200 is presented by way of example only and not limitation. For example, while the actuator 250 is shown in FIGS. 2-5 as being disposed in a given position, in other embodiments, the actuator 250 can be placed at any suitable position along the housing 230. By way of example, in some embodiments, the actuator 250 can be disposed at the junction between the fluid flow path 233, the sequestration chamber 234, and the inlet 231. In such embodiments, a flow of bodily fluid can flow directly from the inlet 231 and into the sequestration chamber 234 when the actuator 250 is in the first state and can flow directly from the inlet 231 to the fluid flow path 254 when the actuator 250 is in the second state. In other words, the actuator

250 can form a portion of the sequestration chamber 234 such that when the actuator 250 is in the first state, bodily fluid flows from the inlet directly into the sequestration chamber 234. When the actuator 250 is actuated, placed, and/or transitioned to the second state, the actuator 250 can, for example, allow bodily fluid to flow directly from the inlet 231 to the fluid flow path 233. In such embodiments, the actuator 250 can prevent the formation of a junction between the inlet 231, the sequestration chamber 234, and the fluid flow path 233. Moreover, when in the second state, the actuator 250 can be operable in at least partially sequestering the sequestration chamber 234 from the inlet 231 and/or the fluid flow path 233.

[1080] In addition, the actuator 250 can be actuated and/or transitioned in any suitable manner. For example, in some embodiments, the actuator 250 can transition between the first and the second state in response to a manual actuation by the user (e.g., exerting a manual force on a button, slider, switch, rotational member, etc.). In other embodiments, the actuator 250 can be configured to automatically transition between the first state and the second state in response to a pressure differential (or lack thereof), a change in potential or kinetic energy, a change in composition or configuration (e.g., a portion of the actuator could at least partially dissolve or transform), and/or the like. In still other embodiments, the actuator 250 can be mechanically and/or electrically actuated or transitioned based on a predetermined time, volumetric flow rate, flow velocity, etc. While examples of actuators and/or ways in which an actuator can transition are provided herein, it should be understood that they have been presented by way of example only and not limitation. Thus, a control device 200 can include any suitable actuator configured to transition in any suitable manner.

[1081] As described above, the device 200 can be used to procure a bodily fluid sample having reduced contamination from microbes such as, for example, dermally residing microbes, and/or the like. For example, in some instances, a user such as a doctor, physician, nurse, phlebotomist, technician, etc. can manipulate the device 200 to establish fluid communication between the inlet 231 and the bodily fluid source (e.g., a vein of a patient). Once the inlet 231 is placed in fluid communication with the bodily fluid source (e.g., the portion of the patient), the outlet 236 can be fluidically coupled to the fluid collection device. As described above, in the embodiment shown in FIGS. 2-5, the fluid collection device can be, for example, an evacuated reservoir or container that defines a negative pressure and/or can be any other suitable negative pressure source.

[1082] Coupling the outlet 236 to the fluid collection device selectively exposes at least a portion of the fluid flow path 254 to the negative pressure within the fluid collection device. As described above, the flow controller 242 is in fluid communication with the fluid flow path

254 and the sequestration chamber 234. Thus, coupling the outlet 236 to the fluid collection device exposes the sequestration chamber to the negative pressure of the fluid collection device, thereby resulting in a negative pressure differential operable in drawing bodily fluid from the bodily fluid source (e.g., the patient), through the inlet 231, and into the housing 230. As described above with reference to the control device 100, the arrangement of the housing 230 is such that when a volume of bodily fluid is transferred to and/or through the inlet 231, an initial portion of the volume of bodily fluid (also referred to herein as an "initial volume" or a "first volume") flows from the inlet 231, through at least a portion of the fluid flow path 233, and into the sequestration chamber 234. That is to say, in some embodiments, the control device 200 and/or the housing 230 can be in first or initial state in which the initial portion or volume of bodily fluid can flow in or through at least a portion the fluid flow path 233 and into the sequestration chamber 234.

[1083] As described above, the housing 230 and/or the control device 200 can be in the initial state when the flow controller 242 and the actuator 250 are in a first state, position, configuration, etc. As such, the actuator 250 isolates, separates, segregates, sequesters and/or otherwise prevents direct fluid communication between the fluid flow paths 233 and 254. In addition, the inlet 231 is exposed to the negative pressure differential via the sequestration chamber 234. In other words, the negative pressure within the fluid collection device can result in a negative pressure (or negative pressure differential) within at least a portion of the sequestration chamber 234 that is operable in drawing an initial flow of bodily fluid from the inlet 233 into the sequestration chamber 234 when the housing 230 and/or control device 200 is in the first or initial state.

[1084] When the flow controller 242 is in the first or initial state, the flow controller 242 can allow a flow of fluid (e.g., a gas or air) therethrough in response to the negative pressure of the fluid collection device (e.g., a sample reservoir, a syringe, or other source of potential energy used to create negative pressure), as described above with reference to the housing 130. In some instances, it may be desirable to modulate and/or control a magnitude of the negative pressure differential. In the embodiment shown in FIGS. 2-5, for example, the housing 230 defines a restricted flow path 232 that places the flow controller 242 in fluid communication with the fluid flow path 254. More specifically, the restricted flow path 232 is a fluid flow path having a smaller diameter than at least the fluid flow path 254.

[1085] For example, in some embodiments, the restricted flow path 232 can have a diameter of about 0.0005", about 0.001", about 0.003", about 0.005", about 0.01", about 0.1", about 0.5" or more. In other embodiments, the restricted flow path 232 can have a diameter

less than 0.0005" or greater than 0.5". In some embodiments, the restricted flow path 232 can have a predetermined and/or desired length of about 0.01", about 0.05", about 0.1", about 0.15", about 0.2", about 0.5", or more. In other embodiments, the restricted flow path 232 can have a predetermined and/or desired length that is less than 0.01" or more than about 0.5". Moreover, in some embodiments, a restricted flow path 232 can have any suitable combination of diameter and length to allow for and/or to provide a desired flow characteristic through at least a portion of the control device 200.

[1086] In this embodiment, the restricted flow path 232 having a smaller diameter results in a lower magnitude of negative pressure being applied through the sequestration chamber than a magnitude of negative pressure when the restricted flow path has a larger diameter. In some instances, modulating a magnitude of negative pressure can control a rate at which bodily fluid is transferred into the sequestration chamber 234. For example, in some embodiments, a fluid collection device and/or other suitable negative pressure source may produce a negative pressure differential having a magnitude (e.g., a negative magnitude) of about 0.5 pounds per square inch (PSI), about 1.0 PSI, about 2.0 PSI, about 3.0 PSI, about 4.0 PSI, about 5.0 PSI, about 10 PSI, about 12.5 PSI, or about 14.7 PSI (e.g., at or substantially at atmospheric pressure at about sea level). In some embodiments, a fluid collection device such as an evacuated container or the like can have a predetermined negative pressure of about 12.0 PSI. Accordingly, by controlling the diameter and/or length of the restricted flow path 232, the amount of negative pressure to which the sequestration chamber 234 is exposed and/or the rate at which the negative pressure is applied can be controlled, reduced, and/or otherwise modulated. In some instances, the use of the restricted flow path 232 can result in a delay or ramp up of the negative pressure exerted on or in the sequestration chamber.

[1087] Moreover, in this embodiment, the restricted flow path 232 is, for example, a gas flow path configured to receive a flow of gas or air but not a flow of a liquid (e.g., bodily fluid). In some embodiments, the diameter of the restricted flow path 232 can be sufficiently small to limit and/or prevent a flow of a liquid therethrough. In addition, the arrangement of the restricted flow path 232 being disposed between the fluid flow path 254 and the flow controller 242 is such that a flow of bodily fluid and/or any other liquid is substantially prevented by the flow controller 242 (e.g., a selectively permeable barrier or seal).

[1088] Although the pressure modulation is described above as being based on a diameter of the restricted flow path 232 (i.e., a single restricted flow path), it should be understood that this is presented by way of example only and not limitation. Other means of modulating the magnitude of negative pressure to which the sequestration chamber is exposed can include, for

example, a porous material, a valve, a membrane, a diaphragm, a specific restriction, a vent, a deformable member or flow path, and/or any other suitable means. In other embodiments, a control device can include any suitable number of restricted flow paths, each of which can have substantially the same diameter or can have varied diameters. For example, in some embodiments, a control device can include up to 100 restricted flow paths or more. In such embodiments, each of the restricted flow paths can have a diameter of between about 0.0005" and about 0.1", between about 0.0005" and about 0.05", or between about 0.0005" and about 0.01". In some embodiments, multiple restricted flow paths can be configured to (1) selectively provide a flow path between the outlet 236 and the sequestration chamber 234 that exposes the sequestration chamber 234 to the negative pressure differential, and (2) act as a flow controller configured to selectively allow the passage of a gas and/or air while substantially preventing the passage of a liquid (e.g., bodily fluid).

[1089] In some embodiments, modulating and/or controlling a magnitude of the pressure to which the sequestration chamber 234 is exposed can, in turn, modulate a magnitude of pressure exerted on the bodily fluid and/or within a vein of a patient. In some instances, such pressure modulation can reduce, for example, hemolysis of a blood sample and/or a likelihood of collapsing a vein. In some instances, the ability to modulate and/or control an amount or magnitude of negative pressure can allow the control device 200 to be used across a large spectrum of patients that may have physiological challenges whereby negative pressure is often needed to facilitate collection of bodily fluid such as, for example, blood (i.e. pressure differential between atmospheric pressure and a patient's vascular pressure is not sufficient to facilitate consistent and sufficiently forceful flow) but not so much pressure that a rapid force flattens, collapses, caves-in, and/or otherwise inhibits patency and ability to collect blood.

[1090] The initial portion and/or amount of bodily fluid can be any suitable volume of bodily fluid, as described in detail above with reference to the control device 100. For example, in some instances, the initial volume can be associated with and/or at least partially based on an amount or volume of bodily fluid that is sufficient to fully wet or saturate the flow controller 242. In other words, in some embodiments, the initial volume of bodily fluid can be a volume sufficient to transition the flow controller 242 to a second state (e.g., a saturated or fully wetted state). In some embodiments, the flow controller 242 is placed in a sealed configuration when transitioned to the second state. That is to say, saturating and/or fully wetting the flow controller 242 (e.g., the semi-permeable material) places the flow controller 242 in a sealed configuration in which the flow controller 242 substantially prevents a flow of a liquid and a gas therethrough. Thus, transitioning the flow controller 242 to the second state sequesters,

blocks, isolates, separates, segregates, and/or otherwise prevents flow through the flow controller 242 between the restricted flow path 232 and the sequestration chamber 234.

[1091] After the initial volume of bodily fluid is transferred and/or diverted into the sequestration chamber 234, the control device 200 and/or the housing 230 can be transitioned to its second state or operating mode to sequester, segregate, retain, contain, isolate, etc. the initial volume in the sequestration chamber 234. For example, as described above, the flow controller 242 is placed in the sealed configuration. In addition, the actuator 250 can be actuated to transition from its first state to its second state to establish fluid communication between the fluid flow paths 233 and 254. As such, the negative pressure otherwise exerted on or through the sequestration chamber 234 is now exerted on or through the fluid flow paths 233 and 254. In response, bodily fluid can flow from the inlet 231, through the fluid flow paths 233 and 254, through the outlet 236, and into the fluid collection device. In some embodiments, the transitioning of the flow controller 242 and the actuator 250 from their respective first states to their respective second states is operable to sequester and/or retain the initial portion of the bodily fluid in the sequestration chamber 234. As described in further detail herein, in some instances, contaminants such as, for example, dermally residing microbes or the like dislodged during the venipuncture event, can be entrained and/or included in the initial volume of the bodily fluid and thus, are sequestered in the sequestration chamber 234 when the initial volume is sequestered therein.

[1092] With the fluid collection device fluidically coupled to the outlet 236 and with the control device 200 and/or the housing 230 being in the second state (e.g., the initial volume of bodily fluid is sequestered in or by the sequestration chamber 234), any subsequent volume(s) of the bodily fluid can flow from the inlet 231, through the fluid flow paths 233 and 254, through the outlet 236, and into the fluid collection device. Thus, as described above, sequestering the initial volume of bodily fluid in the sequestration chamber 234 prior to collecting or procuring one or more sample volumes of bodily fluid reduces and/or substantially eliminates an amount of contaminants in the one or more sample volumes. Moreover, in some embodiments, the arrangement of the control device 200 and/or the housing 230 can be such that the control device 200 and/or the housing 230 cannot transition to the second state prior to collecting and sequestering the initial volume in the sequestration chamber 234.

[1093] While the control device 200 is described above with reference to FIGS. 2-5 as including the actuator 250 configured to be moved (e.g., via a force applied by a user) between the first state and the second state, in other embodiments, a control device can include any suitable member, device, mechanism, etc. configured to selectively establish fluid

communication between two or more fluid flow paths. For example, FIGS. 6-8 illustrate a fluid control device 300 according to an embodiment. The fluid control device 300 can be similar in at least form and/or function to the fluid control device 100 described above with reference to FIG. 1 and/or the fluid control device 200 described above with reference to FIGS. 2-5. Accordingly, portions of the fluid control device 300 that can be similar to portions of the fluid control devices 100 and/or 200 are not described in further detail herein.

[1094] As shown in FIGS. 6-8, the fluid control device 300 (also referred to herein as "control device" or "device") includes a housing 330 having an inlet 331 and an outlet 336, and including or being coupled to an actuator 350. As described above with reference to the control devices 100 and/or 200, the inlet 331 is configured to be placed in fluid communication with a bodily fluid source to receive a flow of bodily fluid therefrom (e.g., via a lumen-containing device such as a needle or the like). The outlet 336 is configured to be fluidically coupled to a fluid collection device (not shown in FIGS. 6-8).

[1095] As described above with reference to the housings 130 and/or 230, the housing 330 defines one or more fluid flow paths 333, 354A, and 354B configured to selectively place the inlet 331 in fluid communication with the sequestration chamber 334 and/or the outlet 336. The housing 330 of the device 300 can be any suitable shape, size, and/or configuration. For example, in some embodiments, the housing 330 can be substantially similar in at least form and/or function to the housings 130 and/or 230 described above. In some embodiments, the housing 330 can have a size that is at least partially based on a volume of bodily fluid at least temporarily stored, for example, in the sequestration chamber 334. The sequestration chamber 334 of the housing 330 is at least temporarily placed in fluid communication with the inlet 331 via the fluid flow path(s) 333. Moreover, the sequestration chamber 334 can be selectively placed in fluid communication with the fluid flow path 354A such that at least air or gas can be transferred therebetween, as described in further detail herein.

[1096] As described in further detail herein, the sequestration chamber 334 is configured to (1) receive a flow and/or volume of bodily fluid from the inlet 331 and (2) sequester (e.g., separate, segregate, contain, retain, isolate, etc.) the flow and/or volume of bodily fluid therein. The sequestration chamber 334 can have any suitable shape, size, and/or configuration. For example, in some embodiments, the sequestration chamber 334 can be substantially similar to the sequestration chamber 234 described above with reference to FIGS. 2-5 and thus, is not described in further detail herein. Likewise, the housing 330 and/or the sequestration chamber 334 include, form, and/or define a flow controller 342 that can be substantially similar to the flow controller 242 described above. As such, the flow controller 342 is positioned within the

housing 330 to selectively establish fluid communication between the sequestration chamber 334 and the fluid flow path 354A, as described in further detail herein.

[1097] The outlet 336 of the housing 330 is in fluid communication with and/or is configured to be placed in fluid communication with the fluid flow paths 333, 354A, and/or 354B. In addition, the outlet 336 is configured to be fluidically coupled to a fluid collection device such as, for example, a sample reservoir, container, vial, negative pressure source, syringe, and/or intermediate control and/or transfer device (not shown in FIGS. 6-8). The outlet 336 and the fluid collection device can each be substantially similar to the outlet 236 and fluid collection device, respectively, described above with reference to the control device 200. Thus, the outlet 336 and fluid collection device are not described in further detail herein.

[1098] As shown in FIGS. 6-8, the housing 330 includes and/or is coupled to the actuator 350, which is configured to selectively control a flow of bodily fluid through the housing 330. In some embodiments, the actuator 350 can be substantially similar in at least function to the actuator 250 described above with reference to FIGS. 2-5. In this embodiment, however, the actuator 350 is arranged as a plunger and includes a set of seals 365 disposed along an outer surface of the plunger. Moreover, the actuator 350 has a substantially annular shape and is configured to at least temporarily receive and/or otherwise be disposed about a portion of the flow controller 342, as shown in FIG. 8. As described above with reference to the actuator 250, the actuator 350 is configured to isolate, sequester, separate, and/or otherwise prevent fluid communication between the fluid flow path 333 and the fluid flow path 354B when in the first state and is configured to place the fluid flow path 333 in fluid communication with the fluid flow path 354B when in the second state.

[1099] As described above, the device 300 can be used to procure a bodily fluid sample having reduced contamination from microbes such as, for example, dermally residing microbes, and/or the like. For example, in some instances, a user such as a doctor, physician, nurse, phlebotomist, technician, etc. can manipulate the device 300 to establish fluid communication between the inlet 331 and the bodily fluid source (e.g., a vein of a patient). Once the inlet 331 is placed in fluid communication with the bodily fluid source (e.g., the portion of the patient), the outlet 336 can be fluidically coupled to the fluid collection device. As described above, in the embodiment shown in FIGS. 6-8, the fluid collection device can be, for example, an evacuated reservoir, a syringe, and/or any container that defines a negative pressure.

[1100] Coupling the outlet 336 to the fluid collection device selectively exposes at least a portion of the fluid flow paths 354A and 354B to the negative pressure within and/or produced

by the fluid collection device. The arrangement of the actuator 350 when in its first state, configuration, and/or position is such that the actuator 350 isolates the fluid flow path 354B from the fluid flow path 333 and as such, the fluid flow path 333 is not exposed to the negative pressure differential produced by the fluid collection device. As described above, the flow controller 342 is in fluid communication with the fluid flow path 354A and the sequestration chamber 334. More particularly, the annular arrangement of the actuator 350 allows the flow controller 342 to be in fluid communication with the fluid flow path 354A (see e.g., FIG. 8). Thus, coupling the outlet 336 to the fluid collection device exposes the sequestration chamber 334 to the negative pressure of the fluid collection device, thereby resulting in a negative pressure differential operable in drawing bodily fluid from the bodily fluid source (e.g., the patient), through the inlet 331, and into the housing 330. As described above with reference to the control devices 100 and 200, the arrangement of the housing 330 is such that when a volume of bodily fluid is transferred to and/or through the inlet 331, an initial portion of the volume of bodily fluid (also referred to herein as an "initial volume" or a "first volume") flows from the inlet 331 and into the sequestration chamber 334. That is to say, in some embodiments, the housing 330 can be in first or initial state in which the initial portion or volume of bodily fluid can flow from the inlet 331 and into the sequestration chamber 334.

[1101] As described above, the housing 330 and/or the control device 300 can be in the initial state when the flow controller 342 and the actuator 350 are in a first state, position, configuration, etc. As such, the actuator 350 isolates, separates, segregates, sequesters and/or otherwise prevents direct fluid communication between the fluid flow paths 333 and 354B. In addition, the inlet 331 is exposed to the negative pressure differential via the sequestration chamber 334. In other words, the negative pressure within or produced by the fluid collection device can result in a negative pressure (or negative pressure differential) within at least a portion of the sequestration chamber 334 that is operable in drawing an initial flow of bodily fluid from the inlet 331 into the sequestration chamber 334 when the housing 330 and/or control device 300 is in the first or initial state. As described in detail above, in some instances, it may be desirable to modulate and/or control a magnitude of the negative pressure differential by any suitable means such as those described herein.

[1102] The initial portion and/or amount of bodily fluid can be any suitable volume of bodily fluid, as described in detail above with reference to the control devices 100 and/or 200. For example, in some instances, the initial volume can be associated with and/or at least partially based on an amount or volume of bodily fluid that is sufficient to fully wet or saturate the flow controller 342. In other words, in some embodiments, the initial volume of bodily

fluid can be a volume sufficient to transition the flow controller 342 to a second state (e.g., a saturated or fully wetted state). As described above with reference to the flow controller 242, the flow controller 342 is placed in a sealed configuration when transitioned to the second state. Thus, transitioning the flow controller 342 to the second state sequesters, blocks, isolates, separates, segregates, and/or otherwise prevents flow through the flow controller 342.

[1103] After the initial volume of bodily fluid is transferred and/or diverted into the sequestration chamber 334, the control device 300 and/or the housing 330 can be transitioned to its second state or operating mode to sequester, segregate, retain, contain, isolate, etc. the initial volume in the sequestration chamber 334. As described above, the flow controller 342 is placed in the sealed configuration and thus, substantially prevents a flow of fluid therethrough. In this embodiment, the arrangement of the actuator 350 is such that when the flow controller 342 is placed in the sealed configuration, at least a portion of the negative pressure otherwise being exerted through the flow controller 342 is instead exerted on the actuator 350, which in turn, is sufficient to transition the actuator 350 from its first state to its second state. For example, in some embodiments, the negative pressure is operable to move the actuator 350 from a first position (e.g., the first state) to a second position (e.g., the second state), thereby establishing fluid communication between the fluid flow paths 333 and 354B.

[1104] More particularly, moving the actuator 350 to its second position (or otherwise transitioning the actuator 350 to its second state), moves and/or transitions the seals 365 relative to the fluid flow paths 333 and 354B such that fluid communication is established therebetween. As such, the negative pressure otherwise exerted on or through the sequestration chamber 334 is now exerted on or through the fluid flow paths 333 and 354B. In response, bodily fluid can flow from the inlet 331, through the fluid flow paths 333 and 354B, through the outlet 336, and into the fluid collection device. In some embodiments, the transitioning of the flow controller 342 and the actuator 350 from their respective first states to their respective second states is operable to sequester and/or retain the initial portion of the bodily fluid in the sequestration chamber 334. As described in further detail herein, in some instances, contaminants such as, for example, dermally residing microbes or the like dislodged during the venipuncture event, can be entrained and/or included in the initial volume of the bodily fluid and thus, are sequestered in the sequestration chamber 334 when the initial volume is sequestered therein.

[1105] With the fluid collection device fluidically coupled to the outlet 336 and with the control device 300 and/or the housing 330 being in the second state (e.g., the initial volume of bodily fluid is sequestered in or by the sequestration chamber 334), any subsequent volume(s)

of the bodily fluid can flow from the inlet 331, through the fluid flow paths 333 and 354B, through the outlet 336, and into the fluid collection device. Thus, as described above, sequestering the initial volume of bodily fluid in the sequestration chamber 334 prior to collecting or procuring one or more sample volumes of bodily fluid reduces and/or substantially eliminates an amount of contaminants in the one or more sample volumes. Moreover, in some embodiments, the arrangement of the housing 330 can be such that housing 330 cannot transition to the second state prior to collecting and sequestering the initial volume in the sequestration chamber 334.

[1106] FIGS. 9 and 10 illustrate a fluid control device 400 according to an embodiment. The fluid control device 400 can be similar in at least form and/or function to the fluid control device 100 described above with reference to FIG. 1, the fluid control device 200 described above with reference to FIGS. 2-5, and/or the fluid control device 300 described above with reference to FIGS. 6-8. Accordingly, portions of the fluid control device 400 that can be similar to portions of the fluid control devices 100, 200, and/or 300 are not described in further detail herein.

[1107] As shown in FIGS. 9 and 10, the fluid control device 400 (also referred to herein as "control device" or "device") includes a housing 430 having an inlet 431 and an outlet 436, and having and/or being coupled to an actuator 450. As described above with reference to the control devices 100, 200, and/or 300, the inlet 431 is configured to be placed in fluid communication with a bodily fluid source to receive a flow of bodily fluid therefrom (e.g., via a lumen-containing device such as a needle or the like). The outlet 436 is configured to be fluidically coupled to a fluid collection device (not shown in FIGS. 9 and 10).

[1108] As described above, the housing 430 of the control device 400 is configured to (1) receive a flow and/or volume of bodily fluid via the inlet 431 and (2) sequester (e.g., separate, segregate, contain, retain, isolate, etc.) the flow and/or volume of bodily fluid within the sequestration chamber 434. The housing 430 can be any suitable shape, size, and/or configuration. In some embodiments, the housing 430 can have a size that is at least partially based on a volume of bodily fluid at least temporarily stored, for example, in the sequestration chamber 434. For example, in the embodiment shown in FIGS. 9 and 10, the housing 430 is arranged (at least in part) as a syringe-like device or the like, as described in further detail herein.

[1109] The housing 430 defines fluid flow paths 433 and 454 that are selectively in fluid communication with the outlet 436 and that selectively receive a flow of fluid therethrough (e.g., a liquid and/or a gas). The outlet 436 of the housing 430 is in fluid communication with

and/or is configured to be placed in fluid communication with the fluid flow paths 433 and/or 454. In addition, the outlet 436 is configured to be fluidically coupled to a fluid collection device (not shown in FIGS. 9 and 10). The outlet 436 and the fluid collection device can each be substantially similar to the outlet 236 and fluid collection device, respectively, described above with reference to the control device 200. Thus, the outlet 436 and fluid collection device are not described in further detail herein.

[1110] The housing 430 includes and/or is coupled to the actuator 450 configured to selectively control a flow of bodily fluid through the housing 430. In this embodiment, the actuator 450 includes a first plunger 460 and a second plunger 461 movably disposed within the housing 430 and configured to at least partially define the sequestration chamber 434. More specifically, the actuator 450 is configured to move between a first state in which the inlet 431 is placed in fluid communication with the sequestration chamber 434 (FIG. 9) and a second state in which the inlet 431 is placed in fluid communication with the outlet 436 via the fluid flow path 454 (FIG. 10). In this embodiment, when the actuator 450 and/or housing 430 is in the first state, the inlet 431 is in fluid communication with a portion of the housing 430 defined between the first plunger 460 and the second plunger 461.

[1111] When in the first state, the first plunger 460 is disposed in a position such that a dampening chamber 437 is defined by the housing 430 on a side of the first plunger 460 opposite the sequestration chamber 434. As shown, the dampening chamber 437 is configured to be placed in fluid communication with the fluid flow path 433 via a port 435. The port 435 can be an opening, a valve, a membrane, a diaphragm, and/or any other suitable flow controller or the like configured to at least selectively establish fluid communication between the fluid flow path 433 and the dampening chamber 437. Furthermore, when the actuator 450 and/or the housing 430 is in the first state, the dampening chamber 437 includes and/or contains a dampening fluid 456 such as a gas (compressed or uncompressed) and/or a liquid (e.g., water, oil, dampening fluid, and/or any other suitable liquid).

[1112] When the actuator 450 and/or housing 430 are in the first state, the second plunger 461 is disposed in a position within the housing 430 such that one or more seals 465 formed by or coupled to the second plunger 461 fluidically isolate, separate, and/or sequester the inlet 431 from the fluid flow path 454. In addition, the second plunger 461 and/or the seals 465 formed by or coupled thereto fluidically isolate the fluid flow path 454 from the sequestration chamber 434. Thus, when the actuator 450 and/or control device 400 are in the first state, the inlet 431 is in fluid communication with the sequestration chamber 434 and is fluidically isolated from the fluid flow paths 433 and 454 as well as the outlet 436 (see FIG. 9). As

described in further detail herein, the actuator 450 and/or the control device 400 can be configured to transition to the second state in which the sequestration chamber 434 is sequestered within the housing 430 and the inlet 431 is placed in fluid communication with the fluid flow path 454 (see FIG. 10).

[1113] As described above, the device 400 can be used to procure a bodily fluid sample having reduced contamination from microbes such as, for example, dermally residing microbes, and/or the like. For example, in some instances, a user such as a doctor, physician, nurse, phlebotomist, technician, etc. can manipulate the device 400 to establish fluid communication between the inlet 431 and the bodily fluid source (e.g., a vein of a patient). Once the inlet 431 is placed in fluid communication with the bodily fluid source (e.g., the portion of the patient), the outlet 436 can be fluidically coupled to the fluid collection device. As described above, in the embodiment shown in FIGS. 9 and 10 the fluid collection device can be, for example, an evacuated reservoir or container that defines a negative pressure.

[1114] As shown in FIG. 9, the actuator 450 and/or the control device 400 can be in a first or initial state prior to coupling the outlet 436 to the fluid collection device. Thus, the fluid flow path 433 is in fluid communication with the dampening chamber 437 and the fluid flow path 454 is fluidically isolated from the inlet 431 and the sequestration chamber 434 (e.g., via the second plunger 461). As described above, coupling the outlet 436 to the fluid collection device exposes at least a portion of the fluid flow paths 433 and 454 to the negative pressure within the fluid collection device. When the actuator 450 and/or the control device 400 are in the first state, the second plunger 461 isolates the housing 430 and/or the sequestration chamber 434 from the negative pressure exerted via the fluid flow path 454. Conversely, the negative pressure exerted through the fluid flow path 433 can be operable in exerting at least a portion of the negative pressure on the dampening chamber 437 (e.g., via the port 435). In some embodiments, for example, the port 435 can be transitioned from a closed configuration to an open configuration in response to the negative pressure.

[1115] The negative pressure exerted through the fluid flow path 433 is operable in transitioning the actuator 450 from a first state to a second state. For example, in some embodiments, the negative pressure differential draws the dampening fluid 456 from the dampening chamber 437 and into the fluid flow path 433 or a secondary chamber or the like. Moreover, the negative pressure urges the first plunger 460 to transition and/or move relative to the housing 430 from a first configuration or position to a second configuration or position. In some embodiments, the transitioning and/or moving of the first plunger 460 can be such that a volume of the housing 430 defined between the first plunger 460 and the second plunger 461

is increased (i.e., a volume of the sequestration chamber 434 is increased). In some embodiments, the increase in the volume of the sequestration chamber 434 results in a negative pressure therein, which in turn, can be operable in drawing an initial volume of bodily fluid through the inlet 431 and into the sequestration chamber 434. In other words, the negative pressure of the fluid collection device indirectly results in a negative pressure differential between the inlet 431 and the sequestration chamber 434 that is operable in drawing the initial volume of bodily fluid into the sequestration chamber 434.

[1116] As shown in FIG. 10, movement of the first plunger 460 results in a similar movement of the second plunger 461. For example, in some embodiments, the arrangement of the actuator 450 is such that after the first plunger 460 has moved a predetermined amount (and/or after the volume of the sequestration chamber 434 has been increased a predetermined amount) and an initial volume of bodily fluid has been drawn into the sequestration chamber 434, the second plunger 461 is moved or transitioned from a first position and/or configuration to a second position and/or configuration. As such, the actuator 450 is placed in its second state in which the sequestration chamber 434 is sequestered from the inlet 431. In addition, the second plunger 461 and/or the seals 465 coupled thereto place the inlet 431 in fluid communication with the fluid flow path 454. Thus, the negative pressure otherwise exerted on or through the fluid flow path 433 is now exerted on or through the fluid flow path 454. In response, bodily fluid can flow from the inlet 431, through the fluid flow path 454, through the outlet 436, and into the fluid collection device.

[1117] In some embodiments, the transitioning of the actuator 450 from the first state to the second state is operable to sequester and/or retain the initial portion of the bodily fluid in the sequestration chamber 434. As described in further detail herein, in some instances, contaminants such as, for example, dermally residing microbes or the like dislodged during the venipuncture event, can be entrained and/or included in the initial volume of the bodily fluid and thus, are sequestered in the sequestration chamber 434 when the initial volume is sequestered therein. Thus, as described above, sequestering the initial volume of bodily fluid in the sequestration chamber 434 prior to collecting or procuring one or more sample volumes of bodily fluid reduces and/or substantially eliminates an amount of contaminants in the one or more sample volumes. Moreover, in some embodiments, the arrangement of the housing 430 can be such that housing 430 cannot transition to the second state prior to collecting and sequestering the initial volume in the sequestration chamber 434.

[1118] As described above with reference to the control devices 100, 200, and/or 300, the control device 400 is configured to modulate an amount of negative pressure exerted on the

first plunger 460 when the actuator 450 is in the first state. Specifically, in this embodiment, the dampening fluid 456 disposed in the dampening chamber 437 reduces a magnitude of the negative pressure exerted on the first plunger 460. As such, the rate at which the actuator 450 and/or control device 400 is transitioned from the first state to the second state can be controlled. Moreover, in some instances, exposing the housing 430 to the full magnitude of the negative pressure may result transitioning the actuator 450 and/or the control device 400 from the first state to the second state prior to receiving the initial volume of bodily fluid in the sequestration chamber 434. Thus, modulating the magnitude of the pressure can ensure a desired volume of bodily fluid is transferred into the sequestration chamber 434. Although shown in FIGS. 9 and 10 as modulating the negative pressure via the dampening fluid 456, it should be understood that this is presented by way of example only and not limitation. Any other suitable means of dampening and/or modulating a magnitude of the negative pressure can be used to control the transitioning of the actuator 450 and/or housing 430.

[1119] Although the housing 430 is shown in FIGS. 9 and 10 and described above as including the plungers 460 and 461 and being in a syringe-like configuration, in other embodiments, a housing can include any other suitable means for controlling fluid flow therethrough. For example, FIG. 11 and 12 illustrate a fluid control device 500 according to an embodiment. The fluid control device 500 can be similar in at least form and/or function to any of the fluid control devices 100, 200, 300, and/or 400. Accordingly, portions of the fluid control device 500 that can be similar to portions of the fluid control devices 100, 200, 300, and/or 400 are not described in further detail herein. As shown in FIGS. 11 and 12, the fluid control device 500 (also referred to herein as "control device" or "device") includes a housing 530 having an inlet 531 and an outlet 536, and having and/or being coupled to an actuator 550. As described above with reference to the control devices 100, 200, 300, and/or 400, the inlet 531 is configured to be placed in fluid communication with a bodily fluid source to receive a fluid of bodily fluid therefrom (e.g., via a lumen-containing device such as a needle or the like). The outlet 536 is configured to be fluidically coupled to a fluid collection device (not shown in FIGS. 11 and 12). The inlet 531, the outlet 536, and the fluid collection device can be substantially similar to those described above and thus, are not described in further detail herein.

[1120] As described above, the housing 530 of the control device 500 is configured to (1) receive a flow and/or volume of bodily fluid via the inlet 531 and (2) sequester (e.g., separate, segregate, contain, retain, isolate, etc.) the flow and/or volume of bodily fluid within the sequestration chamber 534. The housing 530 can be any suitable shape, size, and/or

configuration. In some embodiments, the housing 530 can have a size that is at least partially based on a volume of bodily fluid at least temporarily stored, for example, in the sequestration chamber 534. For example, in the embodiment shown in FIGS. 11 and 12, the housing 530 can be arranged in a substantially similar manner as the housing 430 described above with reference to FIGS. 9 and 10. As described in further detail herein, the housing 530 can differ from the housing 430, by arranging the actuator 550 as, for example, a diaphragm rather than one or more plungers.

[1121] The housing 530 defines a set of fluid flow paths 533 and 554 in fluid communication with the outlet 536 and configured to selectively receive a flow of fluid therethrough (e.g., a liquid and/or a gas). The housing 530 includes and/or is coupled to the actuator 550 configured to selectively control a flow of bodily fluid through the housing 530. In this embodiment, the actuator 550 includes a diaphragm 576 movably disposed within the housing 530 and configured to at least partially define the sequestration chamber 534. More specifically, the actuator 550 is configured to move between a first state in which the inlet 531 is placed in fluid communication with the sequestration chamber 534 (FIG. 11) and a second state in which the inlet 531 is placed in fluid communication with the outlet 536 via the fluid flow path 554 (FIG. 12).

[1122] As shown in FIG. 11, when the actuator 550 and/or control device 500 is in the first state, the inlet 531 is in fluid communication with a portion of the housing 530 defined between the diaphragm 576 and one or more seals 565. Moreover, the diaphragm 576 is disposed in a first state such that a dampening chamber 537 is defined by the housing 530 on a side of the diaphragm 576 opposite the sequestration chamber 534, as described above with reference to the housing 430. As shown, the dampening chamber 537 is configured to be placed in fluid communication with the fluid flow path 533 via a port 535. The port 535 can be an opening, a valve, a membrane, a diaphragm, and/or any other suitable flow controller or the like configured to at least selectively establish fluid communication between the fluid flow path 533 and the dampening chamber 537. Furthermore, when the actuator 550 and/or the control device 500 is in the first state, the dampening chamber 537 includes and/or contains a dampening fluid such as a gas (compressed or uncompressed) and/or a liquid (e.g., water, oil, dampening fluid, and/or any other suitable liquid). As described above with reference to the control devices 400, the arrangement of the dampening chamber 537, the dampening fluid, and the port 535 can be configured to modulate an amount of negative pressure exerted on the diaphragm 576 when the actuator 550 is in the first state. Although shown in FIGS. 11 and 12 as modulating the negative pressure via the dampening fluid, it should be understood that this

is presented by way of example only and not limitation. Any other suitable means of dampening and/or modulating a magnitude of the negative pressure can be used to control the transitioning of the actuator 550 and/or the control device 500.

[1123] As described above with reference to the actuator 450, when the actuator 550 and/or the control device 500 are in the first state, the one or more seals 565 are disposed in a position within the housing 530 such that the one or more seals 565 fluidically isolate, separate, and/or sequester the inlet 531 from the fluid flow path 554. In addition, the one or more seals 565 fluidically isolate the fluid flow path 554 from the sequestration chamber 534. Thus, when the actuator 550 and/or the control device 500 are in the first state, the inlet 531 is in fluid communication with the sequestration chamber 534 and fluidically isolated from the fluid flow paths 533 and 554 as well as the outlet 536 (see FIG. 11). As described in further detail herein, the actuator 550 and/or the control device 500 housing 530 can be configured to transition to the second state in which the sequestration chamber 534 is sequestered within the housing 530 and the inlet 531 is placed in fluid communication with the fluid flow path 554 (see FIG. 12).

[1124] As described in detail above, the device 500 can be used to procure a bodily fluid sample having reduced contamination from microbes such as, for example, dermally residing microbes, and/or the like. For example, in some instances, a user can place the inlet 531 in fluid communication with the bodily fluid source (e.g., the portion of the patient) and can fluidically couple the outlet 536 to the fluid collection device. As shown in FIG. 11, the actuator 550 and/or the device 500 can be in a first or initial state prior to coupling the outlet 536 to the fluid collection device. Thus, the fluid flow path 533 is in fluid communication with the dampening chamber 537 and the fluid flow path 554 is fluidically isolated from the inlet 531 and the sequestration chamber 534 (e.g., via the one or more seals 565), as described in detail above with reference to the control device 400 of FIGS. 9 and 10.

[1125] Coupling the outlet 536 to the fluid collection device selectively exposes at least a portion of the fluid flow paths 533 and 554 to the negative pressure within and/or produced by the fluid collection device. When the actuator 550 and/or the device 500 are in the first state, the one or more seals 565 isolate the housing 530 and/or the sequestration chamber 534 from the negative pressure exerted via the fluid flow path 554. Conversely, the negative pressure exerted through the fluid flow path 533 can be operable in exerting at least a portion of the negative pressure on the dampening chamber 537 (e.g., via the port 535). In some embodiments, for example, the port 535 can be transitioned from a closed configuration to an open configuration in response to the negative pressure. The negative pressure exerted through the fluid flow path 533 is operable in transitioning the actuator 550 from a first state to a second

state. For example, in some embodiments, the negative pressure differential draws the dampening fluid from the dampening chamber 537 and into the fluid flow path 533. Moreover, the negative pressure urges the diaphragm 576 to transition, flip, move, switch, deform, etc., from a first configuration or state (FIG. 11) to a second configuration or state (FIG. 12). As described above with reference to the actuator 450, the transitioning of the diaphragm 576 from the first state to the second state can be such that a volume of the housing 530 defined between the diaphragm 576 and the one or more seals 565 is increased (i.e., a volume of the sequestration chamber 534 is increased), which in turn, results in a negative pressure therein that can be operable in drawing an initial volume of bodily fluid through the inlet 531 and into the sequestration chamber 534.

[1126] As shown in FIG. 12, movement of the diaphragm 576 results in a similar movement of the one or more seals 565 such that the one or more seals 565 are disposed on the same side of the inlet 531 as the diaphragm 576. Thus, the sequestration chamber 534 is sequestered within the housing 530. In addition, moving the one or more seals 565 is such that fluid communication is established between the inlet 531 and the fluid flow path 554. Thus, the negative pressure otherwise exerted on or through the fluid flow path 533 is now exerted on or through the fluid flow path 554. In response, bodily fluid can flow from the inlet 531, through the fluid flow path 554, through the outlet 536, and into the fluid collection device, as described in detail above. In some embodiments, the transitioning of the actuator 550 from the first state to the second state is operable to sequester and/or retain the initial portion of the bodily fluid in the sequestration chamber 534, which can include contaminants such as, for example, dermally residing microbes or the like dislodged during the venipuncture event. Thus, as described above, sequestering the initial volume of bodily fluid in the sequestration chamber 534 prior to collecting or procuring one or more sample volumes of bodily fluid reduces and/or substantially eliminates an amount of contaminants in the one or more sample volumes. Moreover, in some embodiments, the arrangement of the control device 500 and/or the housing 530 can be such that the control device 500 and/or the housing 530 cannot transition to the second state prior to collecting and sequestering the initial volume in the sequestration chamber 534.

[1127] FIGS. 13-15 illustrate a fluid control device 600 according to an embodiment. The fluid control device 600 can be similar in at least form and/or function to any of the fluid control devices 100, 200, 300, 400, and/or 500. Accordingly, portions of the fluid control device 600 that can be similar to portions of the fluid control devices 100, 200, 300, 400, and/or 500 are not described in further detail herein. As shown in FIGS. 13-15, the fluid control device 600

(also referred to herein as "control device" or "device") includes a housing 630 having an inlet 631 and an outlet 636, and having and/or being coupled to an actuator 650. As described above with reference to the control devices 100, 200, 300, 500, and/or 500, the inlet 631 is configured to be placed in fluid communication with a bodily fluid source to receive a fluid of bodily fluid therefrom (e.g., via a lumen-containing device such as a needle or the like). The outlet 636 is configured to be fluidically coupled to a fluid collection device (not shown in FIGS. 13-15). The inlet 631, the outlet 636, and the fluid collection device can be substantially similar to those described above and thus, are not described in further detail herein.

[1128] As described above, the housing 630 of the control device 600 is configured to (1) receive a flow and/or volume of bodily fluid via the inlet 631 and (2) sequester (e.g., separate, segregate, contain, retain, isolate, etc.) the flow and/or volume of bodily fluid within a sequestration chamber 634 included in and/or at least partially formed by the housing 630. The housing 630 can be any suitable shape, size, and/or configuration. In some embodiments, the housing 630 can have a size that is at least partially based on a volume of bodily fluid at least temporarily stored, for example, in the sequestration chamber 634. For example, in the embodiment shown in FIGS. 13-15, the housing 630 can be arranged in a substantially similar manner as the housing 530 described above with reference to FIGS. 11 and 12. That is to say, the housing 630 includes an actuator 650 that is arranged as a diaphragm.

[1129] The housing 630 defines a set of fluid flow paths 633 and 654 in fluid communication with the outlet 636 and configured to selectively receive a flow of fluid therethrough (e.g., a liquid and/or a gas). The housing 630 includes and/or is coupled to the actuator 650 configured to selectively control a flow of bodily fluid through the housing 630. In this embodiment, the actuator 650 includes a diaphragm 676 movably disposed within the housing 630 and configured to at least partially define the sequestration chamber 634. More specifically, the actuator 650 is configured to move between a first state in which the inlet 631 is placed in fluid communication with the sequestration chamber 634 and a second state in which the inlet 631 is placed in fluid communication with the outlet 636 via the fluid flow path 654, as described in detail above with reference to the control device 500.

[1130] As shown in FIGS. 14 and 15, when the actuator 650 and/or the device 600 is in the first state, the inlet 631 is in fluid communication with a portion of the housing 630 defined between the diaphragm 676 and one or more seals 665. Moreover, the diaphragm 676 is disposed in a first state such that a dampening chamber 637 is defined by the housing 630 on a side of the diaphragm 676 opposite the sequestration chamber 634, as described above with reference to the housing 530. As shown, the dampening chamber 637 is configured to be placed

in fluid communication with the fluid flow path 654 via a port 635 (such as those described above). Although not shown, when the actuator 650 and/or the device 600 is in the first state, the dampening chamber 637 includes and/or contains a dampening fluid such as a gas (compressed or uncompressed) and/or a liquid (e.g., water, oil, dampening fluid, and/or any other suitable liquid), that can be configured to modulate an amount of negative pressure exerted on the diaphragm, as described in detail above with reference to the control device 500. Although described as modulating the negative pressure via the dampening fluid, it should be understood that this is presented by way of example only and not limitation. Any other suitable means of dampening and/or modulating a magnitude of the negative pressure can be used to control the transitioning of the actuator 650 and/or device 600.

[1131] As described above with reference to the actuator 550, when the actuator 650 and/or the device 600 are in the first state, the seal 665 is disposed in a position within the housing 630 such that the seal 665 fluidically isolates, separates, and/or sequesters the inlet 631 from the fluid flow path 654. In addition, the seal 665 fluidically isolates the fluid flow path 654 from the sequestration chamber 634. Thus, when the actuator 650 and/or the device 600 are in the first state, the inlet 631 is in fluid communication with the sequestration chamber 634 and fluidically isolated from the fluid flow path 654 as well as the outlet 636. The actuator 650 and/or the device 600 can be configured to transition to the second state in which the sequestration chamber 634 is sequestered within the housing 630 and the inlet 631 is placed in fluid communication with the fluid flow path 654. Accordingly, the device 600 can be used to procure a bodily fluid sample having reduced contamination from microbes (e.g., dermally residing microbes and/or the like), in a substantially similar manner as the device 500 described above with reference to FIGS. 11 and 12. Thus, the functioning of the device 600 is not described in further detail herein.

[1132] FIGS. 16-18 illustrate a fluid control device 700 according to an embodiment. The fluid control device 700 can be similar in at least form and/or function to any of the fluid control devices 100, 200, 300, 400, 500, and/or 600. Accordingly, portions of the fluid control device 700 that can be similar to portions of the fluid control devices 100, 200, 300, 400, 500, and/or 600 are not described in further detail herein. As shown in FIGS. 16-18, the fluid control device 700 (also referred to herein as "control device" or "device") includes a housing 730 having an inlet 731 and an outlet 736, and having or being coupled to an actuator 750. As described above with reference to the control devices 100, 200, 300, 400, 500, and/or 600, the inlet 731 is configured to be placed in fluid communication with a bodily fluid source to receive a fluid of bodily fluid therefrom (e.g., via a lumen-containing device such as a needle or the

like). The outlet 736 is configured to be fluidically coupled to a fluid collection device (not shown in FIGS. 16-18). The inlet 731, the outlet 736, and the fluid collection device can be substantially similar to those described above and thus, are not described in further detail herein.

[1133] As described above, the housing 730 of the control device 700 is configured to (1) receive a flow and/or volume of bodily fluid via the inlet 731 and (2) sequester (e.g., separate, segregate, contain, retain, isolate, etc.) the flow and/or volume of bodily fluid within the sequestration chamber 734. The housing 730 can be any suitable shape, size, and/or configuration. In some embodiments, the housing 730 can have a size that is at least partially based on a volume of bodily fluid at least temporarily stored, for example, in the sequestration chamber 734. For example, in the embodiment shown in FIGS. 16-18, the housing 730 can be arranged in a substantially similar manner as the housings 530 and/or 630. That is to say, the housing 530 includes and/or is coupled to the actuator 750 that is arranged as a diaphragm.

[1134] The housing 730 defines a set of fluid flow paths 733 and 754 in fluid communication with the outlet 736 (see e.g., FIGS. 17A and 17B) and configured to selectively receive a flow of fluid therethrough (e.g., a liquid and/or a gas). The housing 730 includes and/or is coupled to the actuator 750 configured to selectively control a flow of bodily fluid through the housing 730. In this embodiment, the actuator 750 includes a diaphragm 776 movably disposed within the housing 730 and configured to at least partially define the sequestration chamber 734. More specifically, the actuator 750 is configured to move between a first state in which the inlet 731 is placed in fluid communication with the sequestration chamber 734 and a second state in which the inlet 731 is placed in fluid communication with the outlet 736 via the fluid flow path 754, as described in detail above with reference to the control device 500.

[1135] In the embodiment shown in FIGS. 16-18, when the actuator 750 and/or the device 700 are in the first state, the inlet 731 is in fluid communication with the sequestration chamber 734 formed by a portion of the housing 730 defined between the diaphragm 776 and a flow controller 742 (e.g., a selectively permeable fluid barrier or seal, and/or any other flow controller such as any of those described above). Moreover, the diaphragm 776 is disposed in a first state such that the fluid flow path 733 is in fluid communication with the sequestration chamber 734. As described above with reference to the actuator 550, when in the actuator 750 and/or device 700 are in the first state, the diaphragm 776 and/or the seal 765 are disposed in a position within the housing 730 such that the diaphragm 776 and/or the seal 765 fluidically isolate, separate, and/or sequester the inlet 731 from the fluid flow path 754. In addition, the

diaphragm 776 and/or the seal 765 fluidically isolate the fluid flow path 754 from the sequestration chamber 734. Thus, when the actuator 750 and/or the device 700 are in the first state, the inlet 731 is in fluid communication with the sequestration chamber 734 and fluidically isolated from the fluid flow path 754.

[1136] As described above with reference to, for example, the control device 200, when the actuator 750 and/or the device 700 are in the first state, a negative pressure differential within the sequestration chamber 734 can result from the coupling of the fluid collection device to the outlet 736. More specifically, the fluid flow path 733 can be in fluid communication with the outlet 736 and the flow controller 742. When the flow controller 742 is in a first state, the flow controller 742 can allow a gas or air to pass therethrough. Thus, the negative pressure differential within the sequestration chamber 734 can result from the coupling of the fluid collection device to the outlet 736.

[1137] As shown in FIG. 18, the actuator 750 and/or the device 700 can be configured to transition to the second state in which the sequestration chamber 734 is sequestered within the housing 730 and the inlet 731 is placed in fluid communication with the fluid flow path 754, as described in detail above with reference to the control device 600. More particularly, an initial volume of bodily fluid can be transferred into the sequestration chamber 734, which in turn, can saturate, can wet, and/or otherwise can transition the flow controller 742 from the first or open state to a second or closed state. In some embodiments, the transitioning of the flow controller 742 from the first state to the second state is operable in isolating the fluid flow path 733 from the outlet 736. As such, a negative pressure exerted through the fluid flow path 754 can be operable in transitioning, switching, flipping, moving, deforming, and/or otherwise reconfiguring the diaphragm 776 such that the actuator 750 is placed in its second state. As such, the negative pressure of the fluid collection device can draw bodily fluid from the inlet 731, through the housing 730 (bypassing the sequestration chamber 734), through the fluid flow path 754 and the outlet 736, and into the fluid collection device, as described in detail above. Accordingly, the device 700 can be used to procure a bodily fluid sample having reduced contamination from microbes (e.g., dermally residing microbes and/or the like), in a manner substantially similar to one or more of the control devices 100, 200, 300, 400, 500, and/or 600 described in detail above. Thus, the functioning of the device 700 is not described in further detail herein.

[1138] In some embodiments, any of the control devices 100, 200, 300, 400, 500, 600, and/or 700 can be formed from any suitable components that can be manufactured, assembled, sterilized, and packaged as an assembly or integrated device. In such embodiments, a user can,

for example, open a packaging containing such an assembly or integrated device and can use the device as described above with reference to the control devices 100, 200, 300, 400, 500, 600, and/or 700. In some embodiments, any of the control devices can be monolithically formed in whole or at least in part.

[1139] In some embodiments any of the control devices can be physically coupled, attached, formed, and/or otherwise mated to a fluid collection device (e.g., a sample reservoir, a syringe, a blood culture bottle, a collection vial, a fluid transfer container, and/or any other suitable reservoir, collection device, and/or transfer device) during a manufacturing process. This can be done prior to sterilization so the collection pathway(s) and connection interface(s) (e.g., where the control device couples to the fluid collection device) maintain a closed-system, mechanical diversion device within a sterile environment that is not subject to touch-point contamination from external sources. In this manner, in order for a user to transfer a sample volume to the fluid collection device, the user would be forced first to sequester, segregate, and/or isolate at least a portion of the initial bodily fluid volume or flow. In some embodiments, the coupling, mating, and/or attachment of the fluid control device to the fluid collection device can be executed such that the control device can be removed (physically decoupled, removed with a specific "key," and/or any other approach used to separate the control device from the fluid collection device) after use to allow access to the fluid collection device, which can then be placed in an incubator and/or any other type of analytical machine, and accessed for analysis and/or otherwise further processed. In some embodiments, such decoupling may be blocked, limited, and/or substantially prevented prior to use and unblocked or allowed after use. In other embodiments, the fluid control device and the fluid collection device can be permanently coupled and/or monolithically formed (at least in part) to prevent such decoupling.

[1140] While described above as being coupled and/or assembled, for example, during manufacturing, in other embodiments, however, a control device can include one or more modular components that can be selected by a user based on a desired use, preference, patient, etc. In such embodiments, the user can couple one or more modular components (packaged together or packaged separately) to form the desired fluid control device. For example, FIGS. 19-25 illustrate a modular fluid control device 800 according to an embodiment. The fluid control device 800 can be similar in at least form and/or function to the fluid control devices described herein. More specifically, portions of the fluid control device 800 can be similar to and/or substantially the same as corresponding portions of the fluid control device 200 described above with reference to FIGS. 2-5. Accordingly, such portions of the fluid control device 800 are not described in further detail herein.

[1141] The fluid control device 800 (also referred to herein as "control device" or "device") includes a housing 830 and an actuator 850. As described above, the control device 800 can be at least partially monolithically formed or can be otherwise preassembled during manufacturing. In other embodiments, the control device 800 can be at least partially modular such that a user can physically and fluidically couple the housing 830 and the actuator 850 to form the control device 800. The housing 830 of the device 800 can be any suitable shape, size, and/or configuration. For example, in the embodiment shown in FIGS. 19-25, the housing 830 can be, for example, relatively thin and substantially rectangular. In some embodiments, portions of the housing 830 can be substantially similar in at least form and/or function to the housing 230 described above with reference to FIGS. 2-5. Thus, while such portions are identified, similar components, features, and/or functions are not described in further detail herein.

[1142] As shown in FIGS. 19 and 20, the housing 830 forms and/or defines a sequestration chamber 834 that is in selective fluid communication with a first port 845 and a second port 846. The first port 845 and the second port 846 are configured to be at least fluidically coupled to a portion of the actuator 850 to allow for selective fluid flow between the housing 830 and the actuator 850. As described in further detail herein, the sequestration chamber 834 is configured (1) to receive a selective flow and/or volume of bodily fluid from a portion of the actuator 850 via the first port 845, and (2) to sequester (e.g., separate, segregate, contain, retain, isolate, etc.) the flow and/or volume of bodily fluid (e.g., an initial or first flow and/or volume of bodily fluid or any portion thereof) within the sequestration chamber 834. The sequestration chamber 834 can have any suitable shape, size, and/or configuration. For example, in some embodiments, the sequestration chamber 834 can have any suitable size, volume, and/or fluid capacity such as, for example, those described above with reference to the sequestration chamber 134. In the embodiment shown in FIGS. 19-25, the sequestration chamber 834 can be, for example, a fluid flow path that extends through and/or that is defined by at least a portion of the housing 830. In some embodiments, the sequestration chamber 834 can be substantially similar in at least form and/or function to the sequestration chamber 234 described above with reference to FIGS. 2-5 and thus, is not described in further detail herein.

[1143] As shown in FIG. 20, the housing 830 includes and/or defines a flow controller 842 and a restricted flow path 832. The flow controller 842 can be, for example, a valve, membrane, diaphragm, restrictor, vent, a selectively permeable member, port, etc. configured to selectively control (at least in part) a flow of fluids into and/or out of the sequestration chamber 834 and/or any other suitable portion of the housing 830. For example, the flow controller 842 can be a

selectively permeable fluid barrier (e.g., a blood barrier) that includes and/or is formed of a porous material configured to selectively allow a flow of gas therethrough but to prevent a flow of a liquid therethrough. In some embodiments, the flow controller 842 can be substantially similar to the flow controller 242 described in detail above with reference to FIGS. 2-5 and thus, is not described in further detail herein.

[1144] As shown, the restricted flow path 832 defined by the housing 830 is in fluid communication with the second port 846 and is positioned between the second port 846 and the flow controller 842 (or a portion of the housing 830 receiving or housing the flow controller 842). As described above with reference to the restricted flow path 232 shown in FIGS. 2-5, the restricted flow path 832 is a fluid flow path having a smaller diameter than, for example, one or more other flow paths defined by the housing 830 and/or actuator 850. For example, in some embodiments, the restricted flow path 832 can have a diameter between about 0.0005" to about 0.5" and can have a length between about 0.01" and about 0.5", as described above with reference to the restricted flow path 232. As described above, the smaller diameter of the restricted flow path 832 results in a lower magnitude of negative pressure being applied through the sequestration chamber 834 than a magnitude of negative pressure when the restricted flow path 832 has a larger diameter. In other words, the restricted flow path 832 can be configured to modulate an amount of negative pressure to which the sequestration chamber 834 is exposed. In some instances, modulating the amount of negative pressure can control a rate at which bodily fluid is transferred into the sequestration chamber 834. Moreover, in this embodiment, the restricted flow path 832 is, for example, a gas flow path configured to receive a flow of gas or air but not a flow of a liquid (e.g., bodily fluid), which can allow for a negative pressure differential sufficient to successfully collect the initial volume of bodily fluid and/or sufficient to transition at least a portion of the control device 800 to a second state, while limiting and/or substantially preventing a portion of the initial or first volume of bodily fluid from being drawn through the sequestration chamber 834 and the second port 846.

[1145] As shown in FIGS. 19-24, the actuator 850 includes a body 851 and an actuator rod 862. The body 851 of the actuator 850 includes an inlet 852 and an outlet 853. The inlet 852 and the outlet 853 can be substantially similar in at least form and/or function to the inlet 231 and the outlet 236, respectively, described above with reference to FIGS. 2-5. Thus, the inlet 852 is configured to be placed in fluid communication with a bodily fluid source to receive a flow of bodily fluid therefrom (e.g., via a lumen-containing device such as a needle, IV catheter, PICC line, or the like). The outlet 853 is configured to be fluidically coupled to a fluid collection device 880 such as, for example, a sample reservoir, a syringe, and/or other

intermediary bodily fluid transfer device, adapter, or vessel (see e.g., FIG. 25) such as, for example, a transfer device similar to those described in the '510 publication.

[1146] As shown in FIG. 21, the body 851 of the actuator 850 includes and/or defines a first port 858 and a second port 859. The first port 858 is in fluid communication with the inlet 852 and the second port 859 is in fluid communication with the outlet 853. In addition, the first port 858 and the second port 859 are configured to be at least fluidically coupled to the first port 845 and the second port 846, respectively, of the housing 830. As described in further detail herein, the actuator 850 can be transitioned between a first operating mode or state and a second operating mode or state to selectively control fluid flow through the ports 858 and 859 of the actuator 850 and the ports 845 and 846 of the housing 830, which in turn, can selectively control a flow of bodily fluid into and/or out of the sequestration chamber 834 of the housing 830.

[1147] In some embodiments, the arrangement of the ports 858 and 859 of the actuator 850 and the ports 845 and 846 of the housing 830 can allow for and/or otherwise can provide a means of physically coupling the housing 830 to the actuator 850 as well as fluidically coupling the housing 830 to the actuator 850. For example, in some embodiments, the ports 858 and 859 of the actuator 850 and the ports 845 and 846 of the housing 830 can form a friction fit, a press fit, an interference fit, and/or the like. In other embodiments, the ports 858 and 859 of the actuator 850 can be coupled to the ports 845 and 846, respectively, of the housing 830 via an adhesive, a mechanical fastener, an elastomeric coupling, a gasket, an o-ring(s), and/or any other suitable coupling means. In still other embodiments, the ports 858 and 859 of the actuator 850 can be physically and fluidically coupled to the ports 845 and 846, respectively, of the housing 830 via an intervening structure such as, for example, one or more sterile, flexible tubing(s). As such, the device 800 can be and/or can have, for example, a modular configuration in which the housing 830 can be at least fluidically coupled to the actuator 850.

[1148] In some embodiments, such a modular arrangement can allow a user to select a housing (or actuator) with one or more desired characteristics based on, for example, the intended purpose and/or use of the assembled device. In other embodiments, the modular arrangement can allow and/or facilitate one or more components with desired characteristics to be coupled and/or assembled during manufacturing. For example, in some instances, it may be desirable to select a housing that includes and/or defines a sequestration chamber having a particular or desired volume. As a specific example, when the device is being used to procure bodily fluid from a pediatric patient and/or a very sick patient (for example), it may be desirable to select a housing that defines and/or includes a sequestration chamber with a smaller volume

than may otherwise be selected when the device is being used to procure bodily fluid from a seemingly healthy adult patient. Accordingly, such a modular arrangement can allow a user (e.g., a doctor, physician, nurse, technician, phlebotomist, etc.) to select a housing or an actuator having one or more desired characteristics based on, for example, the intended use of the device. In other instances, the modular arrangement can allow or facilitate assembly of a housing or an actuator having one or more desired characteristics during manufacturing without making significant changes to one or more manufacturing processes.

[1149] The actuator rod 862 of the actuator 850 is movably disposed within a portion of the body 851. The actuator rod 862 includes a first end portion 863 and a second end portion 864, at least one of which extends beyond the body 851 of the actuator 850 with the actuator rod 862 is disposed within the body 851 (see e.g., FIGS. 23 and 24). A portion of the actuator rod 862 includes and/or is coupled to a set of seals 865. The seals 865 can be, for example, o-rings, elastomeric over-molds, proud or raised dimensions or fittings, and/or the like. The arrangement of the actuator 862 and the body 851 of the actuator 850 can be such that an inner portion of the seals 865 forms a fluid tight seal with a surface of the actuator rod 862 and an outer portion of the seals 865 forms a fluid tight seal with an inner surface of the body 851. In other words, the seals 865 form one or more fluid tight seals between the actuator rod 862 and the inner surface of the body 851. As shown in FIGS. 23 and 24, the actuator rod 862 includes and/or is coupled to three seals 865 which form and/or define a first fluid flow path 833 within the body 851 of the actuator 850 and a second fluid flow path 854 within the body 851 of the actuator 850.

[1150] The actuator rod 862 is configured to be moved or transitioned relative to the body 851 between a first position or configuration and a second position or configuration. For example, in some instances, a force can be exerted on the first end portion 863 of the actuator rod 862 to place the actuator rod 862 in its first position and/or configuration, as shown in FIG. 23. The force exerted on the first end portion 863 of the actuator rod 862 can come from any suitable source. For example, a user can create the force with his or her hand or finger, a syringe, a positive or negative pressure source, and/or any other external energy source. When in the first position and/or configuration, the inlet 852 of the actuator 850 is in fluid communication with the first fluid flow path 833 and the outlet 853 of the actuator 850 is in fluid communication with the second fluid flow path 854. In some instances, a force can be exerted on the second end portion 864 of the actuator rod 862 to place the actuator rod 862 in its second position and/or configuration, as shown in FIG. 24. When in the second position and/or configuration, the inlet 852 and the outlet 853 of the actuator 850 are each in fluid

communication with the second fluid flow path 854 while the first fluid flow path is sequestered, isolated, and/or otherwise not in fluid communication with the inlet 852 and the outlet 853. Although not shown, the first port 858 of the actuator 850 is in fluid communication with the first fluid flow path 833 and the second port 859 of the actuator 850 is in fluid communication with the second fluid flow path 854. As such, moving and/or transitioning the actuator rod 862 (or the actuator 850 in general) between the first position and the second position can be operable in selectively controlling a flow of fluid (e.g., bodily fluid) between the inlet 852 of the actuator 850 and the housing 830, or between the inlet 852 of the actuator 850 and the outlet 853 of the actuator 850, as described in further detail herein.

[1151] As described above, the device 800 can be used to procure a bodily fluid sample having reduced contamination from microbes such as, for example, dermally residing microbes, microbes external to the bodily fluid source, and/or the like. For example, in some instances, a user such as a doctor, physician, nurse, phlebotomist, technician, etc. can manipulate the device 800 to establish fluid communication between the inlet 852 and the bodily fluid source (e.g., a vein of a patient). Once the inlet 852 is placed in fluid communication with the bodily fluid source (e.g., the portion of the patient), the outlet 853 can be fluidically coupled to the fluid collection device 880. In the embodiment shown in FIGS. 19-25, the fluid collection device 880 can be, for example, a syringe (as shown in FIG. 25), and/or any other suitable container or device configured to define or produce a negative pressure or energy source.

[1152] As described in detail above with reference to, for example, the device 200, coupling the outlet 853 to the fluid collection device 880 selectively exposes at least a portion of the control device 800 to a negative pressure within and/or produced by the fluid collection device 880. More specifically, in the embodiment shown in FIGS. 19-25, coupling the outlet 853 to the fluid collection device 880 exposes the outlet 853 of the actuator 850 and the second fluid flow path 854 to the negative pressure within and/or produced by the fluid collection device 880. In addition, the second port 859 of the actuator 850 is in fluid communication with the second fluid flow path 854 and the second port 846 of the housing 830. The second port 846 of the housing 830, in turn, is in selective fluid communication with the sequestration chamber 834 via the flow controller 842 and the restricted flow path 832. For example, the device 800 and/or the flow controller 842 can be in a first operating state or mode in which the flow controller 842 allows a flow of gas (e.g., air) through the flow controller 842 while limiting and/or preventing a flow of liquid (e.g., bodily fluid such as blood) through the flow controller 842. Thus, coupling the fluid collection device 880 to the outlet 853 results in a

negative pressure differential between the fluid collection device 880 (and/or any suitable negative pressure source) and the sequestration chamber 834.

[1153] As described above, the control device 800 can be in a first or initial state when the flow controller 842 and/or the actuator 850 are in a first state, position, configuration, etc. As such, the actuator rod 862 can be in its first position and/or configuration in which the first fluid flow path 833 is in fluid communication with the inlet 852. In addition, the first port 858 of the actuator 850 and the first port 845 of the housing 830 establish fluid communication between the sequestration chamber 834 and the first fluid flow path 833. Thus, the negative pressure within the fluid collection device 880 can result in a negative pressure (or negative pressure differential) within at least a portion of the sequestration chamber 834 that is operable in drawing an initial flow, portion, amount, or volume of bodily fluid from the inlet 852, through the first fluid flow path 833, and into the sequestration chamber 834 when the actuator 850 and/or control device 800 is in the first or initial state (e.g., when the actuator rod 862 is in its first state, position, and/or configuration). In some instances, the arrangement of the flow controller 842 and/or the restricted flow path 832 can be configured to restrict, limit, control, and/or otherwise modulate an amount or magnitude of negative pressure exerted on or through the sequestration chamber 834, as described in detail above with reference to the device 200.

[1154] The initial portion and/or amount of bodily fluid can be any suitable volume of bodily fluid, as described in detail above with reference to the control device 100. For example, in some instances, the initial volume can be associated with and/or at least partially based on an amount or volume of bodily fluid that is sufficient to fully wet or saturate the flow controller 842. In other words, in some embodiments, the initial volume of bodily fluid can be a volume sufficient to transition the flow controller 842 from a first state to a second state (e.g., a saturated or fully wetted state). In some embodiments, the flow controller 842 is placed in a sealed configuration when transitioned to the second state. That is to say, saturating and/or fully wetting the flow controller 842 (e.g., the semi-permeable material) places the flow controller 842 in a sealed configuration in which the flow controller 842 substantially prevents a flow of a liquid and a gas therethrough. Thus, transitioning the flow controller 842 to the second state sequesters, blocks, isolates, separates, segregates, and/or otherwise prevents flow through the flow controller 842 between the restricted flow path 832 and the sequestration chamber 834.

[1155] After the initial volume of bodily fluid is transferred and/or diverted into the sequestration chamber 834, the control device 800 and/or the actuator 850 can be transitioned to its second state or operating mode to sequester, segregate, retain, contain, isolate, etc. the

initial volume in the sequestration chamber 834. For example, the actuator 850 can be actuated to transition from its first state to its second state, for example, by exerting a force on the second end portion 864 of the actuator rod 862. As such, the actuator rod 862 is moved and/or transitioned to its second state, position, and/or configuration in which the first fluid flow path 833 is sequestered and/or isolated from the inlet 852. With the flow controller 842 in the sealed configuration in response to the initial volume of bodily fluid being disposed in the sequestration chamber 834 and with the initial fluid flow path 833 sequestered and/or isolated from the inlet 852, the initial volume of bodily fluid is sequestered in the sequestration chamber 834. As described in detail above, in some instances, contaminants such as, for example, dermally residing microbes or the like dislodged during the venipuncture event, can be entrained and/or included in the initial volume of the bodily fluid and thus, are sequestered in the sequestration chamber 834 when the initial volume is sequestered therein.

[1156] As shown in FIG. 24, moving and/or transitioning the control device 800 and/or the actuator 850 to its second state or configuration establishes fluid communication between the inlet 852 and the outlet 853 via the second fluid flow path 854. As such, the negative pressure otherwise exerted on or through the sequestration chamber 834 is now exerted on or through the fluid flow path 854. In response, bodily fluid can flow from the inlet 852, through the fluid flow path 854, through the outlet 853, and into the fluid collection device 880. Thus, as described above, sequestering the initial volume of bodily fluid in the sequestration chamber 834 prior to collecting or procuring one or more sample volumes of bodily fluid reduces and/or substantially eliminates an amount of contaminants in the one or more sample volumes. Moreover, in some embodiments, the arrangement of the control device 800 can be such that the control device 800 cannot transition to the second state prior to collecting and sequestering the initial volume in the sequestration chamber 834, thereby reducing the likelihood of contaminants being transferred to the fluid collection device 880.

[1157] In some instances, it may be desirable to isolate the negative pressure source (e.g., the fluid collection device 880 from the inlet 853 such as, for example, if it is desirable to collect multiple samples of bodily fluid using multiple fluid collection device 880 (e.g., syringes). For example, in some instances, after filling the fluid collection device 880 the user can engage the actuator 850 and exert a force on the first end portion 863 of the actuator rod 862 to move and/or transition the actuator rod 862 from its second position and/or configuration toward its first position and/or configuration. As such, the second fluid flow path 854 no longer places the inlet 852 in fluid communication with the outlet 853. Moreover, the flow controller 842 can remain in the sealed state or configuration (e.g., fully saturated, wetted, and/or

otherwise preventing flow therethrough) such that the outlet 853 is substantially sequestered or isolated from the rest of the control device 800. In some instances, the user can then remove the filled fluid collection device 880 (e.g., syringe) and can couple a new fluid collection device 880 (e.g., syringe) to the outlet 853. With the new fluid collection device 880 coupled to the outlet 853, the user can, for example, exert a force on the second end portion 864 of the actuator rod 862 to move and/or transition the actuator rod 862 back to its second position, state, and/or configuration, as described above.

[1158] While the fluid collection device 880 coupled to the device 800 is shown in FIG. 25 as being a syringe, in other embodiments, a control device can be physically and/or fluidically coupled to any suitable collection device. For example, FIG. 26 illustrates a fluid control device 900. As described above with reference to the control device 800, the fluid control device 900 includes a housing 930 and an actuator 950, which can be arranged, for example, in a modular configuration or the like. The actuator 950 includes an inlet 952 configured to be placed in fluid communication with a bodily fluid source and an outlet 953 configured to be coupled to a fluid collection device 980. In the embodiment shown in FIG. 26, the fluid collection device 980 is a transfer adapter configured to be coupled to one or more reservoirs such as, for example, an evacuated container, a sample bottle, a culture bottle, etc. In such embodiments, the reservoir can be sealed prior to being coupled to the transfer adapter (i.e., the fluid collection device 980) and once coupled the seal can be punctured, displaced, deformed, and/or otherwise unsealed to expose the outlet 953 to the negative pressure within the reservoir. Thus, the fluid control device 900 can function in a substantially similar manner to the control device 800 described above with reference to FIGS. 19-25.

[1159] While the fluid control device 800 is shown as including the actuator rod 862 that includes the first end portion 863 and the second portion 864 on which a force can be exerted to transition the device 800 between its first and second configurations, states, and/or positions, in other embodiments, a control device can include an actuator having any suitable configuration. For example, the fluid control device 900 includes an actuator rod 962 having only a single end portion that extends beyond the body 951 of the actuator 950, as shown in FIG. 26. In such embodiments, the device 900 can be used to fill a fluid collection device such as, for example, a sample reservoir, container, bottle, etc. and if it is desirable for more than one sample to be collected, the user can, for example, decouple the inlet 952 from a lumen-containing device and/or any suitable device otherwise placing the inlet 952 in fluid communication with the bodily fluid source. Once decoupled, the user can couple the inlet of a new control device 900 to the lumen-containing device and/or the like and can collect one or

more additional samples in a manner similar to that described above with reference to the control device 800.

[1160] As described above, some fluid control device described herein can be and/or can have a modular configuration in which one or more components can be coupled to collectively form a fluid control device having a desired set of characteristics or the like. For example, the fluid control device 800 shown in FIGS. 19-25 includes the housing 830 and the actuator 850 in one modular arrangement. It should be understood, however, that a control device can have any suitable modular arrangement. For example, FIG. 27 illustrates a modular fluid control device 1000 according to an embodiment. The fluid control device (also referred to herein as "device") includes a housing 1030 forming and/or defining a sequestration chamber 1034, and an actuator 1050 forming and/or having an inlet 1052 and an outlet 1053. The device 1000 can be substantially similar to the control device 800 described in detail above but can be arranged such that housing 1030 is disposed in different position and/or orientation relative to the actuator 1050. In some embodiments, varying the arrangement may, for example, enhance usability, visibility, and/or the like and/or may otherwise allow for a more compact design.

[1161] As another example, FIG. 28 illustrates a modular fluid control device 1100 according to an embodiment. The fluid control device (also referred to herein as "device") includes a housing 1130 forming and/or defining a sequestration chamber 1134, and an actuator 1150 forming and/or having an inlet 1152 and an outlet 1153. The device 1100 can be substantially similar to the control device 800 described in detail above but can be arranged such that housing 1130 is disposed in different position and/or orientation relative to the actuator 1150. Moreover, as shown in FIG. 28, the actuator 1150 can be arranged such that the inlet 1152 and the outlet 1153 are disposed in substantially perpendicular positions relative to one another. As described above, in some embodiments, varying the arrangement may, for example, enhance usability, visibility, and/or the like and/or may otherwise allow for a more compact design. While examples of modular fluid control devices are shown herein, it should be understood that such embodiments are presented by way of example and not limitation. Thus, while specific arrangements and/or orientations may be described herein, the devices and/or concepts described herein are not intended to be limited to those shown herein.

[1162] While the housings 230, 330, 830, 930, 1030, and 1130 have been shown and described herein as including and/or defining a sequestration chamber that is arranged in a serpentine-like configuration, in other embodiments, a housing and/or any other suitable portion of a control device can include and/or can define a sequestration chamber having any suitable configuration. For example, FIGS. 29-34 illustrate a fluid control device 1200

according to an embodiment. The fluid control device 1200 can be similar in at least form and/or function to the fluid control devices described herein. More specifically, portions of the fluid control device 1200 can be similar to and/or substantially the same as corresponding portions of the fluid control devices 200, 300, 800, 900, 1000, and/or 1100 described above. Accordingly, such portions of the fluid control device 1200 are not described in further detail herein.

[1163] The fluid control device 1200 (also referred to herein as "control device" or "device") includes a housing 1230 and an actuator 1250. As described above with reference to the control device 800, the control device 1200 can be arranged in a modular configuration such that the housing 1230 and the actuator 1250 can be physically and fluidically coupled to form the control device 1200. In other embodiments, the control device 1200 need not be modular. That is to say, in some embodiments, the control device 1200 can be assembled during manufacturing and delivered to a supplier and/or end user as an assembled device. In other embodiments, the control device can be monolithically formed and/or coupled to a fluid collection device in any suitable manner, as described in detail above.

[1164] The housing 1230 of the control device 1200 can be any suitable shape, size, and/or configuration. For example, in some embodiments, the housing 1230 can be substantially similar in at least form and/or function to the housing 830 described in detail above. Accordingly, such similar portions of the housing 1230 are identified below but may not be described in further detail herein.

[1165] As shown in FIGS. 29-31, the housing 1230 forms and/or defines a sequestration chamber 1234 that is in selective fluid communication with a first port 1245 and a second port 1246. The second port 1246 is configured to receive, include, and/or define a flow controller 1242 (see e.g., FIG. 30) and a restricted flow path 1232 (see e.g., FIG. 31). Although shown as including the restricted flow path 1232, in other embodiments, a housing need not include or receive a restricted flow path (e.g., when excessive negative pressure being applied to the sequestration chamber 1234 is unlikely or otherwise not intended such as when a fluid collection device is a syringe or the like). The first port 1245 and the second port 1246 are configured to be at least fluidically coupled to a portion of the actuator 1250 to allow for selective fluid flow between the housing 1230 and the actuator 1250. As described in further detail herein, the sequestration chamber 1234 is configured (1) to receive a selective flow and/or volume of bodily fluid from a portion of the actuator 1250 via the first port 1245, and (2) to sequester (e.g., separate, segregate, contain, retain, isolate, etc.) the flow and/or volume

of bodily fluid (e.g., an initial or first flow and/or volume of bodily fluid or any portion thereof) within the sequestration chamber 1234.

[1166] The sequestration chamber 1234 can have any suitable shape, size, and/or configuration. For example, in some embodiments, the sequestration chamber 1234 can have any suitable size, volume, and/or fluid capacity such as, for example, those described above with reference to the sequestration chamber 134. In the embodiment shown in FIGS. 29-34, the sequestration chamber 1234 can be, for example, a fluid flow path that extends through and/or that is defined by at least a portion of the housing 1230. In some embodiments, the sequestration chamber 1234 can be substantially similar in at least form and/or function to the sequestration chamber 834 described above with reference to FIGS. 19-25. The sequestration chamber 1234 and/or the housing 1230 can differ from the sequestration chamber 834 and/or the housing 830 by being arranged in a spiral configuration with the first port 1245 being in fluid communication with, for example, an inner portion of the spiraled sequestration chamber 1234 and the second port 1246 being in fluid communication with, for example, an outer portion of the spiraled sequestration chamber, as shown in FIG. 30. In some embodiments, the sequestration chamber 1234 can be, for example, a channel or the like formed in a portion of the housing 1230.

[1167] In some embodiments, the channel forming at least a portion of the sequestration chamber 1234 can have a relatively small cross-sectional shape and/or size that can reduce and/or substantially prevent a mixing of an initial volume of bodily fluid drawn into the sequestration chamber 1234 (channel) and a volume of air within the sequestration chamber 1234 (e.g., a volume of air that has not been vented or purged, as described in further detail herein). For example, in some instances, the relatively small cross-sectional shape and/or size of the sequestration chamber 1234 (channel), a surface tension associated with the bodily fluid flowing into the sequestration chamber 1234, and a contact angle between a surface of the housing 1230 forming the sequestration chamber 1234 and the bodily fluid flowing into the sequestration chamber 1234 can collectively limit and/or substantially prevent a mixing of the bodily fluid and a volume of air within the sequestration chamber 1234.

[1168] As shown in FIG. 30, the housing 1230 can include and/or can be coupled to a cover 1238 configured to enclose the channel, thereby forming the sequestration chamber 1234. The cover 1238 can be coupled to the housing 1230 in any suitable manner (e.g., via a friction fit, snap fit, interference fit, an adhesive, one or more mechanical fasteners, laser welding, ultrasonic welding, plasma techniques, annealing, heat boding and/or any other suitable coupling means or combination thereof). In other embodiments, the cover 1238 is

monolithically formed with and/or coupled to the housing 1230. Moreover, in some embodiments, the cover 1238 can be at least partially transparent to allow a user to visualize a flow of bodily fluid through the sequestration chamber 1234. In some embodiments, the arrangement of the housing 1230 and the cover 1238 can, for example, facilitate one or more manufacturing processes and/or can facilitate use of the control device 1200.

[1169] As shown in FIG. 30, the housing 1230 includes and/or defines a flow controller 1242 and a restricted flow path 1232. The flow controller 1242 can be, for example, a valve, membrane, diaphragm, restrictor, vent, a selectively permeable member, port, etc. configured to selectively control (at least in part) a flow of fluids into and/or out of the sequestration chamber 1234 and/or any other suitable portion of the housing 1230. For example, the flow controller 1242 can be a selectively permeable fluid barrier (e.g., a blood barrier) that includes and/or is formed of a porous material configured to selectively allow a flow of gas therethrough but to prevent a flow of a liquid therethrough. As such, the flow controller 1242 can be configured to vent and/or purge a volume of air within the sequestration chamber 1234 through the flow controller 1242 in response to a negative pressure differential within a portion of the control device 1200. Such a venting and/or purging of the volume of air within the sequestration chamber 1234 can result in a suction force and/or negative pressure differential being exerted and/or applied in or on the sequestration chamber 1234 that is operable to draw in the initial volume of bodily fluid. Moreover, the use of a selectively permeable fluid barrier can allow for the venting and/or purging of air without allowing a volume of bodily fluid to pass through the flow controller 1242. Accordingly, in some embodiments, the flow controller 1242 can be substantially similar to the flow controller 242 described in detail above with reference to FIGS. 2-5 and thus, is not described in further detail herein.

[1170] The actuator 1250 of the control device 1200 can be any suitable shape, size, and/or configuration. For example, in some embodiments, the actuator 1250 can be substantially similar in at least form and/or function to the actuator 850 described in detail above. Accordingly, such similar portions of the actuator 1250 are identified below but may not be described in further detail herein.

[1171] As shown in FIGS. 32-34, the actuator 1250 includes a body 1251 and an actuator rod 1262. The body 1251 of the actuator 1250 includes an inlet 1252 and an outlet 1253. The inlet 1252 and the outlet 1253 can be substantially similar in at least form and/or function to the inlet 852 and the outlet 853, respectively, described above with reference to FIGS. 19-25. Thus, the inlet 1252 is configured to be placed in fluid communication with a bodily fluid source to receive a flow of bodily fluid therefrom (e.g., via a lumen-containing device such as

a needle, IV catheter, PICC line, or the like). The outlet 1253 is configured to be fluidically coupled to a fluid collection device (not shown in FIGS. 29-34) such as, for example, a sample reservoir, a syringe, and/or other intermediary bodily fluid transfer device, adapter, or vessel such as, for example, a transfer device similar to those described in the '510 publication. In some embodiments, such a transfer device can provide a negative pressure and/or can act as an external energy source to enable desired functionality and fluid flow path dynamics/characteristics of the control device 1200.

[1172] The body 1251 of the actuator 1250 includes and/or defines a first port 1258 and a second port 1259. The first port 1258 is in fluid communication with the inlet 1252 and the second port 1259 is in fluid communication with the outlet 1252. In addition, the first port 1258 and the second port 1259 are configured to be at least fluidically coupled to the first port 1245 and the second port 1246, respectively, of the housing 1230. In some embodiments, the arrangement of the ports 1258 and 1259 of the actuator 1250 and the ports 1245 and 1246 of the housing 1230 can allow for and/or otherwise can provide a means of physically coupling the housing 1230 to the actuator 1250 as well as fluidically coupling the housing 1230 to the actuator 1250. That is to say, in some embodiments, the arrangement of the ports 1258 and 1259 of the actuator 1250 and the ports 1245 and 1246 of the housing 1230 can allow for a modular configuration or arrangement as described above with reference to the control device 800. In other embodiments, the housing 1230 and/or actuator 1250 need not be modular.

[1173] In some embodiments, the body 1251 and the actuator rod 1262 collectively include and/or collectively form a lock configured to at least temporarily lock the actuator 1250. For example, in some embodiments, the body 1251 and the actuator rod 1262 can each define an opening 1257 in or through which a locking member can be disposed. In such embodiments, when the locking member (not shown in FIG. 32) is disposed in the openings 1257, the locking member can limit and/or substantially prevent the actuator rod 1262 from being moved relative to the body 1251. On the other hand, removing the locking member from the openings 1257 can allow the actuator rod 1262 to be moved relative to the body 1251. While described as forming a lock, in some embodiments, the body 1251 and the actuator rod 1262 collectively include and/or collectively form a feature and/or arrangement that can limit and/or substantially prevent the actuator rod 1262 from being pulled out of the body 1251. In such embodiments, the feature can be a snap, a lock, a catch, and/or any other suitable feature and/or arrangement.

[1174] As shown in FIGS. 33 and 34, a portion of the actuator rod 1262 includes and/or is coupled to a set of seals 1265. The seals 1265 can be, for example, o-rings, over-molded elastomeric material, raised protrusions, and/or the like. The arrangement of the actuator 1262

and the body 1251 of the actuator 1250 can be such that the seals 1265 form one or more fluid tight seals between the actuator rod 1262 and the inner surface of the body 1251, as described above with reference to the actuator 850. In the embodiment shown in FIGS. 33 and 34, the actuator rod 1262 includes and/or is coupled to three seals 1265 which form and/or define a first fluid flow path 1233 within the body 1251 of the actuator 1250 and a second fluid flow path 1254 within the body 1251 of the actuator 1250. In other embodiments, any number of seals may be used to achieve desired performance.

[1175] As described above with reference to the device 800, the device 1200 can be used to procure a bodily fluid sample having reduced contamination from microbes such as, for example, dermally residing microbes, microbes external to the bodily fluid source, and/or the like. For example, the actuator rod 1262 is configured to be moved or transitioned relative to the body 1251 between a first position or configuration and a second position or configuration. In some embodiments, the transition of the actuator rod 1262 can be achieved by and/or can otherwise result from user interaction and manipulation of the actuator rod 1262, automatically in response to negative pressure and associated flow dynamics within the device 1200, and/or enacted by or in response to an external energy source which creates dynamics that result in the transitioning of the actuator rod 1262. As shown in FIG. 33, when in the first position and/or configuration, the inlet 1252 of the actuator 1250 is in fluid communication with the first fluid flow path 1233, which in turn, is in fluid communication with the first port 1258. The outlet 1253 of the actuator 1250 is in fluid communication with the second fluid flow path 1254, which in turn, is in fluid communication with the second port 1259. Thus, when in the actuator 1250 and/or actuator rod 1262 is in the first position and/or configuration (e.g., when the control device 1200 is in a first state or operating mode), the negative pressure within the fluid collection device (not shown in FIGS. 29-34) can result in a negative pressure (or negative pressure differential) within at least a portion of the sequestration chamber 1234 that is operable in drawing at least a portion of an initial flow, amount, or volume of bodily fluid from the inlet 1252, through the first fluid flow path 1233, and into the sequestration chamber 1234. Moreover, in some instances, the initial volume and/or flow of bodily fluid can be transferred into the sequestration chamber 1234 until, for example, the bodily fluid disposed within the sequestration chamber 1234 transitions the flow controller 1242 from an open or unsealed configuration or state (e.g., one in which a flow of gas or air can be drawn therethrough) to a sealed configuration or state (e.g., one in which a flow of gas and liquid cannot be drawn therethrough).

[1176] In some instances, a force can be exerted on the end portion 1263 of the actuator rod 1262 to place the actuator rod 1262 and/or actuator 1250 in its second position and/or configuration, as shown in FIG. 34. As described above, in some instances, prior to exerting the force on the end portion 1263 of the actuator rod 1262, the actuator 1250 may be transitioned from a locked configuration or state to an unlocked configuration or state. When the actuator rod 1262 and/or the actuator 1250 is placed in its second position and/or configuration (e.g., when the control device 1200 is transitioned to a second state or operating mode), the inlet 1252 and the outlet 1253 of the actuator 1250 are each in fluid communication with the second fluid flow path 1254 while the first fluid flow path 1233 is sequestered, isolated, and/or otherwise not in fluid communication with the inlet 1252 and the outlet 1253. As described in detail above, in some instances, contaminants such as, for example, dermally residing microbes or the like dislodged during the venipuncture event or throughout the bodily fluid collection process, can be entrained and/or included in the initial volume of the bodily fluid and thus, are sequestered in the sequestration chamber 1234 when the initial volume is sequestered therein. As such, the negative pressure otherwise exerted on or through the sequestration chamber 1234 is now exerted on or through the second fluid flow path 1254. In response, bodily fluid can flow from the inlet 1252, through the second fluid flow path 1254, through the outlet 1253, and into the fluid collection device coupled to the outlet 1253. Accordingly, the device 1200 can function in a manner substantially similar to that of the device 800 and thus, the function of the device 1200 is not described in further detail herein.

[1177] FIGS. 35-40 illustrate a fluid control device 1300 according to an embodiment. The fluid control device 1300 can be similar in at least form and/or function to the fluid control devices described herein. More specifically, portions of the fluid control device 1300 can be similar to and/or substantially the same as corresponding portions of the fluid control devices 200, 300, 800, 900, 1000, 1100, and/or 1200 described above. Accordingly, such portions of the fluid control device 1300 are not described in further detail herein.

[1178] The fluid control device 1300 (also referred to herein as "control device" or "device") includes a housing 1330 and an actuator 1350. As described above with reference to the control devices 800, the control device 1300 can be arranged in a modular configuration such that the housing 1330 and the actuator 1350 can be physically and fluidically coupled to form the control device 1300. In other embodiments, the control device 1300 need not be modular. That is to say, in some embodiments, the control device 1300 can be assembled during manufacturing and delivered to a supplier and/or end user as an assembled device. In

other embodiments, the device 1300 can be monolithically formed and/or collectively formed with, for example, a fluid collection device, as described above.

[1179] The housing 1330 of the control device 1300 can be any suitable shape, size, and/or configuration. As shown in FIGS. 35-37, the housing 1330 forms and/or defines a sequestration chamber 1334 that is in selective fluid communication with a first port 1345 and a second port 1346. The second port 1346 is configured to receive, include, and/or define a flow controller 1342 (see e.g., FIG. 36) and a restricted flow path 1332 (see e.g., FIG. 37). The first port 1345 and the second port 1346 are configured to be at least fluidically coupled to a portion of the actuator 1350 to allow for selective fluid flow between the housing 1330 and the actuator 1350. As described in further detail herein, the sequestration chamber 1334 is configured (1) to receive a selective flow and/or volume of bodily fluid from a portion of the actuator 1350 via the first port 1345, and (2) to sequester (e.g., separate, segregate, contain, retain, isolate, etc.) the flow and/or volume of bodily fluid (e.g., at least a portion of an initial or first flow and/or volume of bodily fluid) within the sequestration chamber 1334. The sequestration chamber 1334 can have any suitable shape, size, and/or configuration. For example, in some embodiments, the sequestration chamber 1334 can be, for example, a channel or the like formed in a portion of the housing 1330 and the housing 1330 can include and/or can be coupled to a cover 1338 configured to enclose the channel, thereby forming the sequestration chamber 1334. In some embodiments, the housing 1330 can be substantially similar in at least form and/or function to the housing 1230 described in detail above with reference to FIGS. 29-34. Accordingly, the housing 1330 is not described in further detail herein.

[1180] The actuator 1350 of the control device 1300 can be any suitable shape, size, and/or configuration. For example, in some embodiments, the actuator 1350 can be substantially similar in at least form and/or function to the actuators 850 and/or 1250 described in detail above. Accordingly, such similar portions of the actuator 1350 are identified below but may not be described in further detail herein.

[1181] As shown in FIGS. 38-40, the actuator 1350 includes a body 1351 and an actuator rod 1362. The body 1351 of the actuator 1350 includes an inlet 1352 and an outlet 1353. The inlet 1352 and the outlet 1353 can be substantially similar in at least form and/or function to the inlet 852 and the outlet 853, respectively, described above with reference to FIGS. 19-25. Thus, the inlet 1352 is configured to be placed in fluid communication with a bodily fluid source to receive a flow of bodily fluid therefrom (e.g., via a lumen-containing device such as a needle, IV catheter, surgical tubing, other standard bodily-fluid transfer device, PICC line, or

the like). The outlet 1353 is configured to be fluidically coupled to a fluid collection device (not shown in FIGS. 35-40) such as, for example, a sample reservoir, a syringe, and/or other intermediary bodily fluid transfer device, adapter, or vessel such as, for example, a transfer device similar to those described in the '510 publication.

[1182] The body 1351 of the actuator 1350 includes and/or defines a first port 1358 and a second port 1359. The first port 1358 is in fluid communication with the inlet 1352 and the second port 1359 is in fluid communication with the outlet 1353. In addition, the first port 1358 and the second port 1359 are configured to be at least fluidically coupled to the first port 1345 and the second port 1346, respectively, of the housing 1330. In some embodiments, the arrangement of the ports 1358 and 1359 of the actuator 1350 and the ports 1345 and 1346 of the housing 1330 can allow for and/or otherwise can provide a means of physically coupling the housing 1330 to the actuator 1350 as well as fluidically coupling the housing 1330 to the actuator 1350. That is to say, in some embodiments, the arrangement of the ports 1358 and 1359 of the actuator 1350 and the ports 1345 and 1346 of the housing 1330 can allow for a modular configuration or arrangement as described above with reference to the control device 800. In other embodiments, the housing 1330 and/or actuator 1350 need not be modular.

[1183] As shown in FIGS. 39 and 40, a portion of the actuator rod 1362 includes and/or is coupled to a set of seals 1365. The seals 1365 can be, for example, o-rings, elastomeric material, silicone or any other suitable material or configuration as described above with reference to the seals 1265. The arrangement of the actuator 1362 and the body 1351 of the actuator 1350 can be such that the seals 1365 form one or more fluid tight seals between the actuator rod 1362 and the inner surface of the body 1351, as described above with reference to the actuator 850. In the embodiment shown in FIGS. 33 and 34, the actuator rod 1362 includes and/or is coupled to three seals 1365 which form and/or define a first fluid flow path 1333 within the body 1351 of the actuator 1350 and a second fluid flow path 1354 within the body 1351 of the actuator 1350.

[1184] As described above with reference to the device 800, the device 1300 can be used to procure a bodily fluid sample having reduced contamination from microbes such as, for example, dermally residing microbes, microbes external to the bodily fluid source, and/or the like. For example, the actuator rod 1362 is configured to be moved or transitioned relative to the body 1351 between a first position or configuration and a second position or configuration. As shown in FIG. 39, when in the first position and/or configuration, the inlet 1352 of the actuator 1350 is in fluid communication with the first fluid flow path 1333, which in turn, is in fluid communication with the first port 1358. The outlet 1353 of the actuator 1350 is in fluid

communication with the second fluid flow path 1354, which in turn, is in fluid communication with the second port 1359. Thus, when in the actuator 1350 and/or actuator rod 1362 is in the first position and/or configuration (e.g., when the control device 1300 is in a first state or operating mode), the negative pressure within the fluid collection device (not shown in FIGS. 35-40) can result in a negative pressure (or negative pressure differential) within at least a portion of the sequestration chamber 1334 that is operable in drawing at least a portion of an initial flow, amount, or volume of bodily fluid from the inlet 1352, through the first fluid flow path 1333, and into the sequestration chamber 1334. Moreover, in some instances, the initial volume and/or flow of bodily fluid can be transferred into the sequestration chamber 1334 until, for example, the bodily fluid disposed within the sequestration chamber 1334 transitions the flow controller 1342 from an open or unsealed configuration or state (e.g., one in which a flow of gas or air can be drawn therethrough) to a sealed configuration or state (e.g., one in which a flow of gas and liquid cannot be drawn therethrough).

[1185] In some instances, a force can be exerted on a first end portion 1363 of the actuator rod 1362 to place the actuator rod 1362 and/or actuator 1350 in its second position, state, operating mode, and/or configuration, as shown in FIG. 35. As described above, in some instances, prior to exerting the force on the first end portion 1363 of the actuator rod 1362, the actuator 1350 may be transitioned from a locked configuration or state to an unlocked configuration or state. In some embodiments, the transition of the actuator rod 1362 can be achieved by and/or can otherwise result from user interaction and manipulation of the actuator rod 1362, automatically in response to negative pressure and associated flow dynamics within the device 1300, and/or enacted by or in response to an external energy source which creates dynamics that result in the transitioning of the actuator rod 1362.

[1186] When the actuator rod 1362 and/or the actuator 1350 is placed in its second position and/or configuration (e.g., when the control device 1300 is transitioned to a second state or operating mode), the inlet 1352 and the outlet 1353 of the actuator 1350 are each in fluid communication with the second fluid flow path 1354 while the first fluid flow path 1333 is sequestered, isolated, and/or otherwise not in fluid communication with the inlet 1352 and the outlet 1353. As described in detail above, in some instances, contaminants such as, for example, dermally residing microbes or the like dislodged during the venipuncture event or throughout the bodily-fluid collection process, can be entrained and/or included in the initial volume of the bodily fluid and thus, are sequestered in the sequestration chamber 1334 when the initial volume is sequestered therein. As such, the negative pressure otherwise exerted on or through the sequestration chamber 1334 is now exerted on or through the second fluid flow

path 1354. In response, bodily fluid can flow from the inlet 1352, through the second fluid flow path 1354, through the outlet 1353, and into the fluid collection device coupled to the outlet 1353. Accordingly, the device 1300 can function in a manner substantially similar to that of the device 800 and thus, the function of the device 1300 is not described in further detail herein.

[1187] In some instances, it may be desirable to isolate the negative pressure source (e.g., the fluid collection device from the inlet 1353 such as, for example, if it is desirable to collect multiple samples of bodily fluid using multiple fluid collection devices (e.g., syringes or the like). For example, in some instances, after filling the fluid collection device the user can engage the actuator 1350 and exert a force on a second end portion 1364 of the actuator rod 1362 to move and/or transition the actuator rod 1362 from its second position and/or configuration toward its first position and/or configuration. As such, the second fluid flow path 1354 no longer places the inlet 1352 in fluid communication with the outlet 1353. Moreover, the flow controller 1342 can remain in the sealed state or configuration (e.g., fully saturated, wetted, and/or otherwise preventing flow therethrough) such that the outlet 1353 is substantially sequestered or isolated from the rest of the control device 1300. In some instances, the user can then remove the filled fluid collection device and can couple a new fluid collection device to the outlet 1353. With the new fluid collection device coupled to the outlet 1353, the user can, for example, exert a force on the first end portion 1363 of the actuator rod 1362 to move and/or transition the actuator rod 1362 back to its second position, state, and/or configuration, as described above with reference to the actuator 850.

[1188] FIGS. 41-44 illustrate a fluid control device 1400 according to an embodiment. The fluid control device 1400 can be similar in at least form and/or function to the fluid control devices described herein. More specifically, portions of the fluid control device 1400 can be similar to and/or substantially the same as corresponding portions of the fluid control devices 200, 300, 800, 900, 1000, 1100, 1200, and/or 1300 described above. Accordingly, such portions of the fluid control device 1400 are not described in further detail herein.

[1189] The fluid control device 1400 (also referred to herein as "control device" or "device") includes a housing 1430 and an actuator 1450. As described above with reference to the control device 800, the control device 1400 can be arranged in a modular configuration such that the housing 1430 and the actuator 1450 can be physically and fluidically coupled to form the control device 1400. In other embodiments, the control device 1400 need not be modular. That is to say, in some embodiments, the control device 1400 can be assembled during manufacturing and delivered to a supplier and/or end user as an assembled device. In

other embodiments, the device 1400 can be monolithically formed and/or collectively formed with, for example, a fluid collection device, as described above.

[1190] The housing 1430 of the control device 1400 can be any suitable shape, size, and/or configuration. The housing 1430 is configured to be in selective fluid communication with a portion of the actuator 1450 via a first port 1458 and a second port 1459. As shown in FIGS. 43 and 44, the housing 1430 includes a bladder 1478 that can be transitioned from a first configuration and/or state to a second configuration and/or state to form and/or define a sequestration chamber 1434. As described in further detail herein, the bladder 1478 is configured to transition from the first configuration and/or state (FIG. 43) to the second configuration and/or state (FIG. 44) to form and/or define the sequestration chamber 1434, which in turn, is configured to receive a selective flow and/or volume of bodily fluid from a portion of the actuator 1450 via the first port 1458. After the bladder 1478 is placed in the second configuration and/or state, the sequestration chamber 1434 can sequester (e.g., separate, segregate, contain, retain, isolate, etc.) the flow and/or volume of bodily fluid (e.g., at least a portion of an initial or first flow and/or volume of bodily fluid) within the sequestration chamber 1434.

[1191] While the bladder 1478 is particularly shown in FIGS. 43 and 44, in other embodiments, the bladder 1478 can be any suitable shape, size, and/or configuration. Similarly, the bladder 1478 can be formed of any suitable material (e.g., any suitable biocompatible material such as those described herein and/or any other suitable material). In some embodiments, the bladder 1478 can be arranged and/or configured as, for example, a bellows, an expandable bag, a flexible pouch, and/or any other suitable reconfigurable container or the like. In addition, the sequestration chamber 1434 formed by the bladder 1478 can have any suitable shape, size, and/or configuration. In some embodiments, the housing 1430 can be substantially similar in at least form and/or function to the housing 1230 and/or 1330 described in detail above with reference to FIGS. 29-34 and FIGS. 35-40, respectively. Accordingly, the housing 1430 is not described in further detail herein.

[1192] The actuator 1450 of the control device 1400 can be any suitable shape, size, and/or configuration. For example, in some embodiments, the actuator 1450 can be substantially similar in at least form and/or function to the actuators 850, 1250, and/or 1350 described in detail above. Accordingly, such similar portions of the actuator 1450 are identified below but may not be described in further detail herein.

[1193] As shown in FIGS. 41-44, the actuator 1450 includes a body 1451 and an actuator rod 1462. The body 1451 of the actuator 1450 includes an inlet 1452 and an outlet 1453. The

inlet 1452 and the outlet 1453 can be substantially similar in at least form and/or function to the inlet 1252 and the outlet 1253, respectively, described above with reference to FIGS. 29-34. Thus, the inlet 1452 is configured to be placed in fluid communication with a bodily fluid source to receive a flow of bodily fluid therefrom (e.g., via a lumen-containing device such as a needle, IV catheter, surgical tubing, other standard bodily-fluid transfer device, PICC line, or the like). The outlet 1453 is configured to be fluidically coupled to a fluid collection device (not shown in FIGS. 41-44) such as, for example, a sample reservoir, a syringe, and/or other intermediary bodily fluid transfer device, adapter, or vessel such as, for example, a transfer device similar to those described in the '510 publication.

[1194] The body 1451 of the actuator 1450 includes and/or defines the first port 1458 and the second port 1459. Although not shown, the first port 1458 is configured to be in fluid communication with the inlet 1452 and the second port 1459 is configured to be in fluid communication with the outlet 1453. In addition, the first port 1458 is configured to be in fluid communication with the housing 1430 and more particularly, an inner volume or an inlet side of the bladder 1478 that forms the sequestration chamber 1434. The second port 1459 is configured to be in fluid communication with a portion of the housing 1430 defined between an inner surface of the housing 1430 and an outer surface of the bladder 1478. In other words, the second port 1459 is in fluid communication with a portion of the housing 1430 that is isolated and/or sequestered from the inner volume of the bladder 1478 that forms the sequestration chamber 1434. In some embodiments, the arrangement of the ports 1458 and 1459 of the actuator 1450 can allow for and/or otherwise can provide a means of physically coupling the housing 1430 to the actuator 1450 as well as fluidically coupling the housing 1430 to the actuator 1450. That is to say, in some embodiments, the arrangement of the ports 1458 and 1459 of the actuator 1450 can allow for a modular configuration or arrangement as described above with reference to the control device 800. In other embodiments, the housing 1430 and/or actuator 1450 need not be modular.

[1195] Although not shown in FIGS. 41-44, a portion of the actuator rod 1462 includes and/or is coupled to a set of seals. The seals can be, for example, o-rings, elastomeric material, silicone or any other suitable material or configuration as described above with reference to the seals 1265 and/or 1365. The arrangement of the actuator rod 1462 and the body 1451 of the actuator 1450 can be such that the seals form one or more fluid tight seals between the actuator rod 1462 and the inner surface of the body 1451, as described above with reference to the actuators 850, 1250, and/or 1350. Moreover, as described above with reference to the actuators 1250 and/or 1350, the actuator rod 1462 can include and/or can be coupled to a set seals which

selectively form and/or define a first fluid flow path configured to place the inlet 1452 of the actuator 1450 in fluid communication with the first port 1458 (e.g., when in a first position, state, operating mode, and/or configuration) and a second fluid flow path configured to place the inlet 1452 in fluid communication with the outlet 1453 (e.g., when in a second position, state, operating mode, and/or configuration).

[1196] As described above with reference to the devices 800, 1200, and/or 1300, the device 1400 can be used to procure a bodily fluid sample having reduced contamination from microbes such as, for example, dermally residing microbes, microbes external to the bodily fluid source, and/or the like. For example, as described above with reference to the devices 1200 and/or 1300, the actuator rod 1462 can be configured to be moved or transitioned relative to the body 1451 between a first position or configuration and a second position or configuration. When in the first position and/or configuration, the inlet 1452 of the actuator 1450 is in fluid communication with, for example, the first fluid flow path, which in turn, is in fluid communication with the first port 1458 (not shown in FIGS. 41-44). The outlet 1453 of the actuator 1450 is in fluid communication with the second fluid flow path 1454, which in turn, is in fluid communication with the second port 1459. Thus, when in the actuator 1450 and/or actuator rod 1462 is in the first position and/or configuration (e.g., when the control device 1400 is in a first state or operating mode), the negative pressure within the fluid collection device (not shown in FIGS. 41-44) can result in a negative pressure (or negative pressure differential) within the portion of the housing 1430 defined between the inner surface of the housing 1430 and the outer surface of the bladder 1478.

[1197] As shown in FIG. 43, the bladder 1478 can be in a first state and/or configuration prior to the fluid collection device being coupled to the outlet 1453. In some embodiments, for example, the bladder 1478 can have a flipped, inverted, collapsed, and/or empty configuration prior to coupling the fluid collection device to the outlet 1453. As shown in FIG. 44, the bladder 1478 can be configured to transition from the first state and/or configuration to a second state and/or configuration in response to the negative pressure differential resulting from the coupling of the fluid collection device to the outlet 1453. In other words, the negative pressure differential can be operable to transition the bladder 1478 from a collapsed or unexpanded configuration and/or state to an expanded configuration and/or state. For example, in some embodiments, the transitioning of the bladder 1478 can be similar to the transitioning and/or "flipping" of the diaphragm 576, described above with reference to FIGS. 11 and 12.

[1198] As described above, the bladder 1478 can be configured to transition from the first configuration and/or state to the second configuration and/or state to form and/or define the

sequestration chamber 1434. In some embodiments, the transitioning of the bladder 1478 results in an increase in an inner volume of the bladder 1478 (i.e., the sequestration chamber 1434). The increase in the inner volume can, in turn, result in a negative pressure differential between the sequestration chamber 1434 defined by the bladder 1478 and the inlet 1452 that is operable in drawing at least a portion of an initial flow, amount, or volume of bodily fluid from the inlet 1452, through the first port 1458, and into the sequestration chamber 1434. Moreover, in some instances, the initial volume and/or flow of bodily fluid can be transferred into the sequestration chamber 1434 until, for example, the bladder 1478 is fully expanded, and/or until the negative pressure differential is reduced and/or equalized.

[1199] Having transferred the initial volume of bodily fluid into the sequestration chamber 1434, a force can be exerted on a first end portion 1463 of the actuator rod 1462 to place the actuator rod 1462 and/or actuator 1450 in its second position, state, operating mode, and/or configuration, as described in detail above with reference to the devices 1200 and/or 1300. As described above, in some instances, prior to exerting the force on the first end portion 1463 of the actuator rod 1462, the actuator 1450 may be transitioned from a locked configuration or state to an unlocked configuration or state. In some embodiments, the transition of the actuator rod 1462 can be achieved by and/or can otherwise result from user interaction and manipulation of the actuator rod 1462, automatically in response to negative pressure and associated flow dynamics within the device 1400, and/or enacted by or in response to an external energy source which creates dynamics that result in the transitioning of the actuator rod 1462.

[1200] When the actuator rod 1462 and/or the actuator 1450 is placed in its second position and/or configuration (e.g., when the control device 1400 is transitioned to a second state or operating mode), the inlet 1452 and the outlet 1453 of the actuator 1450 are placed in fluid communication (e.g., via the second fluid flow path (not shown)) while the first fluid flow path (not shown) and/or the first port 1458 is sequestered, isolated, and/or otherwise not in fluid communication with the inlet 1452 and/or the outlet 1453. As described in detail above, in some instances, contaminants such as, for example, dermally residing microbes or the like dislodged during the venipuncture event or throughout the bodily-fluid collection process, can be entrained and/or included in the initial volume of the bodily fluid and thus, are sequestered in the sequestration chamber 1434 when the initial volume is sequestered therein. As such, the negative pressure otherwise exerted on or through the housing 1430 is now exerted on or through the outlet 1453 and the inlet 1452 via, for example, the second fluid flow path (not shown). In response, bodily fluid can flow from the inlet 1452, through the body 1451 of the actuator 1450, through the outlet 1453, and into the fluid collection device coupled to the outlet

1453. Accordingly, the device 1400 can function in a manner substantially similar to that of the devices 800, 1200, and/or 1300 and thus, the function of the device 1400 is not described in further detail herein.

[1201] While the device 1400 is described above as including the housing 1430 and the actuator 1450, in other embodiments, a fluid control device can have, for example, at least a partially integrated design. For example, FIGS. 45-50 illustrate a fluid control device 1500 according to an embodiment. The fluid control device 1500 can be similar in at least form and/or function to the fluid control devices described herein. More specifically, portions of the fluid control device 1500 can be similar to and/or substantially the same as corresponding portions of at least the fluid control device 1400 described above with reference to FIGS. 41-44. Accordingly, such portions of the fluid control device 1500 are not described in further detail herein.

[1202] The fluid control device 1500 (also referred to herein as "control device" or "device") includes an actuator 1550 having an actuator body 1551 and an actuator rod 1562. The actuator 1550 can be any suitable shape, size, and/or configuration. For example, in some embodiments, the actuator 1550 can be substantially similar in at least form and/or function to the actuators 850, 1250, 1350, and/or 1450 described in detail above. Accordingly, such similar portions of the actuator 1550 are identified below but may not be described in further detail herein.

[1203] As shown in FIGS. 45-50, the actuator 1550 includes an inlet 1552 and an outlet 1553, each of which is in fluid communication with the body 1551. The inlet 1552 and the outlet 1553 can be substantially similar in at least form and/or function to the inlet 1252 and the outlet 1253, respectively, described above with reference to FIGS. 29-34. Thus, the inlet 1552 is configured to be placed in fluid communication with a bodily fluid source to receive a flow of bodily fluid therefrom (e.g., via a lumen-containing device such as a needle, IV catheter, surgical tubing, other standard bodily-fluid transfer device, PICC line, or the like). The outlet 1553 is configured to be fluidically coupled to a fluid collection device (not shown in FIGS. 45-50) such as, for example, a sample reservoir, a syringe, and/or other intermediary bodily fluid transfer device, adapter, or vessel such as, for example, a transfer device similar to those described in the '510 publication.

[1204] As shown in FIGS. 48-50, the actuator 1550 includes a bladder 1578 that can be transitioned from a first configuration and/or state (FIG. 48) to a second configuration and/or state (FIG. 49) to form and/or define a sequestration chamber 1534. As described in further detail herein, the bladder 1578 is configured to transition from the first configuration and/or

state (FIG. 48) to the second configuration and/or state (FIGS. 49 and 50) to form and/or define the sequestration chamber 1534, which in turn, is configured to receive a selective flow and/or volume of bodily fluid from the inlet 1552. After the bladder 1578 is placed in the second configuration and/or state, the sequestration chamber 1534 can sequester (e.g., separate, segregate, contain, retain, isolate, etc.) the flow and/or volume of bodily fluid (e.g., at least a portion of an initial or first flow and/or volume of bodily fluid) within the sequestration chamber 1534. As such, the bladder 1578 can be substantially similar in at least form and/or function to the bladder 1478 described above with reference to FIGS. 41-44 and thus, is not described in further detail herein.

[1205] As shown in FIGS. 46 and 48-50, the body 1551 of the actuator 1550 includes and/or defines a port 1559 configured to be in fluid communication with the outlet 1553. In addition, the port 1559 defines a fluid flow path that is configured to be in fluid communication with a portion of the actuator 1550 defined between an inner surface of the body 1551 and an outer surface of the bladder 1578. In other words, the port 1559 is in fluid communication with a portion of the actuator 1550 that is isolated and/or sequestered from the inner volume of the bladder 1578 that forms and/or that is configured to form the sequestration chamber 1534.

[1206] As described above with reference to the devices 1200, 1300, and/or 1400, a portion of the actuator rod 1562 includes and/or is coupled to a set of seals 1565. The seals 1565 can be, for example, o-rings, elastomeric material, silicone or any other suitable material or configuration as described above with reference to the seals 1265 and/or 1365. The arrangement of the actuator rod 1562 and the body 1551 of the actuator 1550 can be such that the seals 1565 form one or more fluid tight seals between the actuator rod 1562 and the inner surface of the body 1551, as described above with reference to the actuators 850, 1250, and/or 1350. Moreover, as described above with reference to the actuators 1250 and/or 1350, the set seals 1565 can be arranged along the actuator rod 1562 to selectively form and/or define a fluid flow path 1554 that is sequestered from and/or fluidically isolated from the inlet 1552 when the actuator rod 1562 is in a first position and/or configuration and that is configured to place the inlet 1552 in fluid communication with the outlet 1553 when the actuator rod 1562 is in a second position and/or configuration.

[1207] As described above with reference to the devices 800, 1200, 1300, and/or 1400, the device 1500 can be used to procure a bodily fluid sample having reduced contamination from microbes such as, for example, dermally residing microbes, microbes external to the bodily fluid source, and/or the like. For example, as described above with reference to the devices 1200, 1300, and/or 1400, the actuator rod 1562 can be configured to be moved or transitioned

relative to the body 1551 between the first position or configuration and the second position or configuration. When in the first position and/or configuration, the inlet 1552 of the actuator 1550 is in fluid communication with a fluid flow path, which in turn, is in fluid communication with a portion of the body 1551 that is disposed on an inlet side of the bladder 1578. In other words, the fluid flow path establishes fluid communication between the inlet 1553 and the bladder 1578 and/or the sequestration chamber 1534 at least partially defined by the bladder 1578 when the bladder 1578 is transitioned to the second configuration and/or state. The outlet 1553 of the actuator 1550 is in fluid communication with the port 1559. Thus, when in the actuator 1550 and/or actuator rod 1562 is in the first position and/or configuration (e.g., when the control device 1500 is in a first state or operating mode), the negative pressure within the fluid collection device (not shown in FIGS. 45-50) can result in a negative pressure (or negative pressure differential) within the portion of the actuator body 1551 defined between the inner surface of the body 1551 and the outer surface of the bladder 1578, as described above with reference to the device 1400.

[1208] As shown in FIG. 48, the bladder 1578 can be in a first state and/or configuration prior to the fluid collection device being coupled to the outlet 1553. In some embodiments, for example, the bladder 1578 can have a flipped, inverted, collapsed, and/or empty configuration prior to coupling the fluid collection device to the outlet 1553. Moreover, when the actuator rod 1562 is in the first position and/or configuration, the fluid flow path 1554 is fluidically isolated from the inlet 1552. Accordingly, as shown in FIG. 49, the bladder 1578 can be configured to transition from the first state and/or configuration to a second state and/or configuration in response to the negative pressure differential resulting from the coupling of the fluid collection device to the outlet 1553. In other words, the negative pressure differential can be operable to transition the bladder 1578 from a collapsed or unexpanded configuration and/or state to an expanded configuration and/or state. For example, in some embodiments, the transitioning of the bladder 1578 can be similar to the transitioning and/or "flipping" of the diaphragm 576, described above with reference to FIGS. 11 and 12. In other embodiments, the bladder 1578 can be configured to transition between a first state and/or configuration to a second state and/or configuration in any suitable manner such as any of those described herein.

[1209] As described above, the bladder 1578 can be configured to transition from the first configuration and/or state to the second configuration and/or state to form and/or define the sequestration chamber 1534. In some embodiments, the transitioning of the bladder 1578 results in an increase in an inner volume of the bladder 1578 (i.e., the sequestration chamber 1534). The increase in the inner volume can, in turn, result in a negative pressure differential

between the sequestration chamber 1534 defined by the bladder 1578 and the inlet 1552 that is operable in drawing at least a portion of an initial flow, amount, or volume of bodily fluid from the inlet 1552 and a portion of the actuator body 1551, and into the sequestration chamber 1534. Moreover, in some instances, the initial volume and/or flow of bodily fluid can be transferred into the sequestration chamber 1534 until, for example, the bladder 1578 is fully expanded, and/or until the negative pressure differential is reduced and/or equalized.

[1210] Having transferred the initial volume of bodily fluid into the sequestration chamber 1534, a force can be exerted on a first end portion 1563 of the actuator rod 1562 to place the actuator rod 1562 and/or actuator 1550 in its second position, state, operating mode, and/or configuration, as described in detail above with reference to the devices 1200 and/or 1300. As described above, in some instances, prior to exerting the force on the first end portion 1563 of the actuator rod 1562, the actuator 1550 may be transitioned from a locked configuration or state to an unlocked configuration or state. In some embodiments, the transition of the actuator rod 1562 can be achieved by and/or can otherwise result from user interaction and manipulation of the actuator rod 1562, automatically in response to negative pressure and associated flow dynamics within the device 1500, and/or enacted by or in response to an external energy source which creates dynamics that result in the transitioning of the actuator rod 1562.

[1211] When the actuator rod 1562 and/or the actuator 1550 is placed in its second position and/or configuration (e.g., when the control device 1500 is transitioned to a second state or operating mode), the inlet 1552 and the outlet 1553 of the actuator 1550 are placed in fluid communication via the fluid flow path 1554 while the sequestration chamber 1534 is sequestered, isolated, and/or otherwise not in fluid communication with the inlet 1552 and/or the outlet 1553. As described in detail above, in some instances, contaminants such as, for example, dermally residing microbes or the like dislodged during the venipuncture event or throughout the bodily-fluid collection process, can be entrained and/or included in the initial volume of the bodily fluid and thus, are sequestered in the sequestration chamber 1534 when the initial volume is sequestered therein.

[1212] As described above with reference to the devices 1200 and/or 1300, transitioning the actuator rod 1562 to the second position and/or configuration is such that the fluid flow path 1554 places the inlet 1552 in fluid communication with the outlet 1553. For example, transitioning the actuator rod 1562 to the second position and/or configuration can move the seals 1565 relative to the inlet 1552 such that the fluid flow path 1554 is placed in fluid communication with both the inlet 1552 and the outlet 1553. As such, the negative pressure otherwise exerted on the outer surface of the bladder 1578 is now exerted on or through the

outlet 1553 and the inlet 1552 via the fluid flow path 1554. In response, bodily fluid can flow from the inlet 1552, through the fluid flow path 1554, through the outlet 1553, and into the fluid collection device coupled to the outlet 1553. Accordingly, the device 1500 can function in a manner substantially similar to that of the devices 800, 1200, 1300, and/or 1400 and thus, the function of the device 1500 is not described in further detail herein.

[1213] While the actuators 850, 1250, 1350, 1450, and 1550 have been described in detail above as being transitioned in response to an external force such as, for example, a force exerted by a user, in other embodiments, a fluid control device can include one or more actuators that can be transitioned in response to any suitable force, input, change of state or configuration, etc. For example, FIGS. 51 and 52 illustrate a portion of a fluid control device 1600 according to an embodiment. The fluid control device 1600 can be similar in at least form and/or function to the fluid control devices described herein. More specifically, portions of the fluid control device 1600 can be similar to and/or substantially the same as corresponding portions of at least the fluid control devices 500, 600, and/or 700 described above. Accordingly, such portions of the fluid control device 1600 are not described in further detail herein.

[1214] As shown in FIGS. 51 and 52, the fluid control device 1600 (also referred to herein as "control device" or "device") includes a housing 1630 having an inlet 1631 and an outlet 1636, and having and/or being coupled to an actuator 1650. As described in further detail herein, the housing 1630 defines a set of fluid flow paths 1633 and 1654 configured to establish fluid communication between one or more portions of the housing 1630 to selectively receive a flow of fluid therethrough (e.g., a liquid and/or a gas). The inlet 1631 is configured to be placed in fluid communication with a bodily fluid source to receive a flow of bodily fluid therefrom (e.g., via a lumen-containing device such as a needle or the like, as described in detail above). The outlet 1636 is configured to be fluidically coupled to a fluid collection device (not shown in FIGS. 51 and 52). The inlet 1631, the outlet 1636, and the fluid collection device can be substantially similar to those described above and thus, are not described in further detail herein.

[1215] The housing 1630 can be any suitable shape, size, and/or configuration. In some embodiments, the housing 1630 can have a size that is at least partially based on a volume of bodily fluid configured to be at least temporarily stored within one or more portions of the housing 1630. As described above, the housing 1630 of the control device 1600 is configured to (1) receive a flow and/or volume of bodily fluid via the inlet 1631 and (2) sequester (e.g., separate, segregate, contain, retain, isolate, etc.) the flow and/or volume of bodily fluid within a sequestration chamber 1634 included in and/or at least partially formed by the housing 1630.

In some embodiments, aspects of the housing 1630 can be substantially similar, for example, to aspects of the housings 630, 730, and/or 830. Accordingly, some portions and/or aspects of the housing 1630 are not described in further detail herein.

[1216] The housing 1630 includes and/or is coupled to the actuator 1650 configured to selectively control a flow of bodily fluid through the housing 1630. In this embodiment, the actuator 1650 includes a diaphragm 1676 and an actuator rod 1662 having a set of seals (e.g., seals 1665 and 1666). As described in further detail herein, the diaphragm 1676 and the actuator rod 1662 are configured to transition, move, and/or otherwise reconfigure within the housing 1630 in response to a negative pressure differential within at least a portion of the device. More specifically, the actuator 1650 is configured to move between a first state in which the inlet 1631 is placed in fluid communication with the sequestration chamber 1634 and a second state in which the inlet 1631 is placed in fluid communication with the outlet 1636 via the fluid flow path 1654, as described in detail above with reference to the control device 500.

[1217] In some embodiments, the diaphragm 1676 can be similar to, for example, the diaphragms 576, 676, and/or 776 described in detail above. Accordingly, the diaphragm 1676 can be at least partially disposed in a sequestration portion of the housing 1630 to define and/or to form at least a portion of the sequestration chamber 1634. As described in detail above, the diaphragm 1676 can be configured to transition, move, flip, and/or otherwise reconfigure from a first state to a second state in response to a negative pressure differential, which can be operable to draw an initial volume of bodily fluid into the sequestration chamber 1634 and/or to sequester the initial volume of bodily fluid in the sequestration chamber 1634 once disposed therein. Moreover, as shown in FIGS. 51 and 52, the diaphragm 1676 can include and/or can be coupled to a flow controller 1642. The flow controller 1642 can be any suitable flow controller such as any of those described herein. For example, in some embodiments, the flow controller 1642 can be a semi-permeable member or membrane such as an air permeable/liquid impermeable barrier (e.g., a blood barrier).

[1218] As described in detail above, the flow controller 1642 can be configured to transition from a first state in which the flow controller 1642 allows a flow of gas (e.g., air) to pass through the flow controller 1642 while preventing a flow of liquid (e.g., bodily fluid) to pass therethrough, to a second state in which the flow controller 1642 limits and/or substantially prevents a flow of gas and liquid to pass through the flow controller 1642. In some embodiments, the flow controller 1642 can be configured to transition from the first state to the second state in response to contact with, for example, the initial volume of bodily fluid

(e.g., at least a portion of the initial volume of bodily fluid can wet or saturate the flow controller 1642 to place the flow controller 1642 in the second state).

[1219] While the diaphragms 576, 676, and 776 are shown and described above as including a pin, rod, post, and/or the like that include and/or are coupled to one or more seals (e.g., the seals 565, 665, and 765, respectively), in the embodiment shown in FIGS. 51 and 52, the diaphragm 1676 includes a pin 1677 (e.g., a rod, an extension, a protrusion, a latch, a lock, and/or any other suitable feature, member, and/or mechanism) that does not include and/or is not coupled to a seal. For example, in this embodiment, the pin 1677 extends through a portion of the housing 1630 to selectively engage a portion of the actuator rod 1662, which in turn includes one or more seals (e.g., the seals 1665 and 1666), as described in further detail herein.

[1220] As shown in FIGS. 51 and 52, the actuator rod 1662 is movably disposed in, for example, an actuator portion 1639 of the housing 1630. The actuator rod 1662 includes a first seal 1665 and a second seal 1666 and is in contact with an energy storage member 1667 such as a spring or the like disposed within the actuator portion 1639 of the housing 1630. In the embodiment shown in FIGS. 51 and 52, the arrangement of the actuator 1650 can be such that a first end portion of the actuator rod 1662 is in selective contact with the pin 1677 of the diaphragm 1676 and a second end portion of the actuator rod 1662 (opposite the first end portion) is in contact with and/or otherwise is engaged with the energy storage member 1667.

[1221] As shown in FIG. 51, when the actuator 1650 is in a first state, the pin 1677 of the diaphragm 1676 can engage the actuator rod 1662 to maintain the actuator rod 1662 in a first or initial state and/or position in which the energy storage member 1667 has a relatively high potential energy (e.g., the energy storage member 1667 can be a spring maintained and/or held in a compressed state when in the first state). Furthermore, the first seal 1665 coupled to and/or disposed on the actuator 1662 is in a first or initial position in which the fluid flow path 1633 establishes fluid communication between the inlet 1631 and the sequestration chamber 1634 when the actuator 1650 is in the first state. As shown, the second seal 1666 coupled to and/or disposed on the actuator rod 1662 is likewise in a first or initial position in which the second seal 1666 is spaced apart from a seal surface 1640 formed by at least a portion of the actuator portion 1639 of the housing 1630.

[1222] In some embodiments, the separation of the second seal 1666 from the seal surface 1640 can be such that the fluid flow path 1654 places the outlet 1636 in fluid communication with the sequestration chamber 1634 via a restricted flow path 1632 (see FIG. 52). In some embodiments, the restricted flow path 1632 can be similar in at least form and/or function to any of the restricted flow paths described herein (e.g., the restricted flow paths 232, 832, 1232,

and/or 1332). As such, the restricted flow path 1632 can be configured to modulate a magnitude of a negative pressure differential applied on or in the sequestration chamber 1634 and/or a rate at which a negative pressure differential increases within the sequestration chamber 1634. In other embodiments, the outlet 1636 can be in fluid communication with the sequestration chamber 1634 via any suitable flow path, port, opening, valve, etc. In other words, in some embodiments, the control device 1600 need not include the restricted flow path 1632.

[1223] As shown in FIG. 51, when the actuator 1650 is in the first state, the actuator rod 1662 can be maintained in a first state or position in which the fluid flow path 1633 places the inlet 1631 in fluid communication with the sequestration chamber 1634, and the fluid flow path 1654 places the outlet 1636 in fluid communication with the sequestration chamber 1634 via the restricted flow path 1632. Accordingly, when a fluid collection device (such as those described herein) is coupled to the outlet 1636, a negative pressure defined in and/or otherwise produced by the fluid collection device can be operable to draw the initial volume of bodily fluid into the sequestration chamber 1634.

[1224] As described in detail above, the actuator 1650 can be transitioned to a second state and/or configuration in response to the initial volume being transferred into the sequestration chamber 1634. For example, in some embodiments, the initial volume of bodily fluid can be drawn into the sequestration chamber 1634 in response to a negative pressure being exerted through the flow controller 1642 (e.g., the selectively permeable membrane). In some instances, at least a portion of the bodily fluid drawn into the sequestration chamber 1634 can come into contact with the flow controller 1642, which in turn, can transition the flow controller 1642 from the first state to the second state (e.g., the flow controller 1642 limits and/or substantially prevents a flow of gas and liquid therethrough). As such, a negative pressure exerted on a surface of the diaphragm 1676 can build and can become sufficient to transition, move, and/or flip the diaphragm from a first state and/or configuration to a second state and/or configuration (see FIG. 52). In some embodiments, the transitioning of the diaphragm 1676 can correspond with and/or can be in response to the flow controller 1642 being transitioned from the first state to the second state (e.g., becoming fully wetted or the like, as described in detail above). In other embodiments, the diaphragm 1676 can transition before or after the flow controller 1642 has transitioned from the first state to the second state. In still other embodiments, the control device 1600 need not include the flow controller 1642 and the diaphragm 1676 can be configured to transition in response to being exposed to the negative pressure differential produced by the fluid collection device. In some such embodiments, the

diaphragm 1676 (and/or at least a portion thereof) can be configured to act in a similar manner to the flow controller 1642 by transitioning from the first state to the second state in a predictable and/or predetermined manner after being exposed to a predetermined negative pressure differential or a predetermined rate of change in negative pressure. Moreover, the transitioning of the diaphragm 1676 can be automatic (e.g., is not a result of user intervention).

[1225] As shown in FIG. 52, when the diaphragm 1676 is transitioned, moved, flipped, etc., the pin 1677 can be moved within the housing 1630 and relative to the actuator rod 1662. More particularly, the transitioning of the diaphragm 1676 can move the pin 1677 a sufficient amount that the pin 1677 is disengaged from the actuator rod 1662. As such, the energy storage member 1667 (e.g., spring) can be configured to release and/or convert at least a portion of its potential energy. As a specific example, in this embodiment, moving the pin 1677 can allow the spring 1667 to expand from a first or compressed state to a second or substantially uncompressed state. The transitioning of the energy storage member 1667 (e.g., spring) from the first state to the second state, in turn, moves the actuator rod 1662 within the actuator portion 1639 from a first state and/or position to a second state and/or position.

[1226] As shown in FIG. 52, when the actuator rod 1662 is in the second state and/or position, the first seal 1665 can be placed in a second or subsequent position in which the first seal 1665 sequesters the sequestration chamber 1634 from the inlet 1631. Similarly, the second seal 1666 can be placed in a second or subsequent position in which the second seal 1666 is pushed (e.g., by the energy storage member 1667) against the seal surface 1640, which in turn, sequesters the flow controller 1642 from the fluid flow path 1654. Furthermore, the placement of the first seal 1665 and the second seal 1666 when the actuator rod 1662 is in the second state and/or position is such that the fluid flow path 1633 is placed in fluid communication with the fluid flow path 1654. Thus, a negative pressure differential produced by the fluid collection device coupled to the outlet 1636 can be operable to draw a subsequent volume of bodily fluid from the inlet 1631, through the fluid flow path 1633 and 1654, through the outlet 1636, and into the fluid collection device. Moreover, the collecting and sequestering of the initial volume of bodily fluid can result in the subsequent volume(s) of bodily fluid being substantially free from contaminants, as described in detail above.

[1227] Referring now to FIG. 53, a flowchart is presented illustrating a method 10 of using a fluid control device to obtain a bodily fluid sample with reduced contamination according to an embodiment. The fluid control device can be similar to and/or substantially the same as any of the fluid control devices described in detail above. The method 10 includes establishing fluid communication between a bodily fluid source and an inlet of the fluid collection device,

at 11. For example, in some embodiments, a user can manipulate the fluid control device to physically and/or fluidically couple the inlet to a lumen-containing device (e.g., a needle, IV, PICC line, etc.) in fluid communication with a patient.

[1228] A fluid collection device is coupled to an outlet of the fluid control device, at 12. The coupling of the fluid collection device to the outlet is configured to produce a negative pressure differential within at least a portion of the fluid control device, as described in detail above. In some embodiments, for example, the fluid collection device can be a sample bottle or container that defines a negative pressure. In other embodiments, the fluid collection device can be a syringe or the like that can be manipulated to produce a negative pressure. Accordingly, a negative pressure differential can be produced within one or more portions of the fluid control device, as described above with reference to the control devices 100, 200, 300, 400, 500, 600, 700, 800, 900, 1000, 1100, 1200, 1300, 1400, 1500, and/or 1600.

[1229] An initial volume of bodily fluid is received from the inlet and into a sequestration portion of the fluid control device in response to the negative pressure differential, at 13. For example, in some embodiments, the sequestration portion can be similar to and/or substantially the same as the sequestration chamber 1234 described above with reference to FIGS. 29-34. In other embodiments, the sequestration portion can be similar to and/or substantially the same as the sequestration chamber 1634. In still other embodiments, the sequestration portion can be similar to and/or substantially the same as any of the sequestration chambers described herein. Furthermore, in some instances, the initial volume of bodily fluid can include contaminants entrained therein, which may otherwise result in false results during testing of a bodily fluid sample.

[1230] In response to contact with at least a portion of the initial volume of bodily fluid, a flow controller disposed in the sequestration portion is transitioned from a first state in which the flow controller allows a flow of a gas through the flow controller and prevents a flow of bodily fluid through the flow controller, to a second state in which the flow controller prevents a flow of gas and bodily fluid through the flow controller, at 14. For example, in some embodiments, the flow controller can be a selectively permeable member or membrane (e.g., a fluid or blood barrier and/or the like), as described above with reference to the flow controller 242. In other embodiments, the flow controller can be similar to and/or substantially the same as any of the flow controllers described herein. Thus, in some embodiments, the contact with at least the portion of the initial volume of bodily fluid can, for example, wet or saturate the flow controller such that the flow controller limits and/or substantially prevents a flow of gas and liquid (e.g., bodily fluid) therethrough. In other embodiments, the flow controller can be

a bladder and/or diaphragm that is configured to be transitioned in response to a negative pressure differential. For example, in such embodiments, a flow controller can be a substantially impermeable bladder or diaphragm that can transition from a first state to a second state when a negative pressure differential applied to a surface of the bladder and/or diaphragm exceeds a threshold amount of negative pressure.

[1231] The initial volume of bodily fluid is sequestered in the sequestration portion after the flow controller is transitioned to the second state, at 15. For example, in some embodiments, the fluid control device can include an actuator and/or any other suitable feature or mechanism configured to transition after the flow controller is placed in its second configuration to sequester the initial volume of bodily fluid. In some embodiments, the actuator can transition from a first state to a second state to automatically sequester the initial volume of bodily fluid in the sequestration portion, as described above with reference to, for example, the actuator 1650. In other embodiments, the actuator can transition from a first state to a second state in response to a force exerted by a user, as described above with reference to, for example, the actuator 850. In still other embodiments, the fluid control device can sequester the initial volume of bodily fluid in the sequestration portion in any suitable manner such as those described herein.

[1232] After sequestering the initial volume of bodily fluid, a subsequent volume of bodily fluid is transferred from the inlet, through the outlet, and into the fluid collection device, at 16. As described in detail above, in some instances, sequestering the initial volume of bodily fluid in the sequestration portion of the fluid control device can likewise sequester contaminants contained in the initial volume. Accordingly, contaminants in the subsequent volume of bodily fluid can be reduced or substantially eliminated.

[1233] While various embodiments have been described above, it should be understood that they have been presented by way of example only, and not limitation. Where schematics and/or embodiments described above indicate certain components arranged in certain orientations or positions, the arrangement of components may be modified. While the embodiments have been particularly shown and described, it will be understood that various changes in form and details may be made. For example, while the control devices 100, 200, 300, 400, 500, 600, 700, 800, 900, 1000, 1100, 1200, 1300, 1400, and/or 1500 are described as transferring a bodily fluid into the device as a result of a negative pressure within a fluid collection device, in other embodiments, the devices described herein can be used with any suitable device configured to establish a pressure differential (e.g., a negative pressure differential). For example, in some embodiments, an outlet of a control device can be coupled

to a syringe or pump. In other embodiments, a control device can include a pre-charged sequestration chamber, a vented sequestration chamber, a manually activated device configured to produce a negative pressure, an energy source (e.g., a chemical energy source, a kinetic energy source, and/or the like), and/or any other suitable means of defining and/or forming a pressure differential within a portion of the control device. Moreover, as described above, the control devices can be coupled to such collection devices by a user (e.g., doctor, nurse, technician, physician, etc.) or can be coupled or assembled during manufacturing. In some embodiments, pre-assembling a control device and a collection device (e.g., a sample container or syringe) can, for example, force compliance with a sample procurement protocol that calls for the sequestration of an initial amount of bodily fluid prior to collecting a sample volume of bodily fluid.

[1234] While some of the embodiments described above include a flow controller and/or an actuator having a particular configuration and/or arrangement, in other embodiments, a fluid control device can include any suitable flow controller and/or actuator configured to selectively control a flow of bodily fluid through one or more portions of the fluid control device. For example, while some embodiments include an actuator such as a diaphragm or the like having one or more seals arranged as an O-ring or an elastomeric over-mold, which is/are moved with the diaphragm and relative to a portion of the device (e.g., the inlet, the outlet, or any other suitable portion) when the diaphragm is transitioned or flipped from a first state to a second state, in other embodiments, a fluid control device can include one or more seals having any suitable configuration. For example, in some embodiments, a fluid control device can include one or more seals arranged as an elastomeric sheet or the like that is/are fixedly coupled to a portion of the control device. In such embodiments, a portion of an actuator such as a pin or rod extending from a diaphragm (see e.g., FIGS. 11 and 12) can extend through an opening defined in the one or more elastomeric sheets, which in turn, form a substantially fluid tight seal with an outer surface of the pin or rod. As such, when the actuator (e.g., diaphragm) is transitioned from a first state to a second state, the portion of the actuator (e.g., the pin or rod) can move through one or more of the elastomeric sheets. In other words, the portion of the actuator moves relative to the one or more elastomeric sheets, which in turn, remain in a substantially fixed position relative to the portion of the control device. In some embodiments, the removal or the portion of the actuator can allow a flow of fluid through the opening defined by the one or more elastomeric sheets that was otherwise occluded by the portion of the actuator. Accordingly, the one or more elastomeric sheets can function in a similar manner as any of the seals described herein. Moreover, in some embodiments, such an arrangement may,

for example, reduce an amount of friction associated with forming the desired fluid tight seals, which in turn, may obviate the use of a lubricant otherwise used to facilitate the movement of the seals within the control device.

[1235] While the diaphragms (e.g., diaphragms 576, 676, and 776) are described herein as being configured to transition, move, flip, and/or otherwise reconfigure in response to an amount of negative pressure exerted on a surface of the diaphragm exceeding a threshold amount of negative pressure, in other embodiments, a fluid control device can include any suitable actuator or the like configured to transition, move, flip, and/or otherwise reconfigure in response to being exposed to a desired and/or predetermined amount of negative pressure. For example, in some embodiments, a fluid control device can include an actuator including and/or arranged as a movable member, plug, plunger, occlusion member, seal, and/or the like configured to selectively control a flow of fluid through at least a portion of the fluid control device. More particularly, the movable member or the like can be transitioned from a first state and/or position in which the movable member or the like is disposed in and/or otherwise occludes an opening, to a second state and/or position in which the movable member or the like is removed from the opening. In such embodiments, a negative pressure can be exerted through a portion of the device to transfer, for example, an initial volume of bodily fluid into a sequestration portion and/or chamber.

[1236] As described in detail above, in some embodiments, a device can include a flow controller such as a selectively permeable member or membrane, that can be configured to transition from a first state to a second state in response to being wetted (or otherwise transitioned) by the initial volume of bodily fluid. After transferring the initial volume of bodily fluid and after the flow controller is transitioned to its second state, an amount of negative pressure exerted on a surface of the movable member or the like may build until a magnitude of the negative pressure is sufficient to pull or move the movable member out of the opening, thereby allowing a flow of bodily fluid through the opening that was otherwise occluded by the movable member. In this manner, the movable member can function similar to any of the diaphragms described herein (e.g., the diaphragm 576, 676, and/or 776) that are configured to transition or flip from a first state to a second state. In such embodiments, the movable member can be, for example, an elastomeric plug, cork, plunger, and/or any other suitable member that can be moved or "popped" out of such an opening or portion of a flow path.

[1237] While some of the embodiments described above include a flow controller and/or actuator that selectively establishes fluid communication between a sequestration chamber and

a fluid collection device (e.g., a sample reservoir, a syringe, and/or any other suitable source of negative pressure) in other embodiments, a control device can be arranged to transfer a flow of bodily fluid in response to negative pressure differentials resulting from any suitable portion(s) of the device. For example, while the control device 200 is described above as including the flow controller 242 and the restricted flow path 232 that selectively place the sequestration chamber 234 in fluid communication with the sample reservoir until the flow controller 242 is transitioned to a sealed or closed state (e.g., until the flow controller 242 is sufficiently wetted), in other embodiments, a control device can include a sequestration chamber that is a pre-sealed evacuated and/or charged chamber such that establishing fluid communication between an inlet and the sequestration chamber results in a negative pressure differential that is sufficient to draw an initial volume of bodily fluid into the sequestration chamber. In such embodiments, the control device can be configured to transfer bodily fluid to the sequestration chamber until the pressure differential is sufficiently reduced and/or until pressures otherwise substantially equalize. Moreover, in some such embodiments, the sequestration chamber and/or the inlet can include a coupler, an actuator, a needle, a septum, a port, and/or any other suitable member that can establish fluid communication therebetween (e.g., that can transition the sequestration chamber from a sealed to an unsealed configuration).

[1238] While some of the embodiments described above include a flow controller and/or actuator that physically and/or mechanically sequesters one or more portions of a fluid control device, in other embodiments, a fluid control device need not physically and/or mechanically sequester one or more portions of the fluid control device. For example, in some embodiments, an actuator such as the actuator 1250 can be transitioned from a first state in which an initial volume of bodily fluid can flow from an inlet to a sequestration chamber or portion, to a second state in which (1) the sequestration chamber or portion is physically and/or mechanically sequestered and (2) the inlet is in fluid communication with an outlet of the fluid control device. In other embodiments, however, an actuator and/or any other suitable portion of a fluid control device can transition from a first state in which an initial volume of bodily fluid can flow from an inlet to a sequestration chamber or portion, to a second state in which the inlet is placed in fluid communication with the outlet without physically and/or mechanically sequestering (or isolating) the sequestration chamber or portion. When such a control device is in the second state, one or more features and/or geometries of the control device can result in a preferential flow of bodily fluid from the inlet to the outlet and the initial volume of bodily fluid can be retained in the sequestration chamber or portion without physically and/or mechanically being sequestered or isolated.

[1239] While the restricted flow path 232 is described above as modulating and/or controlling a magnitude of negative pressure applied on or through at least a portion of the device 200, in other embodiments, a control device can include any suitable feature, mechanism, and/or device configured to modulate, create, and/or otherwise control one or more pressure differentials through at least a portion of the control device. For example, in some embodiments, a user can transition and/or move an actuator to change (e.g., reduce or increase) the size of one or more portions of a fluid flow path or fluid flow interface within a portion of the control device to manually modulate and/or otherwise control an amount or magnitude of negative pressure within one or more portions of a control device.

[1240] Although various embodiments have been described as having particular features, concepts, and/or combinations of components, other embodiments are possible having any combination or sub-combination of any features, concepts, and/or components from any of the embodiments described herein. For example, as described above, the device 700 includes concepts, features, and/or elements of the devices 200 and 600. As another example, any of the embodiments described herein can include a lock or other suitable feature configured to at least temporarily maintain one or more components in a desired position, state, arrangement, and/or configuration. As another example, any of the embodiments described herein can include and/or can define a sequestration chamber and/or portion that is configured similar to, for example, the sequestration chamber 1234 described above with reference to FIG. 30. In other words, any of the fluid control devices described herein can include a sequestration chamber that is arranged and/or formed as a channel. In some embodiments, a channel forming at least a portion of a sequestration chamber can have a relatively small cross-sectional shape and/or size that can reduce and/or substantially prevent mixing of air and bodily fluid as the initial volume of bodily fluid is drawn into the channel, as described above with reference to the sequestration chamber 1234. Moreover, such a channel can have a spiral shape and/or configuration similar to the sequestration chamber 1234 described above and/or can have any other suitable shape and/or configuration.

[1241] As another example, any of the control devices described herein can include a flow controller arranged as a selectively permeable member or membrane as described above, for example, with reference to the flow controller 242. More particularly, while the control device 600 is not described as including a flow controller, in other embodiments, a portion of the diaphragm 676 can include and/or can form a flow controller formed, at least in part, of a selectively permeable material. In such embodiments, the flow controller can be configured to allow a volume of the sequestration chamber and/or portion 634 to be vented in response to

being exposed to the negative pressure differential (as described above). In other words, a volume of air can be drawn out of (e.g., vented from or purged from) the sequestration chamber 634 via the flow controller in response to the negative pressure differential within a portion of the fluid control device 600. In some instances, such an arrangement can allow for a reduction in a size and/or volume of the sequestration chamber 634 because a volume of air otherwise occupying a portion of the sequestration chamber 634 is vented or purged through the flow controller in response to the negative pressure differential.

[1242] By way of another example, any of the embodiments described herein can include any suitable actuator and/or flow controller configured to selectively control fluid flow through at least a portion of the device. Specifically, a flow controller or the like can be one or more of a selectively permeable material or membrane, a valve, a diaphragm, and/or any other suitable flow controller. While some of the embodiments have been described as including an actuator rod configured to be transitioned from a first configuration or position to a second configuration or position (e.g., the actuator rod 1262 of the actuator 1250), in other embodiments, any actuator described herein can include an actuator rod configured to transition from between a first position and second position to at least temporarily isolate an outlet of the device from one or more other portions of the device (e.g., as described above with reference to the actuators 850 and/or 1350). In some embodiments, such an actuator can be configured for use with a given and/or predetermined collection device such as, for example, a syringe. In other embodiments, such an actuator can be used with any suitable collection device.

[1243] In some embodiments, the specific configurations of the various components can also be varied. For example, the size and specific shape of the various components can be different from the embodiments shown, while still providing the functions as described herein. For example, while a portion of the actuator body 1551, sequestration chamber 1534, and/or the bladder 1578 are shown in FIGS. 45-50 as being substantially tubular having a round or substantially semi-circular end portion, in other embodiments, the portion of the actuator body 1551, sequestration chamber 1534, and/or bladder 1578 can have any suitable shape and/or size. In some embodiments, varying the size and/or shape of such components may reduce an overall size of the device 1500 and/or may increase the ergonomics of the device 1500 without changing the function of the device 1500. As a specific example, a housing, sequestration chamber, and/or bladder may have a substantially cylindrical shape with a relatively flat end portion or the like. Moreover, in some embodiments, a control device can include a bladder that is configured to "flip" similar to the diaphragms described above in response to being exposed to a negative pressure differential. In other embodiments, a bladder can be configured

to gradually transition (e.g., unroll, unfold, unfurl, and/or otherwise reconfigure) from the first state to the second state. In some instances, controlling a rate at which a bladder is transitioned may allow for a modulation and/or control of a negative pressure differential produced within the sequestration chamber.

[1244] In other embodiments, a device may include a bladder (similar in form and/or function to the bladders 1478 and/or 1578) disposed in a housing having a size, shape, and/or profile similar to the housings 1230 and/or 1330. In some such embodiments, the bladder can define a volume that is similar in shape and/or size the overall size, and/or shape of the housing (e.g., cylindrical with a relatively low profile or height). In some instances, such an arrangement can allow at least a portion of an initial volume of bodily fluid to remain in contact with a surface of the bladder (or diaphragm or other actuator), which can provide a visual indication to the user regarding the bodily fluid being transferred into the sequestration chamber. In other embodiments, a housing similar to the housing 1230 can define a spiral channel or any other suitable channel and can include a bladder disposed within at least a portion of that channel. In such embodiments, the bladder can function similarly to the bladder 1578 in which the bladder expands, opens, and/or otherwise increases in volume in response to being exposed to a negative pressure differential. In some embodiments, a bladder can define an enclosed volume configured to receive an initial volume of bodily fluid. In other embodiments, the bladder and a portion of the housing (e.g., a surface defining the sequestration chamber and/or channel) can collectively define the volume configured to receive the initial volume of bodily fluid. In this manner, a fluid control device can include a bladder configured to conform to any suitable shape, feature, channel, and/or configuration of a housing in which it is disposed. In some embodiments, the size and shape of the various components can be specifically selected for a desired rate and/or volume of bodily fluid flow into a fluid reservoir.

[1245] In some embodiments, the size and/or shape of the various components can be specifically selected for a desired or intended usage. For example, in some embodiments, a device such as those described herein can be configured for use with or on seemingly healthy adult patients. In such embodiments, the device can include a sequestration chamber that has a first volume (e.g., about 0.5 ml to about 5.0 ml). In other embodiments, a device such as those described herein can be configured for use with or on, for example, very sick patients and/or pediatric patients. In such embodiments, the device can include a sequestration chamber that has a second volume that is less than the first volume (e.g., less than about 0.5 ml). Thus, it should be understood that the size, shape, and/or arrangement of the embodiments and/or

components thereof can be adapted for a given use unless the context explicitly states otherwise.

[1246] Although not shown, any of the devices described herein can include an opening, port, coupler, septum, Luer-Lok, gasket, valve, threaded connecter, standard fluidic interface, etc. (referred to for simplicity as a "port") in fluid communication with the sequestration chamber. In some such embodiments, the port can be configured to couple to any suitable device, reservoir, pressure source, etc. For example, in some embodiments, the port can be configured to couple to a reservoir, which in turn, can allow a greater volume of bodily fluid to be diverted and/or transferred into the sequestration chamber. In other embodiments, the port can be coupled to a negative pressure source such as an evacuated container, a pump, a syringe, and/or the like to collect a portion of or the full volume of bodily fluid in the sequestration chamber, channel, reservoir, etc. and use that volume of bodily fluid (e.g., the pre-sample volume) for additional clinical and/or in vitro diagnostic testing purposes. In other embodiments, the port can be configured to receive a probe, sampling tool, testing device, and/or the like that can be used to perform one or more tests (e.g., tests not sensitive to potential contamination) on the initial volume while the initial volume is disposed or sequestered in the sequestration chamber. In still other embodiments, the port can be coupled to any suitable pressure source or infusion device configured to infuse the initial volume of bodily fluid sequestered in the sequestration chamber back into the patient and/or bodily fluid source (e.g., in the case of pediatric patients, very sick patients, patients having a low blood volume, and/or the like). In other embodiments, the sequestration channel, chamber, and/or reservoir can be configured with the addition of other diagnostic testing components integrated into the chamber (e.g., a paper test) such that the initial bodily fluid is used for that test.

[1247] In still other embodiments, the sequestration chamber, channel, and/or reservoir can be designed, sized, and configured to be removable and compatible with testing equipment and/or specifically accessible for other types of bodily fluid tests commonly performed on patients with suspected conditions. By way of example, a patient with suspected sepsis commonly has blood samples collected for lactate testing, procalcitonin testing, and blood culture testing. All of the fluid control devices described herein can be configured such that the sequestration chamber, channel, reservoir, etc. can be removed (e.g., after receiving the initial volume of bodily fluid) and the bodily fluid contained therein can be used for these additional testing purposes before or after the subsequent sample is collected for microbial testing.

[1248] Although not shown, in some embodiments, a fluid control device can include one or more lumen, channels, flow paths, etc. configured to selectively allow for a "bypass" flow of bodily fluid, where an initial amount or volume of bodily fluid can flow from the inlet, through the lumen, cannel, flow path, etc. to bypass the sequestration chamber, and into the collection device. In some embodiments, the fluid control device can include an actuator having, for example, at least three states – a first in which bodily fluid can flow from the inlet to the sequestration chamber, a second in which bodily fluid can flow from the inlet to the outlet after the initial volume is sequestered in the sequestration chamber, and a third in which bodily fluid can flow from the inlet, through the bypass flow path, and to the outlet. In other embodiments, the control device can include a first actuator configured to transition the device between a first and second state, as described in detail above with reference to specific embodiments, and can include a second actuator configured to transition the device to a bypass configuration or the like. In still other embodiments, the control device can include any suitable device, feature, component, mechanism, actuator, controller, etc. configured to selectively place the fluid control device in a bypass configuration or state.

[1249] Any of the embodiments described herein can be used in conjunction with any suitable fluid transfer, fluid collection, and/or fluid storage device such as, for example, the fluid reservoirs described in the '420 patent. In some instances, any of the embodiments described herein can be used in conjunction with any suitable transfer adapter, fluid transfer device, fluid collection device, and/or fluid storage devices such as, for example, the devices described in the '510 Publication and/or any of the devices described in U.S. Patent Publication No. 2015/0246352 entitled, "Apparatus and Methods for Disinfection of a Specimen Container," filed March 3, 2015; U.S. Patent No. 8,535,241 entitled, "Fluid Diversion Mechanism for Bodily-Fluid Sampling," filed October 12, 2012; U.S. Patent No. 9,060,724 entitled, "Fluid Diversion Mechanism for Bodily-Fluid Sampling," filed May 29, 2013; U.S. Patent No. 9,155,495 entitled, "Syringe-Based Fluid Diversion Mechanism for Bodily-Fluid Sampling," filed December 2, 2013; U.S. Patent Publication No. 2016/0361006 entitled, "Devices and Methods for Syringe Based Fluid Transfer for Bodily-Fluid Sampling," filed June 13, 2016; U.S. Patent Publication No. 2018/0140240 entitled, "Systems and Methods for Sample Collection with Reduced Hemolysis," filed November 20, 2017; and/or U.S. Patent Publication No. 2017/0065733 entitled, "Apparatus and Methods for Maintaining Sterility of a Specimen Container," filed September 6, 2016, the disclosures of each of which are incorporated herein by reference in their entireties.

[1250] In some embodiments, a method of using a fluid control device such as those described herein can include the ordered steps of establishing fluid communication between a bodily fluid source (e.g., a vein of a patient or the like) and an inlet of a fluid control device. An outlet of the fluid control device is then placed in fluid communication with and/or otherwise engages a negative pressure source. Such a negative pressure source can be a sample reservoir, a syringe, an evacuated container, an intermediate transfer device, and/or the like. The fluid control device can be in a first state or operating mode when the outlet is coupled to the negative pressure source and, as such, a negative pressure differential is applied through the fluid control device that draws an initial volume of bodily fluid into a sequestration chamber of the fluid control device. For example, a negative pressure within a sample reservoir can be operable in drawing an initial volume of bodily fluid from a patient and into the sequestration chamber. Once the initial volume of bodily fluid is disposed in the sequestration chamber, the fluid control device is transitioned, either automatically or via user intervention, from the first state or operating mode to a second state or operating mode such that (1) the initial volume is sequestered in the sequestration chamber and (2) the fluid communication is established between the inlet and the outlet. The sequestration of the initial volume can be such that contaminants entrained in the flow of the initial volume are likewise sequestered within the sequestration chamber. With the initial volume of bodily fluid sequestered in the sequestration chamber and with fluid communication established between the inlet and the outlet, subsequent volumes of bodily fluid that are substantially free of contamination can be collected in one or more sample reservoirs.

[1251] While the method of using the fluid control device is explicitly described as including the recited ordered steps, in other embodiments, the ordering of certain events and/or procedures in any of the methods or processes described herein may be modified and such modifications are in accordance with the variations of the invention. Additionally, certain events and/or procedures may be performed concurrently in a parallel process when possible, as well as performed sequentially as described above. Certain steps may be partially completed or may be omitted before proceeding to subsequent steps. For example, while the devices are described herein as transitioning from a first state to a second state in a discrete operation or the like, it should be understood that the devices described herein can be configured to automatically and/or passively transition from the first state to the second state and that such a transitioning may occur over a period of time. In other words, the transitioning from the first state to the second state may, in some instances, be relatively gradual such that as a last portion of the initial volume of bodily fluid is being transferred into the sequestration chamber, the

housing begins to transition from the first state to the second state. In some instances, the rate of change when transitioning from the first state to the second state can be selectively controlled to achieve one or more desired characteristics associated with the transition. Moreover, in some such instances, the inflow of the last portion of the initial volume can limit and/or substantially prevent bodily fluid already disposed in the sequestration chamber from escaping therefrom. Accordingly, while the transitioning from the first state to the second state may occur over a given amount of time, the sequestration chamber can nonetheless sequester the volume of bodily fluid disposed therein.

What is claimed:

1. A system, comprising:

a housing having an inlet and an outlet, the inlet configured to be placed in fluid communication with a bodily fluid source, the housing forming a sequestration portion configured to receive an initial volume of bodily fluid from the bodily fluid source;

a flow controller at least partially disposed in the sequestration portion of the housing and configured to transition from a first state to a second state; and

a fluid collection device configured to be fluidically coupled to the outlet to produce a negative pressure differential within at least a portion of the housing, the negative pressure differential produced by the fluid collection device operable to draw the initial volume of bodily fluid into the sequestration portion when the flow controller is in the first state, the negative pressure differential produced by the fluid collection device operable to draw the sample volume of bodily fluid through the outlet and into the fluid collection device when the flow controller is in the second state.

2. The system of claim 1, wherein the flow controller is configured to transition from the first state to the second state automatically.

3. The system of claim 1, wherein the flow controller is configured to transition from the first state to the second state in response to contact with a portion of the initial volume of bodily fluid disposed in the sequestration portion.

4. The system of claim 1, wherein the flow controller includes a selectively permeable material.

5. The system of claim 4, wherein prior to being placed in the second state, the flow controller is configured to allow a flow of a gas through the flow controller and to prevent a flow of bodily fluid through the flow controller.

6. The system of claim 5, wherein the flow controller is configured to prevent a flow of gas and bodily fluid through the flow controller when in the second state.

7. The system of claim 6, wherein the flow controller is configured to be placed in the second state in response to a portion of the initial volume of bodily fluid saturating the selectively permeable material.

8. The system of claim 1, wherein the flow controller is configured to modulate a magnitude of negative pressure exerted on the sequestration portion of the housing prior to the flow controller transitioning to the second state.

9. The system of claim 1, wherein the fluid collection device is a sample reservoir that defines a negative pressure operable to produce the negative pressure differential within at least the portion of the housing when fluidically coupled to the outlet.

10. The system of claim 1, wherein the fluid collection device is a syringe configured to be manipulated by a user after being fluidically coupled to the outlet to produce the negative pressure differential within at least the portion of the housing.

11. The system of claim 1, wherein the housing defines a first fluid flow path and a second fluid flow path, the negative pressure differential is operable to draw the initial volume of bodily fluid through the first fluid flow path from the inlet to the sequestration portion when the flow controller is in the first state, the negative pressure differential is operable to draw the sample volume of bodily fluid through the second fluid flow path from the inlet to the outlet when the flow controller is in the second state.

12. The system of claim 11, further comprising:

an actuator coupled to the housing, the actuator having a first actuator state in which the negative pressure differential is applied to the first fluid flow path and a second actuator state in which the negative pressure differential is applied to the second fluid flow path.

13. The system of claim 12, wherein the actuator is in the first actuator state when the flow controller is in the first state, the actuator is configured to be transitioned from the first actuator state to the second actuator state after the flow controller is transitioned to the second state.

14. The system of claim 13, wherein the negative pressure differential automatically transitions the actuator from the first actuator state to the second actuator state after the flow controller is transitioned to the second state.

15. An apparatus, comprising:

a housing having an inlet configured to be placed in fluid communication with a bodily fluid source and an outlet configured be placed in fluid communication with a fluid collection device, the housing forming a sequestration portion configured to receive an initial volume of bodily fluid from the bodily fluid source; and

an actuator coupled to the housing, the actuator having a first configuration in which a first fluid flow path places the inlet in fluid communication with the sequestration portion and a second configuration in which a second fluid flow path places the inlet in fluid communication with the outlet,

wherein the fluid collection device is configured to be placed in fluid communication with the outlet to produce a negative pressure differential (1) within the first fluid flow path operable to draw the initial volume of bodily fluid into the sequestration portion when the actuator is in the first configuration, and (2) within the second fluid flow path operable to draw a sample volume of bodily fluid into the fluid collection device when the actuator is in the second configuration.

16. The apparatus of claim 15, wherein the initial volume of bodily fluid is sequestered in the sequestration portion when the actuator is in the second configuration.

17. The apparatus of claim 15, wherein sequestering the initial volume in the sequestration portion reduces contamination in the sample volume.

18. The apparatus of claim 15, wherein the fluid collection device is a sample reservoir that defines a negative pressure operable to produce the negative pressure differential within the first fluid flow path and the second fluid flow path.

19. The apparatus of claim 15, wherein the fluid collection device is a syringe configured to be manipulated by a user after being placed in fluid communication with the outlet to produce the negative pressure differential within the first fluid flow path and the second fluid flow path.

20. The apparatus of claim 15, wherein the actuator is configured to transition from the first configuration to the second configuration in response to a force applied by a user on a portion of the actuator.

21. The apparatus of claim 15, wherein the actuator includes at least one seal configured to define a portion of the first fluid flow path when the actuator is in the first configuration, the at least one seal is configured to define a portion of the second fluid flow path when the actuator is in the second configuration.

22. The apparatus of claim 15, wherein the actuator includes a diaphragm configured to transition from a first state to a second state when a negative pressure differential within a portion of the first fluid flow path is greater than a threshold amount of negative pressure.

23. The apparatus of claim 22, wherein the diaphragm is coupled to at least one seal configured to define a portion of the first fluid flow path when the diaphragm is in the first state and configured to define a portion of the second fluid flow path when the diaphragm is in the second state.

24. The apparatus of claim 15, further comprising:

a flow controller at least partially disposed in the sequestration portion of the housing, the flow controller is configured to establish selective fluid communication between the sequestration portion and the actuator.

25. The apparatus of claim 24, wherein the flow controller includes a selectively permeable material.

26. The apparatus of claim 25, wherein the flow controller is configured to transition from a first state in which the selective permeable material allows a flow of a gas through the flow controller and prevents a flow of bodily fluid through the flow controller, to a second state in which the selectively permeable material prevents a flow of gas and bodily fluid through the flow controller.

27. The apparatus of claim 26, wherein the flow controller is configured to be placed in the second state in response to at least a portion of the initial volume of bodily fluid saturating the selectively permeable material.

28. The apparatus of claim 26, wherein the actuator is configured to be transitioned to the second configuration after the flow controller is transitioned to the second state.

29. A method of using a fluid control device to obtain a bodily fluid sample with reduced contamination, the method comprising:

establishing fluid communication between a bodily fluid source and an inlet of the fluid control device;

coupling a fluid collection device to an outlet of the fluid control device, the coupling of the fluid collection device to the outlet configured to produce a negative pressure differential within at least a portion of the fluid control device;

receiving an initial volume of bodily fluid from the inlet and into a sequestration portion of the fluid control device in response to the negative pressure differential;

transitioning, in response to contact with at least a portion of the initial volume of bodily fluid, a flow controller disposed in the sequestration portion from a first state in which the flow controller allows a flow of a gas through the flow controller and prevents a flow of bodily fluid through the flow controller, to a second state in which the flow controller prevents a flow of gas and bodily fluid through the flow controller;

sequestering the initial volume of bodily fluid in the sequestration portion after the flow controller is transitioned to the second state; and

transferring a subsequent volume of bodily fluid from the inlet, through the outlet, and into the fluid collection device.

30. The method of claim 29, wherein the flow controller includes a selectively permeable material.

31. The method of claim 29, wherein the flow controller is configured to be placed in the second state in response to at least a portion of the initial volume of bodily fluid saturating the selectively permeable material.

32. The method of claim 29, wherein the flow controller is configured to automatically transition from the first state to the second state in response to contact with at least the portion of the initial volume of bodily fluid.

33. The method of claim 29, wherein the coupling the fluid collection device to the outlet includes coupling a fluid reservoir to the outlet to produce the negative pressure differential within at least the portion of the fluid control device, the fluid reservoir defining a negative pressure prior to the fluid reservoir being coupled to the outlet.

34. The method of claim 29, wherein coupling the fluid collection device to the outlet includes coupling a syringe to the outlet, the method further comprising:

manipulating the syringe, after coupling the syringe to the outlet, to produce the negative pressure differential within at least the portion of the fluid control device.

35. The method of claim 29, further comprising:

transitioning an actuator of the fluid control device from a first configuration to a second configuration after transitioning the flow controller from the first state to the second state, the actuator defining at least a portion of a first fluid flow path between the inlet and the sequestration portion when in the first configuration, the actuator defining at least a portion of a second fluid flow path between the inlet and the outlet when in the second configuration.

36. The method of claim 29, wherein the sequestering of the initial volume of bodily fluid sequesters contaminants within the sequestration portion such that the subsequent volume of bodily fluid is substantially free of contaminants.

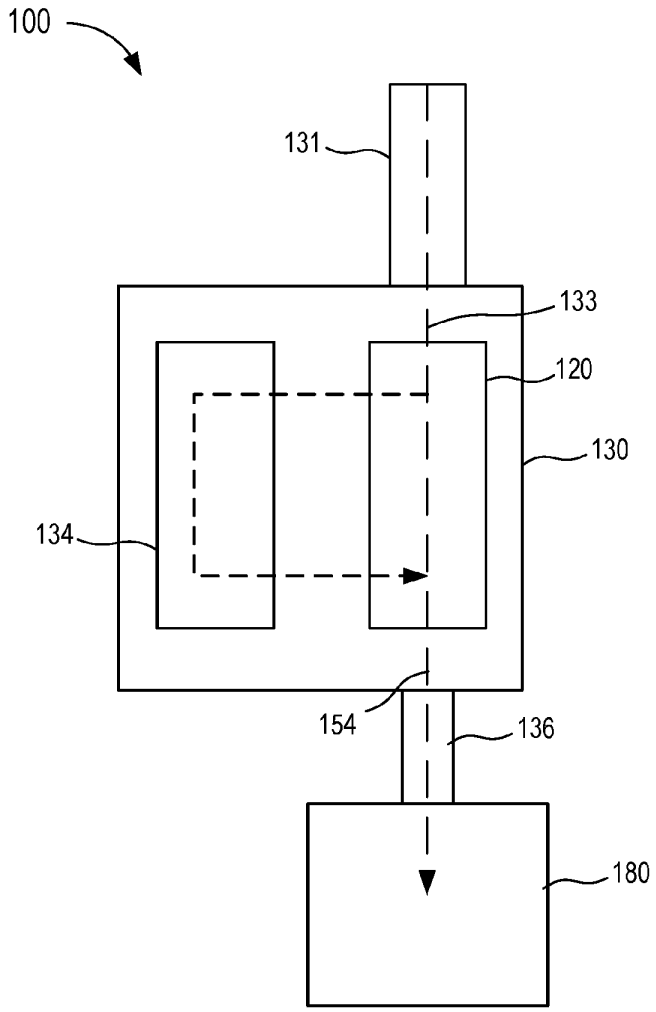


FIG. 1

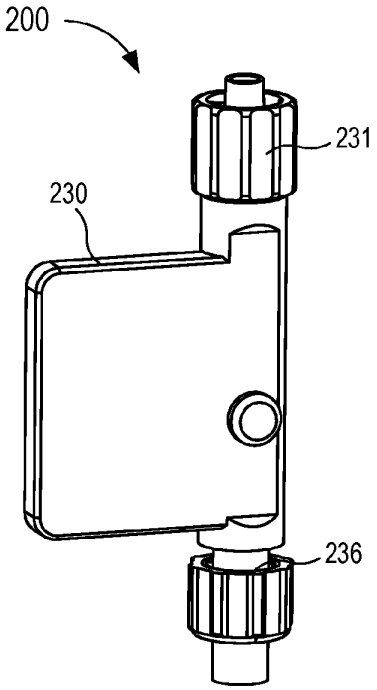


FIG. 2

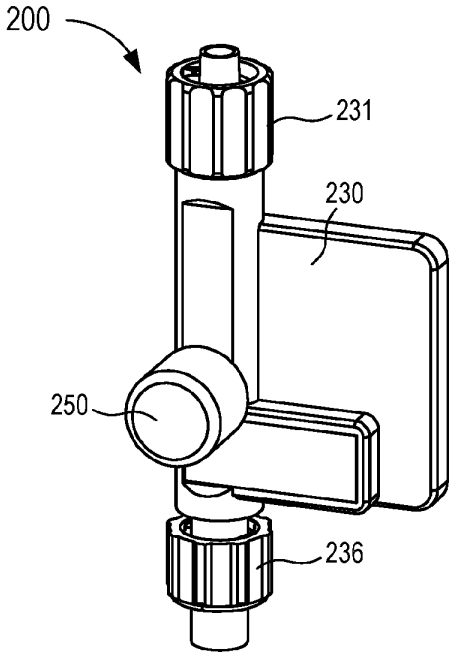


FIG. 3

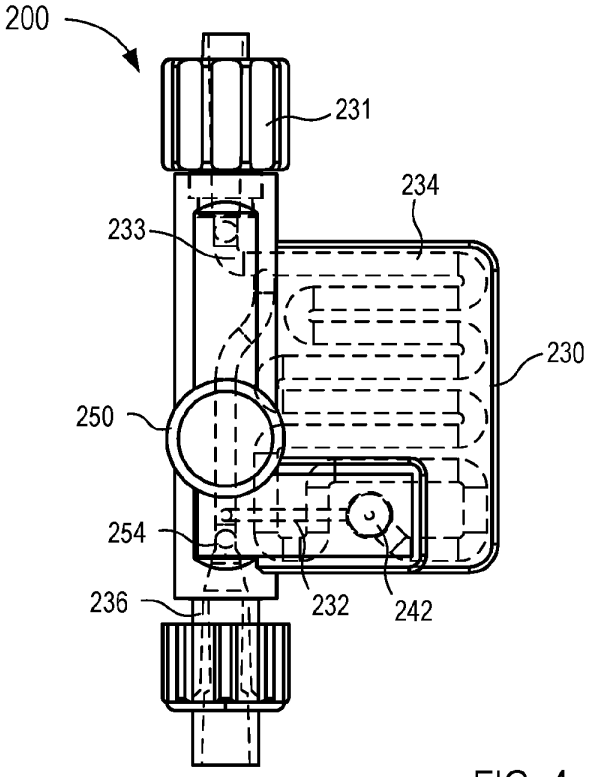


FIG. 4

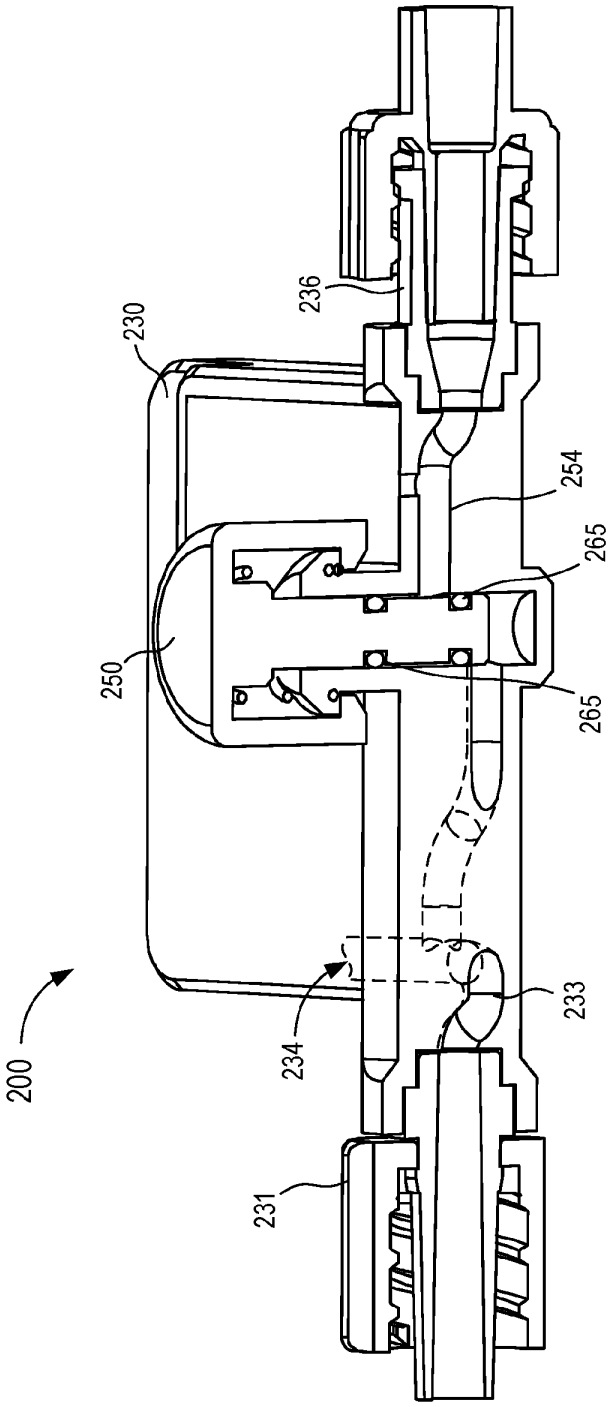


FIG. 5

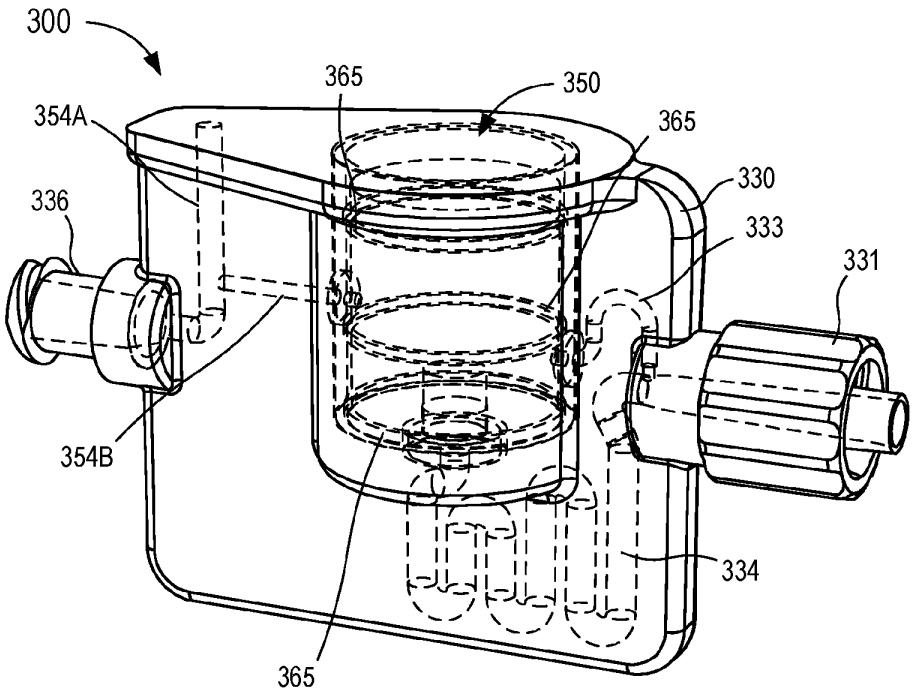

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FIG. 6

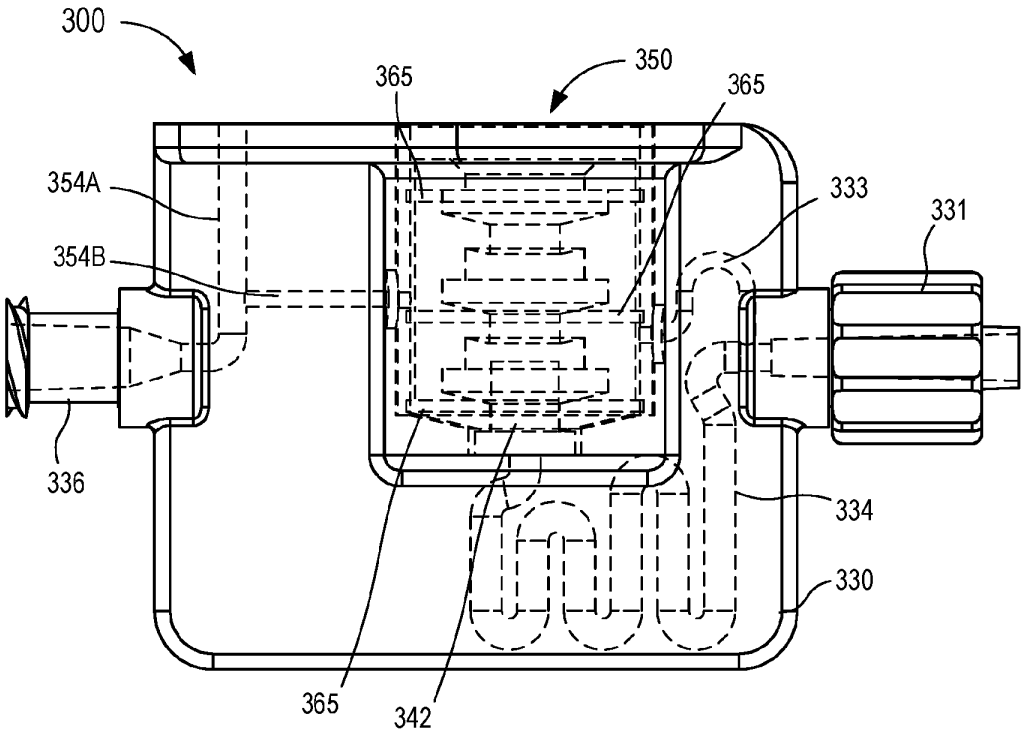

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FIG. 7

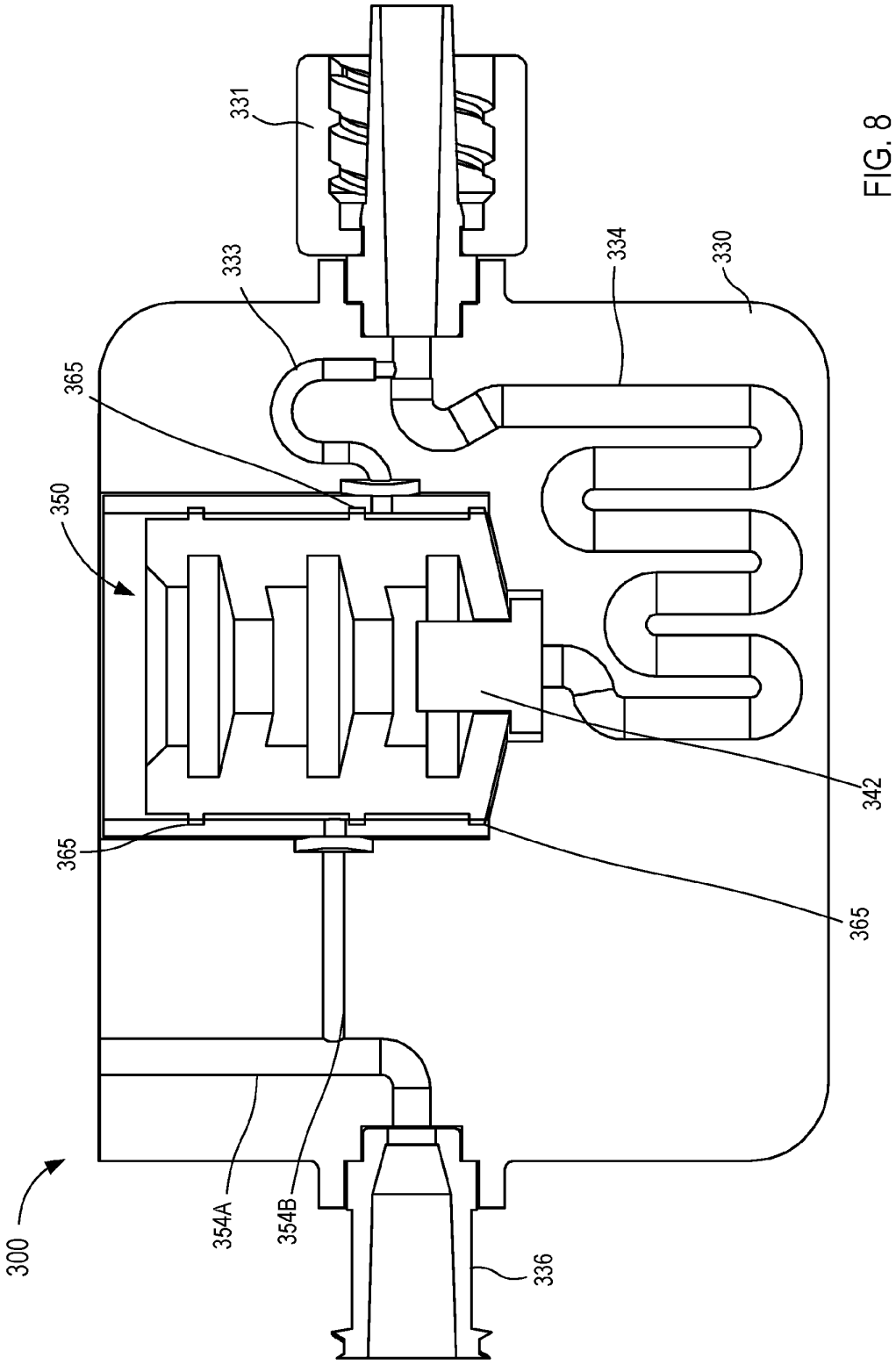


FIG. 8

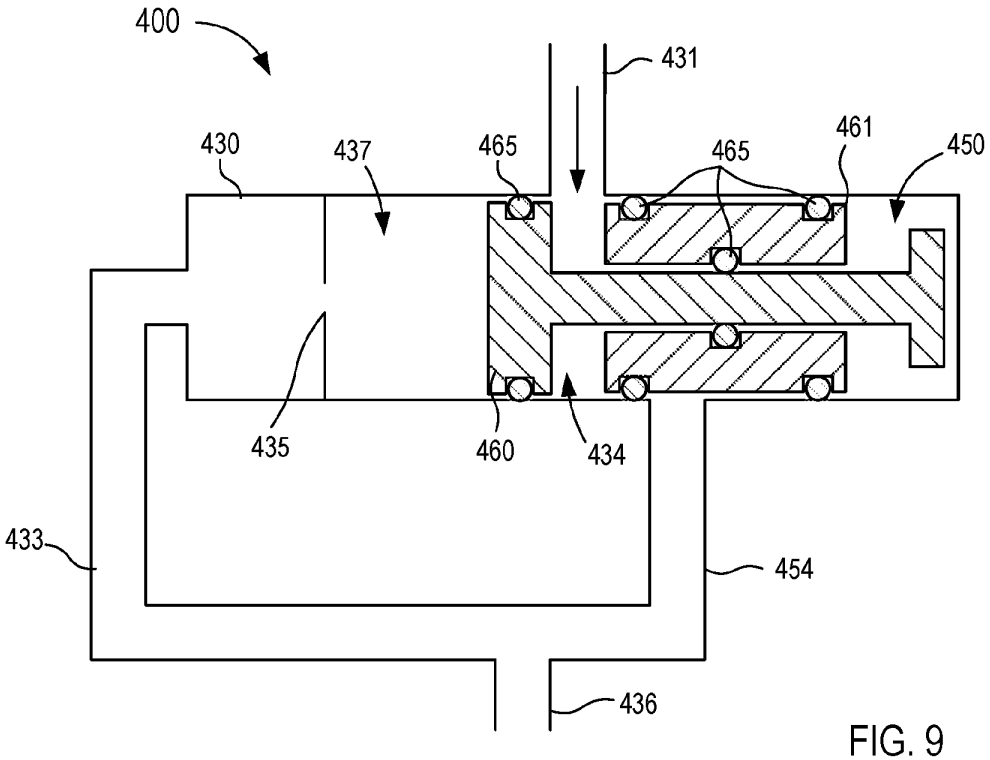

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FIG. 9

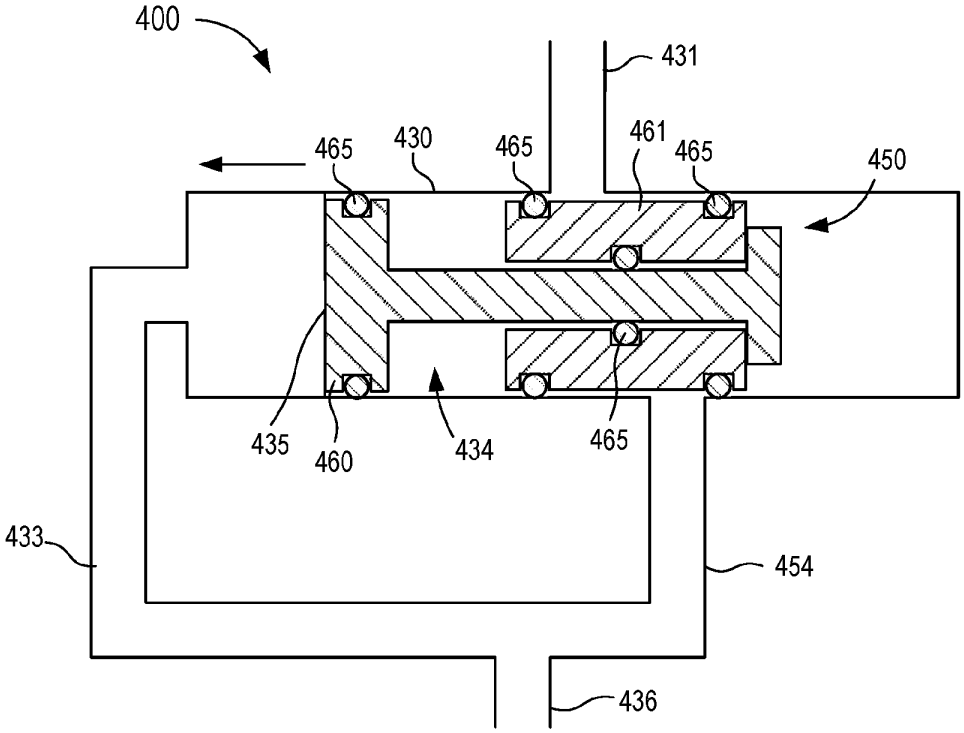

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FIG. 10

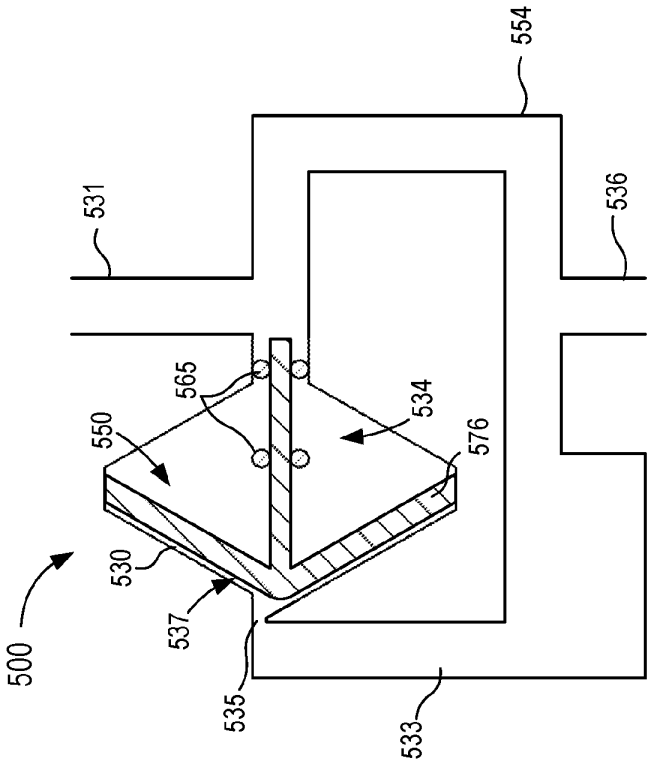

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FIG. 12

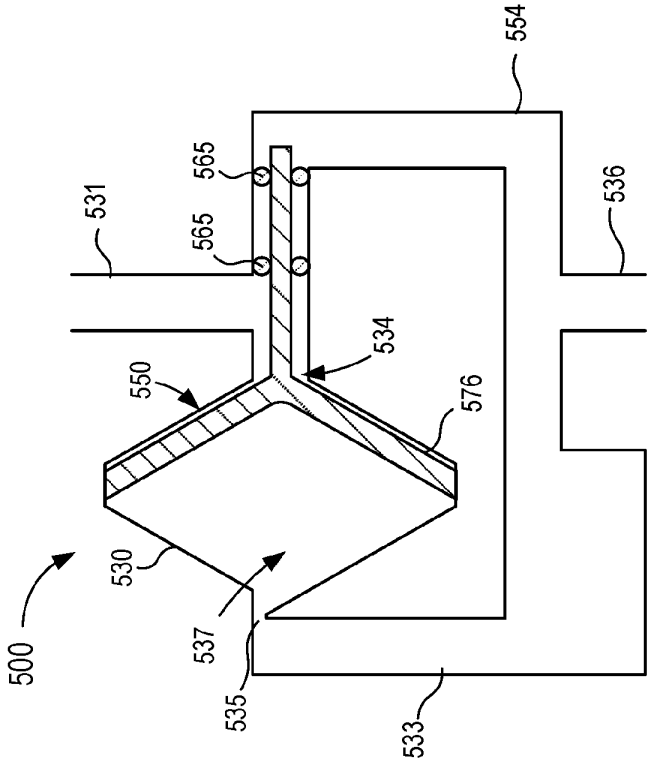

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FIG. 11

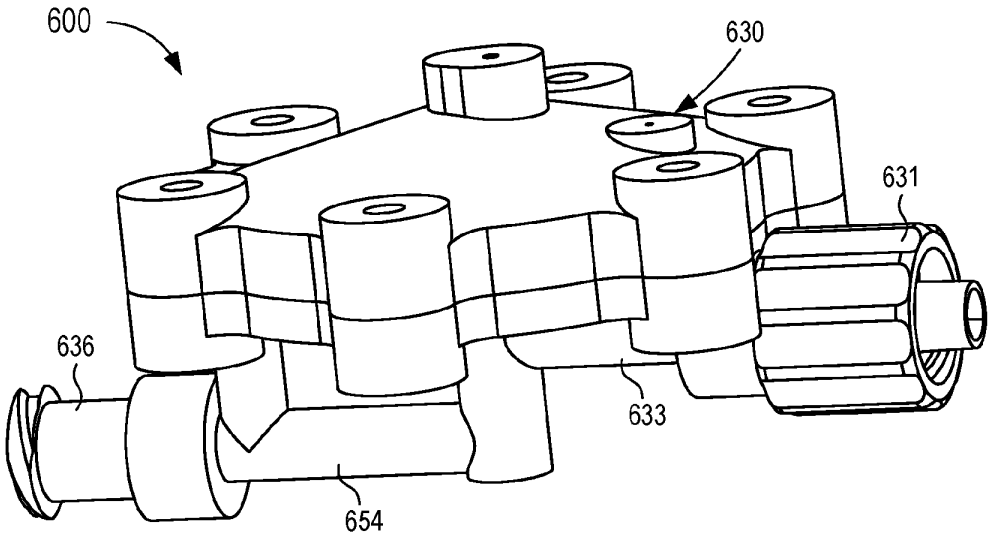

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FIG. 13

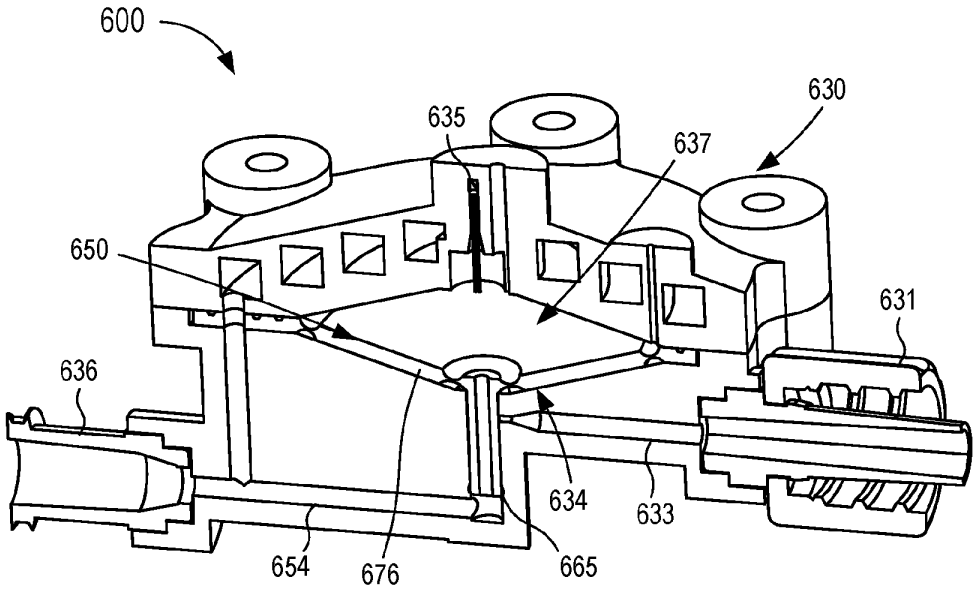

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FIG. 14

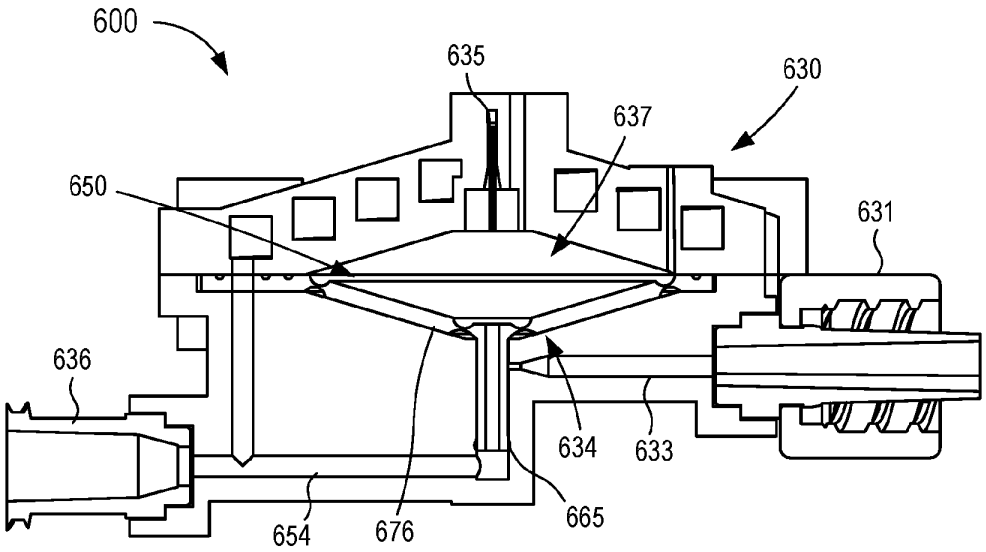


FIG. 15A

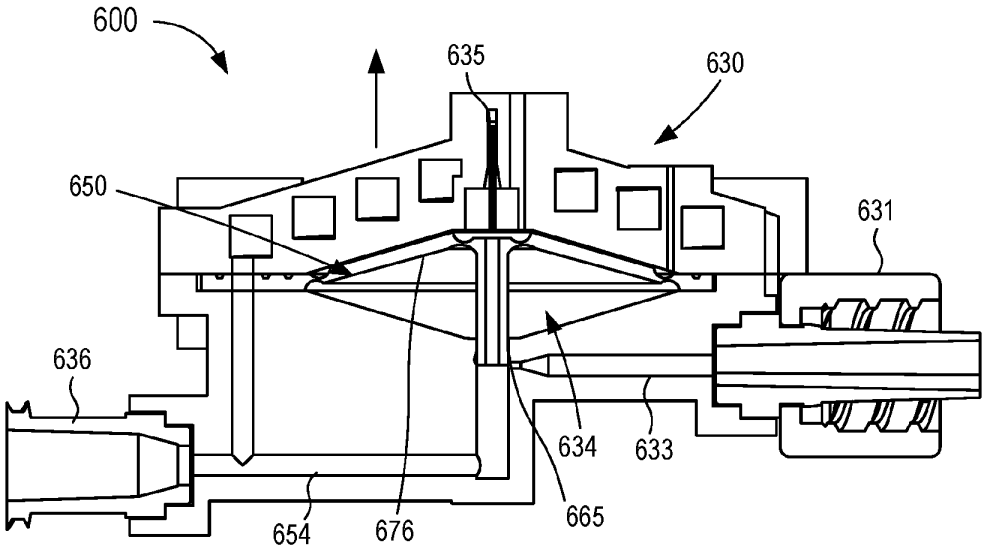


FIG. 15B

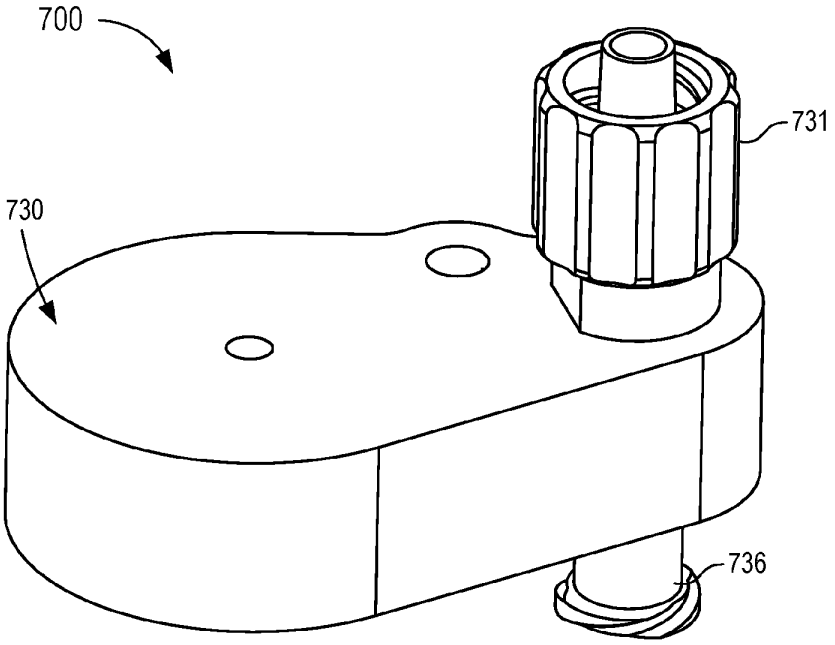


FIG. 16

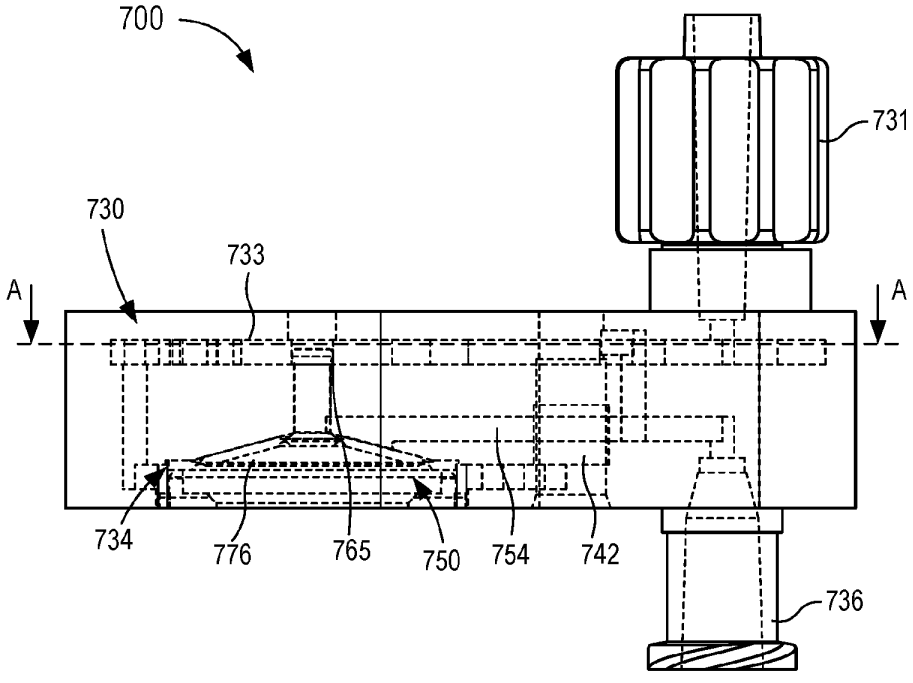


FIG. 17A

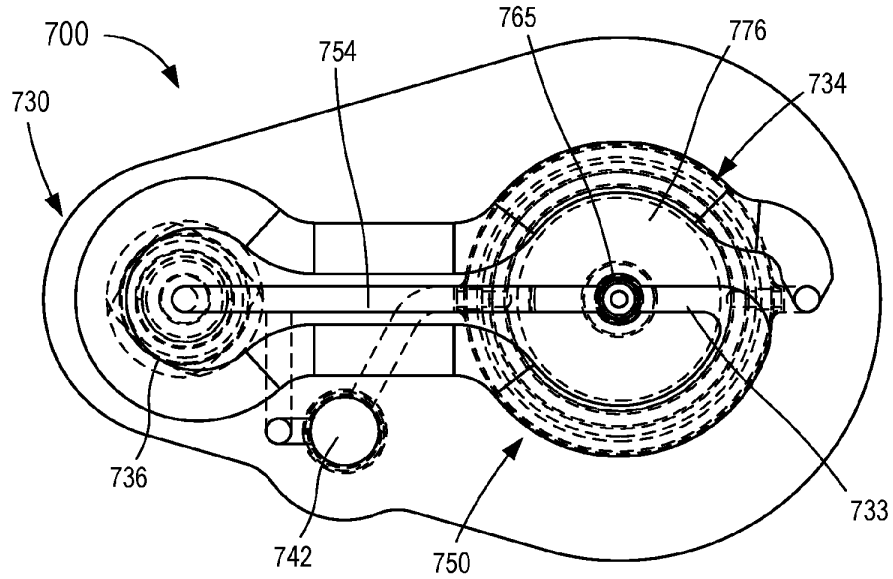


FIG. 17B

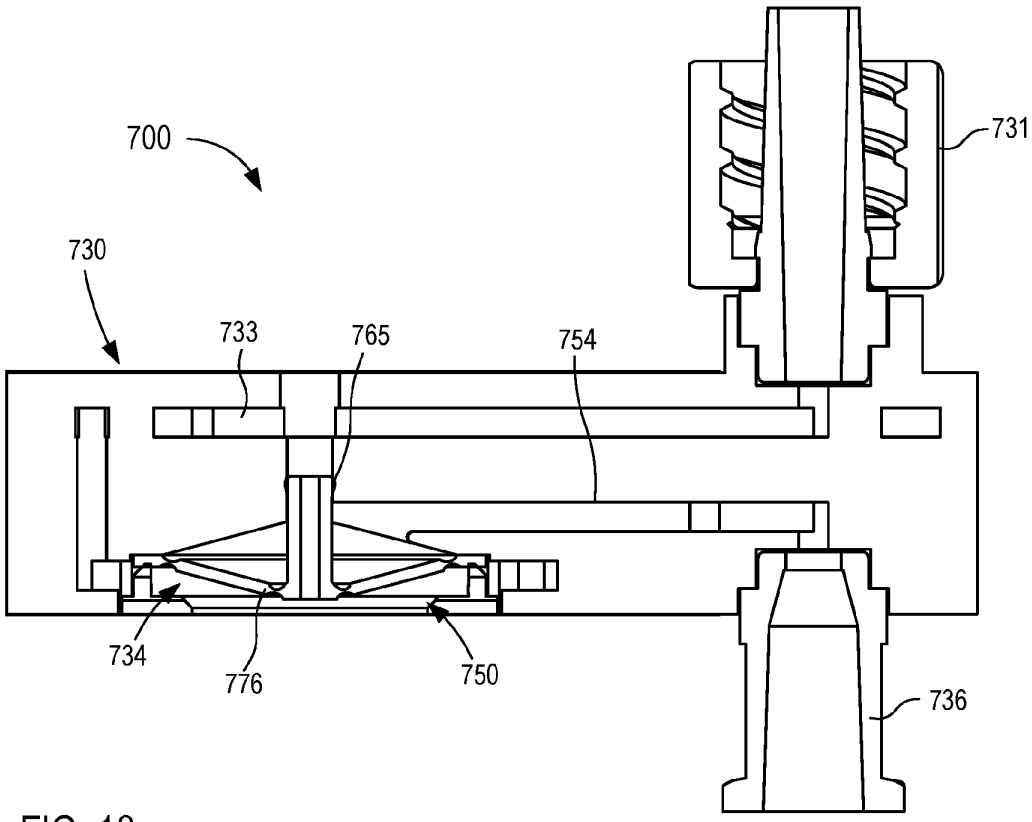


FIG. 18

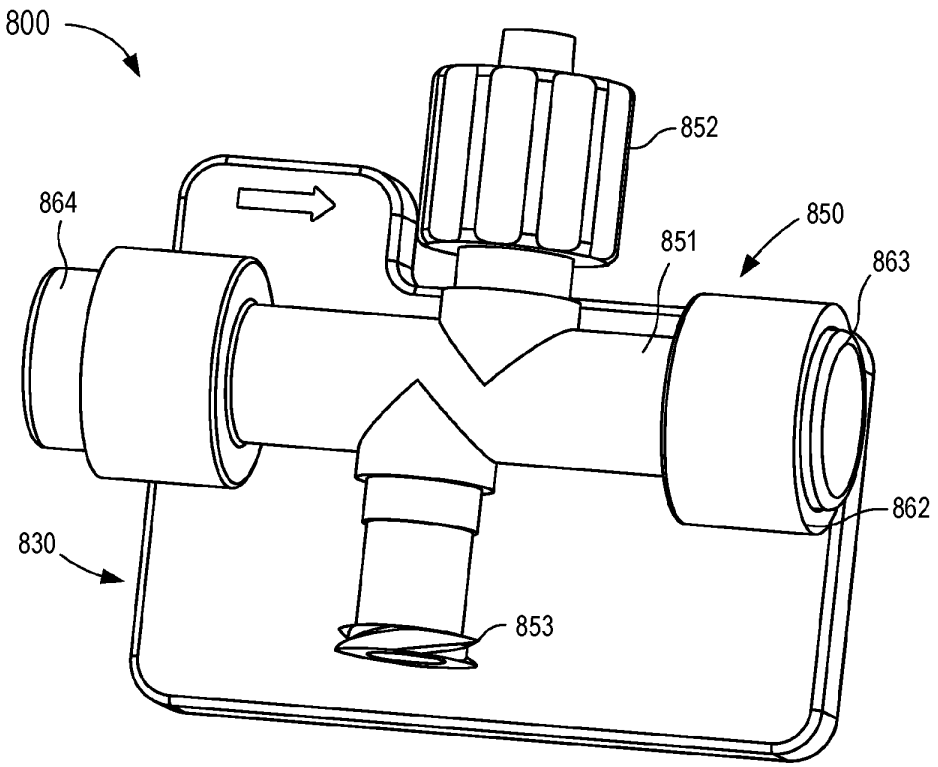


FIG. 19

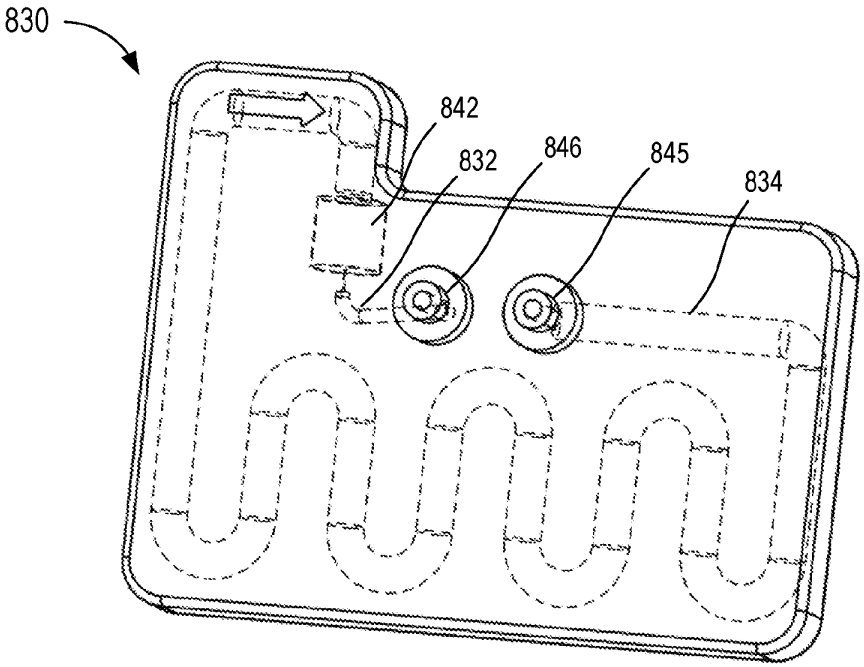


FIG. 20

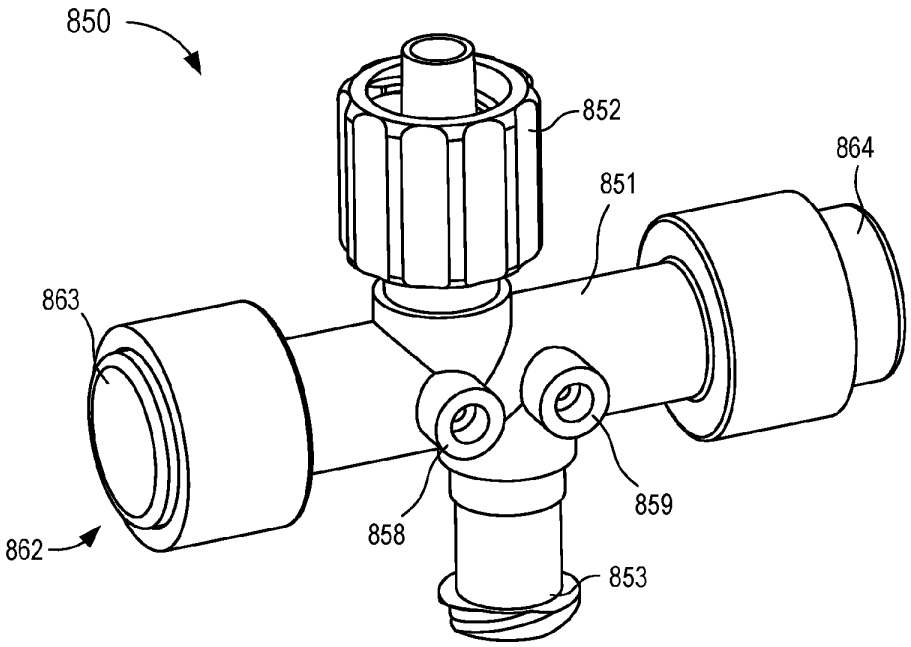


FIG. 21

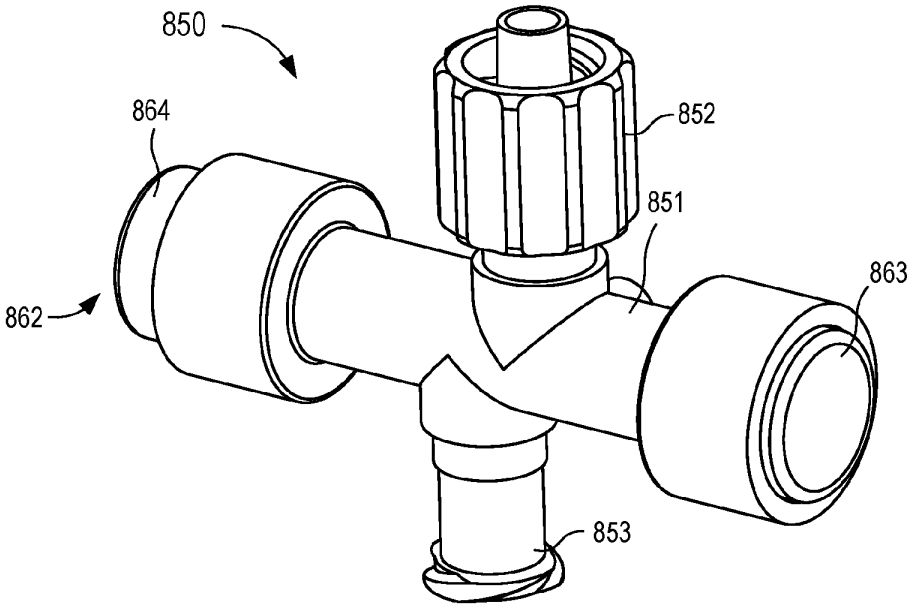


FIG. 22

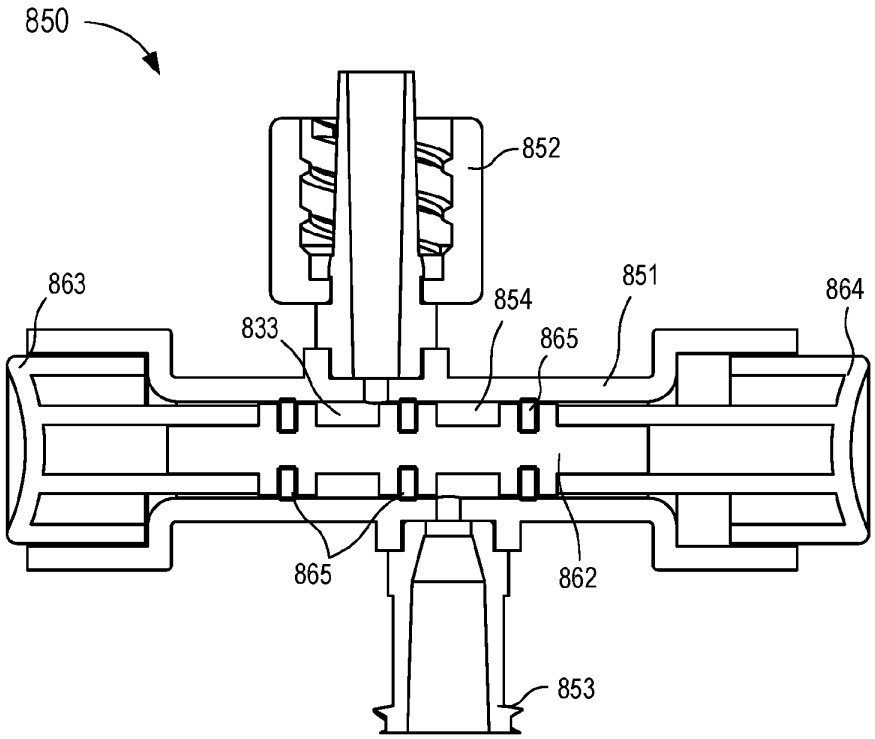

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FIG. 23

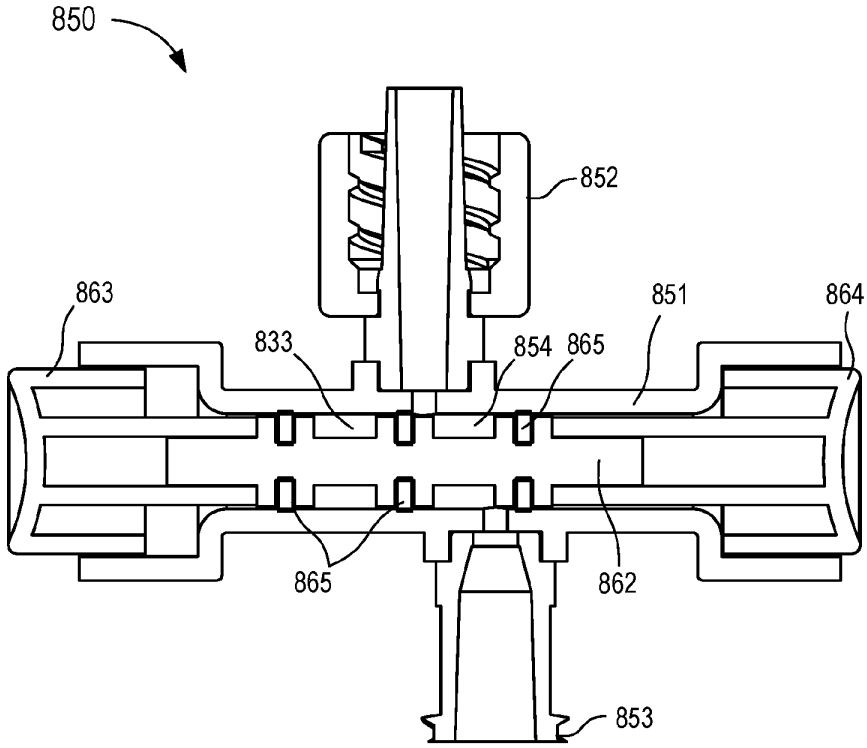

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FIG. 24

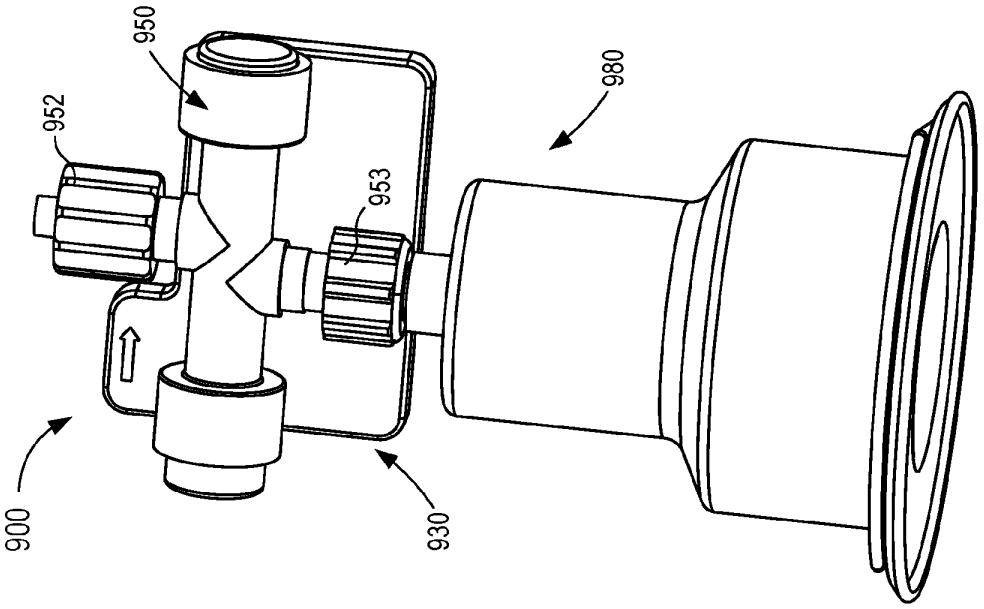


FIG. 26

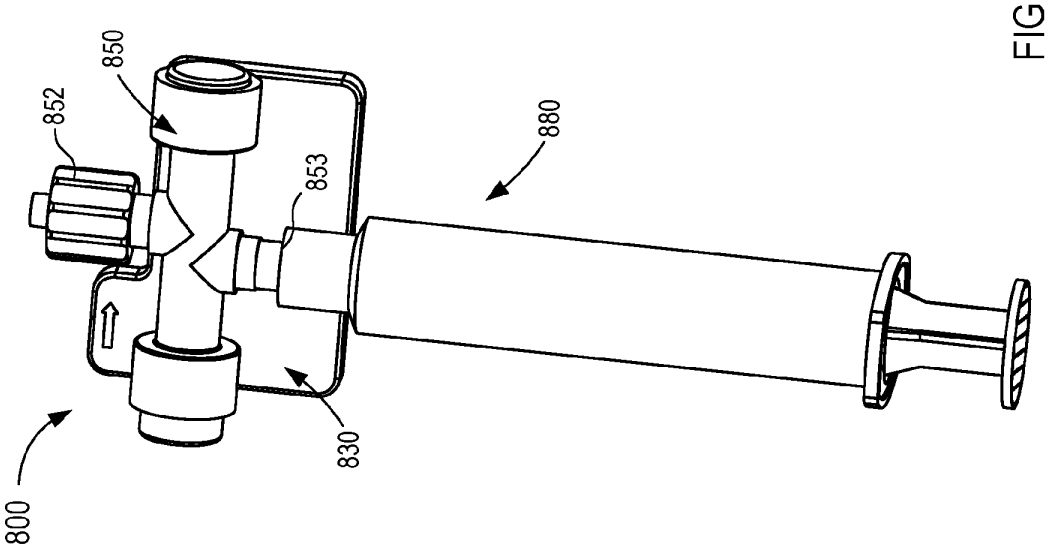


FIG. 25

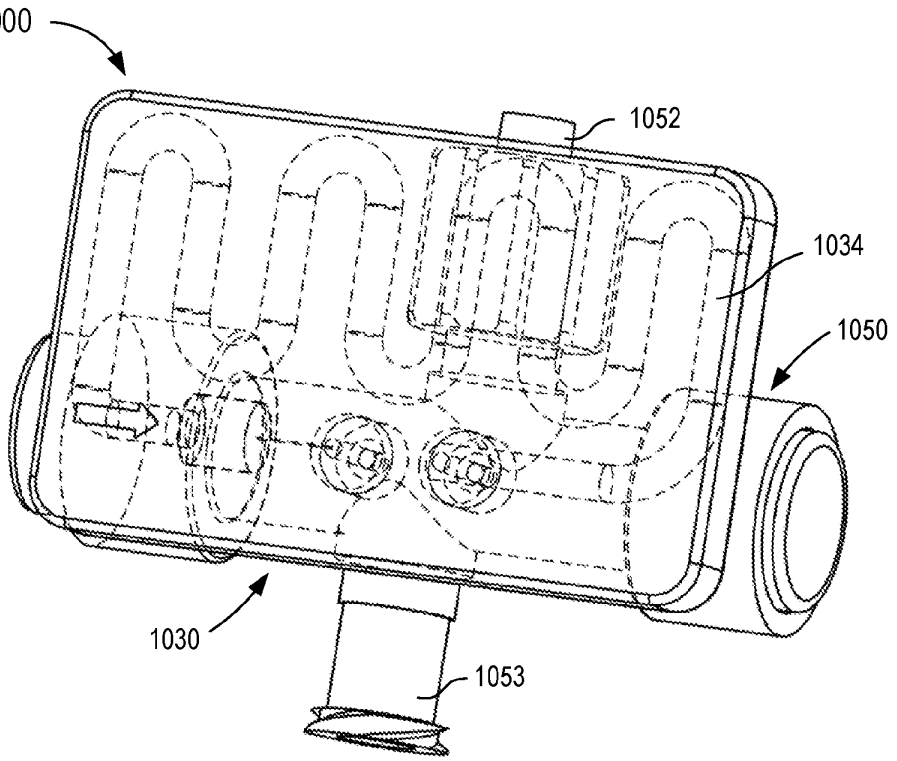


FIG. 27

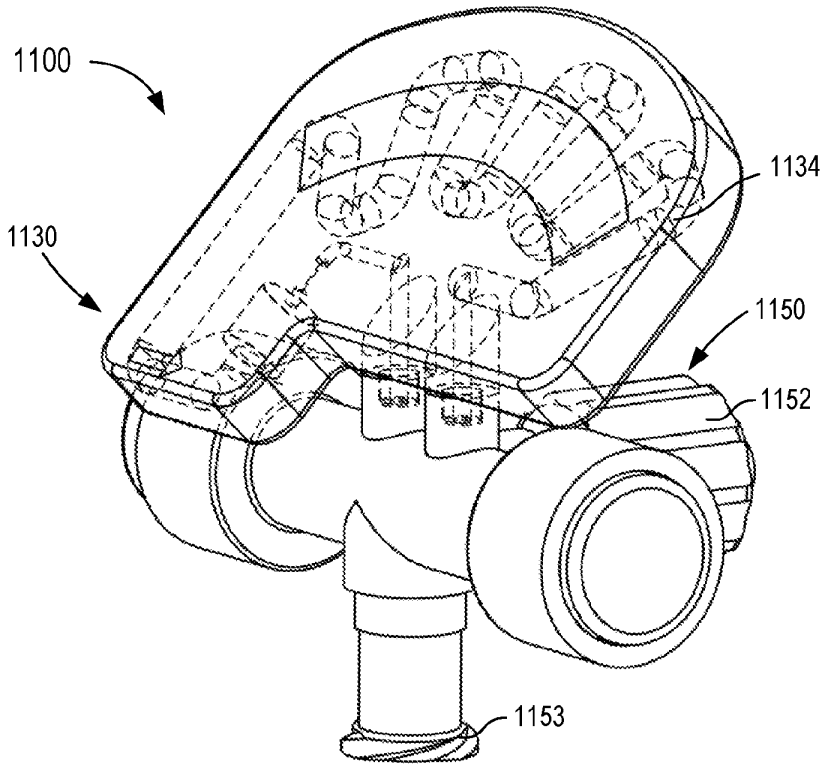


FIG. 28

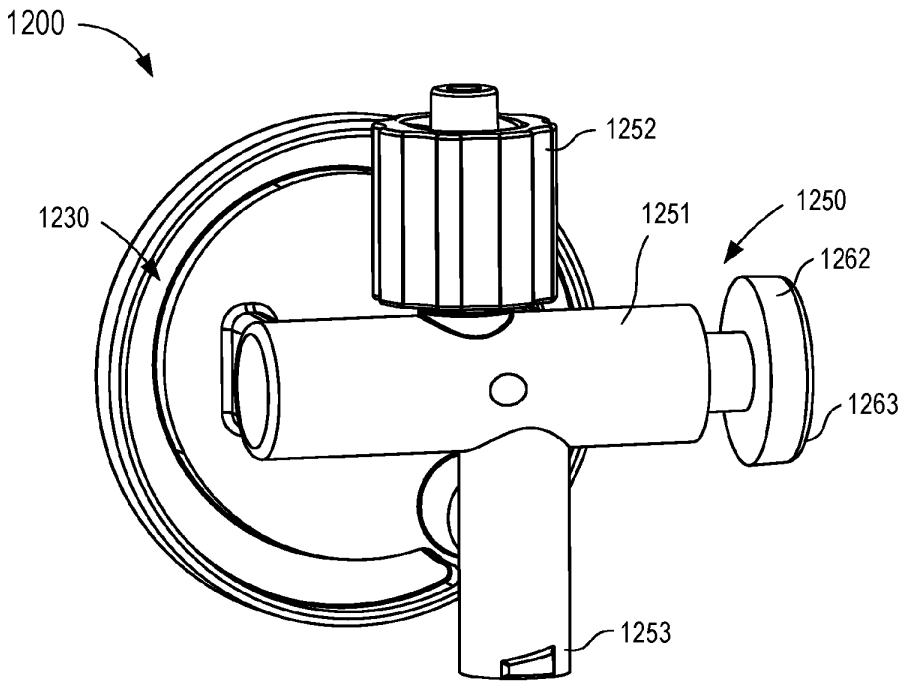

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FIG. 29

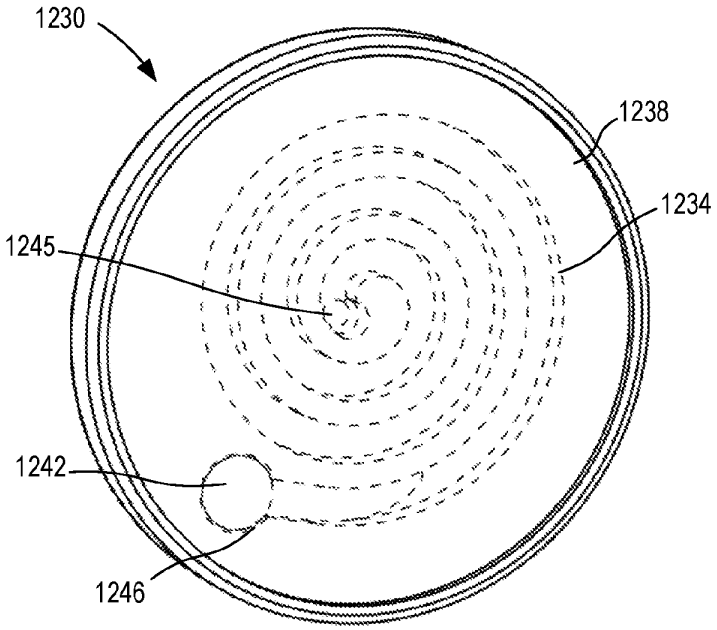

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FIG. 30

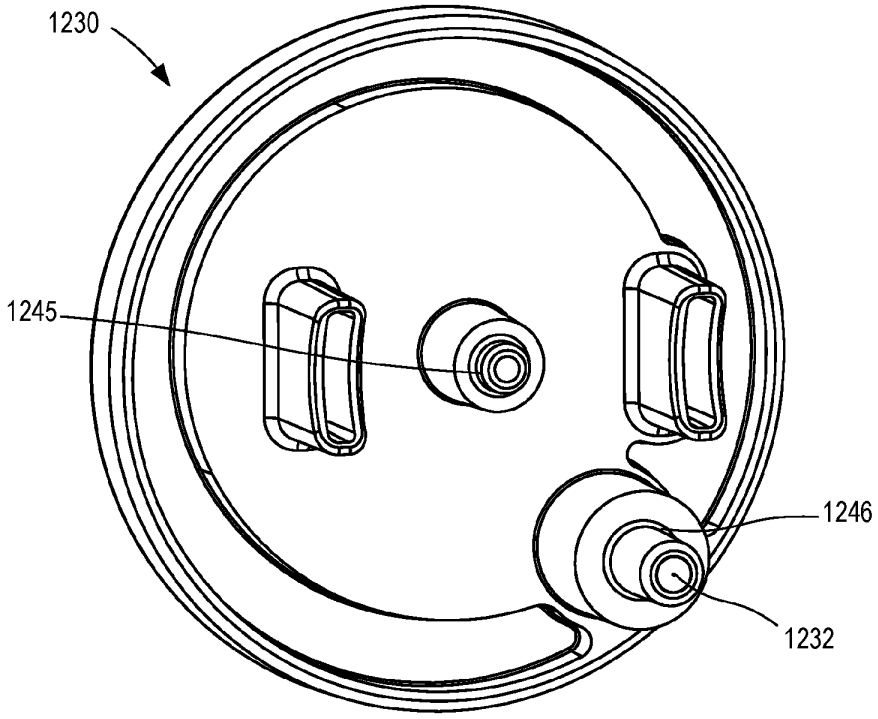

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FIG. 31

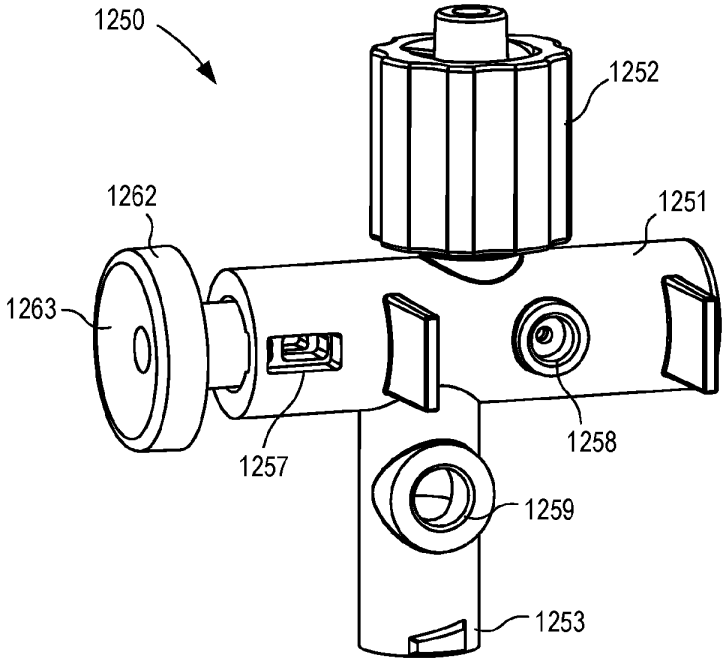

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FIG. 32

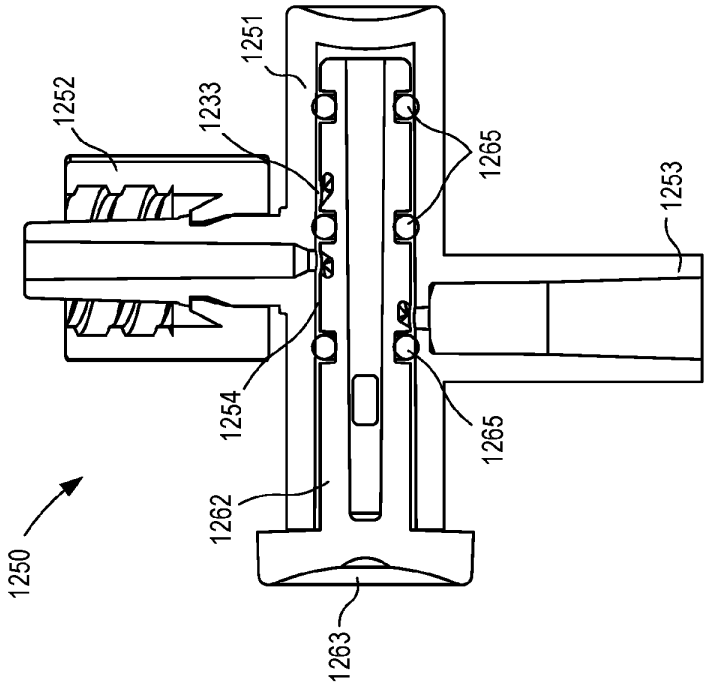

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FIG. 34

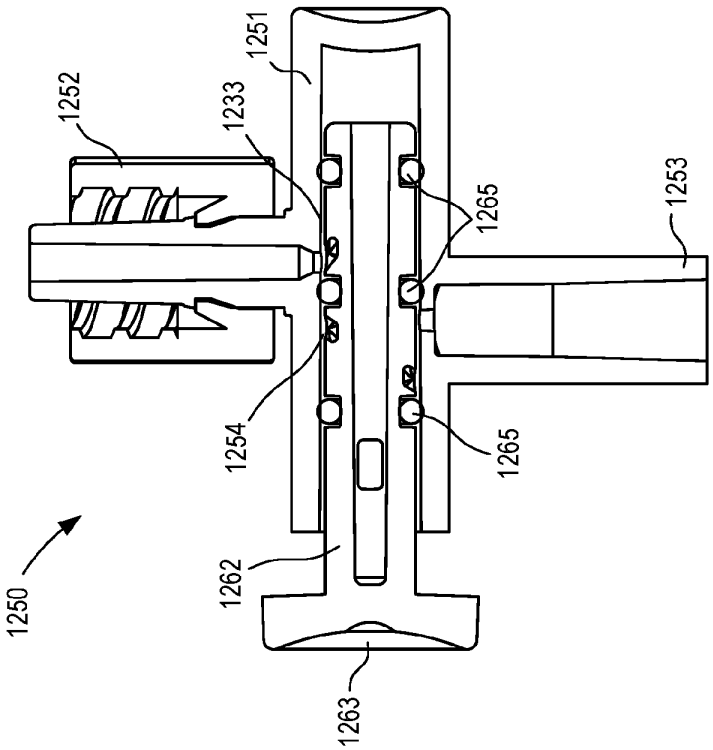

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FIG. 33

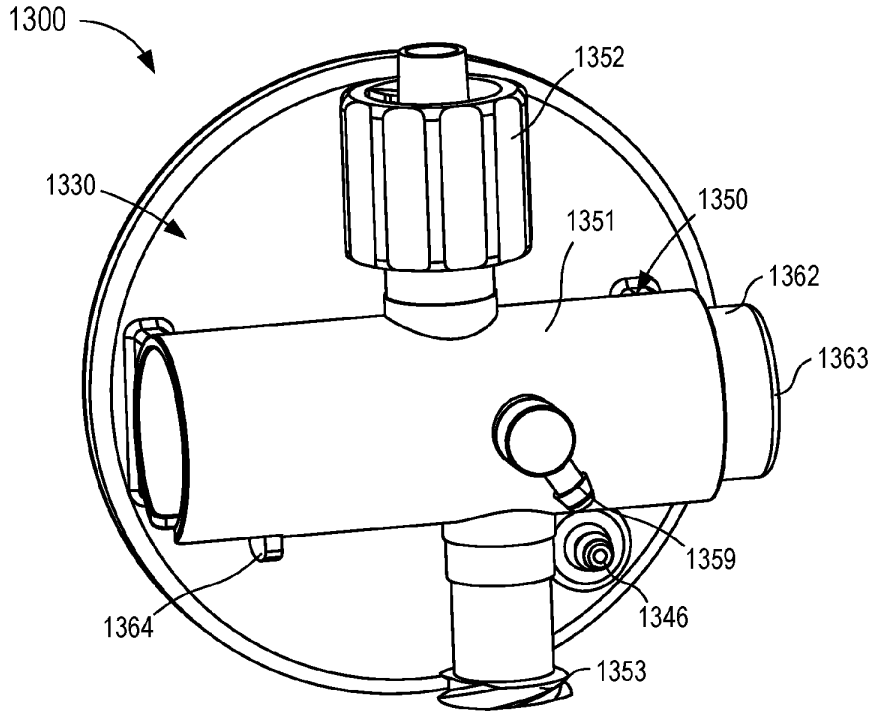

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FIG. 35

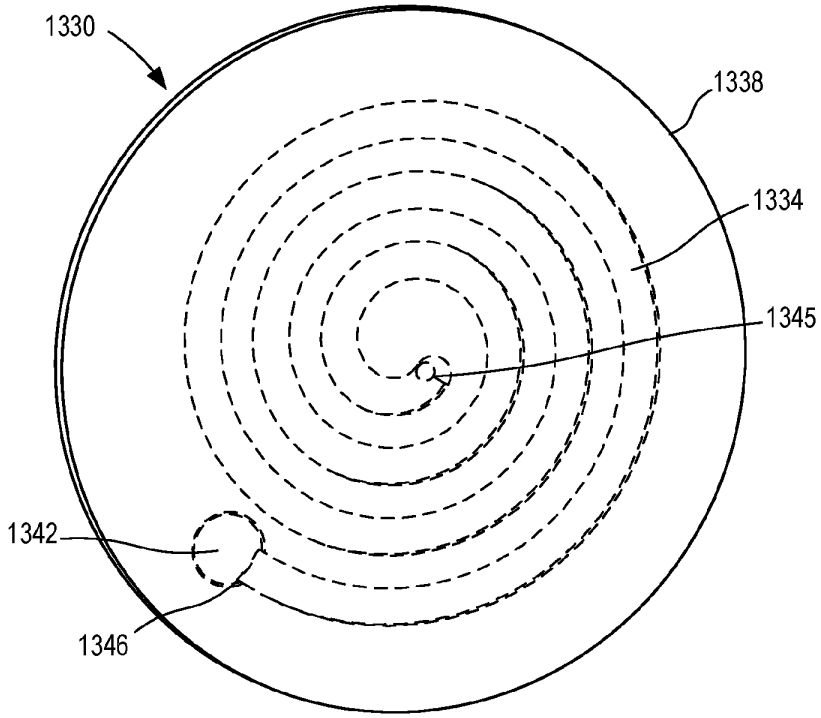

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FIG. 36

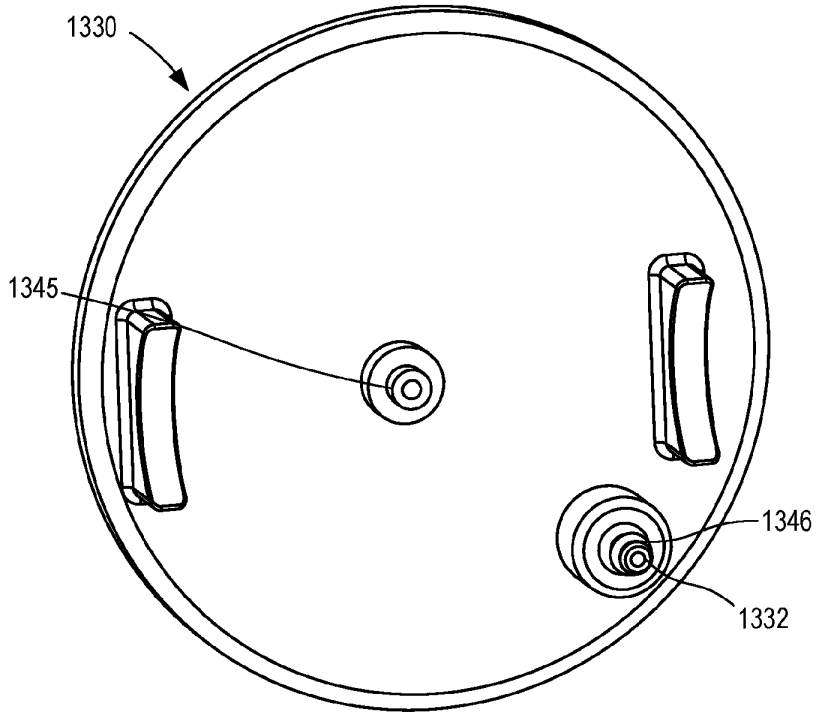


FIG. 37

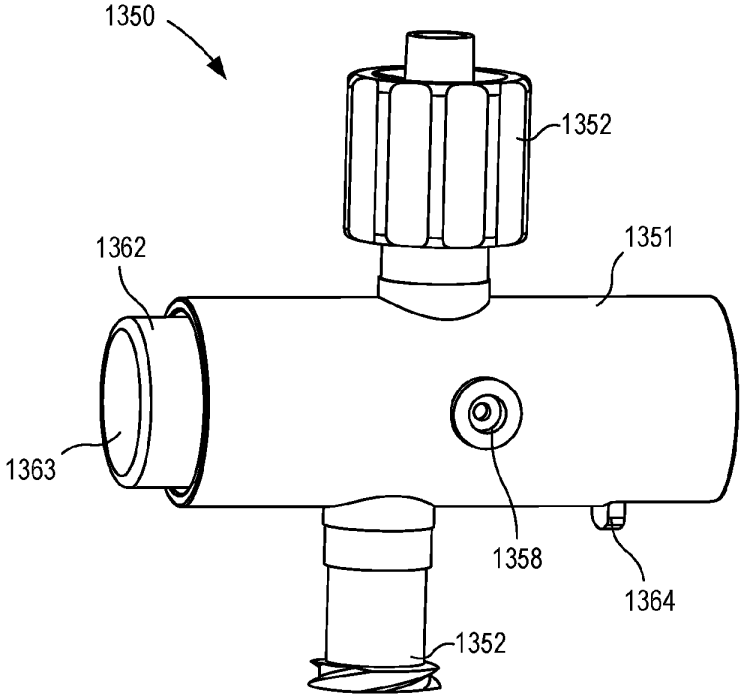


FIG. 38

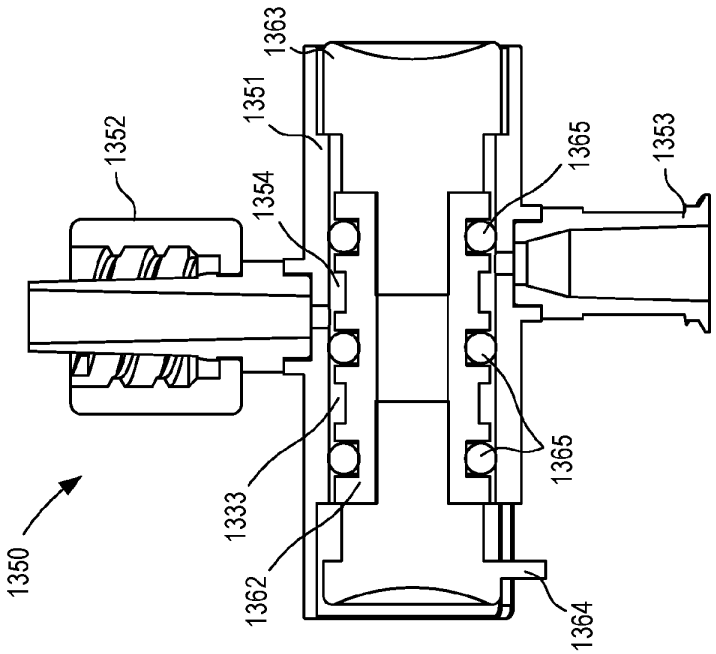

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FIG. 40

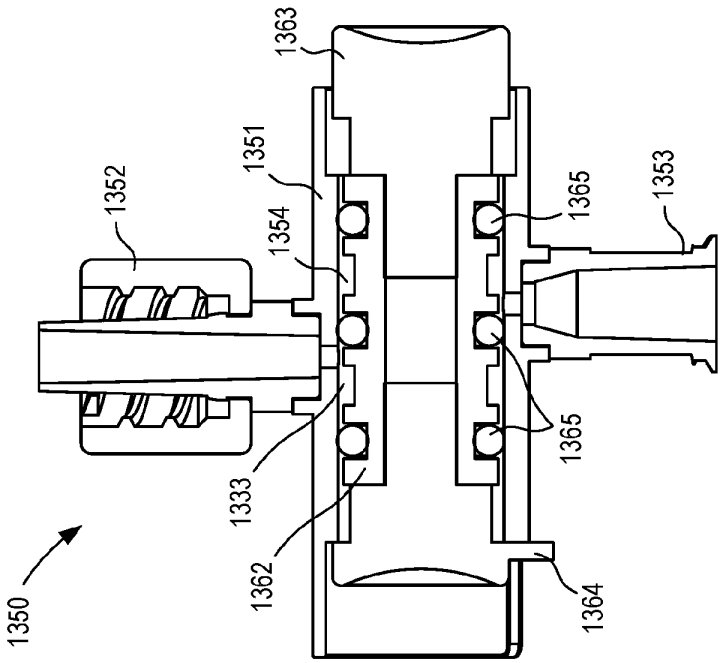

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FIG. 39

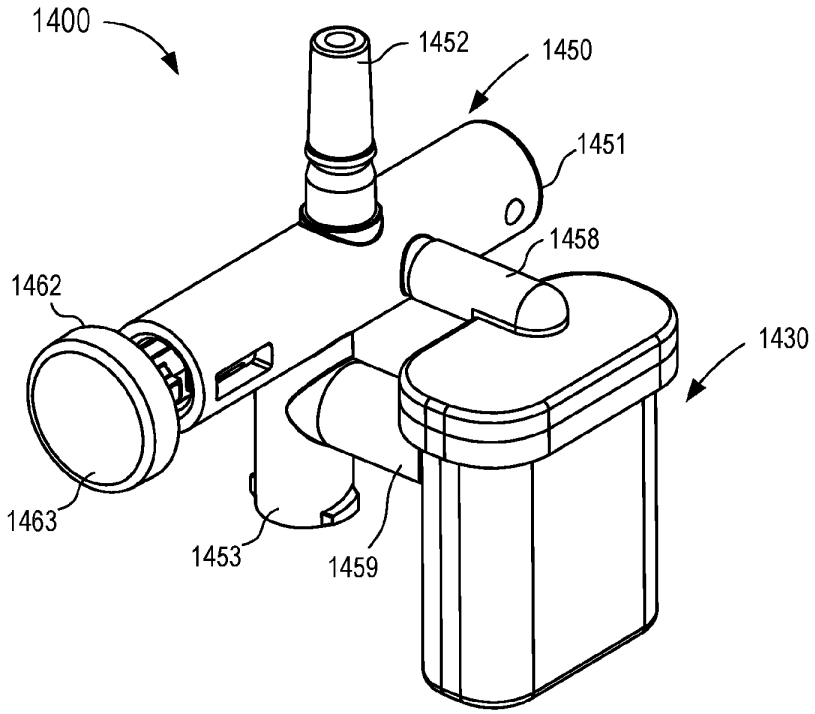

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FIG. 41

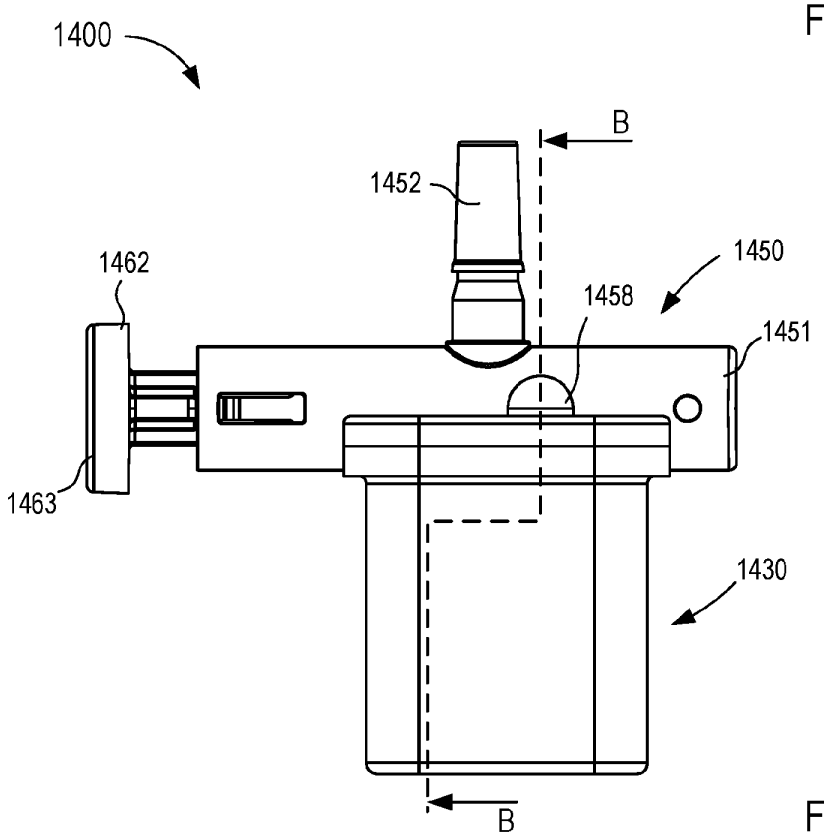

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FIG. 42

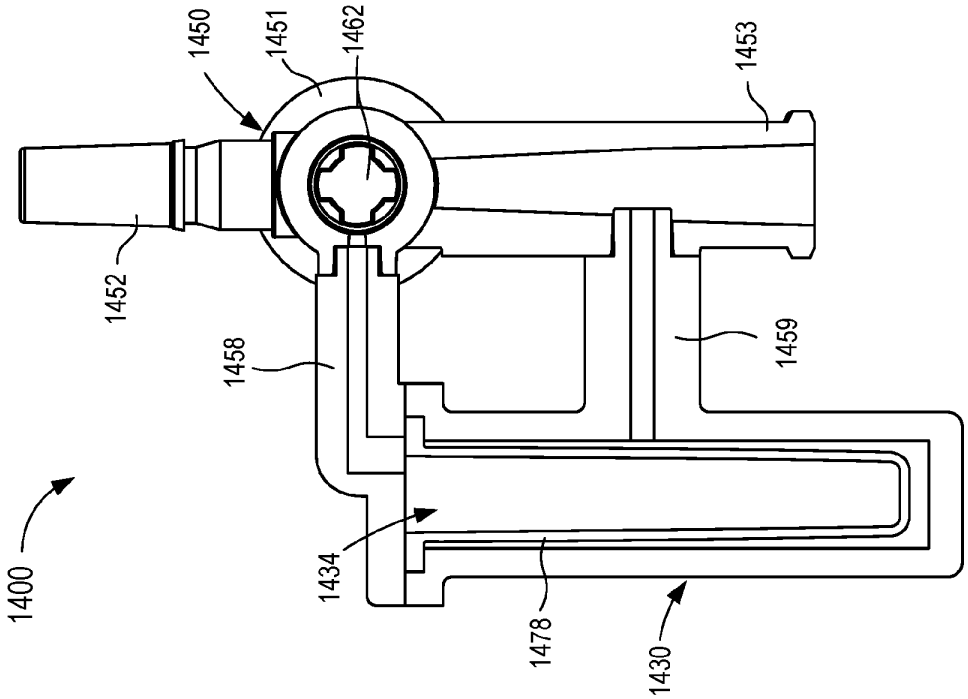

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SECTION B-B

FIG. 44

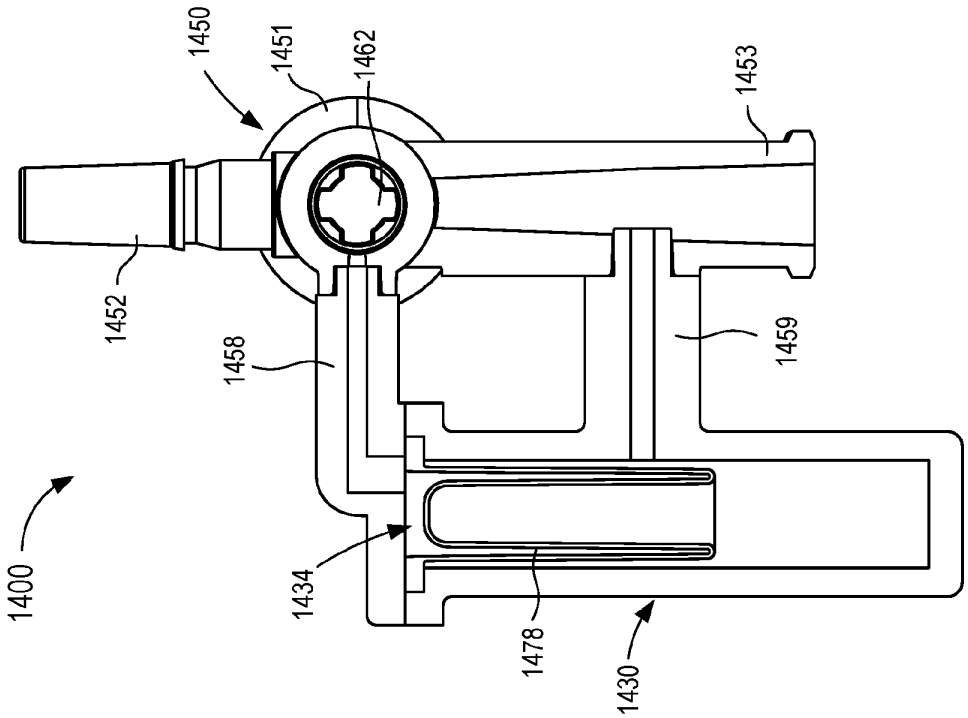

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SECTION B-B

FIG. 43

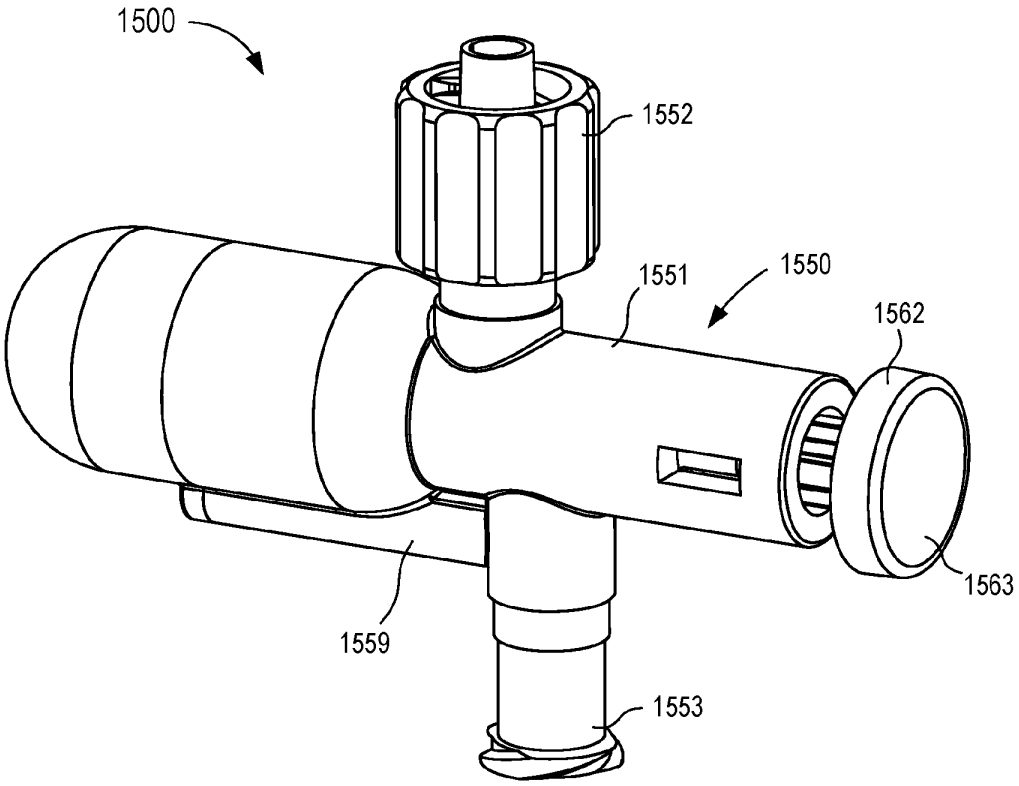

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FIG. 45

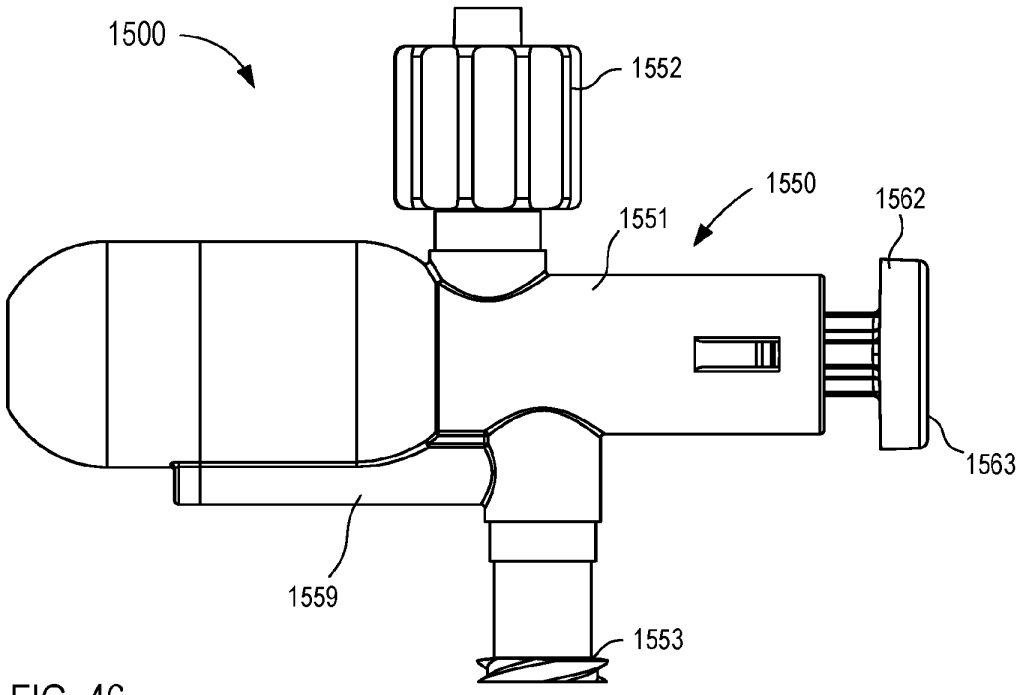

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FIG. 46

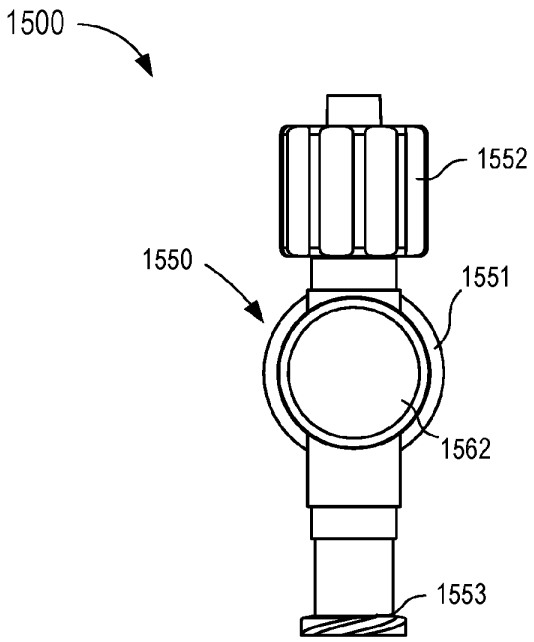

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FIG. 47

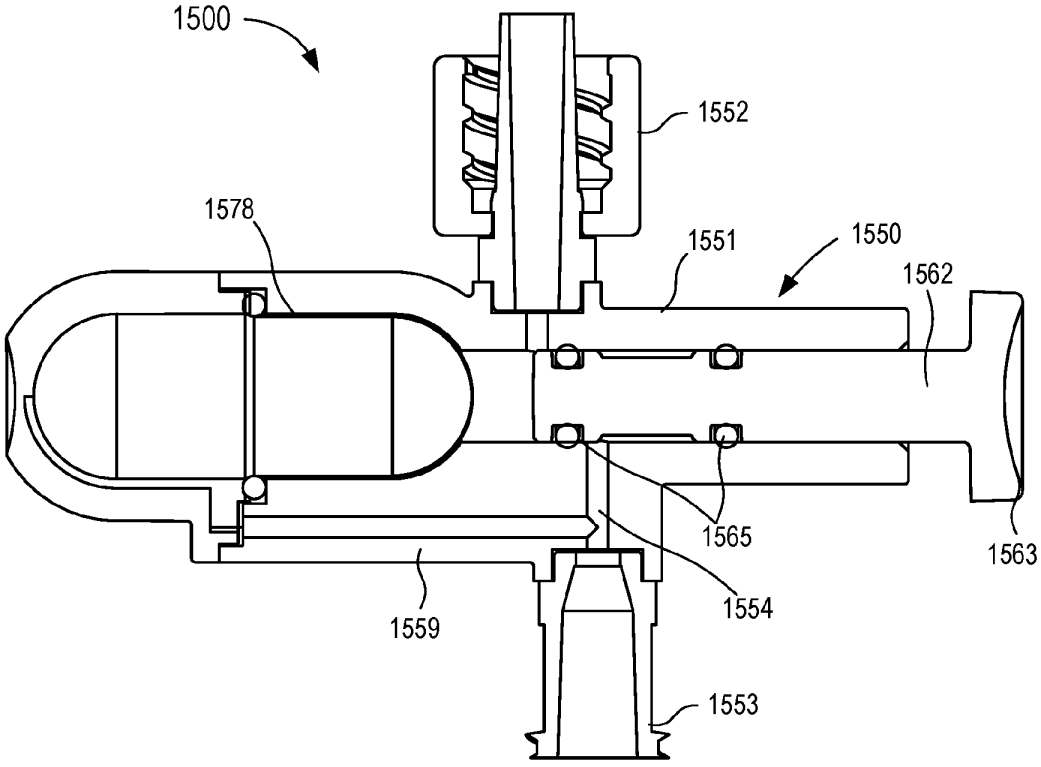

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FIG. 48

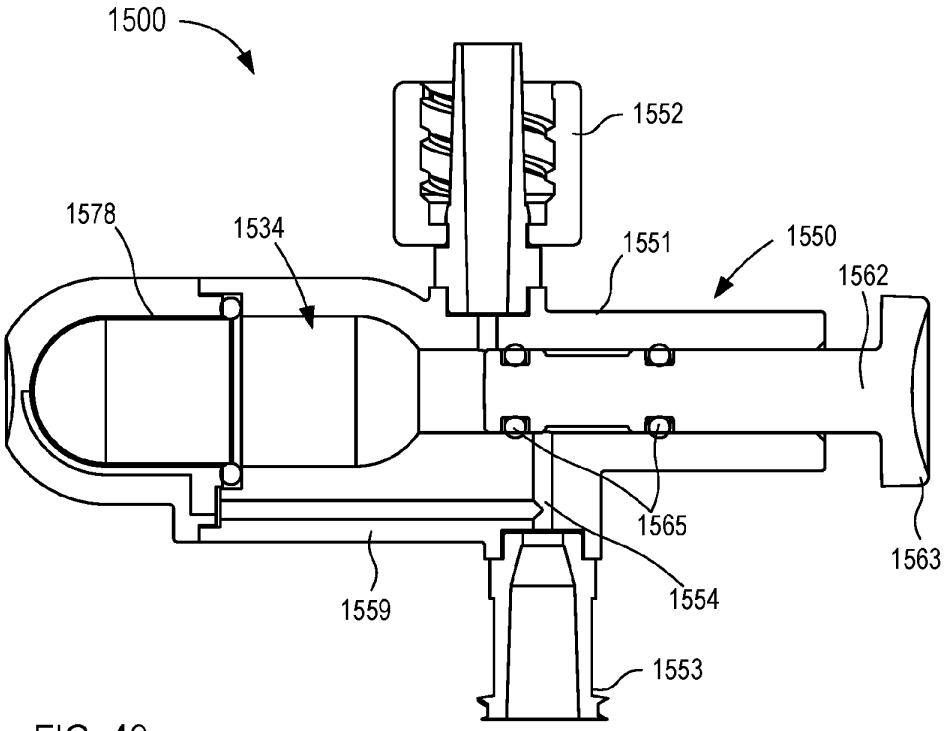

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FIG. 49

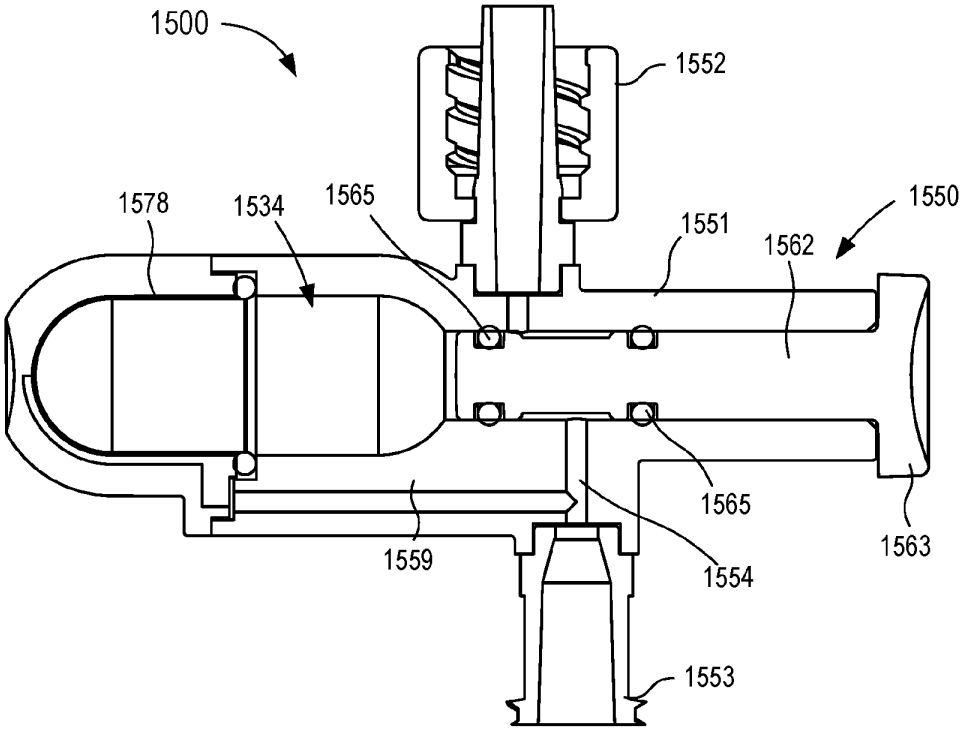

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FIG. 50

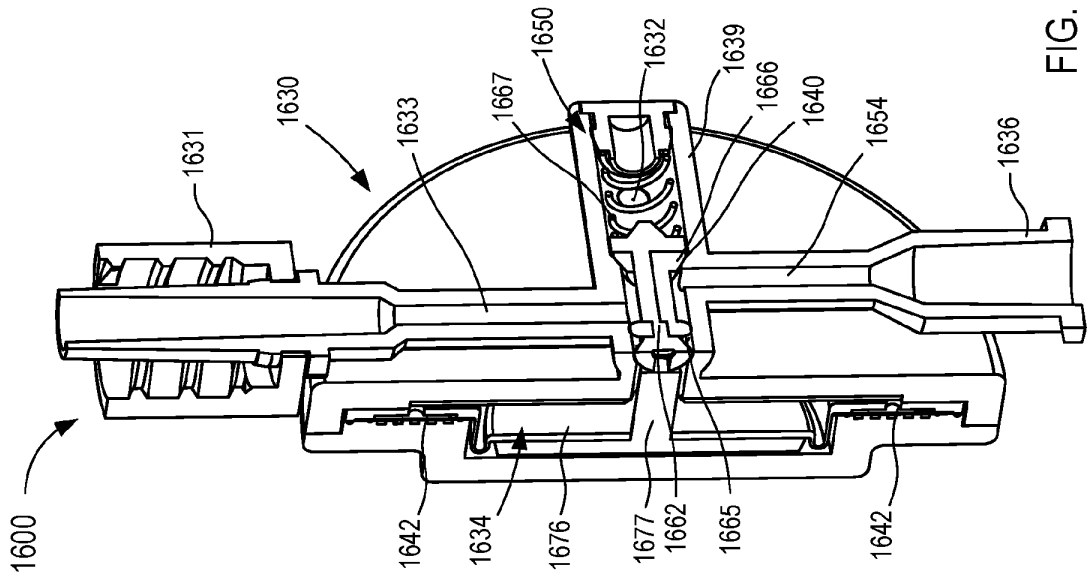

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FIG. 52

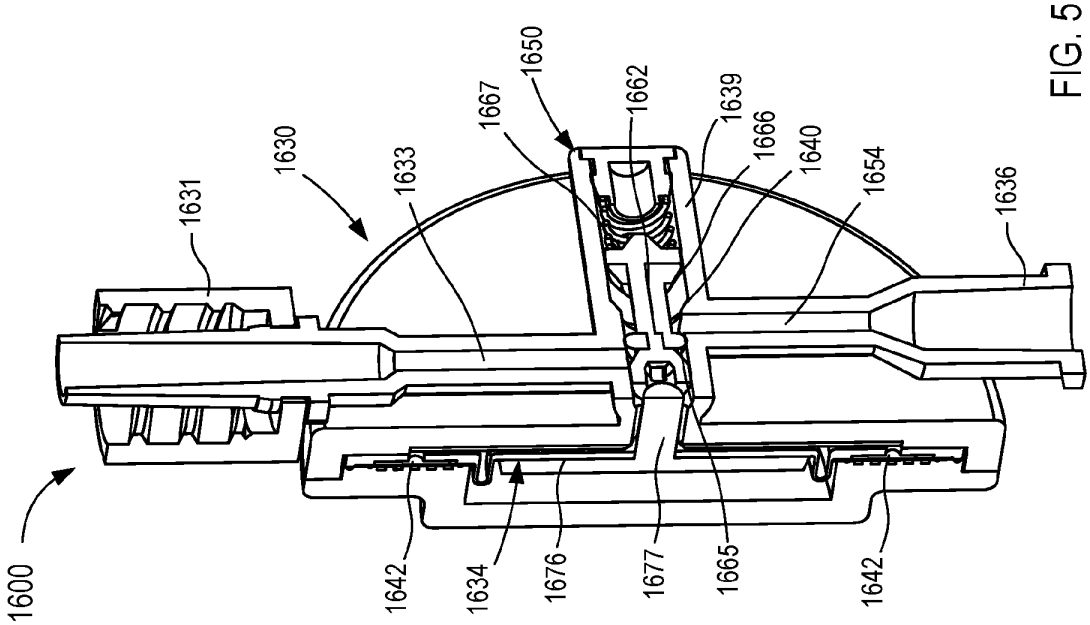

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FIG. 51

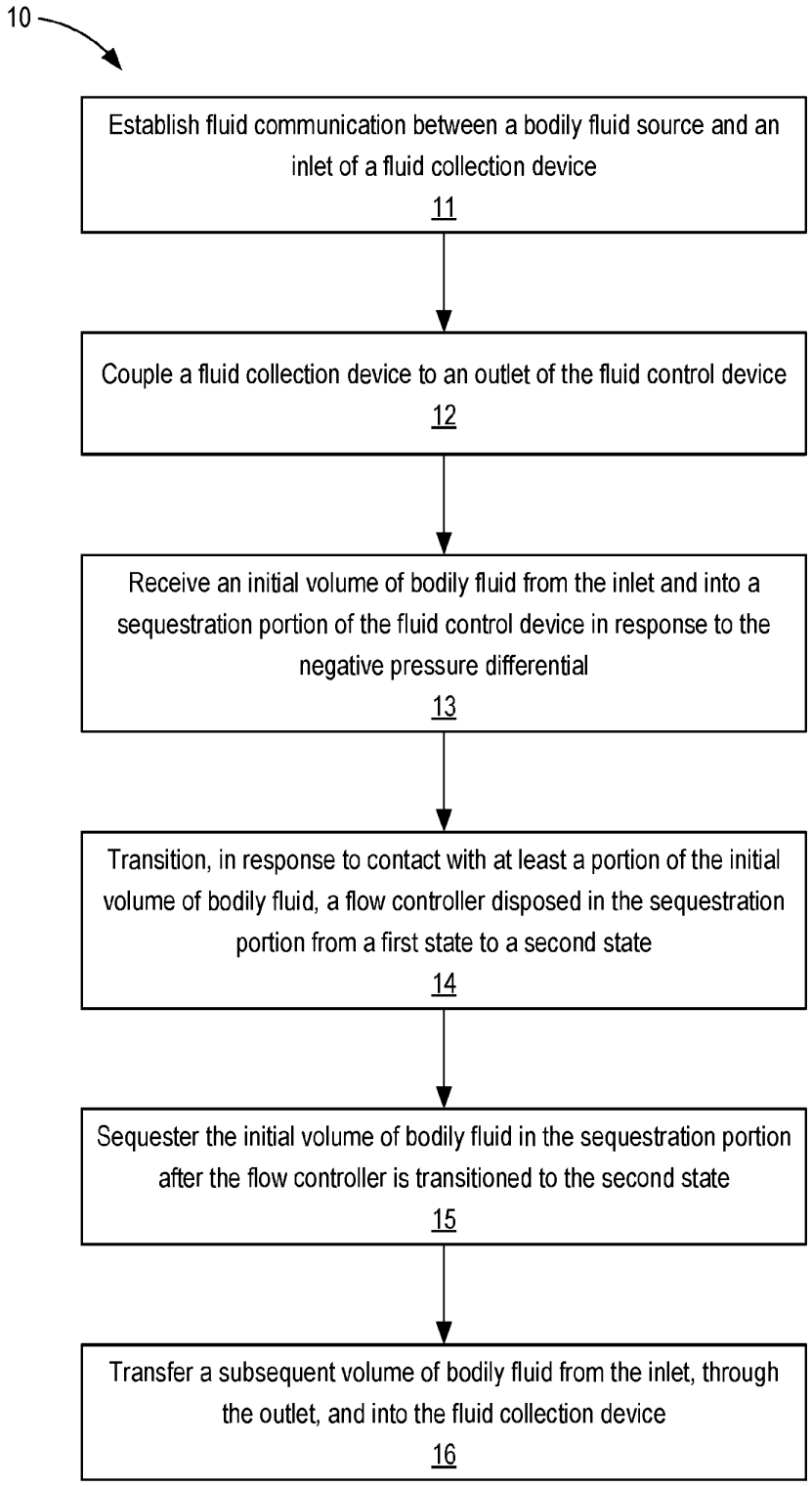

10
Establish fluid communication between a bodily fluid source and an inlet of a fluid collection device
11
Couple a fluid collection device to an outlet of the fluid control device
12
Receive an initial volume of bodily fluid from the inlet and into a sequestration portion of the fluid control device in response to the negative pressure differential
13
Transition, in response to contact with at least a portion of the initial volume of bodily fluid, a flow controller disposed in the sequestration portion from a first state to a second state
14
Sequester the initial volume of bodily fluid in the sequestration portion after the flow controller is transitioned to the second state
15
Transfer a subsequent volume of bodily fluid from the inlet, through the outlet, and into the fluid collection device
16

FIG. 53

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 18/50621

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - A61B 5/00, A61B 17/00, A61M 1/00, A61M 39/00 (2018.01)

CPC - A61B 5/00, A61B 5/02, A61B 5/03, A61B 5/06, A61B 5/14, A61B 5/1405, A61B 5/145, A61B 5/15, A61B 5/150007, A61B 5/150099, A61B 5/150206, A61B 5/150221, A61B 5/150251, A61B 5/150755, A61B 5/153, A61B 5/154, A61B 5/155, A61B 5/157, A61M 1/00, A61M 1/0001, A61M 1/0031, A61M 1/0035, A61M 1/0058, A61M 1/0066, A61M 1/10, A61M 1/1037, A61M 1/1086, A61M 1/34, A61M 1/36, A61M 39/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

See Search History Document

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

See Search History Document

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

See Search History Document

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- Y --- A	US 2014/0163419 A1 (MAGNOLIA MEDICAL TECHNOLOGIES, INC.) 12 June 2014 (12.06.2014), entire document, especially Figs. 11-15; paras [0079]-[0099])	1-3, 8-21, 24, 29, 32-36 --- 4-5, 25, 30 --- 6-7, 22-23, 26-28, 31
Y --- A	US 6,511,439 B1 (TABATA et al.) 28 January 2003 (28.01.2003), entire document, especially Fig. 1; col 4, ln 48-51; col 9; ln 48-51	4-5, 25, 30 --- 6-7, 22-23, 26-28, 31
A	US 8,876,734 B2 (MAGNOLIA MEDICAL TECHNOLOGIES, INC.) 4 November 2014 (04.11.2014), entire document	1-36
A	US 2014/0107564 A1 (MAGNOLIA MEDICAL TECHNOLOGIES, INC.) 17 April 2014 (17.04.2014), entire document	1-36
A	US 2013/0116599 A1 (BULLIUNGTON et al.) 9 May 2013 (09.05.2013), entire document	1-36
A	US 2015/0018715 A1 (WALTERSPIEL) 15 January 2015 (15.01.2015), entire document	1-36
A	US 2017/0020428 A1 (CALLIOPE SOLUTIONS, INC.) 26 January 2017 (26.01.2017), entire document	1-36

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:

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"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
5 November 2018	26 NOV 2018
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-8300	Authorized officer: Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

Form PCT/ISA/210 (second sheet) (January 2015)

(19) Europäisches Patentamt
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(11) EP 3 622 890 A1

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A61B 5/154 *(2006.01)*

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04.04.2016 US 201662318194 P
27.04.2016 US 201615140448
27.04.2016 US 201615140443

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16747682.9 / 3 324 845

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Remarks:
This application was filed on 01-10-2019 as a divisional application to the application mentioned under INID code 62.

(54) BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE

(57) Blood sample optimization systems and methods are described that reduce or eliminate contaminates in collected blood samples, which in turn reduces or eliminates false positive readings in blood cultures or other testing of collected blood samples. A blood sample optimization system can include a blood sequestration device (1500) located between a patient needle and a sample needle. The blood sequestration device can include a sequestration chamber (1508) for sequestering an initial, potentially contaminated aliquot of blood, and may further include a sampling channel (1506) that bypasses the sequestration chamber to convey likely uncontaminated blood between the patient needle and the sample needle after the initial aliquot of blood is sequestered in the sequestration chamber.

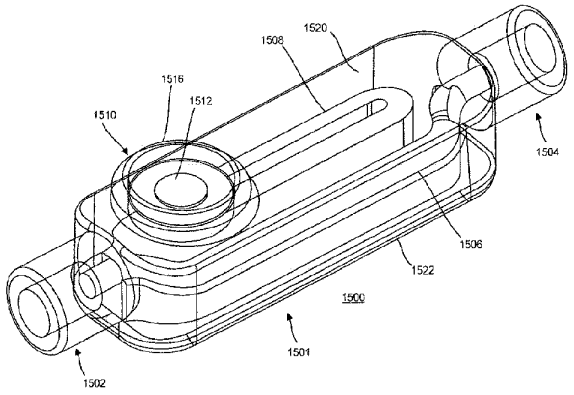


FIG. 15C

EP 3 622 890 A1

Printed by Jouve, 75001 PARIS (FR)

Description

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the benefit of priority of U.S. Non-Provisional Application Serial No. 15/140,443, filed on April 27, 2016 and titled "BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE AND METHOD" and U.S. Non-Provisional Application Serial No. 15/140,448, filed on April 27, 2016 and titled "BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE AND METHOD", both of which claim priority to U.S. Provisional Application Serial No. 62/196,797, filed on July 24, 2015 and titled "BLOOD CULTURE IMPROVEMENT SYSTEM AND METHOD"; U.S. Provisional Application Serial No. 62/238,636, filed on October 7, 2015 and titled "BLOOD SEQUESTRATION SYSTEM FOR NON-CONTAMINATED BLOOD SAMPLING"; and U.S. Provisional Application Serial No. 62/318,194, filed on April 4, 2016 and titled "BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE AND METHOD," the disclosures of which are incorporated by reference in their entirety.

BACKGROUND

[0002] Bacteraemia is the presence of microorganisms in the blood. Sepsis, on the other hand, is bacteraemia in the presence of clinical symptoms and signs such as fever, tachycardia, tachypnea and hypotension. Bacteraemia and sepsis are associated with a high mortality and an increased incidence and duration of hospital stay and associated costs. Many bacteraemias, sepsis, fungaemias and other pathogens actually occur within a hospital or other healthcare settings with catheters and venipunctures being a source of contamination as potential carriers of these pathogens.

[0003] Blood cultures are the standard test used to detect microbial pathogens related to bacteraemia and sepsis in a patient's blood. The term blood culture refers to a single venipuncture, either from a peripheral site or central or arterial line, with the blood inoculated into one or more blood culture bottles or containers. One bottle is considered a blood culture where two or more are considered a set. Multiple sets may be obtained from multiple venipunctures and are associated with different sites on the patient.

[0004] These methods allow for microbial identification and susceptibility testing to be performed, which is a critical component to managing sepsis, however the lack of rapid results and decreased sensitivity for fastidious pathogens has led to the development of improved systems and adjunctive molecular or proteomic testing.

[0005] Collection of blood samples for conducting blood cultures is a critical component of modern patient care and can either positively affect the patient outcome by providing an accurate diagnosis, or can adversely affect the outcome by prolonging unnecessary antimicrobial therapy, the length of hospital stays, and increasing costs.

[0006] One outcome of collection of blood cultures is contamination. Blood culture contamination can lead to a false positive culture result and/or significant increase in healthcare related costs. Sources of blood culture contamination include improper skin antisepsis, improper collection tube disinfection, and contamination of the initial blood draw which may then skew results.

[0007] Blood culture collection kits generally consist of a "butterfly" set, infusion set, or other type of venipuncture device as offered by companies like BD, Smiths, B. Braun and others, and aerobic and anaerobic blood culture bottles. Various different bottles are also available depending on the test requirements. These bottles are specifically designed to optimize recovery of both aerobic and anaerobic organisms. In conventional kits, a bottle used is known generally as a "Vacutainer," which is a blood collection tube formed of a sterile glass or plastic tube with a closure that is evacuated to create a vacuum inside the tube to facilitate the draw of a predetermined volume of liquid such as blood.

[0008] False positive blood cultures are typically a result of poor sampling techniques. They cause the use of antibiotics when not needed, increasing hospital costs and patient anxiety. Blood cultures are drawn from a needlestick into the skin, and then a Vacutainer is attached to capture a sample of blood. Contamination may occur from improper or incomplete disinfection of the skin area in and around the puncture site. It may also occur from the coring of the skin by the needle during insertion, with the cored skin cells and any associated contamination being pulled into the sample.

[0009] Blood flow through a hypodermic needle is laminar, and as such, a velocity gradient can be developed over the flow tube as a pressure drop is applied to the hypodermic needle. Either forceful aspiration of blood, or using a very small hypodermic needle, can cause lysis and a release of potassium from the red blood cells, thereby rendering the blood samples abnormal.

[0010] In other instances, some patients have delicate veins that can collapse under a pressure drop or vacuum, particularly as applied by a syringe's plunger that is drawn too quickly for the patient's condition. Since such condition is impossible to know beforehand, such vein collapses are a risk and very difficult to control.

[0011] Various strategies have been implemented to decrease blood culture contamination rates, e.g. training staff with regard to aseptic collection technique, feedback with regard to contamination rates and implementation of blood culture collection kits. Although skin antisepsis can reduce the burden of contamination, 20% or more of skin organisms are located deep within the dermis and are unaffected by antisepsis. Changing needles before bottle inoculation is not advisable as it increases the risk to acquire needle stick injuries without decreasing con-

tamination rates.

[0012] Some conventional systems and techniques for reducing blood culture contamination include discarding the initial aliquot of blood taken from central venous catheters, venipunctures, and other vascular access systems. However, these systems require the user to mechanically manipulate an intravascular device, or require a complex series of steps that are difficult to ensure being followed.

SUMMARY

[0013] This document presents systems and methods for reducing blood culture contamination, lysing of cells, and vein collapse. In some implementations, a system and method can eliminate user variability in disinfection, and also eliminate the risk of skin cells getting into the blood culture sample. The systems and methods disclosed herein do not require a change in existing clinical processes, other than to potentially indicate when a vacutainer or other blood collection device (i.e., syringe) should be attached for drawing contaminant-free blood samples.

[0014] In some implementations of the systems and methods disclosed herein the withdrawal of blood is accomplished passively by use of the patient's own blood pressure, thereby reducing the risk of vein collapse and eliminating any additional user steps over current practice. The systems and methods can be applied to accommodate short-path direct stick or butterfly venipuncture systems. They can also be used with samples drawn through a catheter.

[0015] In one aspect, a blood sequestration device is presented. The blood sequestration device includes an inlet port and an outlet port. The blood sequestration device further includes a sequestration chamber connected with the inlet port, the sequestration chamber having a vent comprising an air permeable blood barrier. The blood sequestration device further includes a sampling channel having a proximal end connected with the inlet port and a distal end connected with the outlet port.

[0016] In another aspect, a blood sequestration device connected with a blood sampling pathway is described. The blood sampling pathway has a patient needle and a sample collection device. The blood sequestration device includes an inlet port connected with the patient needle, and a sequestration chamber connected with the inlet port, the sequestration chamber having a vent comprising an air permeable blood barrier. The blood sequestration device further includes a sampling channel having a proximal end connected with the inlet port, and an outlet port connected with a distal end of the sampling channel and with the sample collection device.

[0017] In yet another aspect, a blood sequestration device connected with a blood sampling system is described. The blood sampling system includes a patient needle for accessing a blood sample from a patient, and a sample needle that is sealed and adapted for receiving an evacuated blood collection tube. The blood sequestration device includes an inlet port connected with the patient needle to receive the blood sample from the patient. The blood sequestration device further includes a sequestration chamber connected with the inlet port and having a vent comprising an air permeable blood barrier, the sequestration chamber for receiving and sequestering a first portion of the blood sample prior to the sample needle being unsealed by the evacuated blood collection tube. The blood sequestration device further includes a sampling channel having a proximal end connected with the inlet port, the sampling channel for conveying a subsequent portion of the blood sample once the sample needle is unsealed by the evacuated blood collection tube. The blood sequestration device further includes an outlet port connected with a distal end of the sampling channel for conveying the subsequent portion of the blood sample to the sample needle.

[0018] In yet another aspect, a blood sample optimization system is disclosed and described. The blood sample optimization system includes a blood sampling system for accessing and acquiring one or more samples of a patient's blood, and a blood sequestration device for receiving and sequestering a first portion of the one or more samples of the patient's blood which might be contaminated by a venipuncture process and which could result in a false positive identification of a pathogen in the patient's blood.

[0019] The blood sampling system includes a patient needle configured for a venipuncture of a patient to access a sample of blood of a patient, a blood sampling pathway connected with the patient needle for conveying the sample of blood, and a sample needle configured for receiving an evacuated blood collection container to collect and contain a subsequent portion of the sample of blood.

[0020] In yet another aspect, a blood sequestration device is disclosed and described. In some implementations, the blood sequestration device can include an inlet port, an outlet port connected with the inlet port, and a sequestration chamber connected with the inlet port. The sequestration chamber can have a vent comprising an air permeable blood barrier.

[0021] The blood sequestration device is connected along the blood sampling pathway between the patient needle and the sample needle, and includes an inlet port for receiving the sample of blood. The blood sequestration device further includes a sequestration chamber connected with the inlet port for receiving a first amount of the sample of blood, the sequestration chamber having a vent comprising an air permeable blood barrier for sequestering at least a first portion of the first amount of the sample of blood. The blood sequestration device may further include a sampling channel having a proximal end connected with the inlet port, the sampling channel conveying a subsequent amount of the sample of blood to the evacuated blood collection container upon the sequestration chamber sequestering at least the first por-

tion of the first amount of the sample of blood. The blood sequestration device further includes an outlet port connected with a distal end of the sampling channel, the outlet port for outputting the subsequent amount of the sample of blood.

[0022] The details of one or more embodiments are set forth in the accompanying drawings and the description below. Other features and advantages will be apparent from the description and drawings, and from the claims.

BRIEF DESCRIPTION OF THE DRAWINGS

[0023] These and other aspects will now be described in detail with reference to the following drawings.

FIG. 1 illustrates a blood sample optimization system.

FIG. 2 illustrates a blood sample optimization system in accordance with an alternative implementation.

FIG. 3 illustrates a blood sample optimization system in accordance with another alternative implementation.

FIG. 4 illustrates a blood sample optimization system in accordance with another alternative implementation.

FIG. 5 illustrates a blood sample optimization system in accordance with another alternative implementation.

FIG. 6 illustrates a blood sample optimization system in accordance with an alternative implementation.

FIG. 7 is a flowchart of a method for optimizing a quality of a blood culture.

FIGS. 8A - 8E illustrate a blood sequestration system for non-contaminated blood sampling, in accordance with some implementations.

FIG. 9 illustrates a pathway splitter for use in a blood sequestrations system.

FIGS. 10A - 10D illustrate a blood sequestration system for non-contaminated blood sampling, in accordance with alternative implementations.

FIGS. 11A - 11E illustrate a blood sequestration system for non-contaminated blood sampling, in accordance with other alternative implementations.

FIGS. 12A-12D illustrate a blood sample optimization system including a blood sequestration device in accordance with yet other alternative implementations.

FIGS. 13A-13D illustrate a blood sample optimization system 1300 in accordance with yet another alternative implementations.

FIGS. 14A-14E illustrate yet another implementation of a blood sampling system to sequester contaminates of an initial aliquot or sample to reduce false positives in blood cultures or tests performed on a patient's blood sample.

FIGS. 15A-15G illustrate a blood sequestration device and method of using the same, in accordance with yet another implementation.

FIGS. 16A-16D illustrate a blood sequestration device in accordance with yet another implementation.

FIGS. 17A - 17E illustrate a bottom member of a housing for a blood sequestration device.

FIGS. 18A - 18F illustrate a top member of a housing for a blood sequestration device.

FIGS. 19A and 19B illustrate a blood sequestration device having a top member mated with a bottom member.

FIG. 20 shows a blood sample optimization system including a blood sequestration device.

FIG. 21 illustrates a non-vented blood sequestration device using a wicking material chamber.

FIGS. 22A and 22B illustrate a material makeup of a filter for sequestering blood in a sequestration chamber of a blood sequestration device.

FIGS. 23A and 23B illustrate another implementation of a blood sequestration device that uses a vacuum force from a blood collection device.

[0024] Like reference symbols in the various drawings indicate like elements.

DETAILED DESCRIPTION

[0025] This document describes blood sample optimization systems and methods for reducing or eliminating contaminates in collected blood samples, which in turn reduces or eliminates false positive readings in blood cultures or other testing of collected blood samples. In some implementations, a blood sample optimization system includes a patient needle for vascular access to a patient's bloodstream, a sample needle for providing a blood sample to a blood collection container, such as an evacuated blood collection container or tube like a Vacutainer™ or

the like, or other sampling device, and a blood sequestration device located between the patient needle and the sample needle. The blood sequestration device includes a sequestration chamber for sequestering an initial, potentially contaminated aliquot of blood, and may further include a sampling channel that bypasses the sequestration chamber to convey likely uncontaminated blood between the patient needle and the sample needle after the initial aliquot of blood is sequestered in the sequestration chamber.

[0026] FIG. 1 illustrates a blood sample optimization system in accordance with some implementations. The system includes a patient needle 1 to puncture the skin of a patient to access the patient's vein and blood therein. The system further includes a sample needle (i.e., a resealably closed needle for use with Vacutainers™ or the like) 5, which may be contained within and initially sealed by a resealable boot 10, a Luer activated valve, or another collection interface or device. The resealable boot 10 can be pushed aside or around the sample needle 5 by application of a Vacutainer™ bottle (not shown) for drawing the patient's blood. The system can further include a low volume chamber 30 that leads to the sample needle 5, but also includes an orifice or one or more channels 45 that lead to a sequestration chamber 55 formed by a housing 50.

[0027] The sequestration chamber 55 is a chamber, channel, pathway, lock, or other structure for receiving and holding a first aliquot of the patient's blood, which may be in a predetermined or measured amount, depending on a volume of the sequestration chamber 55. The first draw of blood typically contains or is more susceptible to containing organisms that cause bacteraemia and sepsis or other pathogens than subsequent blood draws. The sequestration chamber 55 can be a vessel encased in a solid housing, formed in or defined by the housing itself, or can be implemented as tubing or a lumen. The sequestration chamber 55, regardless how formed and implemented, may have a predetermined volume. In some implementations, the predetermined volume may be based on a volume of the patient needle, i.e. ranging from less than the volume of the patient needle to any volume up to or greater than 20 times or more of the volume of the patient needle. The predetermined volume of the sequestration chamber 55 may also be established to economize or minimize an amount of blood to be sequestered and disposed of.

[0028] The sequestration chamber 55 can be formed, contained or housed in a chamber housing 50, and can be made of plastic, rubber, steel, aluminum or other suitable material. For example, the sequestration chamber 55 could be formed of flexible tubing or other elastomeric materials. The sequestration chamber 55 further includes an air permeable blood barrier 20 that allows air to exit the sequestration chamber 55. As used herein the term "air permeable blood barrier" means an air permeable but substantially blood impermeable substance, material, or structure. Examples may include hydrophobic membranes and coatings, a hydrophilic membrane or coating combined with a hydrophobic membrane or coating, mesh, a filter, a mechanical valve, antimicrobial material, or any other means of allowing air to be displaced from the sequestration chamber 55 as it is filled with blood. In various exemplary embodiments, an air permeable blood barrier may be formed by one or more materials that allow air to pass through until contacted by a liquid, such material then becomes completely or partially sealed to prevent or inhibit the passage of air and/or liquid. In other words, prior to contact with liquid, the material forms a barrier that is air permeable. After contact with a liquid, the material substantially or completely prevents the further passage of air and/or liquid.

[0029] The orifice or channel 45 can be any desired length, cross-sectional shape or size, and/or can be formed to depart from the low volume chamber 30 at any desired angle or orientation. The orifice or channel 45 may also include a one-way flap or valve 60 that maintains an initial aliquot of blood sample within the sequestration chamber 55. In some specific implementations, the orifice or channel 45 can include a "duck bill" or flapper valve 60, or the like, for one-way flow of blood from low volume chamber 30 to the sequestration chamber 55. The air permeable blood barrier 20 can also be constructed of a material that allows air to exit but then seals upon contact with blood, thereby not allowing external air to enter sequestration chamber 55. This sealing would eliminate the need for a valve.

[0030] Valve 60 can be any type of valve or closing mechanism. Chamber 30 is designed to hold virtually no residual blood, and can be designed to be adapted to hold or allow pass-through of a particular volume or rate of blood into sequestration chamber 55. Likewise, sequestration chamber 55 may also include any type of coating, such as an anti-microbial coating, or a coating that aids identification and/or diagnosis of components of the first, sequestered blood draw.

[0031] Housing 50 and 40 can be formed of any suitable material, including plastic, such as acrylonitrile butadiene styrene (ABS) or other thermoplastic or polymeric material, rubber, steel, or aluminum. The air permeable blood barrier 20 can include a color-providing substance, or other signaling mechanism, that is activated upon contact with blood from the initial blood draw, or when air displacement is stopped, or any combination of events with blood in the sequestration chamber 55. The air permeable barrier may also include an outer layer such as a hydrophobic membrane or cover that inhibits or prevents the inadvertent or premature sealing of the filter by an external fluid source, splash etc. Sequestration chamber 55 can also be translucent or clear to enable a user to visually confirm the chamber is filled.

[0032] FIG. 2 illustrates a blood sample optimization system in accordance with some alternative implementations. In the implementation shown in FIG. 2, a sequestration chamber 55, or waste chamber, surrounds the patient needle 1, with an open-ended cuff or housing con-

nected with the waste chamber and encircling the sample needle housing base and housing. The patient needle 1 and sample needle 5 are connected together by a boot 56, which forms a continuous blood draw channel therethrough. The boot 56 includes a single orifice or channel leading from the blood draw channel into sequestration chamber 55. The device can include more than one single orifice or channel, in other implementations. Each orifice or channel can include a one-way valve, and can be sized and adapted for predetermined amount of blood flow.

[0033] The sequestration chamber 55 includes an air permeable blood barrier. The filter can further include a sensor or indicator to sense and/or indicate, respectively, when a predetermined volume of blood has been collected in the sequestration chamber 55. That indication will alert a user to attach an evacuated blood collection tube or bottle, such as a Vacutainer™ to the sample needle 5. The housing for the sequestration chamber 55 can be any size or shape, and can include any type of material to define an interior space or volume therein. The interior space is initially filled only with air, but can also be coated with an agent or substance, such as a decontaminate, solidifying agent, or the like. Once evacuated blood collection tube is attached to the sample needle 5, blood will flow automatically into the patient needle 1, through the blood draw channel and sample needle 5, and into the bottle. The sample needle 5 is covered by a resealable boot, coating or membrane that seals the sample needle when a blood collection bottle is not attached thereon or thereto.

[0034] FIG. 3 illustrates a blood sample optimization system in accordance with some alternative implementations. In the implementation shown, a sample needle 5 is surrounded by a resealable boot or membrane, and is further connected with a patient needle 1. A blood flow channel is formed through the sample needle and the patient needle. The connection between the sample needle and patient needle includes a "T" or "Y" connector 102, which includes a channel, port or aperture leading out from the main blood flow channel to a sequestration chamber 104.

[0035] The T or Y connector 102 may include a flap or one-way valve, and have an opening that is sized and adapted for a predetermined rate of flow of blood. The sequestration chamber 104 can be formed from tubing, or be formed by a solid housing, and is initially filled with air. The sequestration chamber 104 will receive blood that flows out of a patient automatically, i.e. under pressure from the patient's own blood pressure. The sequestration chamber 104 includes an air permeable blood barrier 106, preferably at the distal end of tubing that forms the sequestration chamber 104, and which is connected at the proximal end to the T or Y connector 102. The T or Y connector 102 can branch off at any desired angle for most efficient blood flow, and can be formed so as to minimize an interface between the aperture and channel and the main blood flow channel, so as to minimize or eliminate mixing of the initial aliquot of blood with main blood draw samples.

[0036] In some alternative implementations, the sample needle may be affixed to a tubing of any length, as shown in FIG. 4, connecting at its opposite end to the T or Y connector 102. The sequestration chamber 104 can be any shape or volume so long as it will contain a predetermined amount of blood sample in the initial aliquot. The T or Y connector 102 may also include an opening or channel that is parallel to the main blood flow channel. The air permeable blood barrier may further include an indicator 107 or other mechanism to indicate when a predetermined amount of blood has been collected in the sequestration chamber, or when air being expelled reaches a certain threshold, i.e. to zero. The tubing can also include a clip 109 that can be used to pinch off and prevent fluid flow therethrough.

[0037] Once the air permeable blood barrier and primary chamber are sealed the initial aliquot of blood is trapped in the sequestration chamber 104, an evacuated blood collection tube, such as a Vacutainer™ bottle may be attached to the sample needle 5 to obtain the sample. The blood collection tube can be removed, and the sample needle 5 will be resealed. Any number of follow-on blood collection tubes can then be attached for further blood draws or samples. Upon completion of all blood draws, the system can be discarded, with the initial aliquot of blood remaining trapped in the sequestration chamber 104.

[0038] FIG. 5 illustrates a blood sample optimization system in accordance with some alternative implementations. In the implementation shown, a sample needle 5 is connected with a patient needle by tubing. A "T" or "Y" connector 120 is added along the tubing at any desired location, and includes an aperture, port or channel leading to a sequestration chamber 204, substantially as described above.

[0039] FIG. 6 illustrates a blood sample optimization system in accordance with some alternative implementations, in which a sequestration chamber 304, formed as a primary collection channel, receives an initial aliquot of blood, and is provided adjacent to the blood sampling channel. The sequestration chamber 304 can encircle the blood sampling channel, the patient needle 1, and/or the sample needle 5. The primary collection channel can include a T or Y connector 120, or other type of aperture or channel. The sequestration chamber 304 includes an air permeable blood barrier, which can also include an indicator of being contacted by a fluid such as blood, as described above.

[0040] In some implementations, either the patient needle 1 or the sample needle 5, or both, can be replaced by a Luer lock male or female connector. However, in various implementations, the connector at a sample needle end of the blood sample optimization system is initially sealed to permit the diversion of the initial aliquot of blood to the sequestration chamber, which is pressured at ambient air pressure and includes the air outlet of the air permeable blood barrier. In this way, the system passive-

ly and automatically uses a patient's own blood pressure to overcome the ambient air pressure of the sequestration chamber to push out air through the air permeable blood barrier and displace air in the sequestration chamber with blood.

[0041] FIG. 7 is a flowchart of an exemplary method for optimizing the quality of a blood culture. At 702, a clinician places a needle into a patient's vein. At 704, blood then flows into a sequestration chamber, pushing the air in the sequestration chamber out of the sequestration chamber through an air permeable blood barrier. In some implementations, the volume of the sequestration chamber is less than 0.1 to more than 5 cubic centimeters (cc's), or more. The sequestration chamber is sized and adapted to collect a first portion of a blood sample, which is more prone to contamination than secondary and other subsequent portion of the blood sample or subsequent draws. Since the sequestration chamber has an air-permeable blood barrier through which air can be displaced by blood pushed from the patient's vein, such blood will naturally and automatically flow into the sequestration chamber before it is drawn into or otherwise enters into a Vacutainer or other bottle for receiving and storing a blood sample.

[0042] When the sequestration chamber fills, the blood will gather at or otherwise make contact with the air permeable blood barrier, which will inhibit or prevent blood from passing therethrough. At 706, when the blood comes into contact with the entire internal surface area of the air permeable blood barrier, the air permeable blood barrier is then closed and air no longer flows out or in. At 708, the clinician may be provided an indictor or can see the full chamber, to indicate the evacuated blood collection tube, such as a Vacutainer™ can be attached. The indicator can include visibility into the primary chamber to see whether it is full, the blood barrier changing color, for example, or other indicator. The fill time of the sequestration chamber may be substantially instantaneous, so such indicator, if present, may be only that the sequestration chamber is filled.

[0043] Prior to an evacuated blood collection tube being attached, communication between the needle, sampling channel, and the sequestration chamber is restricted by the sealing of the sequestration chamber blood barrier thereby not permitting air to reenter the system through the sequestration. Sealing the communication path could also be accomplished with a mechanical twist or other movement, a small orifice or tortuous pathway, eliminating the need for a separate valve or mechanical movement or operation by the clinician. At 710, once the evacuated blood collection tube is removed, the self-sealing membrane closes the sample needle, and at 712, additional subsequent evacuated blood collection tubes may be attached. Once samples have been taken, at 714 the device is removed from the patient and discarded.

[0044] FIGS. 8A - 8E illustrate an exemplary blood sample optimization system 800 for non-contaminated blood sampling, in accordance with some implementations. The blood sample optimization system 800 includes an inlet port 802 that can be connected to tubing, a patient needle (or both), or other vascular or venous access device, and a pathway splitter 804 having a first outlet to a sequestration chamber tubing 806 and a second outlet to sample collection tubing 808. One or both of the sequestration chamber tubing 806 and the sample collection tubing 808 can be formed of tubing. In some implementations, the sequestration chamber tubing 806 is sized so as to contain a particular volume of initial blood sample. The sample collection tubing 808 will receive a blood sample once the sequestration chamber tubing 806 is filled. The sample collection tubing 808 can be connected to a Vacutainer™ base or housing 810, or other blood sample collection device.

[0045] The blood sequestration system 800 further includes a blood sequestration device 812 which, as shown in more detail in FIGS. 8B - 8D, includes a housing 818 that includes a sampling channel 820 defining a pathway for the non-contaminated sample collection tubing 808 or connected at either end to the non-contaminated sample collection tubing 808. The sampling channel 820 can be curved through the housing 818 so as to better affix and stabilize the housing 818 at a location along the non-contaminated sample collection tubing 808.

[0046] The blood sequestration device 812 further includes a sequestration chamber 822 connected with the sequestration chamber tubing 806 or other chamber. The sequestration chamber 822 terminates at an air permeable blood barrier 824. The air permeable blood barrier 824 can also include a coloring agent that turns a different color upon full contact with blood, as an indicator that the regular collection of blood samples (i.e. the non-contaminated blood samples) can be initiated. Other indicators may be used, such as a small light, a sound generation mechanism, or the like. In some implementations, the air permeable blood barrier is positioned at a right angle from the direction of sequestration chamber 822, but can be positioned at any distance or orientation in order to conserve space and materials used for the housing 818. The housing 818 and its contents can be formed of any rigid or semi-rigid material or set of materials.

[0047] FIG. 9 illustrates a pathway splitter 900 for use in a blood sequestrations system, such as those shown in FIGS. 8A - 8E, for example. The pathway splitter 900 includes an inlet port 902, a main line outlet port 904, and a sequestration channel outlet port 906. The inlet port 902 can be connected to main tubing that is in turn connected to a patient needle system, or directly to a patient needle. The main line outlet port 904 can be connected to main line tubing to a blood sampling system, such as a vacutainer base or housing, or directly to such blood sampling system. The sequestration channel outlet port 906 can be connected to sequestration tubing for receiving and sequestering a first sample of blood, up to a measured amount or predetermined threshold. Alternatively, the sequestration channel outlet port 906 can be connected to a sequestration chamber. The sequestra-

tion channel outlet port 906 is preferably 20-70 degrees angled from the main line outlet port 904, which in turn is preferably in-line with the inlet port 902. Once the predetermined amount of initial blood sample is sequestered in the sequestration tubing or chamber, in accordance with mechanisms and techniques described herein, follow-on blood samples will flow into the inlet port 902 and directly out the main line outlet port 904, without impedance.

[0048] FIGS. 10A - 10D illustrate a blood sequestration device 1000 in accordance with alternative implementations. The blood sequestration device 1000 includes an inlet port 1002, a main outlet port 1004, and a sequestration channel port 1006. The inlet port 1002 can be connected to a patient needle or related tubing. The main outlet port 1004 can be connected to a blood sample collection device such as a Vacutainer, associated tubing, or a Luer activated valve, or the like. The sequestration channel port 1006 splits off from the main outlet port 1004 to a sequestration chamber 1008. In some implementations, the sequestration chamber 1008 is formed as a helical channel within a housing or other container 1001.

[0049] The sequestration chamber 1008 is connected at the distal end to an air permeable blood barrier 1010, substantially as described above. Air in the sequestration chamber 1008 is displaced through the air permeable blood barrier 1010 by an initial aliquot of blood that is guided into the sequestration channel port 1006. Once the sequestration chamber 1008 is filled, further blood draws through the main outlet port 1004 can be accomplished, where these samples will be non-contaminated.

[0050] FIGS. 11A - 11E illustrate a blood sequestration device 1100 in accordance with other alternative implementations. The blood sequestration device 1100 includes an inlet port 1102, similar to the inlet ports described above, a main outlet port 1104, and a sequestration channel port 1106 that splits off from the main outlet port 1104 and inlet port 1102. The sequestration channel port is connected to a sequestration chamber 1108. In the implementation shown in FIGS. 11A - 11E, the blood sequestration device includes a base member 1101 having a channel therein, which functions as the sequestration chamber 1108. The channel can be formed as a tortuous path through the base member 1101, which is in turn shaped and formed to rest on a limb of a patient.

[0051] A portion of the sequestration chamber 1108 can protrude from the base member or near a top surface of the base member, just before exiting to an air permeable blood barrier 1110, to serve as a blood sequestration indicator 1109. The indicator 1109 can be formed of a clear material, or a material that changes color when in contact with blood.

[0052] In some implementations, the blood sequestration device 1100 can include a blood sampling device 1120 such as a normally closed needle, Vacutainer™ shield or other collection device. The blood sampling device 1120 can be manufactured and sold with the blood sequestration device 1100 for efficiency and convenience, so that a first aliquot of blood that may be contaminated by a patient needle insertion process can be sequestered. Thereafter, the blood sampling device 1120 can draw non-contaminated blood samples to reduce the risk of false positive testing and ensure a non-contaminated sample.

[0053] FIGS. 12A-12D illustrate a blood sample optimization system 1200 in accordance with yet other alternative implementations. The system 1200 includes a blood sequestration device 1202 for attaching to a blood sampling device 1204, such as a Vacutainer™ or other collection and sampling device. The blood sequestration device 1202 is configured and arranged to receive, prior to a Vacutainer™ container or vial being attached to a collection needle of the blood sampling device 1204, a first aliquot or amount of blood, and sequester that first aliquot or amount in a sequestration channel of the blood sequestration device 1202.

[0054] In some implementations, the blood sequestration device 1202 can include an inlet port 1212, a main outlet port, and a sequestration channel port. The inlet port 1212 can be connected to a patient needle or related tubing. The main outlet port 1214 can be connected to a normally closed needle or device to enable connection with an evacuated blood collection container or other collection device such as a Vacutainer™, associated tubing, luer connectors, syringe, a Luer activated valve, or the like. The sequestration channel port splits off from the main outlet port to a sequestration chamber 1218.

[0055] In some implementations, the sequestration chamber 1218 is formed as a channel within the body of a sequestration device 1202. The sequestration chamber 1218 can be a winding channel, such as a U-shaped channel, an S-shaped channel, a helical channel, or any other winding channel. The sequestration device 1202 can include a housing or other containing body, and one or more channels formed therein. As shown in FIGS. 12A and 12B, the sequestration device 1202 includes a main body 1206 and a cap 1208. The main body 1206 is formed with one or more cavities or channels, which are further formed with one or more arms 1210 that extend from the cap 1208, and which abut the cavities or channels in the main body 1206 to form the primary collection port and main outlet port.

[0056] FIGS. 13A-13D illustrate a blood sample optimization system 1300 in accordance with yet other alternative implementations. The system 1300 includes a blood sequestration device 1302 for attaching to a blood sampling device 1304, such as a Vacutainer or other bodily fluid collection and sampling device. The blood sequestration device 1302 is configured and arranged to receive, prior to a Vacutainer container or vial being attached to a collection needle of the blood sampling device 1304, a first aliquot or amount of blood, and to sequester that first aliquot or amount of blood or other bodily fluid in a sequestration channel of the blood sequestration device 1302.

[0057] The blood sequestration device 1302 includes a housing 1301 having an inlet port 1314, a main outlet port 1312, and a sequestration channel port 1316. The inlet port 1314 can be connected to a patient needle or associated tubing. The main outlet port 1312 can be connected to a normally closed needle or device to enable connection with an evacuated blood collection container or other collection device such as a Vacutainer™, associated tubing, luer connectors, syringe, a Luer activated valve, or the like. The sequestration channel port 1316 splits off from the main inlet port 1314 to a sequestration chamber 1318.

[0058] In the implementation shown in FIGS. 13A-D, the sequestration chamber 1318 is formed as a cavity or chamber within housing 1301 or formed by walls that define housing 1301. The sequestration chamber 1318 can be a winding channel, such as a U-shaped channel, an S-shaped channel, a helical channel, or any other winding channel, that is defined by the cooperation and connection of housing 1301 with cap 1307 which cap 1307 can include a protrusion 1305 that provides one or more walls or directors for the winding channel in the sequestration chamber 1318. The protrusion 1305 from the cap 1307 can be straight or curved, and may have various channels, apertures or grooves embedded therein, and can extend from the cap 1307 any angle or orientation. When the cap 1307 is connected with the housing 1301 to complete the formation of the sequestration chamber 1318, the protrusion 1305 forms at least part of the winding channel to sequester a first aliquot or amount of blood or other bodily fluid in a sequestration channel formed in the sequestration chamber 1318 and by the winding channel.

[0059] The sequestration chamber 1318 includes an air permeable blood barrier 1310, substantially as described above. Air in the sequestration chamber 1318 is displaced through the air permeable blood barrier 1310 by an initial aliquot of blood that is provided into the sequestration chamber 1318 by the blood pressure of the patient. Once the sequestration chamber 1318 is filled and the air in the sequestration chamber 1318 displaced, the blood pressure of the patient will be insufficient to drive or provide further blood into the blood sequestration device 1302, and in particular the outlet port 1312, until a force such as a vacuum or other pressure, such as provided by the blood sample collection device like Vacutainer is provided to draw out a next aliquot or amount of blood or bodily fluid. Further blood draws through the main outlet port 1312 can be accomplished, where these samples will be non-contaminated since any contaminants would be sequestered in the sequestration chamber 1318 with the first aliquot of blood.

[0060] FIGS. 14A-14E illustrate yet another implementation of a blood sampling system 1400 to sequester contaminates of an initial aliquot or sample to reduce false positives in blood cultures or tests performed on a patient's blood sample. The blood sampling system 1400 includes a blood sequestration device 1401 that can be connected between a blood sample collection device 1403 and a patient needle (not shown). The blood sample collection device 1403 can be a Vacutainer or the like. The blood sequestration device 1401 includes an inlet port 1402 that can be connected with a patient needle that is inserted into a patient's vascular system for access to and withdrawing of a blood sample. The inlet port 1402 may also be connected with tubing or other conduit that is in turn connected with the patient needle.

[0061] The inlet port 1402 defines an opening into the blood sequestration device 1401, which opening can be the same cross sectional dimensions as tubing or other conduit connected with the patient needle or the patient needle itself. For instance, the opening can be circular with a diameter of approximately 0.045 inches, but can have a diameter of between 0.01 inches or less to 0.2 inches or more. The blood sequestration device 1401 further includes an outlet port 1404, which defines an opening out of the blood sequestration device 1401 and to the blood sample collection device 1403. The outlet port 1404 may also be connected with tubing or other conduit that is in turn connected with the blood sequestration device 1403. The outlet port 1404 can further include a connector device such as a threaded cap, a Luer connector (male or female), a non threaded interference or glue joint fitting for attachment of various devices including but not limited to tubing, or the like.

[0062] The blood sequestration device 1401 further includes a sampling channel 1406 between the inlet port 1402 and the outlet port 1404, and which functions as a blood sample pathway once a first aliquot of blood has been sequestered. The sampling channel 1406 can be any sized, shaped or configured channel, or conduit. In some implementations, the sampling channel 1406 has a substantially similar cross sectional area as the opening of the inlet port 1402. In other implementations, the sampling channel 1406 can gradually widen from the inlet port 1402 to the outlet port 1404.

[0063] The blood sequestration device 1401 further includes a sequestration chamber 1408 that is connected to and split off or diverted from the sampling channel 1406 at any point between the inlet port 1402 and the outlet port 1404, but preferably from a proximal end of the sampling channel 1406 near the inlet port 1402. The sequestration chamber 1408 is at first maintained at atmospheric pressure, and includes an air outlet 1412 at or near a distal end of the sequestration chamber 1408 opposite the diversion point from the sampling channel 1406. The air outlet 1412 includes an air permeable blood barrier 1412. As shown in FIG. 14B, the air permeable blood barrier 1412 can be overlaid with a protective cover 1416. The protective cover 1416 can be sized and configured to inhibit a user from touching the air permeable blood barrier 1412 with their finger or other external implement, while still allowing air to exit the air permeable blood barrier 1412 as the air is displaced from the sequestration chamber 1408 by blood being forced into the sequestration chamber 1408 by a patient's own blood

pressure. In addition the protective cover 1416 can be constructed to inhibit or prevent accidental exposure of the air permeable blood barrier to environmental fluids or splashes. This can be accomplished in a variety of mechanical ways including but not limited to the addition of a hydrophobic membrane to the protective cover.

[0064] As shown in FIGS. 14C and 14D, the sampling channel 1406 can be cylindrical or frusto-conical in shape, going from a smaller diameter to a larger diameter, to minimize a potential to lyse red blood cells. Likewise, the sampling channel 1406 is formed with a minimal amount of or no sharp turns or edges, which can also lyse red blood cells. The sampling channel 1406 splits off to the sequestration chamber 1408 near the inlet port 1402 via a diversion pathway 1409. The diversion pathway 1409 can have any cross-sectional shape or size, but is preferably similar to the cross-sectional shape of at least part of the inlet port 1402.

[0065] In some implementations, the sampling channel 1406 and the sequestration chamber 1408 are formed by grooves, channels, locks or other pathways formed in housing 1414. The housing 1414 can be made of plastic, metal or other rigid or semi-rigid material. The housing 1414 can have a bottom member that sealably mates with a top member. One or both of the bottom member and the top member can include the sampling channel 1406 and the sequestration chamber 1408, as well as the diversion pathway 1409, the inlet port 1402, and the outlet port 1404. In some other implementations, one or more of the diversion pathway 1409, the inlet port 1402, and/or the outlet port 1404 can be at least partially formed by a cap member that is connected to either end of the housing 1414. In some implementations, the top member and the bottom member, as well as the cap member(s), can be coupled together by laser welding, heat sealing, gluing, snapping, screwing, bolting, or the like. In other implementations, some or all of the interior surface of the diversion pathway 1409 and/or sequestration chamber 1408 can be coated or loaded with an agent or substance, such as a decontaminate, solidifying agent, or the like. For instance, a solidifying agent can be provided at the diversion pathway 1409 such that when the sequestration chamber 1408 is filled and the initial aliquot of blood backs up to the diversion pathway 1409, that last amount of sequestered blood could solidify, creating a barrier between the sequestration chamber 1408 and the sampling channel 1406.

[0066] FIGS. 15A-15G illustrate a blood sequestration device 1500. The blood sequestration device 1500 can be connected to a normally closed needle or device to enable connection with an evacuated blood collection container or other collection device such as a Vacutainer™, associated tubing, luer connectors, syringe, a Luer activated valve, or the like.

[0067] The blood sequestration device 1500 includes an inlet port 1502 that can be connected with a patient needle that is inserted into a patient's vascular system for access to and withdrawing of a blood sample. The inlet port 1502 may also be connected with tubing or other conduit that is in turn connected with the patient needle. The inlet port 1502 defines an opening into the blood sequestration device 1500, which opening may be the same cross sectional dimensions as tubing or other conduit connected with the patient needle or the patient needle itself. For instance, the opening can be circular with a diameter of approximately 0.045 inches, but can have a diameter of between 0.01 inches or less to 0.2 inches or more.

[0068] The inlet port 1502 can also include a sealing or fluid-tight connector or connection, such as threading or Luer fitting, or the like. In some implementations, tubing or other conduit associated with the patient needle can be integral with the inlet port 1502, such as by co-molding, gluing, laser weld, or thermally bonding the parts together. In this manner, the blood sequestration device 1500 can be fabricated and sold with the patient needle as a single unit, eliminating the need for connecting the patient needle to the blood sequestration device 1500 at the time of blood draw or sampling.

[0069] The blood sequestration device 1500 further includes an outlet port 1504, which defines an opening out of the blood sequestration device 1500 and to the blood sample collection device. The outlet port 1504 may also be connected with tubing or other conduit that is in turn connected with the blood sequestration device, and may also include a sealing or fluid-tight connector or connection, such as threading or Luer fitting, or the like. Accordingly, as discussed above, the blood sequestration device 1500 can be fabricated and sold with the patient needle and/or tubing and the blood sample collection device as a single unit, eliminating the need for connecting the patient needle and the blood sample collection device to the blood sequestration device 1500 at the time of blood draw or sampling.

[0070] The blood sequestration device 1500 further includes a sampling channel 1506 between the inlet port 1502 and the outlet port 1504, and which functions as a blood sample pathway once a first aliquot of blood has been sequestered. The sampling channel 1506 can be any sized, shaped or configured channel or conduit. In some implementations, the sampling channel 1506 has a substantially similar cross sectional area as the opening of the inlet port 1502. In other implementations, the sampling channel 1506 can gradually widen from the inlet port 1502 to the outlet port 1504.

[0071] The blood sequestration device 1500 further includes a sequestration chamber 1508 that is connected to and split off or diverted from the sampling channel 1506 at any point between the inlet port 1502 and the outlet port 1504, but preferably from a proximal end of the sampling channel 1506 near the inlet port 1502. In some implementations, the diversion includes a Y-shaped junction. The sequestration chamber 1508 is preferably maintained at atmospheric pressure, and includes a vent 1510 at or near a distal end of the sequestration chamber 1508. The vent 1510 includes an air per-

meable blood barrier 1512. FIG. 15C illustrates the blood sequestration device 1500 with the sequestration chamber 1508 filled with a first aliquot or sample of blood from the patient.

[0072] The air permeable blood barrier 1512 can be covered with a protective cover 1516. The protective cover 1516 can be sized and configured to inhibit a user from touching the air permeable blood barrier 1512 with their finger or other external implement, while still allowing air to exit the air permeable blood barrier 1512 as the air is displaced from the sequestration chamber 1508 by blood being forced into the sequestration chamber 1508 by a patient's own blood pressure. The protective cover 1516 can be constructed to inhibit or prevent accidental exposure of the filter to environmental fluids or splashes. This can be accomplished in a variety of mechanical ways including but not limited to the addition of a hydrophobic membrane to the protective cover.

[0073] FIG. 15B is a perspective view of the blood sequestration device 1500 from the outlet port 1504 and top side of a housing 1501 of the blood sequestration device 1500 that includes the vent 1510, and illustrating an initial aliquot of blood filling sequestration chamber 1508 while the sampling channel 1506 is empty, before a sample collection device is activated. FIG. 15G is a perspective view of the blood sequestration device 1500 from the outlet port 1504 and bottom side of the housing 1501 of the blood sequestration device 1500, and illustrating the initial aliquot of blood filling sequestration chamber 1508 while the sampling channel 1506 is empty, before the sample collection device is activated. FIG. 15C is another perspective view of the blood sequestration device 1500 from the inlet port 1502 and top side of a housing 1501 of the blood sequestration device 1500 that includes the vent 1510, and illustrating blood now being drawn through sampling channel 1506 while the sequestered blood remains substantially in the sequestration chamber 1508.

[0074] FIG. 15D is a cross section of the blood sequestration device 1500 in accordance with some implementations, showing the housing 1501 that defines the sampling channel 1506 and the sequestration chamber 1508. FIGS. 15E and 15F illustrate various form factors of a housing for a blood sequestration device, in accordance with one or more implementations described herein.

[0075] The sequestration chamber 1508 can have a larger cross-sectional area than the sampling channel 1506, and the cross-sectional area and length can be configured for a predetermined or specific volume of blood to be sequestered or locked. The sampling channel 1506 can be sized to be compatible with tubing for either or both of the patient needle tubing or the blood collection device tubing.

[0076] The housing 1501 can be formed of multiple parts or a single, unitary part. In some implementations, and as illustrated in FIG. 15D, the housing 1501 includes a top member 1520 and a bottom member 1522 that are mated together, one or both of which having grooves, channels, locks, conduits or other pathways pre-formed therein, such as by an injection molding process or by etching, cutting, drilling, etc. The top member 1520 can be connected with the bottom member 1522 by any mating or connection mechanism, such as by laser welding, thermal bonding, ultrasonic welding, gluing, using screws, rivets, bolts, or the like, or by other mating mechanisms such as latches, grooves, tongues, pins, flanges, or the like.

[0077] In some implementations, such as shown in FIG. 15D, the top member 1520 can include the grooves, channels, locks, conduits or other pathways, while the bottom member 1522 can include a protrusion 1524 that is sized and adapted to fit into at least one of the grooves, channels, locks or other pathways of the top member 1520. The protrusion 1524 can provide a surface feature, such as a partial groove or channel, for instance, to complete the formation of either the sampling channel 1506 and/or the sequestration chamber 1508. In some implementations, the protrusion 1524 can be formed with one or more angled sides or surfaces for a tighter fit within the corresponding groove, channel, lock or other pathway. In yet other implementations, both the top member 1520 and the bottom member can include grooves, channels, locks or other pathways, as well as one or more protrusions 1524.

[0078] In some implementations, the sampling channel 1506 and the sequestration chamber 1508 are formed by grooves, channels, locks or other pathways formed in housing 1501. The housing 1501 can be made of any suitable material, including rubber, plastic, metal or other material. The housing 1501 can be formed of a clear or translucent material, or of an opaque or non-translucent material. In other implementations, the housing 1501 can be mostly opaque or non-translucent, while the housing surface directly adjacent to the sampling channel 1506 and/or the sequestration chamber 1508 is clear or translucent, giving a practitioner a visual cue or sign that the sequestration chamber 1508 is first filled to the extent necessary or desired, and/or then a visual cue or sign that the sequestered blood remains sequestered while a clean sample of blood is drawn through the sampling channel 1506. Other visual cues or signs of the sequestration can include, without limitation: the air permeable blood barrier 1512 turning a different color upon contact, saturation, or partial saturation with blood; a color-coded tab or indicator at any point along or adjacent to the sequestration chamber; an audible signal; a vibratory signal; or other signal.

[0079] After a venipuncture by a patient needle of a patient (not shown), which could gather a number of pathogens from the patient's skin, a first amount of the patient's blood with those pathogens will make its way into the input port 1502 blood sequestration device 1500 and flow into the sequestration chamber 1508 by following the path of least resistance, as the patient's own blood pressure overcomes the atmospheric pressure in the sequestration chamber 1508 to displace air therein through

the air permeable blood barrier 1512. The patient's blood pressure will not be sufficient to overcome the air pressure that builds up in the sealed sampling channel 1506. Eventually, the sequestration chamber 1508, which has a predetermined volume, is filled with blood that displaces air through the air permeable blood barrier 1512. Once the blood hits the air permeable blood barrier, the blood interacts with the air permeable blood barrier 1512 material to completely or partially seal the vent 1510. A signal or indication may be provided that the practitioner can now utilize the Vacutainer capsule or other blood sample collection device to acquire a next amount of the patient's blood for sampling. The blood in the sequestration chamber 1508 is now effectively sequestered in the sequestration chamber.

[0080] Upon filling the blood sequestration pathway 1508 but prior to use of the Vacutainer or other blood sample collection device, the patient's blood pressure may drive compression of the air in the sampling channel 1506, possibly resulting in a small amount of blood moving past the diversion point to the sequestration chamber 1508 and into the sampling channel 1506, queuing up the uncontaminated blood to be drawn through the sampling channel 1506.

[0081] FIGS. 16-19 illustrate yet another implementation of a blood sequestration device. FIGS. 16A-16D illustrate a blood sequestration device 1600 that can be connected between a blood sample collection device, such as an evacuated blood collection container like a Vacutainer™ (not shown), and a patient needle (not shown) and/or associated tubing. FIG. 17 illustrates a bottom member of the blood sequestration device, and FIG. 18 illustrates a top member of the blood sequestration device, which top member and bottom member can be mated together to form an input port, and output port, a sequestration chamber and a sampling channel, as explained more fully below. FIGS. 19A and B show the top member and bottom member mated together. It should be understood that FIGS. 16-19 illustrate one exemplary manner of constructing a blood sequestration device as described herein, and other forms of construction are possible.

[0082] Referring to FIGS. 16A - D, the blood sequestration device 1600 includes an inlet port 1602 that can be connected with a patient needle that is inserted into a patient's vascular system for access to and withdrawing of a blood sample. The inlet port 1602 may also be connected with tubing or other conduit that is in turn connected with the patient needle. The inlet port 1602 defines an opening into the blood sequestration device 1600, which opening can be the same cross sectional dimensions as tubing or other conduit connected with the patient needle or the patient needle itself. For instance, the opening can be circular with a diameter of approximately 0.045 inches, but can have a diameter of between 0.01 inches or less to 0.2 inches or more.

[0083] The inlet port 1602 can also include a sealing or fluid-tight connector or connection, such as threading or Luer fitting, or the like. In some implementations, tubing or other conduit associated with the patient needle can be integral with the inlet port 1602, such as by co-molding, gluing, laser weld, or thermally bonding the parts together. In this manner, the blood sequestration device 1600 can be fabricated and sold with the patient needle and/or tubing as a single unit, eliminating the need for connecting the patient needle to the blood sequestration device 1600 at the time of blood draw or sampling.

[0084] The blood sequestration device 1600 further includes an outlet port 1604, which defines an opening out of the blood sequestration device 1600 and to the blood sample collection device. The outlet port 1604 may also be connected with tubing or other conduit that is in turn connected with the blood sequestration device, and may also include a sealing or fluid-tight connector or connection, such as threading or Luer fitting, or the like. Accordingly, as discussed above, the blood sequestration device 1600 can be fabricated and sold with the patient needle and/or tubing and the blood sample collection device as a single unit, eliminating the need for connecting the patient needle and the blood sample collection device to the blood sequestration device 1600 at the time of blood draw or sampling.

[0085] The blood sequestration device 1600 further includes a sampling channel 1606 between the inlet port 1602 and the outlet port 1604, and a sequestration chamber 1608 that is connected to and split off or diverted from the sampling channel 1606 at any point between the inlet port 1602 and the outlet port 1604. The sampling channel 1606 functions as a blood sampling pathway once a first aliquot of blood has been sequestered in the sequestration chamber 1608. The sampling channel 1606 can be any sized, shaped or configured channel, or conduit. In some implementations, the sampling channel 1606 has a substantially similar cross sectional area as the opening of the inlet port 1602. In other implementations, the sampling channel 1606 can gradually widen from the inlet port 1602 to the outlet port 1604. The sequestration chamber 1608 may have a larger cross section to form a big reservoir toward the sequestration channel path so that the blood will want to enter the reservoir first versus entering a smaller diameter on the sampling channel 1606, as is shown more fully in FIGS. 17 and 19.

[0086] In some exemplary implementations, the diversion between the sampling channel 1606 and the sequestration chamber 1608 is by diverter junction 1607. Diverter junction 1607 may be a substantially Y-shaped, T-shaped, or U-shaped. In some preferred exemplary implementations, and as shown in FIG. 17A -17B, the diverter junction 1607 is configured such that the flow out of the inlet port 1602 is preferentially directed toward the sequestration chamber 1608. The sequestration chamber 1608 may also include or form a curve or ramp to direct the initial blood flow toward and into the sequestration chamber 1608.

[0087] The sequestration chamber 1608 is preferably maintained at atmospheric pressure, and includes a vent

1610 at or near a distal end of the sequestration chamber 1608. The vent 1610 may include an air permeable blood barrier 1612 as described above.

[0088] The blood sequestration device 1600 can include a housing 1601 that can be formed of multiple parts or a single, unitary part. In some implementations, and as illustrated in FIGS. 17A - 17D and FIGS. 18A - 18F, the housing 1601 includes a top member 1620 and a bottom member 1622 that are mated together. The blood sequestration device 1600 can also include a gasket or other sealing member (not shown) so that when the top member 1620 is mechanically attached with the bottom member 1622, the interface between the two is sealed by the gasket or sealing member. The FIGS. 17A - 17D illustrate a bottom member 1622 of a housing for a blood sequestration device 1600. The bottom member 1622 can include grooves, channels, locks, conduits or other pathways pre-formed therein, such as by an injection molding process or by etching, cutting, drilling, etc., to form the sampling channel 1606, the sequestration chamber 1608, and diverter junction 1607.

[0089] The sequestration chamber 1608 may have a larger cross section than the sampling channel 1606 so that the blood will preferentially move into the sequestration chamber first versus entering a smaller diameter on the sampling channel 1606.

[0090] FIGS. 18A - 18F illustrate the top member 1620, which can be connected with the bottom member 1622 by any mating or connection mechanism, such as by laser welding, thermal bonding, gluing, using screws, rivets, bolts, or the like, or by other mating mechanisms such as latches, grooves, tongues, pins, flanges, or the like. The top member 1620 can include some or all of the grooves, channels, locks, conduits or other pathways to form the sampling channel 1606, the sequestration chamber 1608, and the diverter junction 1607. In yet other implementations, both the top member 1620 and the bottom member 1622 can include the grooves, channels, locks or other pathways.

[0091] In some implementations, the sampling channel 1606 and the sequestration chamber 1608 are formed by grooves, channels, locks or other pathways formed in housing 1601. The housing 1601 can be made of rubber, plastic, metal or any other suitable material. The housing 1601 can be formed of a clear or translucent material, or of an opaque or non-translucent material. In other implementations, the housing 1601 can be mostly opaque or non-translucent, while the housing surface directly adjacent to the sampling channel 1606 and/or the sequestration chamber 1608 may be clear or translucent, giving a practitioner a visual cue or sign that the sequestration chamber 1608 is first filled to the extent necessary or desired, and/or then a visual cue or sign that the sequestered blood remains sequestered while a clean sample of blood is drawn through the sampling channel 1606. Other visual cues or signs of the sequestration can include, without limitation: the air permeable blood barrier 1612 turning a different color upon contact, saturation, or partial saturation with blood; a color-coded tab or indicator at any point along or adjacent to the sequestration chamber; an audible signal; a vibratory signal; or other signal.

[0092] As shown in FIGS. 18A - 18F, the air permeable blood barrier 1612 can be covered with, or surrounded by, a protective member 1616. The protective member 1616 can be sized and configured to inhibit a user from touching the air permeable blood barrier 1612 with their finger or other external implement, while still allowing air to exit the air permeable blood barrier 1612 as the air is displaced from the sequestration chamber 1608. In some implementations, the protective member 1616 includes a protrusion that extends up from a top surface of the top member 1620 and around the air permeable blood barrier 1612. The protective cover 1616 can be constructed to inhibit or prevent accidental exposure of the filter to environmental fluids or splashes. This can be accomplished in a variety of mechanical ways including but not limited to the addition of a hydrophobic membrane to the protective cover.

[0093] In use, the blood sequestration device 1600 includes a sampling channel 1606 and a sequestration chamber 1608. Both pathways are initially air-filled at atmospheric pressure, but the sampling channel 1606 is directed to an output port 1604 that will be initially sealed by a Vacutainer or other such sealed blood sampling device, and the sequestration chamber 1608 terminates at a vent 1610 to atmosphere that includes an air permeable blood barrier 1612.

[0094] After a venipuncture by a patient needle of a patient (not shown), which could gather a number of pathogens from the patient's skin, a first amount of the patient's blood with those pathogens will pass through input port 1602 of blood sequestration device 1600. This initial volume of potentially contaminated blood will preferentially flow into the sequestration chamber 1608 by finding the path of least resistance. The patient's own blood pressure overcomes the atmospheric pressure in the vented sequestration chamber 1608 to displace air therein through the air permeable blood barrier 1612, but is not sufficient to overcome the air pressure that builds up in the sealed sampling channel 1606. In various exemplary embodiments, the sequestration chamber 1608 and sampling channel 1606 can be configured such that the force generated by the patient's blood pressure is sufficient to overcome any effect of gravity, regardless of the blood sequestration device's orientation.

[0095] Eventually, the sequestration chamber 1608 fills with blood that displaces air through the air permeable blood barrier 1612. Once the blood contacts the air permeable blood barrier, the blood interacts with the air permeable blood barrier 1612 material to completely or partially seal the vent 1610. A signal or indication may be provided that the practitioner can now utilize the Vacutainer or other blood sampling device.

[0096] Upon filling the blood sequestration pathway 1608 but prior to use of the Vacutainer or other blood

sample collection device, the patient's blood pressure may drive compression of the air in the sampling channel 1606, possibly resulting in a small amount of blood moving past the diversion point into the sampling channel 1606, queuing up the uncontaminated blood to be drawn through the sampling channel 1606.

[0097] FIG. 19A is a side view, and FIG. 19B is a cross-sectional view, of the blood sequestration device 1600, illustrating the top member 1620 mated with the bottom member 1622.

[0098] FIG. 20 shows a blood sample optimization system 2000 that includes a patient needle 2002 for vascular access to a patient's bloodstream, a blood sample collection device 2004 to facilitate the collecting of one or more blood samples, and a conduit 2006 providing a fluid connection between the patient needle 2002 and the blood sample collection device 2004. In some implementations, the blood sample collection device 2004 includes a protective shield that includes a sealed collection needle on which a sealed vacuum-loaded container is placed, which, once pierced by the collection needle, draws in a blood sample under vacuum pressure or force through the conduit 2006 from the patient needle 2002.

[0099] The blood sample optimization system 2000 further includes a blood sequestration device 2008, located at any point on the conduit 2006 between the patient needle 2002 and the blood sample collection device 2004 as described herein.

[0100] FIG. 21 illustrates a non-vented blood sequestration device 2100 using a wicking material chamber. The blood sequestration device 2100 includes a housing 2101 that has a sampling channel 2104 that is at least partially surrounded or abutted by a sequestration chamber 2102 that is filled with a wicking material. An initial aliquot of blood is drawn in from the patient needle into the sampling channel 2104 where it is immediately wicked into the wicking material of the sequestration chamber 2102. The wicking material and/or sequestration chamber 2102 is sized and adapted to receive and hold a predetermined amount of blood, such that follow-on or later blood draws pass by the wicking material and flow straight through the sampling channel 2104 to a sampling device such as a Vacutainer. The wicking material can include a substance such as a solidifier, a decontaminate, or other additive.

[0101] As described herein, an air permeable blood barrier may be created using a wide variety of different structures and materials. As shown in FIGS. 22A and B, an air permeable blood barrier 2202 of a blood sequestration device 2200 can include a polymer bead matrix 2204, in which at least some beads are treated to make them hydrophilic. The air permeable blood barrier 2202 further includes a self-sealing material 2206, such as carboxymethyl cellulose (CMC) or cellulose gum, or other sealing material. The air permeable blood barrier 2202 can further include voids 2208 that permit air flow before contact or during partial contact with a fluid such as blood. As shown in FIG. 22B, contact with a fluid causes the self-sealing material 2206 to swell and close off the voids 2208, occluding air flow through the voids 2208 and creating a complete or partial seal.

[0102] FIGS. 23A and B illustrate yet another implementation of a blood sequestration device 2300, having an inlet port 2302 to connect with a patient needle, an outlet port 2304 to connect with a blood sample collection device, a sequestration chamber 2306, and a sampling channel 2308 that bypasses the sequestration chamber 2306 once the sequestration chamber is filled to an initial aliquot of potentially contaminated blood to be sequestered. The sequestration chamber 2306 includes a hydrophobic plug 2312 at a distal end of the sequestration chamber 2306 that is farthest from the inlet port 2302. A vacuum or other drawing force applied from the outlet port 2304, such as from a Vacutainer or the like, draws in blood into the inlet port 2302 and directly into the sequestration chamber 2306, where the initial aliquot of blood will contact the hydrophobic plug 2312 and cause the initial aliquot of blood to back up into the sequestration chamber 2306 and be sequestered there. A small amount of blood may make its way into the sampling channel 2308, which is initially closed off by valve 2308. Upon release of the valve 2308, and under further force of the vacuum or other force, follow-on amounts of blood will flow into inlet port 2302, bypass the sequestration chamber 2306, and flow into and through sampling channel 2308 toward the outlet port 2304 and to the collection device.

[0103] The sampling channel 2308 can have any suitable geometry and can be formed of plastic tubing or any other suitable material. Valve 2308 can be a clip or other enclosing device to pinch, shunt, bend or otherwise close off the sampling channel before the initial aliquot of blood is sequestered in the sequestration chamber 2306.

[0104] Although a variety of embodiments have been described in detail above, other modifications are possible. Other embodiments may be within the scope of the following claims.

Aspects useful for understanding the invention:

[0105]

1. A blood sequestration device comprising;
an inlet port;
an outlet port;
a sequestration chamber connected with the inlet port, the sequestration chamber having a vent comprising an air permeable blood barrier;
a sampling channel having a proximal end connected with the inlet port and a distal end connected with the outlet port; and
a housing that houses and defines the inlet port, the outlet port, the sequestration chamber, and the sampling channel.

2. The blood sequestration device in accordance

with aspect 1, wherein the air permeable blood barrier includes an air permeable material that seals at least partially upon contact with blood.

3. The blood sequestration device in accordance with aspect 1 or 2, wherein the sequestration chamber includes a sequestration channel defined in the housing.

4. The blood sequestration device in accordance with aspect 3, further comprising a blood sampling pathway connected with the inlet port, and wherein the inlet port defined by the housing has a cross-sectional geometry consistent with the blood sampling pathway.

5. The blood sequestration device in accordance with aspect 3 or 4, wherein the sampling channel defined by the housing has a cross-sectional geometry consistent with the inlet port.

6. The blood sequestration device in accordance with one of the previous aspects, wherein the sequestration chamber and the sampling channel are connected with the inlet port by a junction that is configured to direct a first portion of blood to the sequestration chamber.

7. The blood sequestration device in accordance with one of the previous aspects, wherein the housing comprises a bottom member mated with a top member, each of the bottom member and the top member defining a part of each of the inlet port, the outlet port, the sequestration chamber, and the sampling channel.

8. A blood sequestration device connected with a blood sampling pathway having a patient needle and a sample collection device, the blood sequestration device comprising;
an inlet port connected with the patient needle;
a sequestration chamber connected with the inlet port, the sequestration chamber having a vent comprising an air permeable blood barrier;
a sampling channel having a proximal end connected with the inlet port; and
an outlet port connected with a distal end of the sampling channel and with the sample collection device; and
a housing that houses and defines the inlet port, the outlet port, the sequestration chamber, and the sampling channel.

9. The blood sequestration device in accordance with aspect 8, wherein the inlet port is connected with the patient needle via a first portion of the blood sampling pathway.

10. The blood sequestration device in accordance with aspect 8 or 9, wherein the outlet port is connected with the sample collection device via a second portion of the blood sampling pathway.

11. The blood sequestration device in accordance with one of aspects 8 to 10, wherein the air permeable blood barrier includes an air permeable material that seals at least partially upon contact with blood.

12. The blood sequestration device in accordance with one of aspects 8 to 11, wherein the sequestration chamber includes a sequestration channel defined in the housing.

13. The blood sequestration device in accordance with aspect 12, wherein the sequestration channel has a proximal end connected with the inlet port, and a distal end having the vent comprising an air permeable blood barrier.

14. The blood sequestration device in accordance with one of aspects 8 to 13, wherein the sequestration chamber and the sampling channel are connected with the inlet port by a junction that is configured to direct a first portion of blood to the sequestration chamber.

15. The blood sequestration device in accordance with one of aspects 8 to 14, wherein the sampling channel has a substantially uniform cross-sectional geometry that is consistent with the blood sampling pathway.

16. The blood sequestration device in accordance with aspect 15, wherein the sequestration chamber includes a sequestration chamber that has a cross-sectional area that is larger than the cross-sectional geometry of the sampling channel.

17. A blood sequestration device connected with a blood sampling system comprising a patient needle for accessing a blood sample from a patient, and a sample needle that is sealed, the blood sequestration device comprising;
an inlet port connected with the patient needle to receive the blood sample from the patient;
a sequestration chamber connected with the inlet port and having a vent comprising an air permeable blood barrier, the sequestration chamber for receiving and sequestering a first portion of the blood sample prior to the sample needle being unsealed; and
a sampling channel having a proximal end connected with the inlet port, the sampling channel for conveying a second portion of the blood sample once the sample needle is unsealed;
an outlet port connected with a distal end of the sampling channel for conveying the second portion of

the blood sample to the sample needle; and
a housing that houses and defines the inlet port, the outlet port, the sequestration chamber, and the sampling channel.

18. The blood sequestration device in accordance with aspect 17, wherein the sequestration chamber is at ambient air pressure, and wherein the sequestration chamber receives the first portion of the blood sample by blood pressure of the patient overcoming the ambient air pressure in the sequestration chamber.

19. The blood sequestration device in accordance with aspect 17 or 18, wherein the sampling channel causes the second portion of the blood sample to bypass the sequestered first portion of blood, and exit the outlet port for conveyance to a blood collection device.

20. The blood sequestration device in accordance with aspect 17, 18 or 19, wherein the air permeable blood barrier includes an air permeable material that seals upon contact with blood.

Claims

1. A blood sequestration device (1500) comprising;

   an inlet port (1502);
   a junction (1607) connected with the inlet port (1502);
   a sequestration chamber (1508) having a vent (1510) comprising an air permeable blood barrier (1512);
   a sampling channel (1506) having a proximal end connected with the inlet port (1502) via the junction (1607), and a distal end connected with an outlet port (1504); and
   a housing (1501) that houses and defines the inlet port (1502), the junction (1607), the sequestration chamber (1508), the sampling channel (1506), and the outlet port (1504),
   characterized in that the sequestration chamber (1508) is connected with the
   inlet port (1502) via the junction (1607) which is configured to direct a first portion of blood to the sequestration chamber (1508), and the air permeable blood barrier (1512) includes an air permeable material that seals at least partially upon contact with a portion of the first portion of blood.

2. The blood sequestration device (1500) in accordance with claim 1,
   wherein the sequestration chamber (1508) includes a sequestration channel defined in the housing (1501).

3. The blood sequestration device (1500) in accordance with claim 1 or 2, further comprising a blood sampling pathway connected with the inlet port (1502) opposite the junction (1607), and
   wherein the inlet port (1502) defined by the housing (1501) has a cross-sectional geometry consistent with the blood sampling pathway.

4. The blood sequestration device (1500) in accordance with one of the preceding claims, wherein
   the sampling channel (1506) defined by the housing (1501) has a cross-sectional geometry consistent with the inlet port (1502).

5. The blood sequestration device (1500) in accordance with one of claims 2 to 4, wherein the housing (1501) comprises a bottom member (1522) mated with a top member (1520), each of the bottom member (1522) and the top member (1520) defining a part of each of the inlet port (1502), the outlet port (1504), the sequestration chamber (1508), and the sampling channel (1506).

6. A system of a blood sequestration device (1500), a blood sampling pathway having a patient needle, and a sample collection device, the blood sequestration device (1500) comprising;
   an inlet port (1502) connected with the patient needle;
   a junction (1607) connected with the inlet port (1502) opposite the blood sampling pathway;
   a sequestration chamber (1508) having a vent (1510) comprising an air permeable blood barrier (1512);
   a sampling channel (1506) having a proximal end connected with the inlet port (1502); and
   an outlet port (1504) connected with a distal end of the sampling channel (1506) and with the sample collection device; and
   a housing (1501) that houses and defines the inlet port (1502), the outlet port (1504), the sequestration chamber (1508), and the sampling channel (1506),
   characterized in that the sequestration chamber (1508) is connected with the inlet port (1502) and the air permeable blood barrier (1512) includes an air permeable material that seals at least partially upon contact with blood.

7. The system in accordance with claim 6, wherein the inlet port (1502) is connected with the patient needle via a first portion of the blood sampling pathway.

8. The system in accordance with claim 6 or 7, wherein the outlet port (1504) is connected with the sample collection device via a second portion of the blood sampling pathway.

9. The system in accordance with one of claims 6 to 8,

wherein the sequestration chamber (1508) includes a sequestration channel defined in the housing (1501).

10. The system in accordance with claim 9, wherein the sequestration channel has a proximal end connected with the inlet port (1502), and a distal end having the vent (1510) comprising an air permeable blood barrier (1512).

11. The system in accordance with one of claims 6 to 10, wherein the sequestration chamber (1508) and the sampling channel (1506) are connected with the inlet port (1502) by
the junction (1607) that is configured to direct a first portion of blood to the sequestration chamber (1508).

12. The system in accordance with one of claims 6 to 11, wherein the sampling channel (1506) has a substantially uniform cross-sectional geometry that is consistent with the blood sampling pathway.

13. The system in accordance with claim 12, wherein the sequestration chamber (1506) includes a sequestration chamber that has a cross-sectional area that is larger than the cross-sectional geometry of the sampling channel (1506).

14. The system in accordance with claim 7, member (1520), wherein the housing (1501) comprises a bottom member (1522) mated with a top member (1520), each of the bottom member (1522) and the top member (1520) defining a part of each of the inlet port (1502), the outlet port (1504), the sequestration chamber (1508), and the sampling channel (1506).

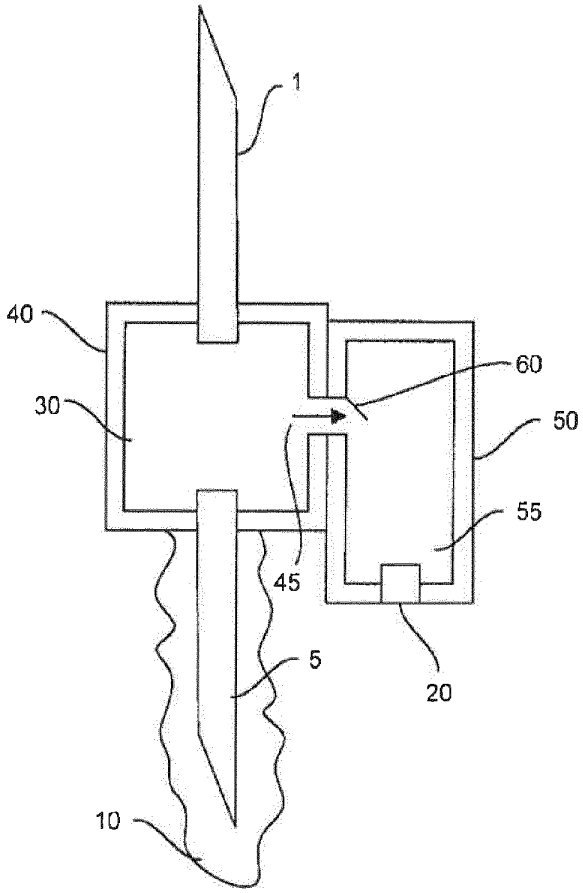


FIG. 1

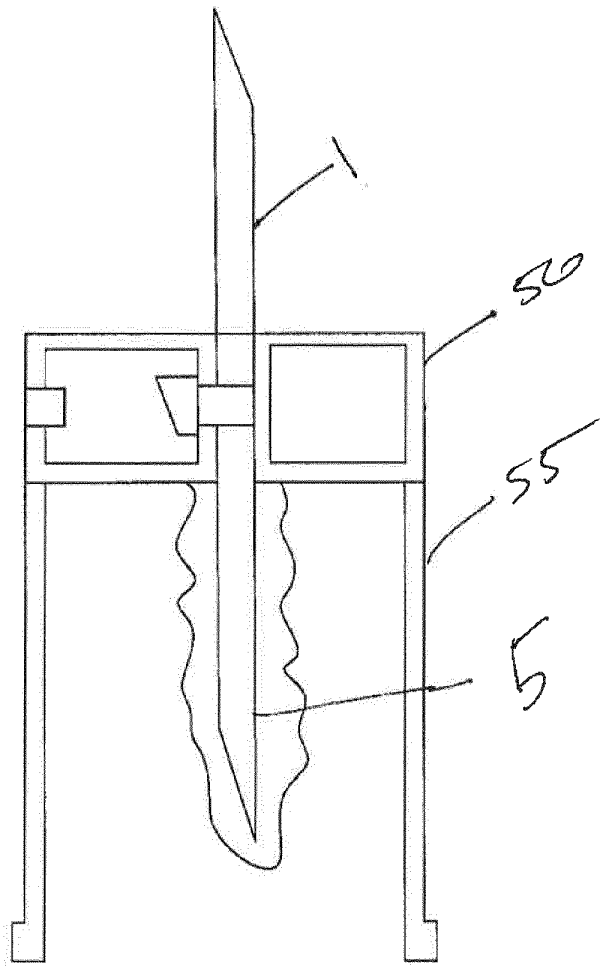


FIG. 2

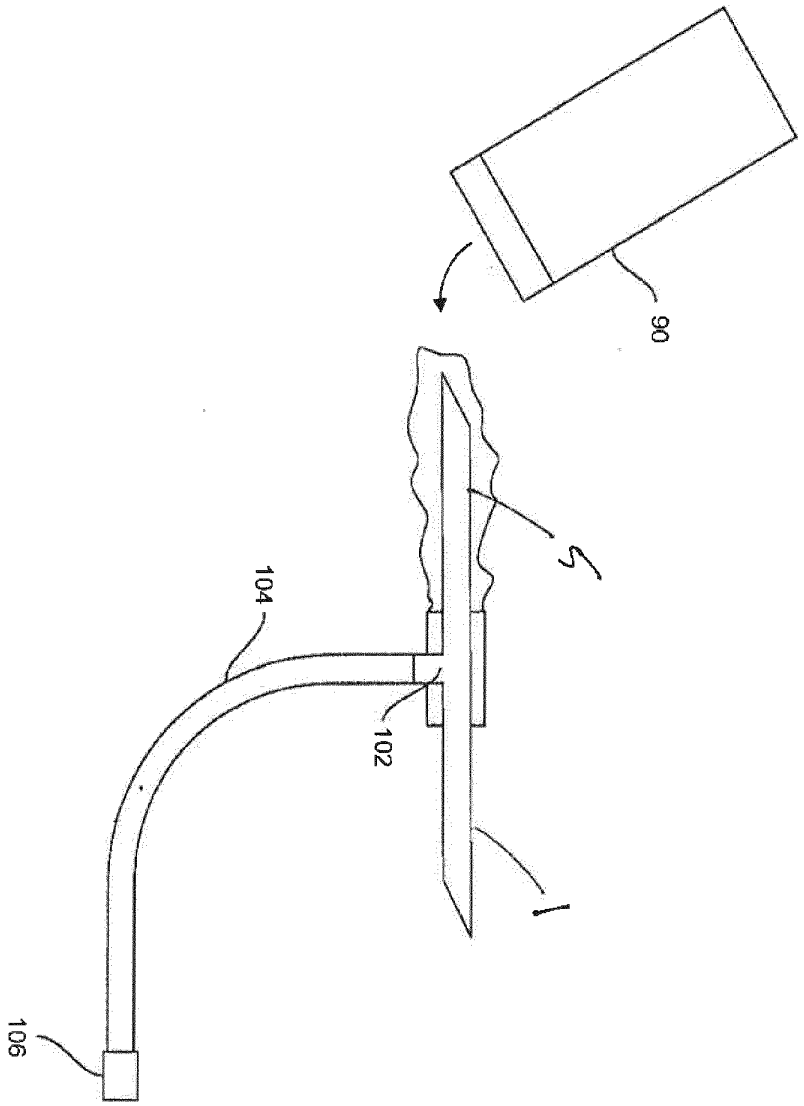


FIG. 3

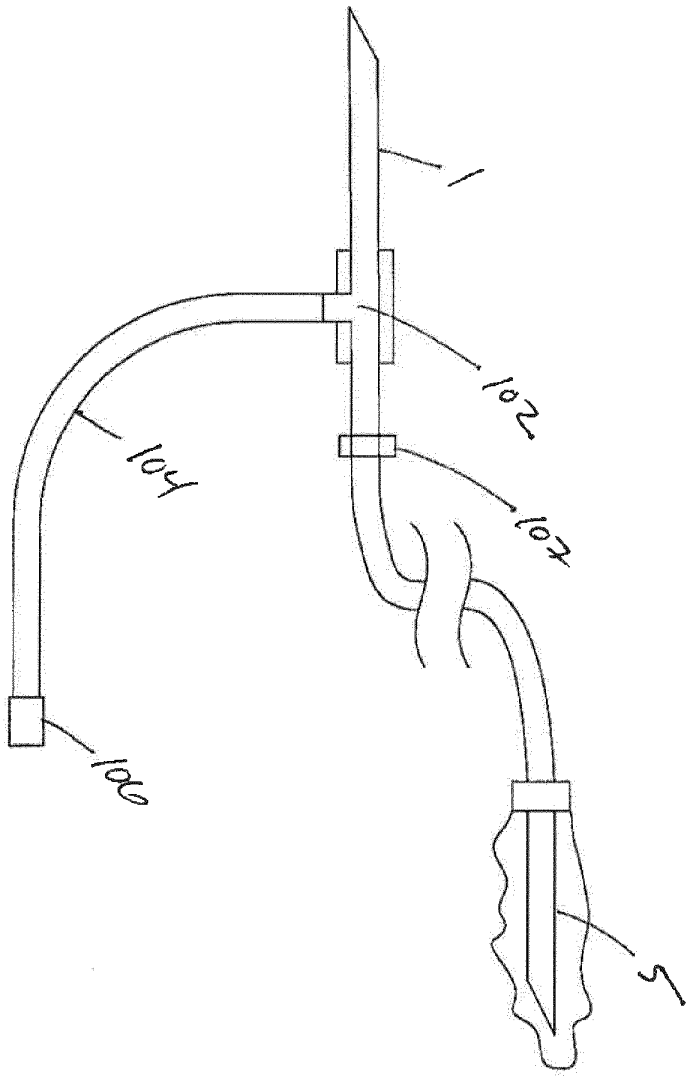


FIG. 4

FIG. 5

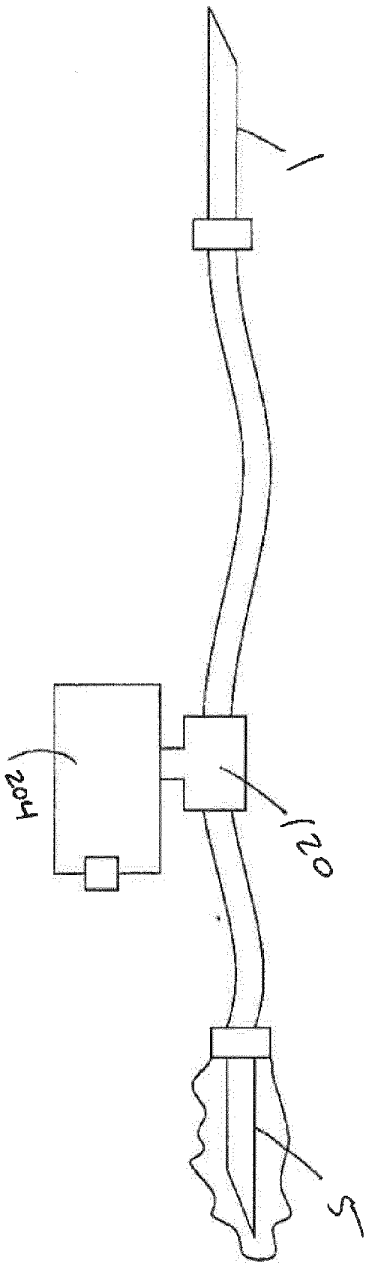
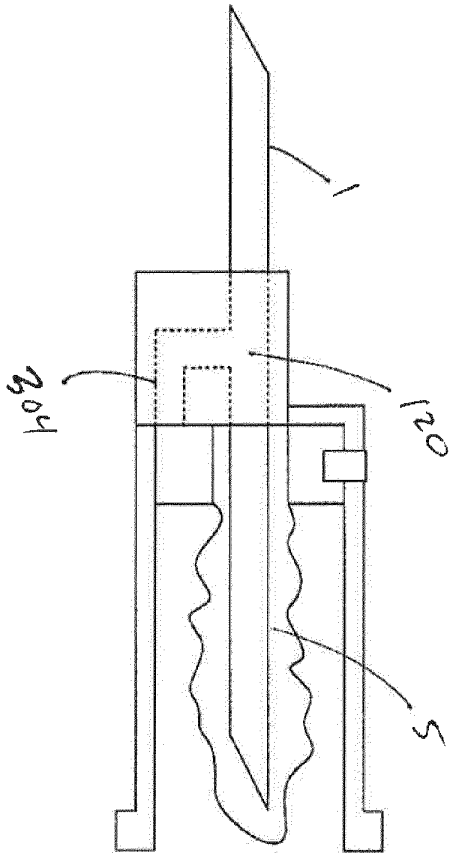


FIG. 6



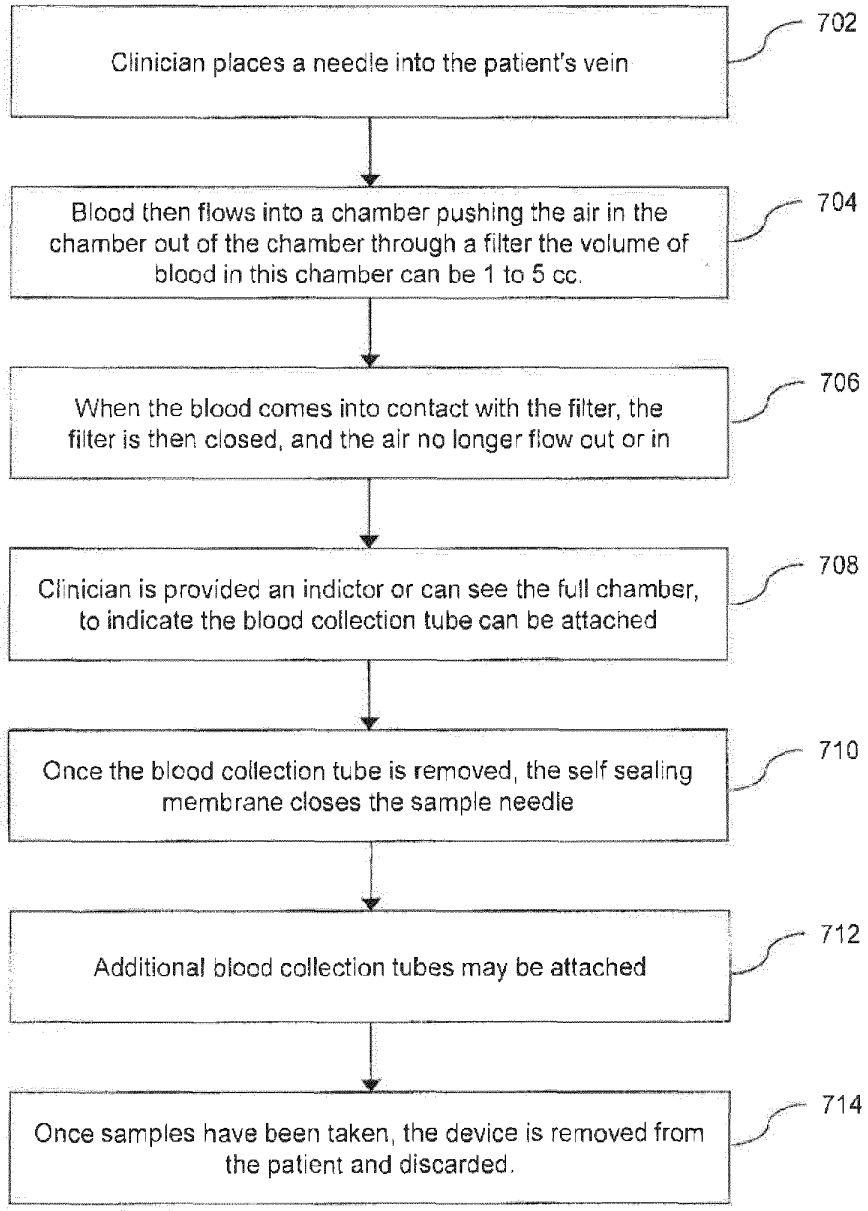

Clinician places a needle into the patient's vein
702
Blood then flows into a chamber pushing the air in the chamber out of the chamber through a filter the volume of blood in this chamber can be 1 to 5 cc.
704
When the blood comes into contact with the filter, the filter is then closed, and the air no longer flow out or in
706
Clinician is provided an indictor or can see the full chamber, to indicate the blood collection tube can be attached
708
Once the blood collection tube is removed, the self sealing membrane closes the sample needle
710
Additional blood collection tubes may be attached
712
Once samples have been taken, the device is removed from the patient and discarded.
714

FIG. 7

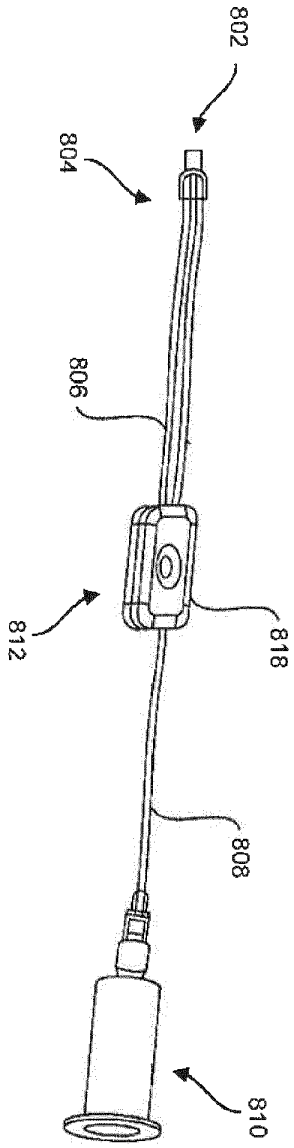


FIG. 8A

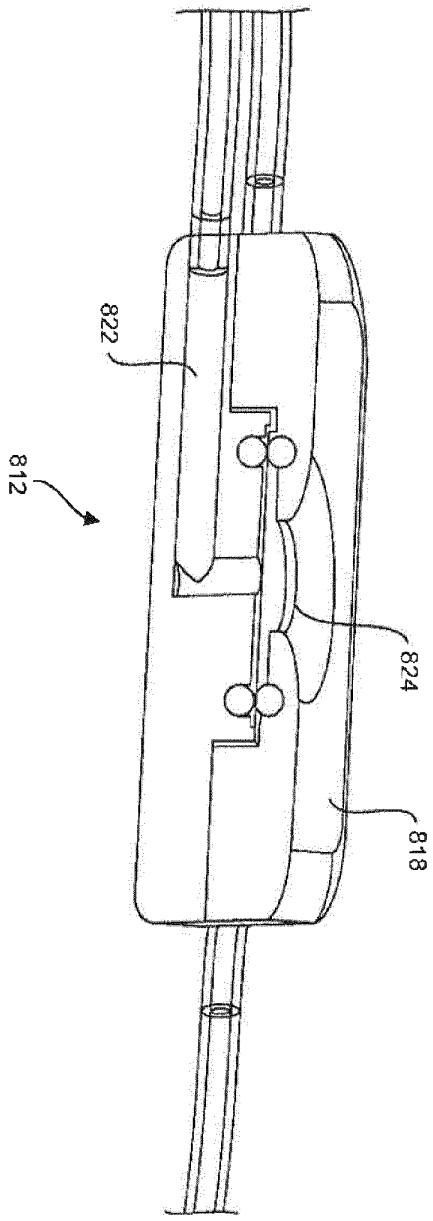


FIG. 8B

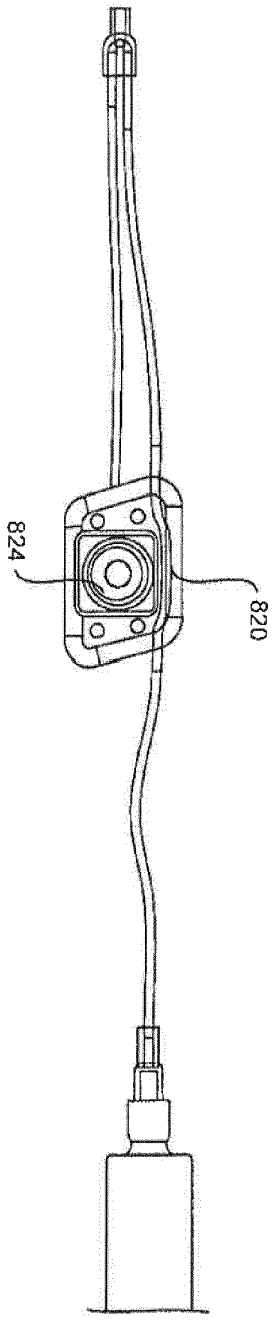


FIG. 8C

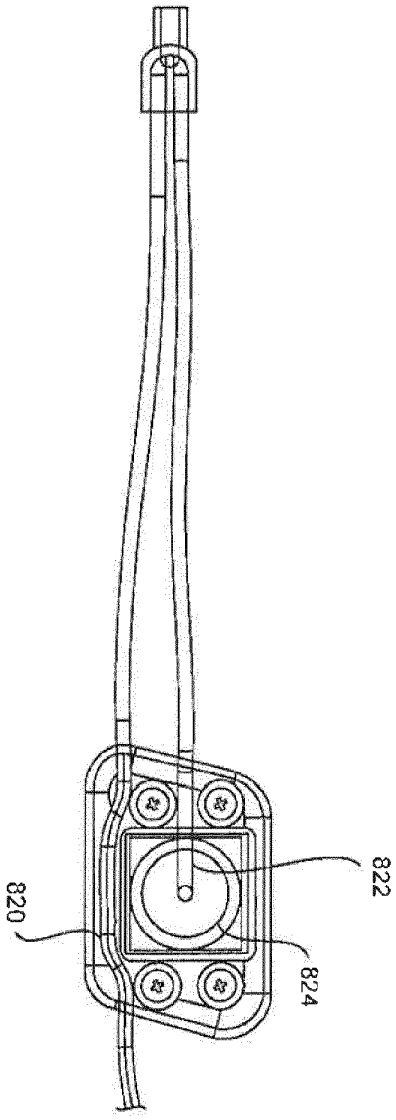


FIG. 8D

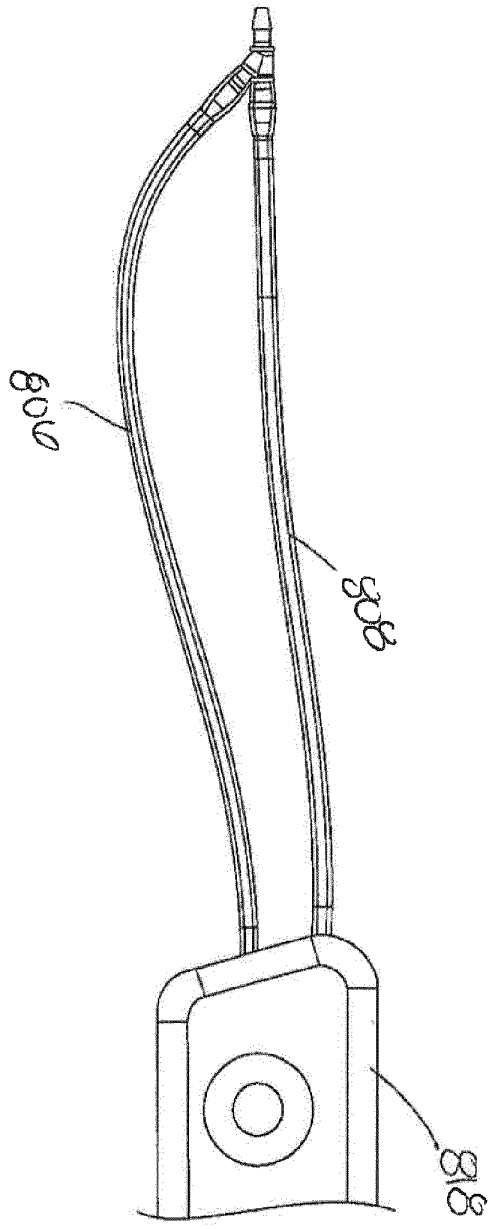


FIG. 8E

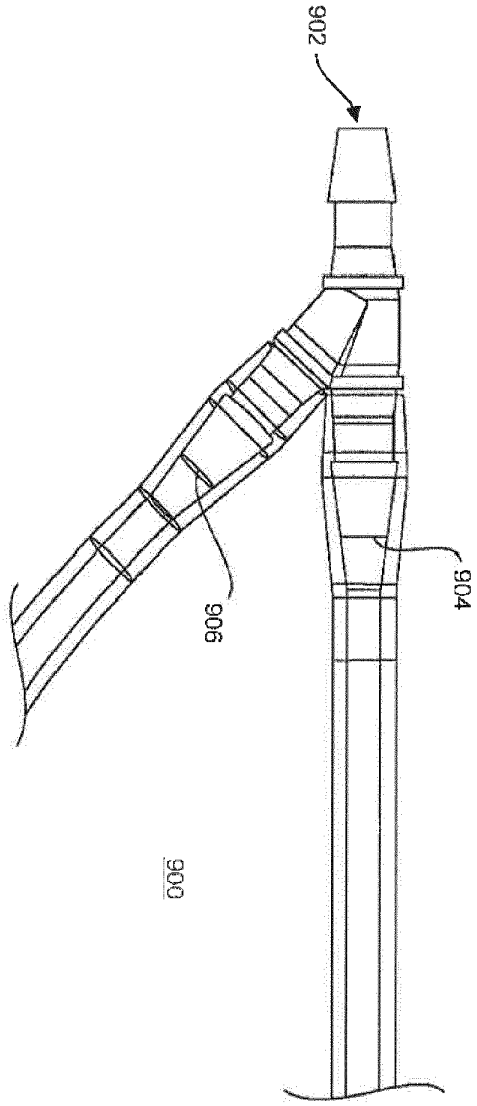


FIG. 9

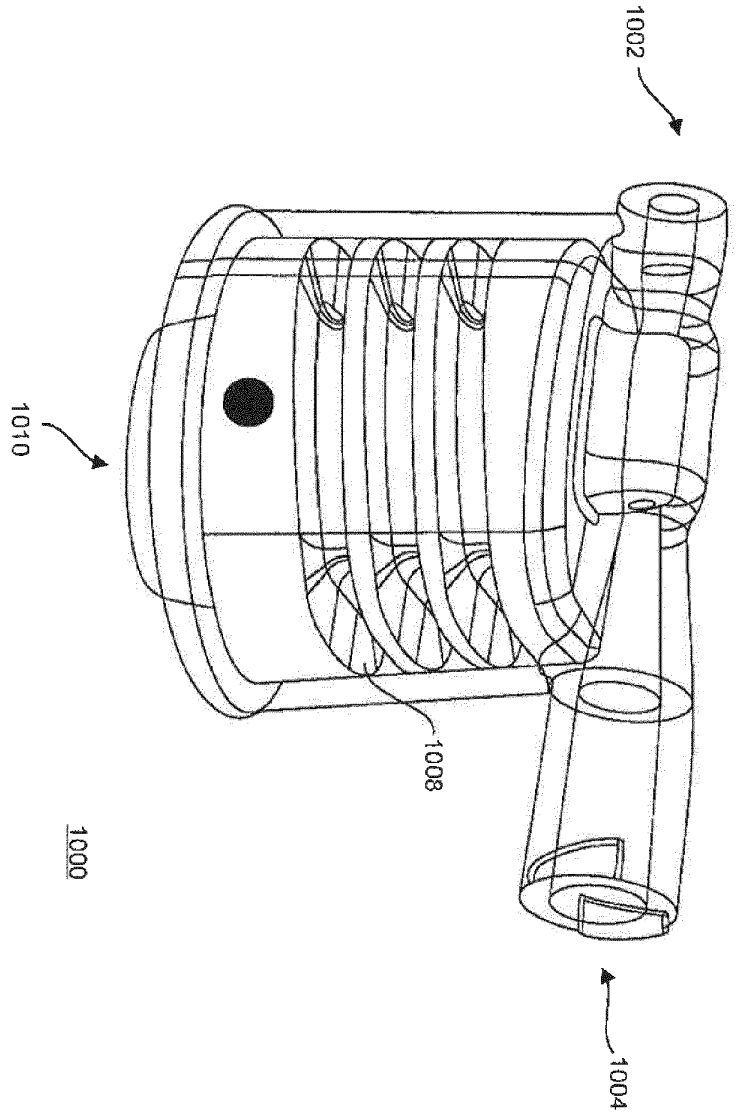


FIG. 10A

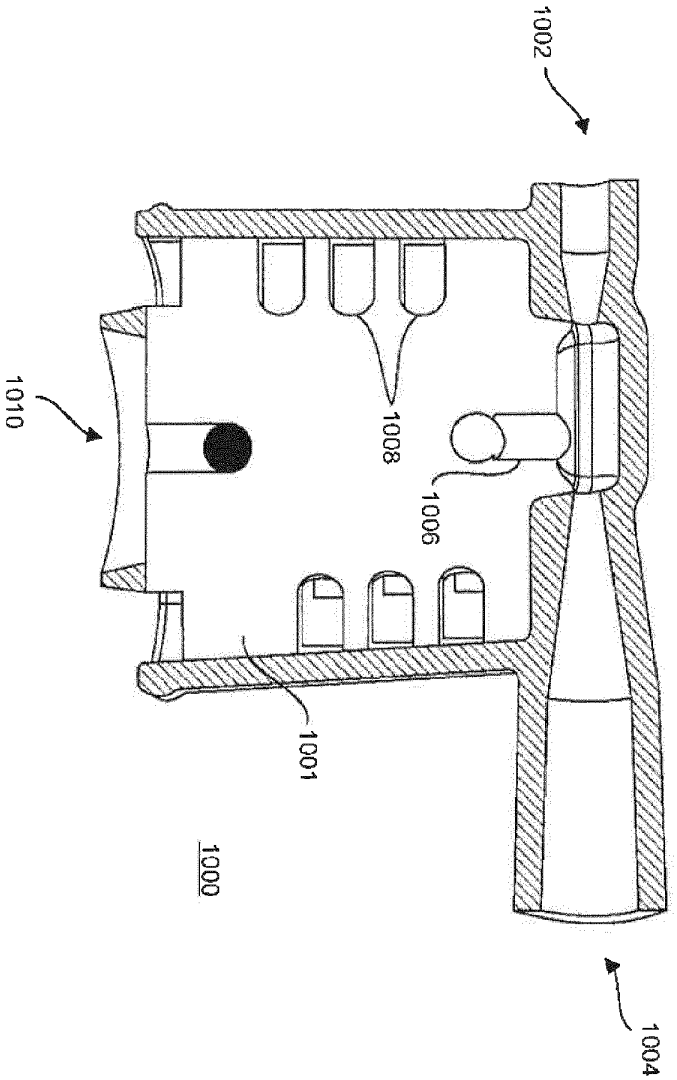


FIG. 10B

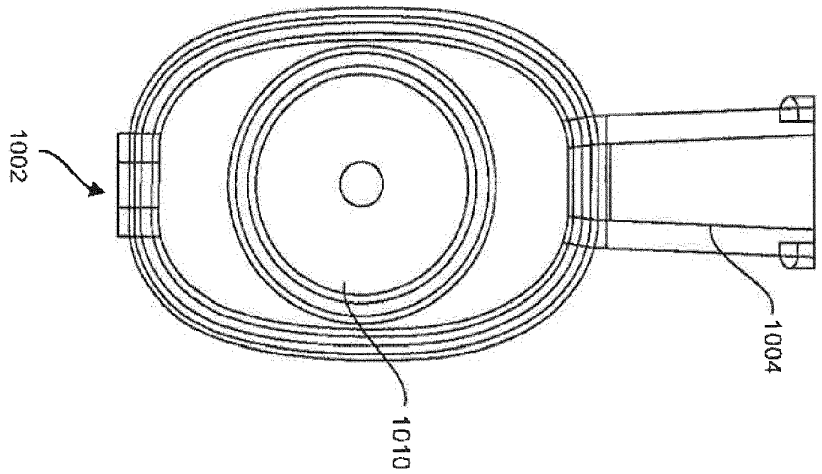


FIG. 10C

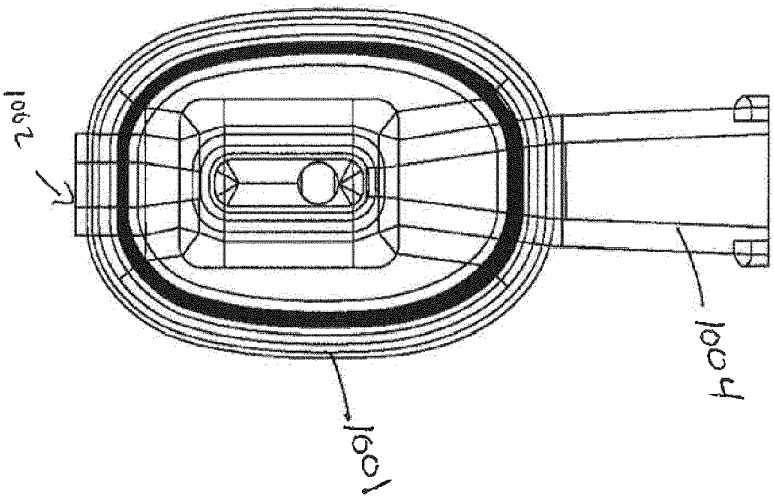
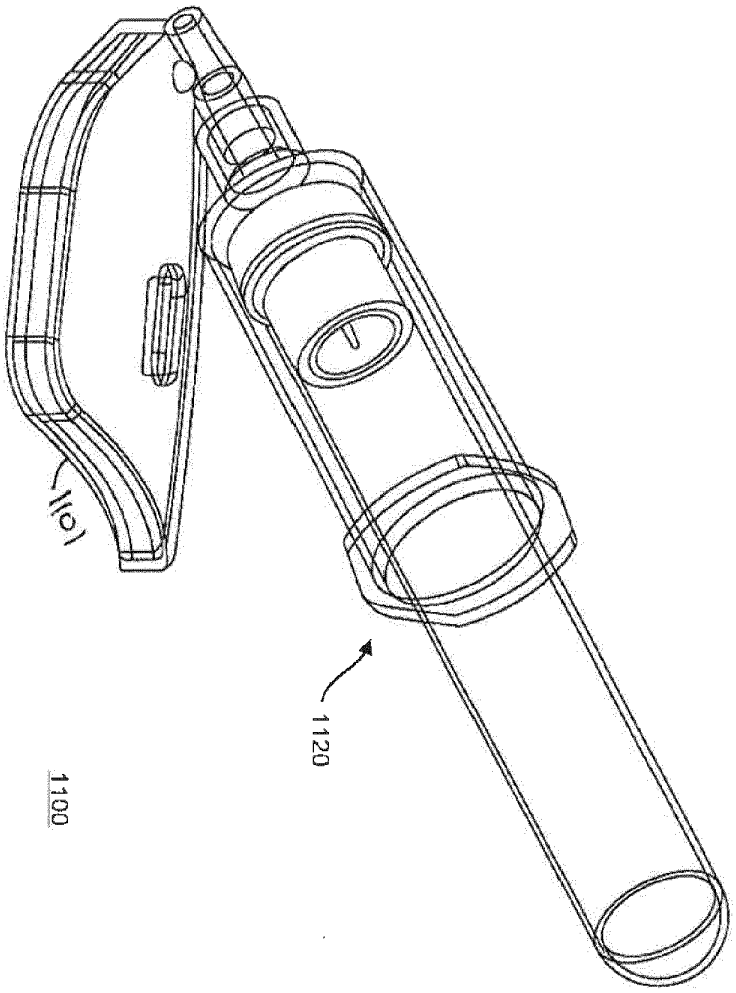


FIG. 10D

FIG. 11A



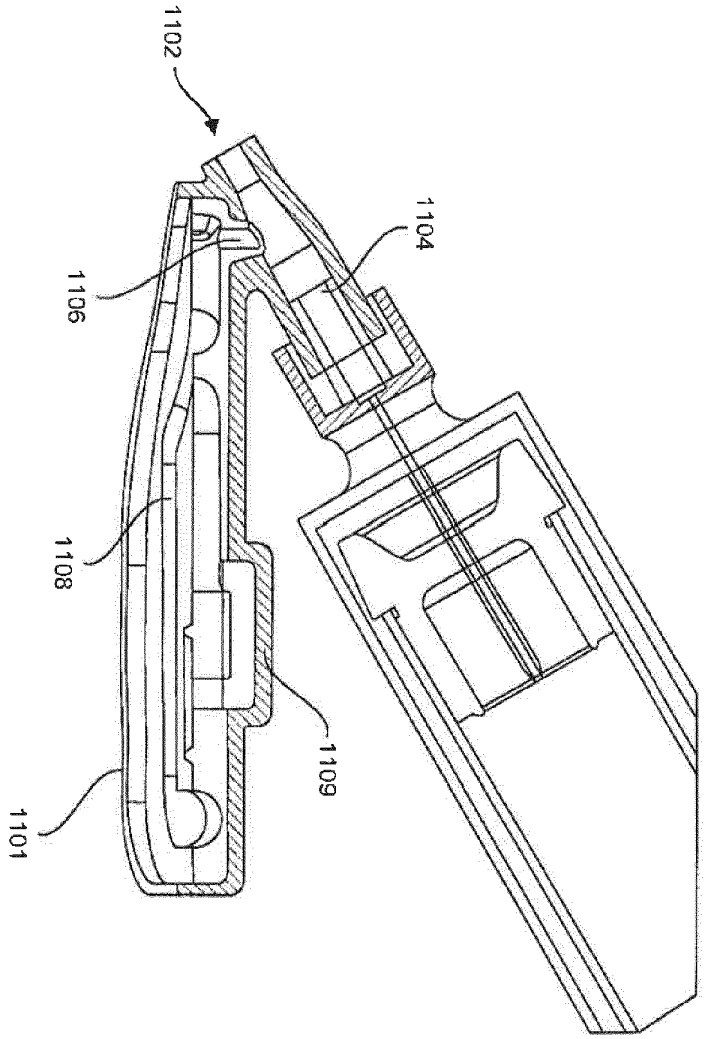


FIG. 11B

FIG. 11C

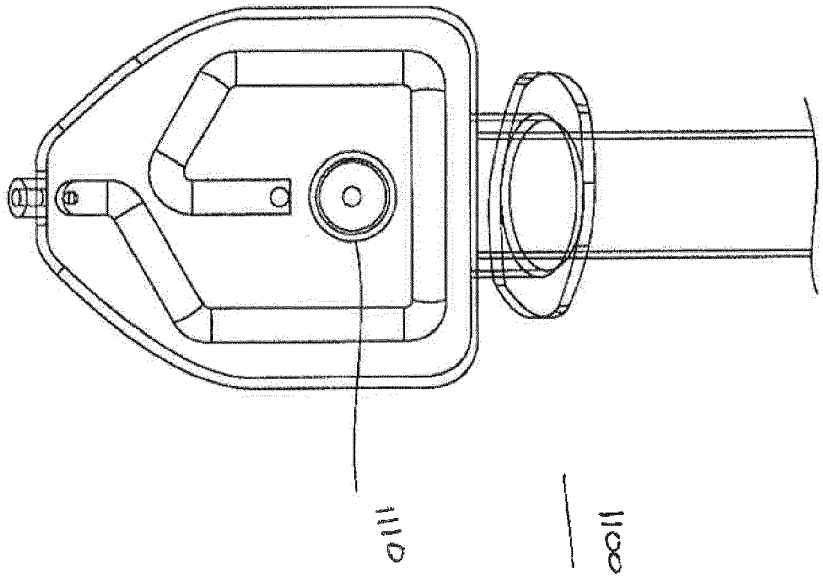
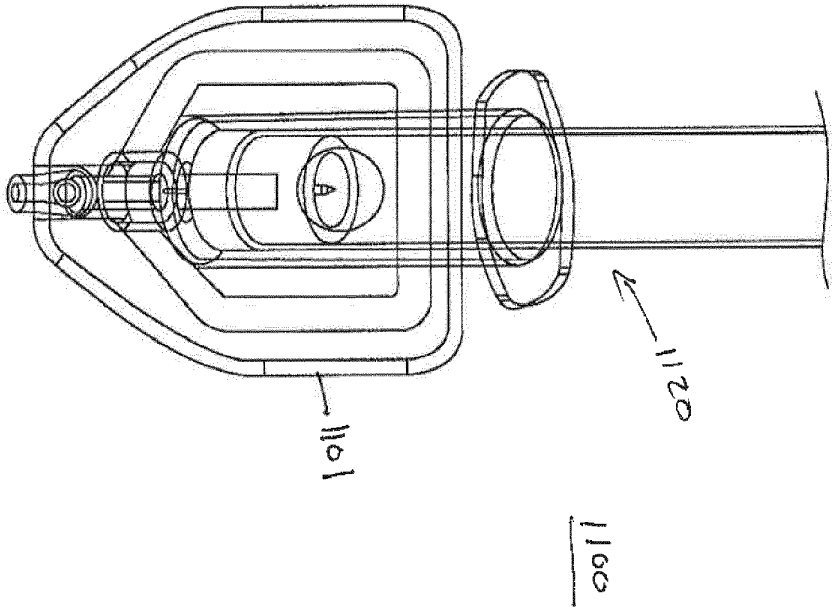


FIG. 11D



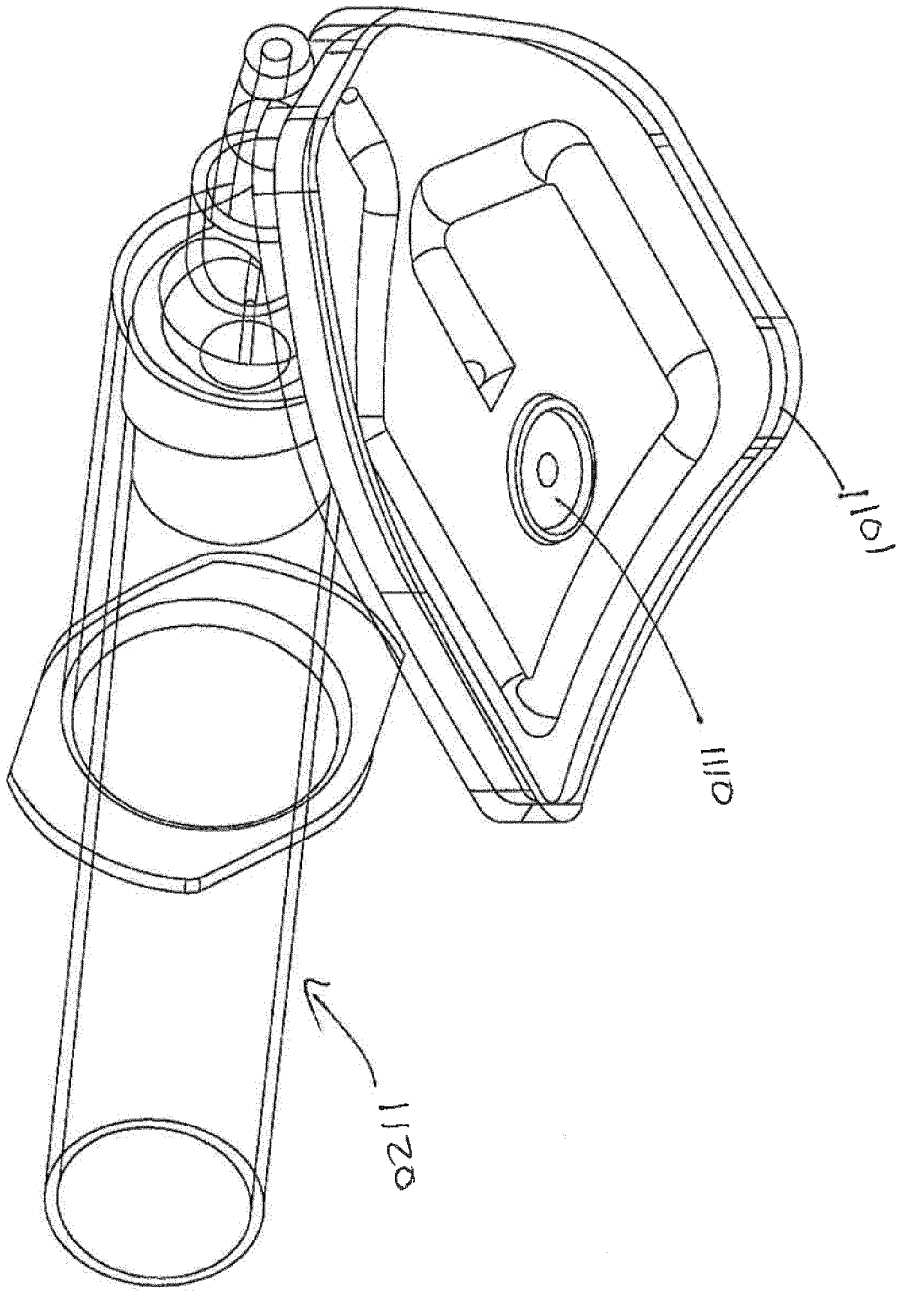


FIG. 11E

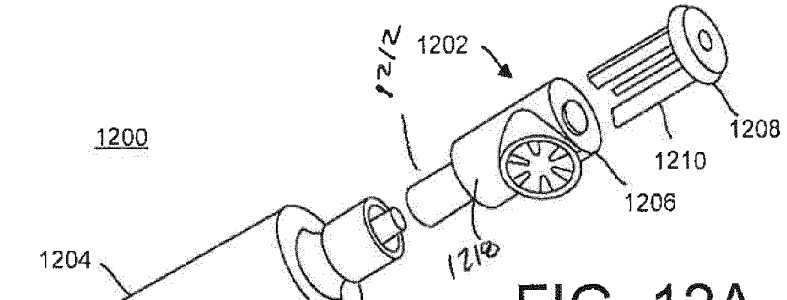


FIG. 12A

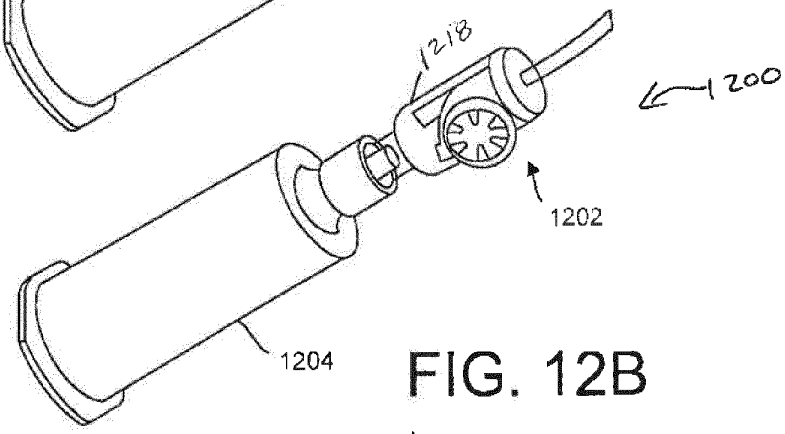


FIG. 12B

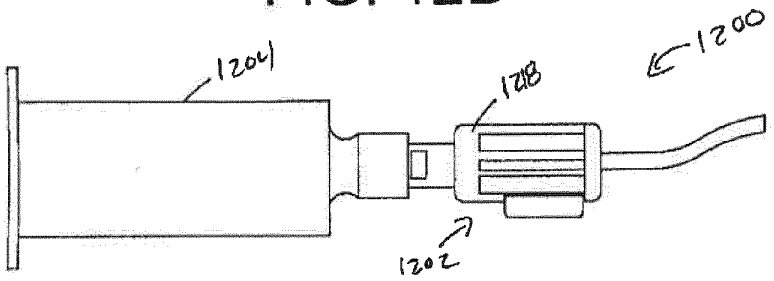


FIG. 12C

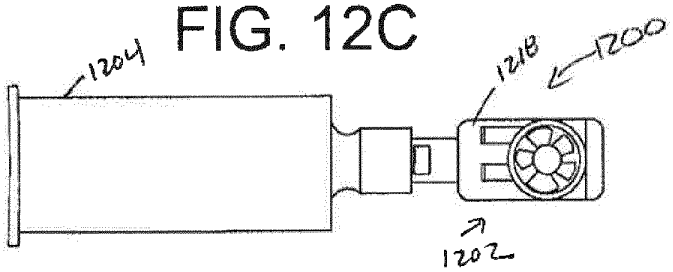


FIG. 12D

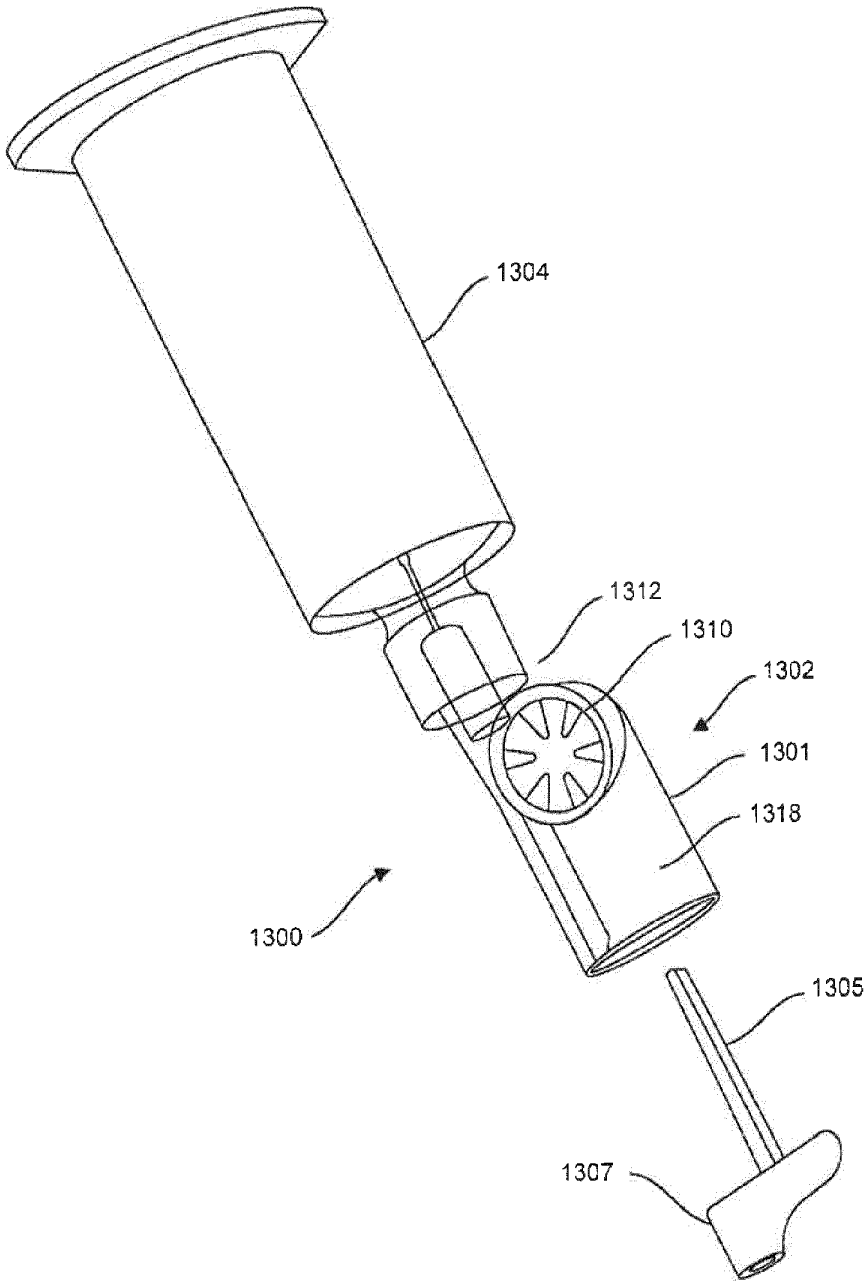


FIG. 13A

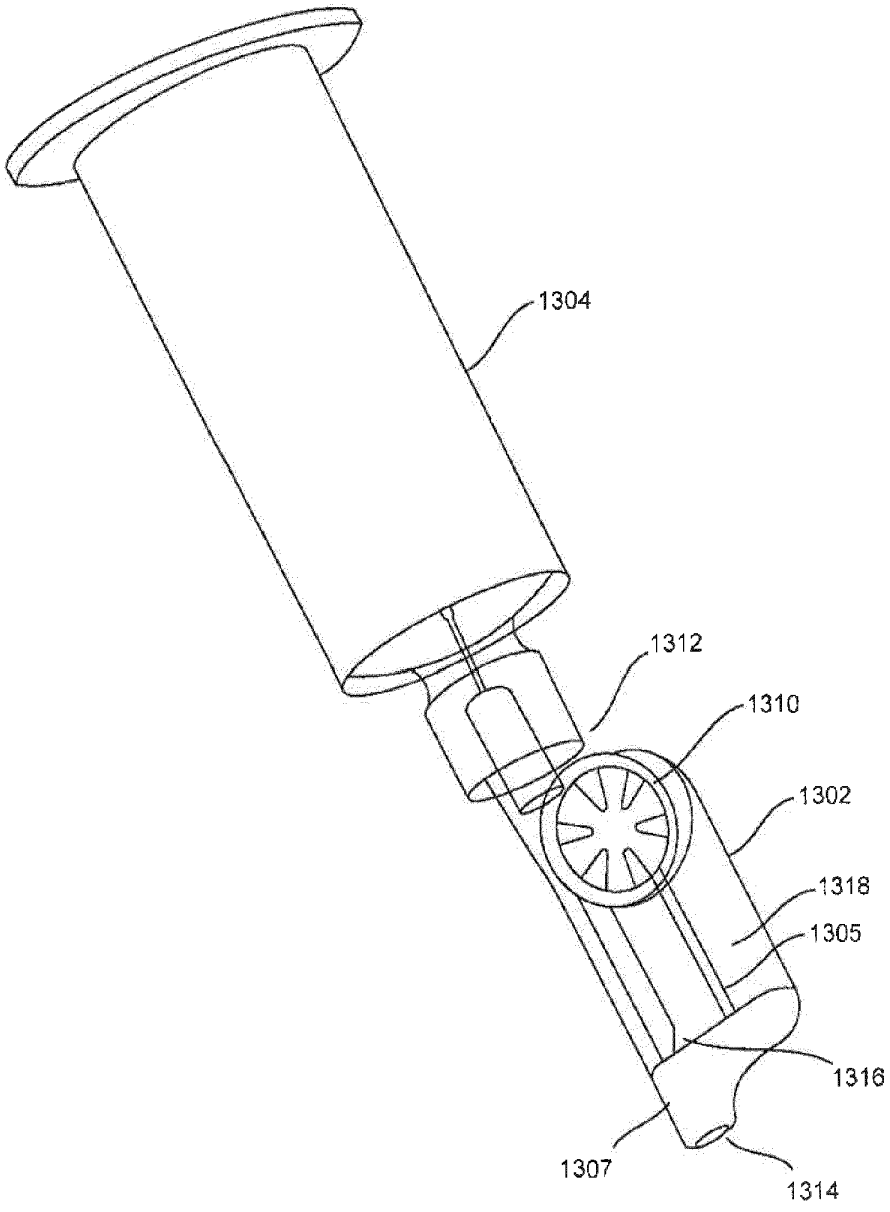


FIG. 13B

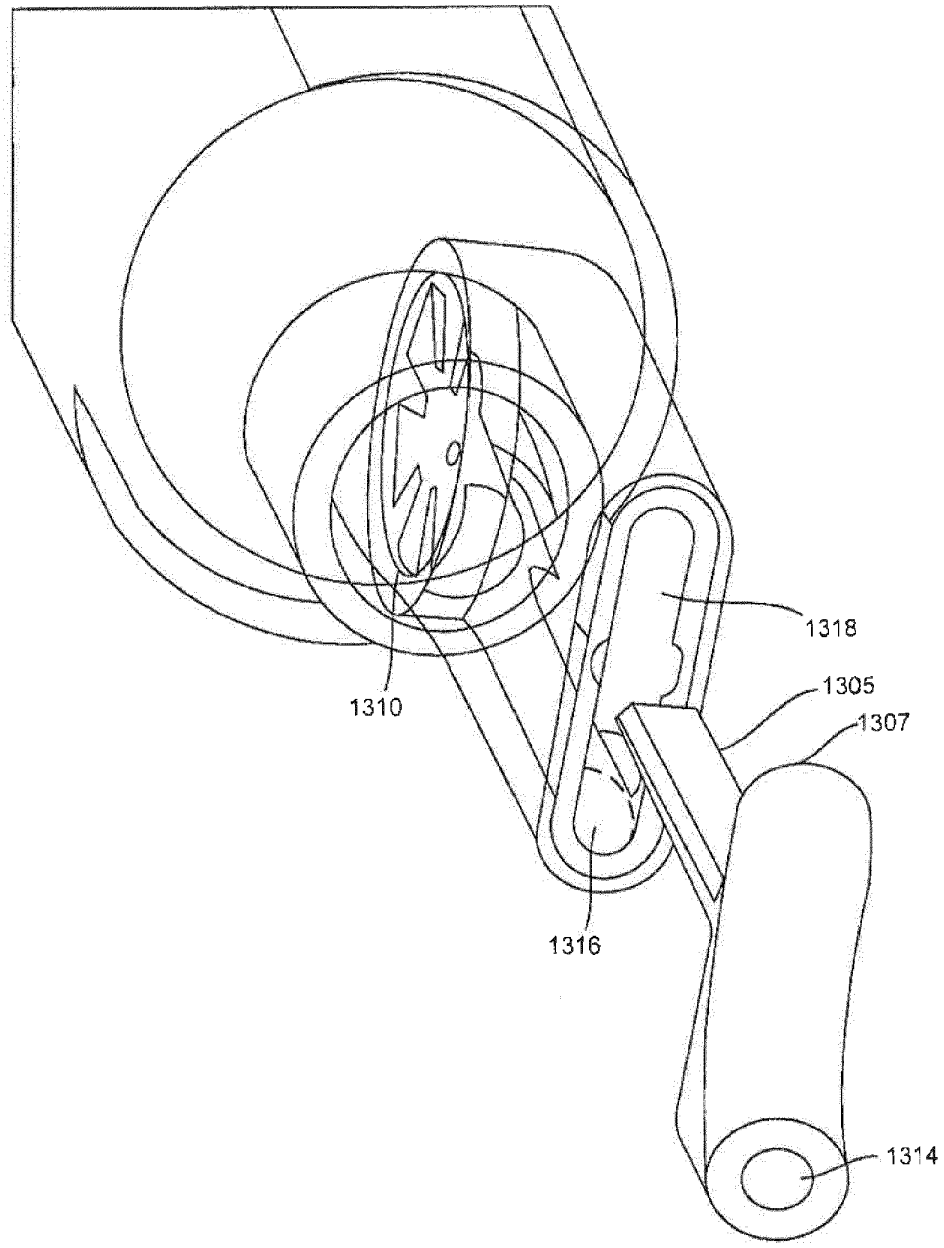


FIG. 13C

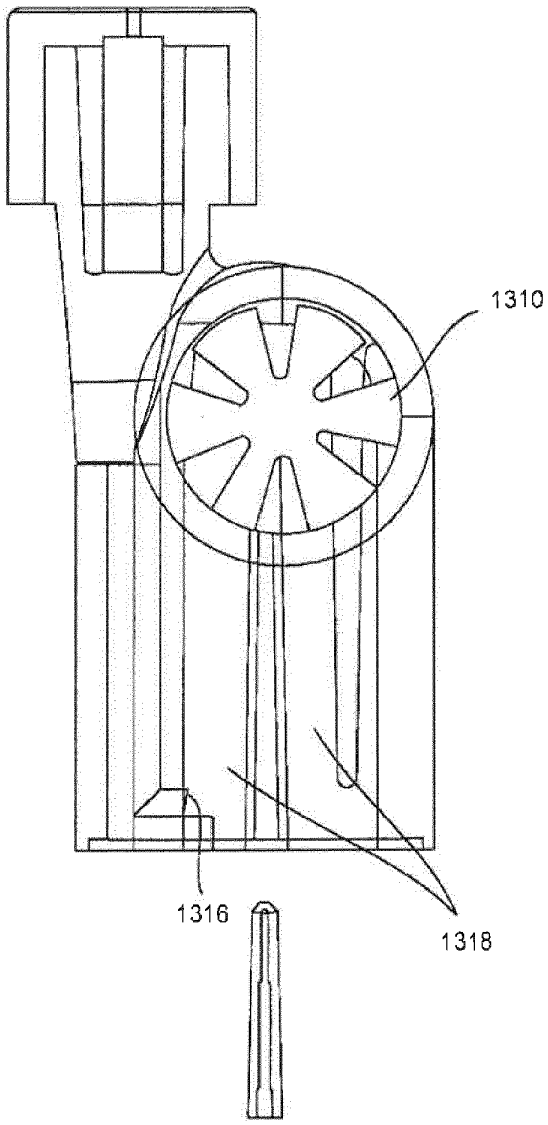


FIG. 13D

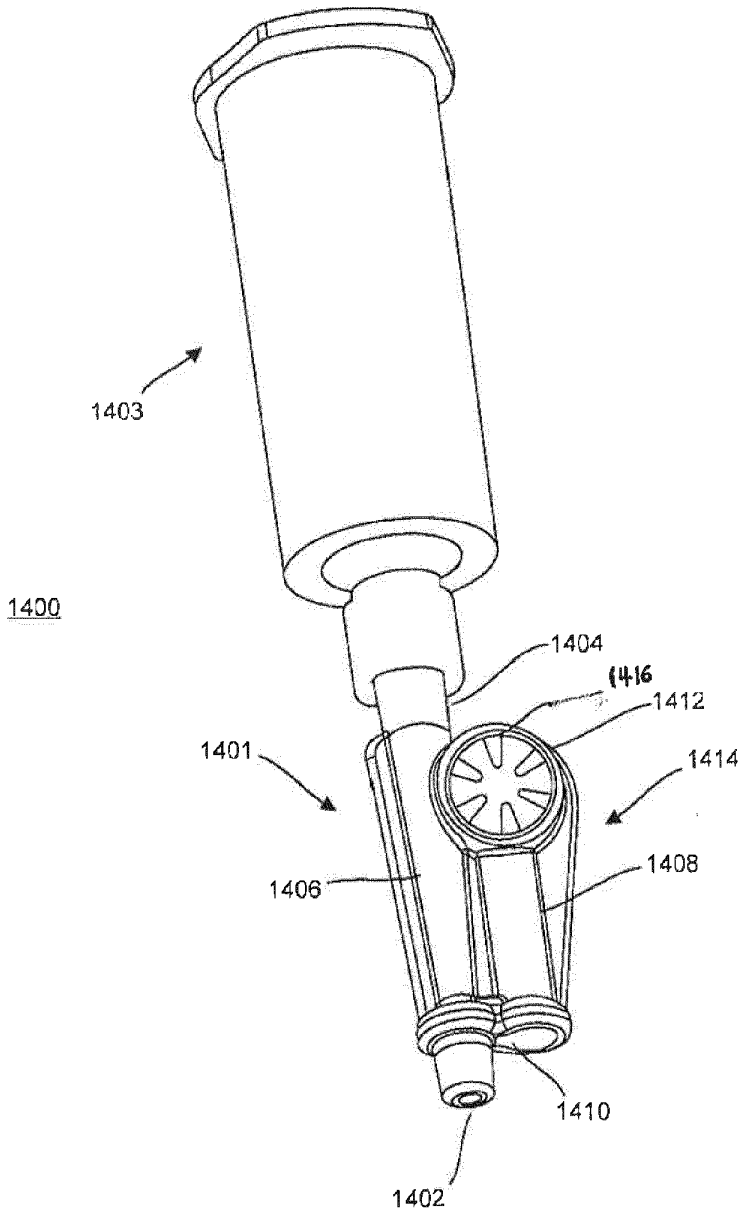


FIG. 14A

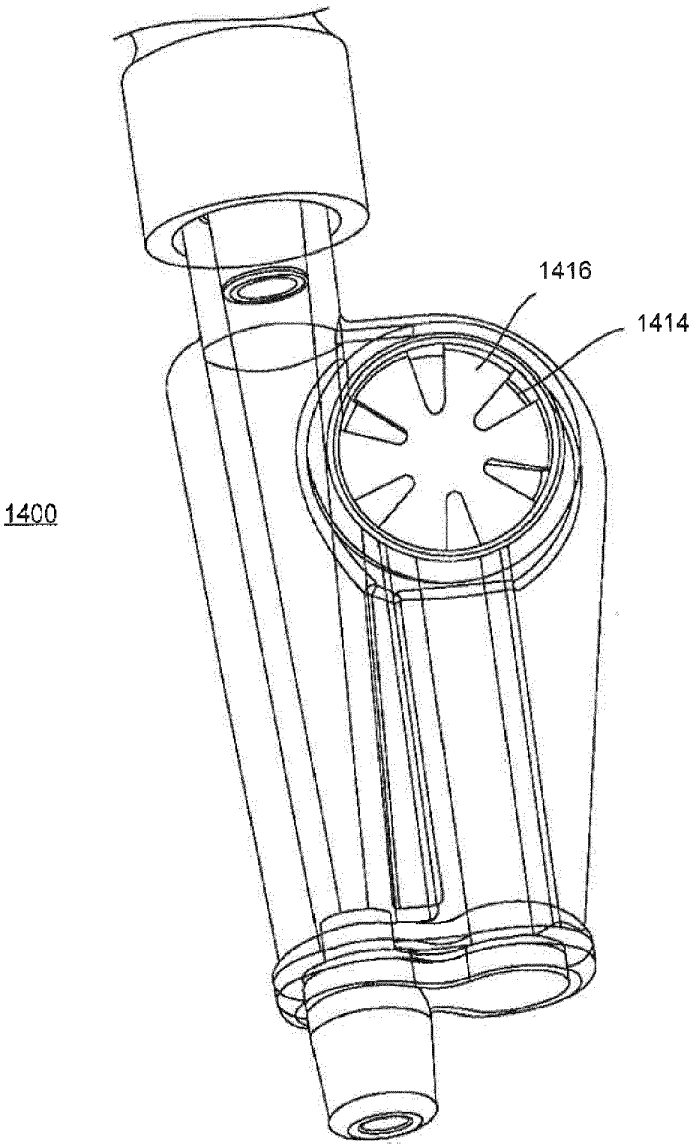


FIG. 14B

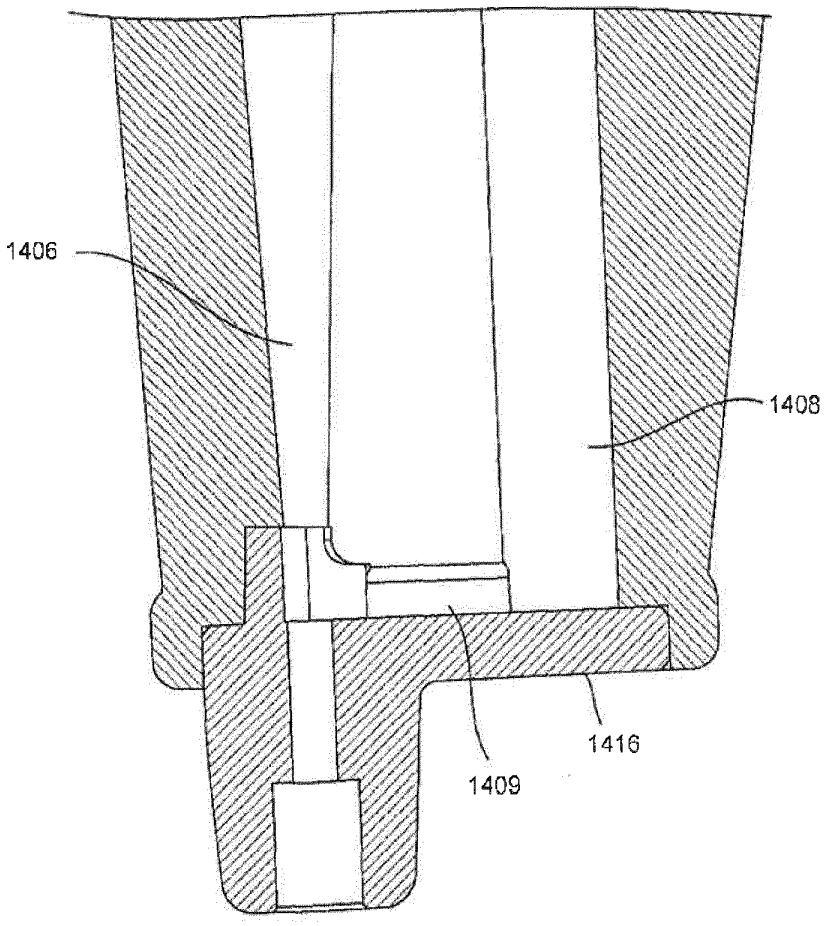


FIG. 14C

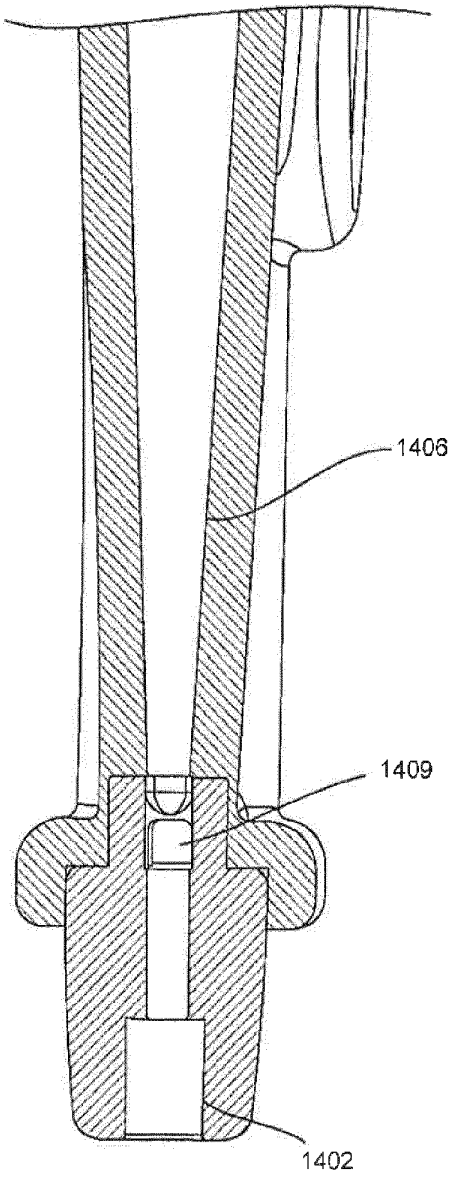


FIG. 14D

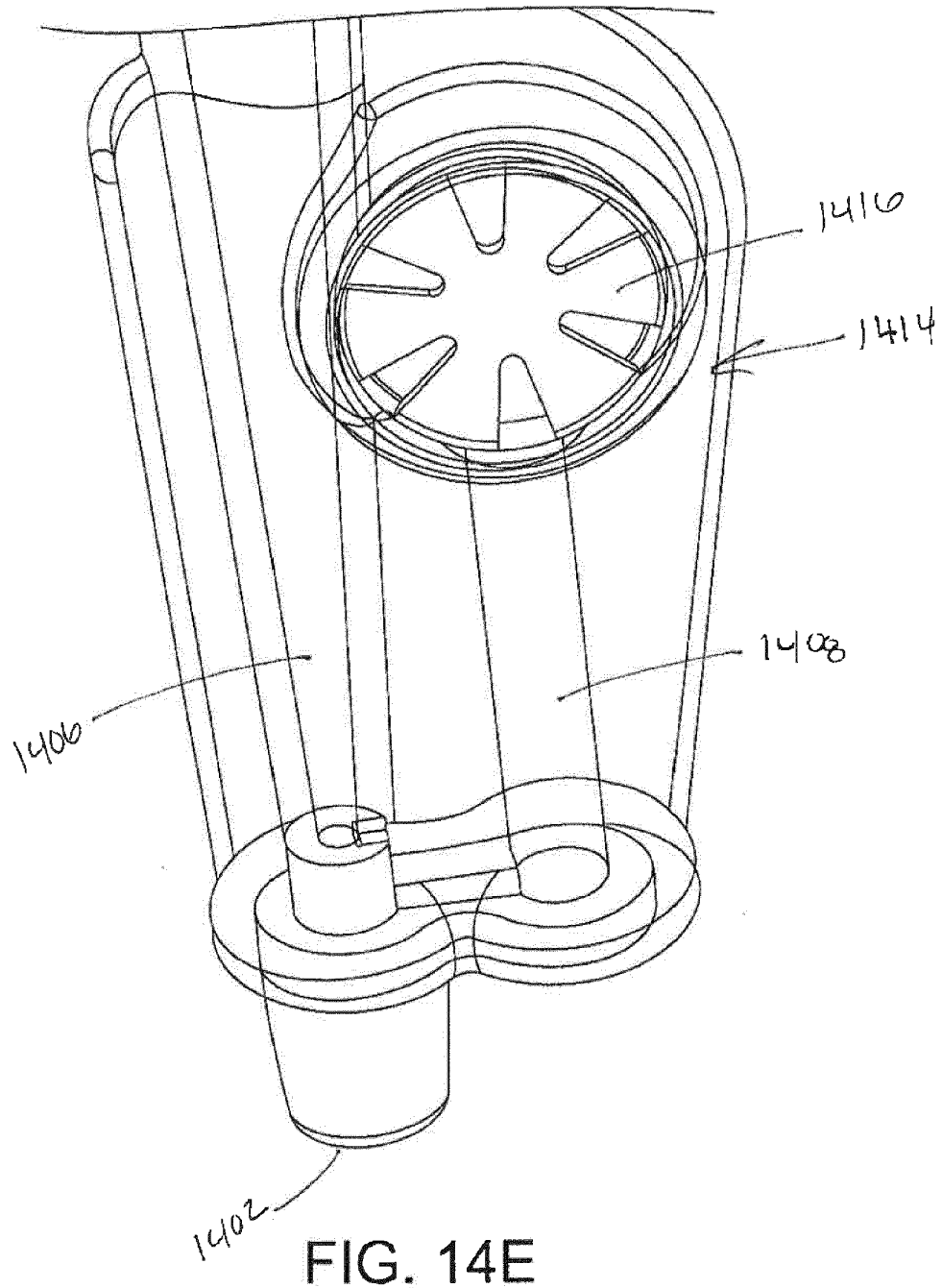


FIG. 14E

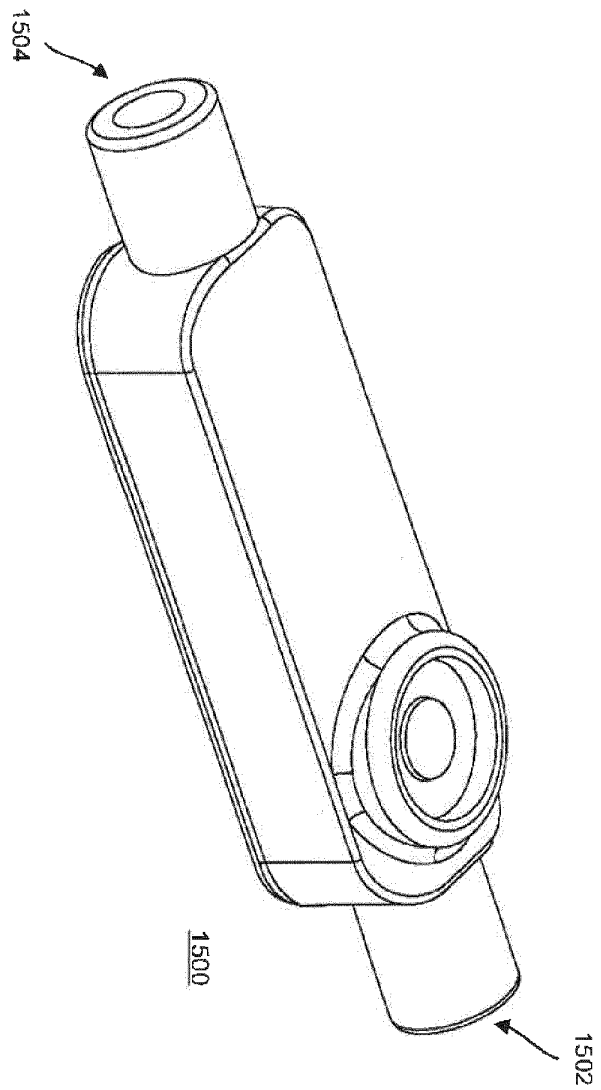


FIG. 15A

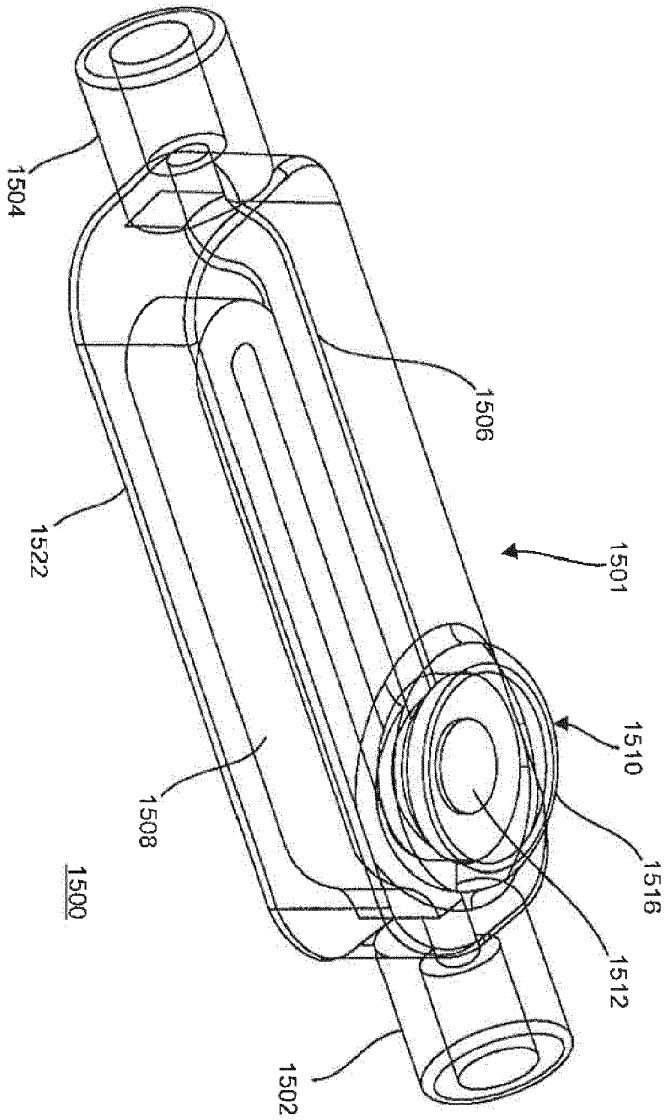


FIG. 15B

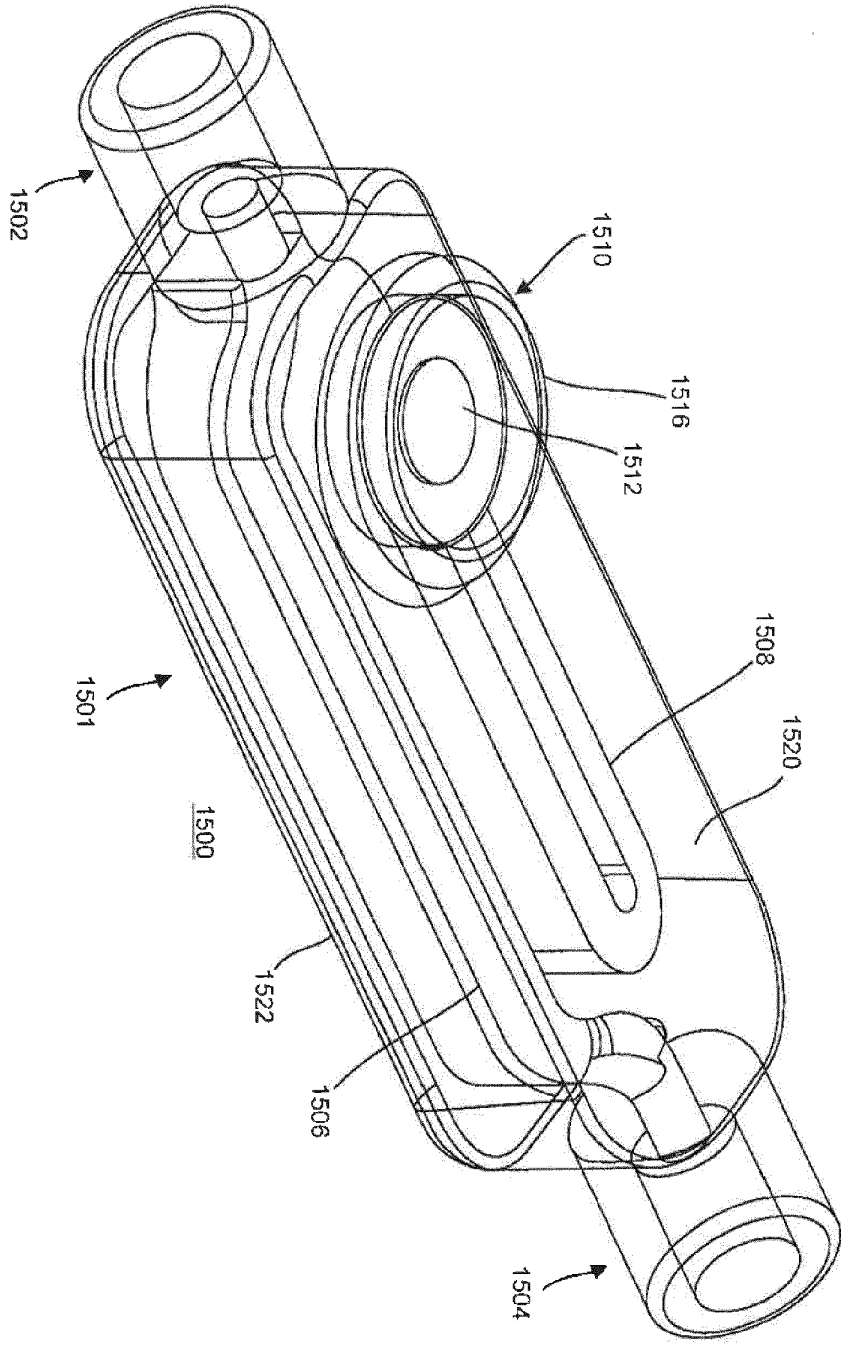


FIG. 15C

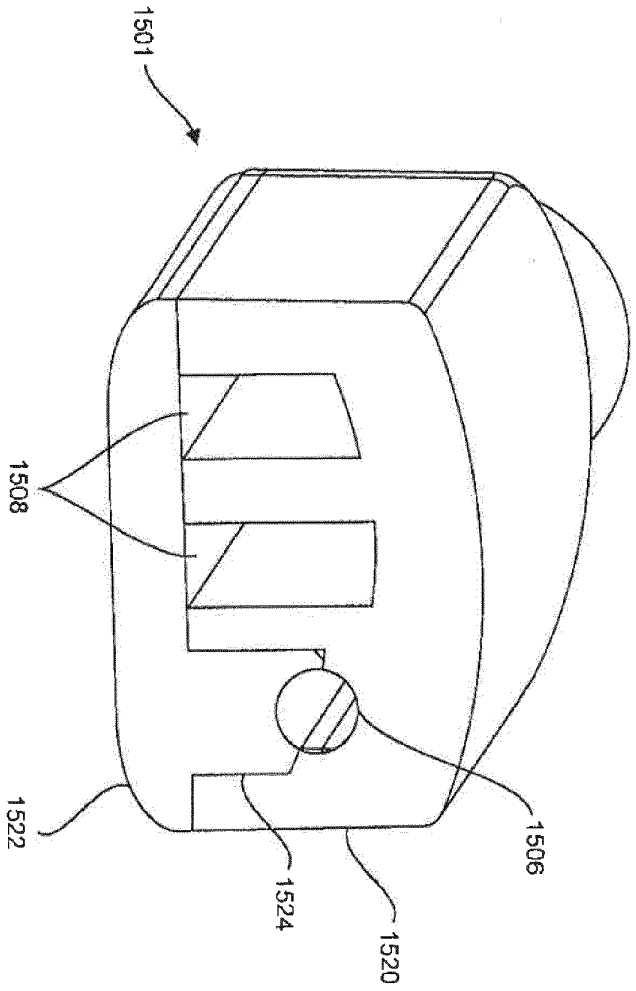


FIG. 15D

FIG. 15E

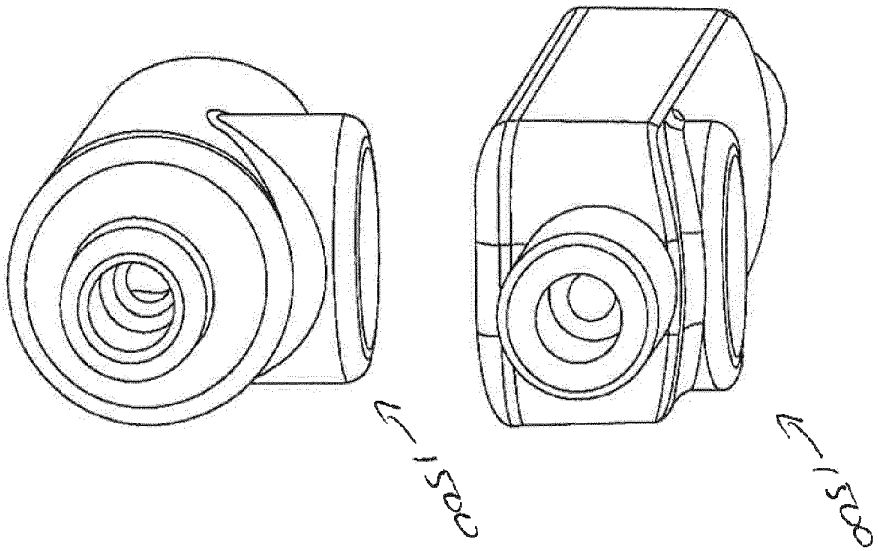
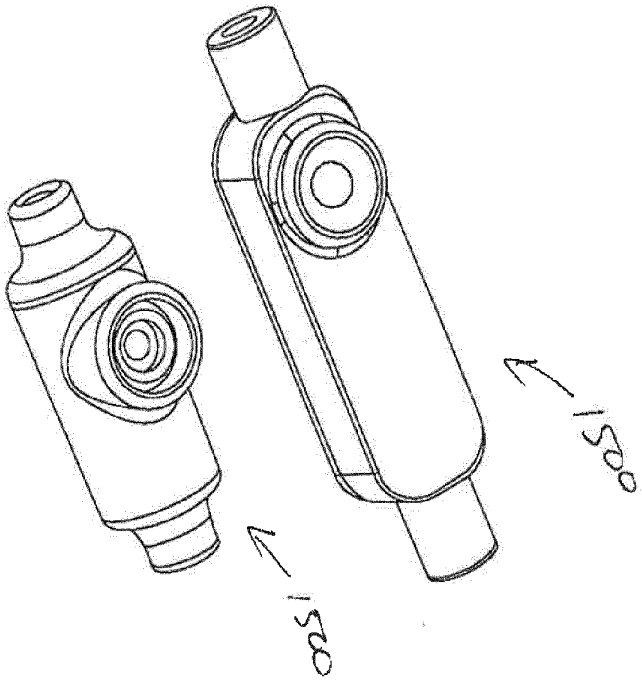


FIG. 15F



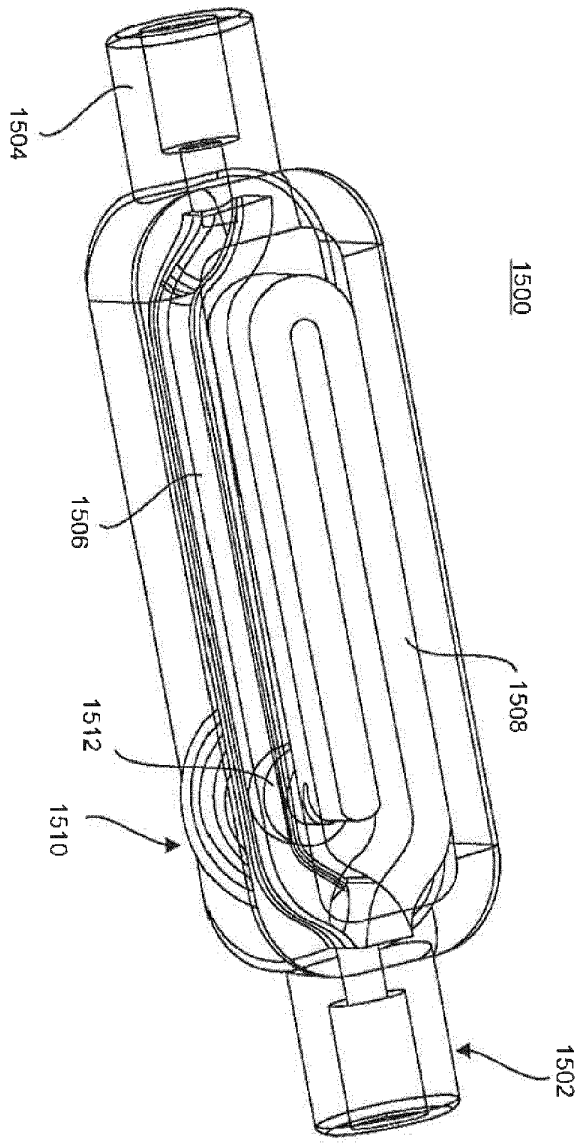


FIG. 15G

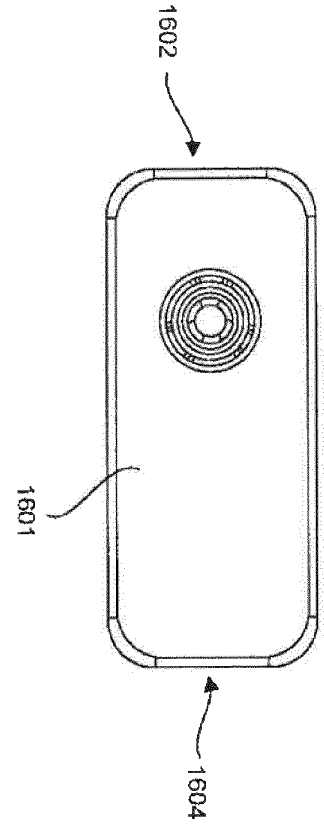


FIG. 16A

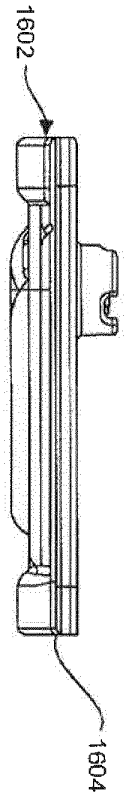


FIG. 16B

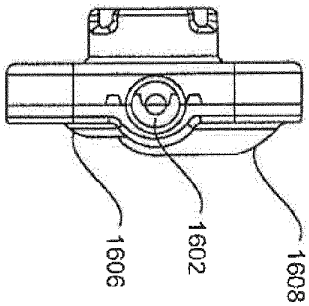


FIG. 16C

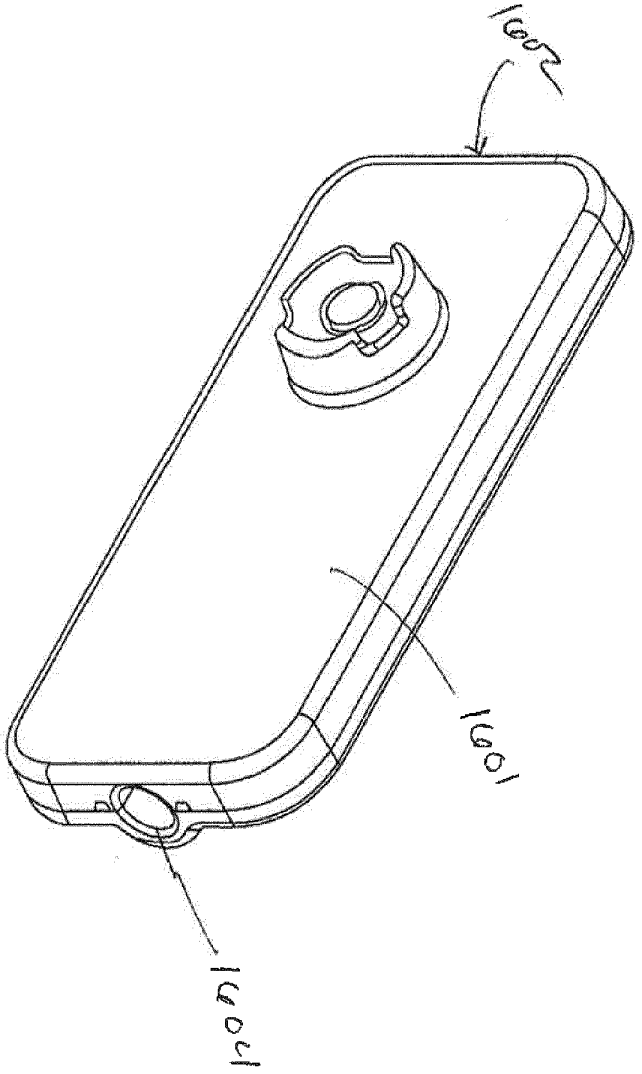


FIG. 16D

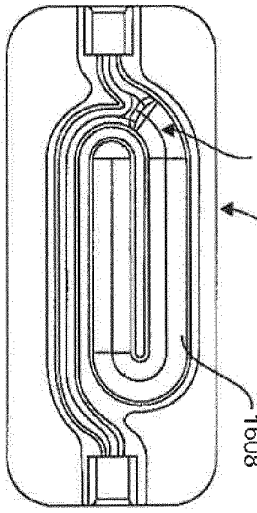


FIG. 17A

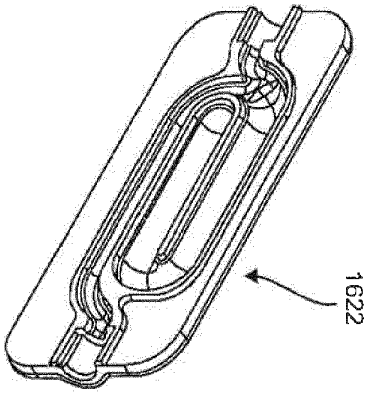


FIG. 17B

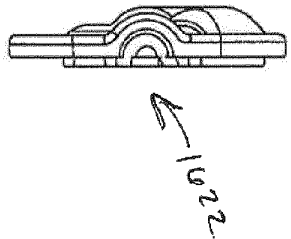


FIG. 17C



FIG. 17D

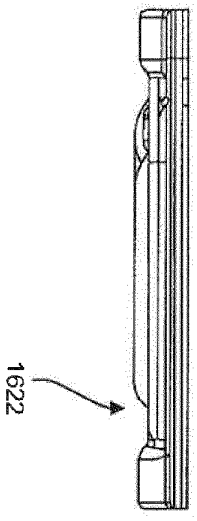


FIG. 17E

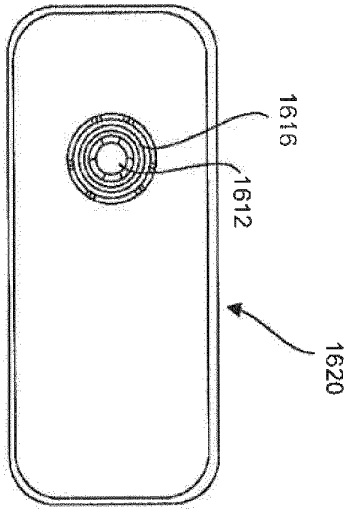


FIG. 18A

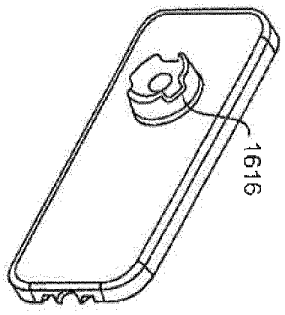


FIG. 18B

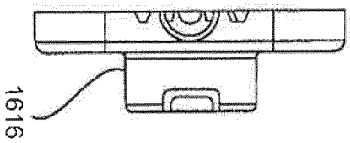


FIG. 18C

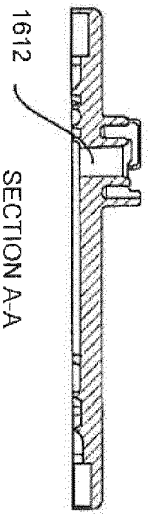


FIG. 18D

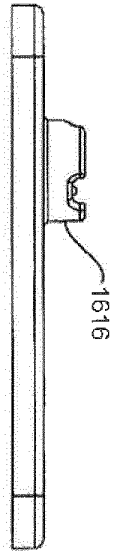


FIG. 18E

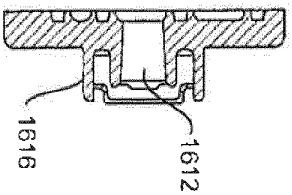


FIG. 18F

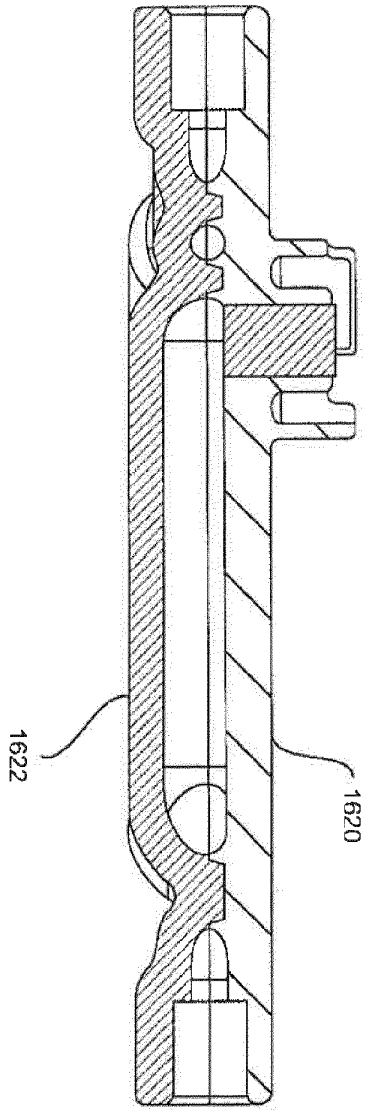


FIG. 19A

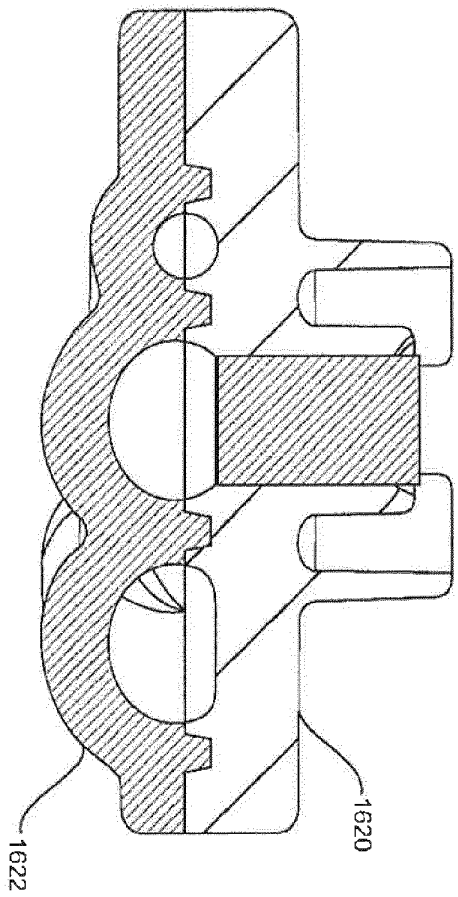


FIG. 19B

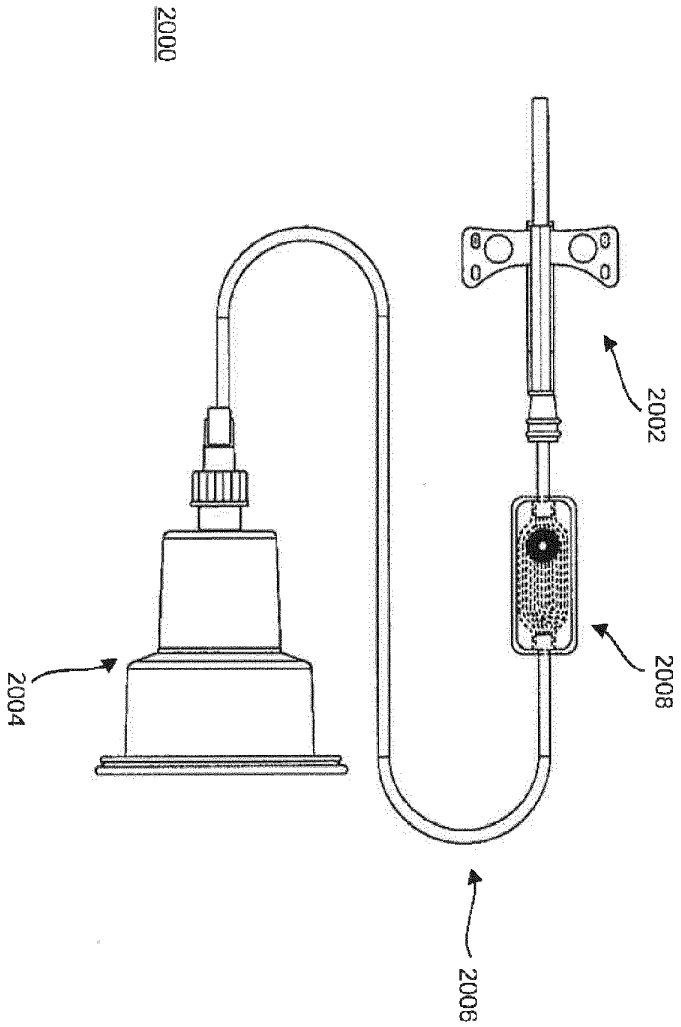


FIG. 20

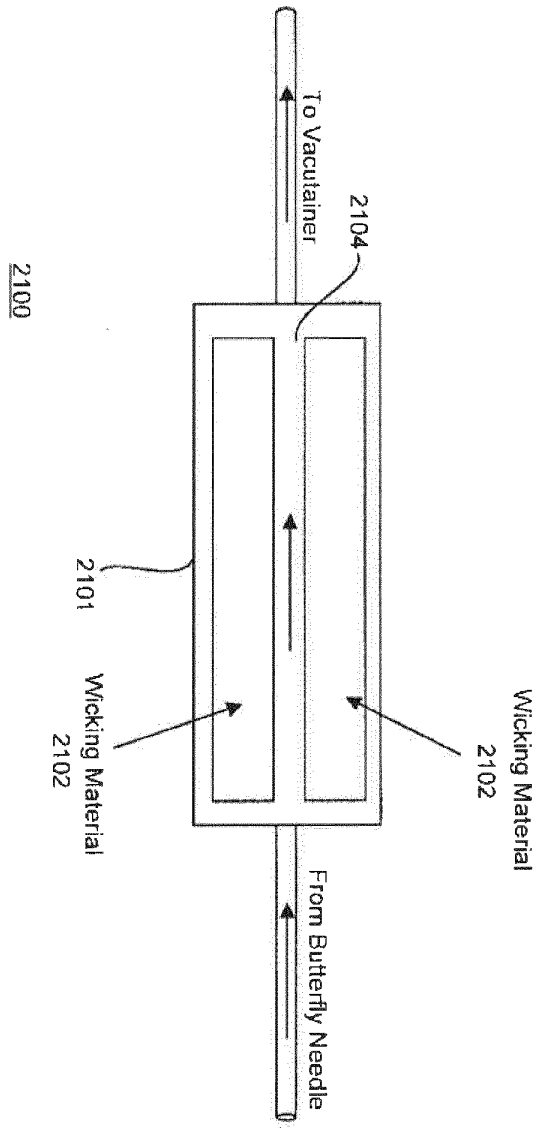

2100
To Vacutainer
2104
2101
Wicking Material
2102
Wicking Material
2102
From Butterfly Needle

FIG. 21

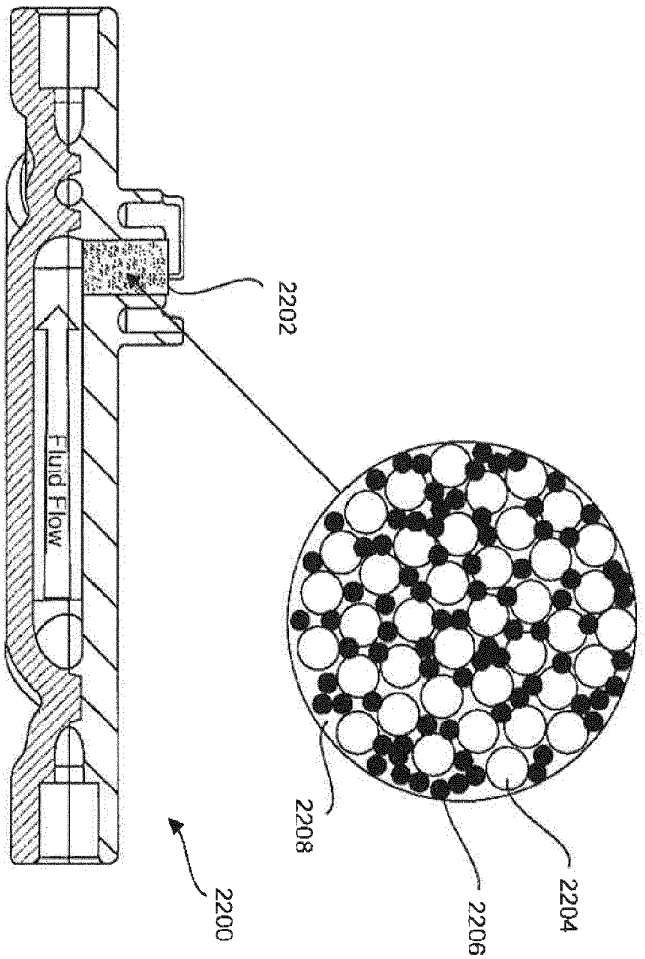


FIG. 22A

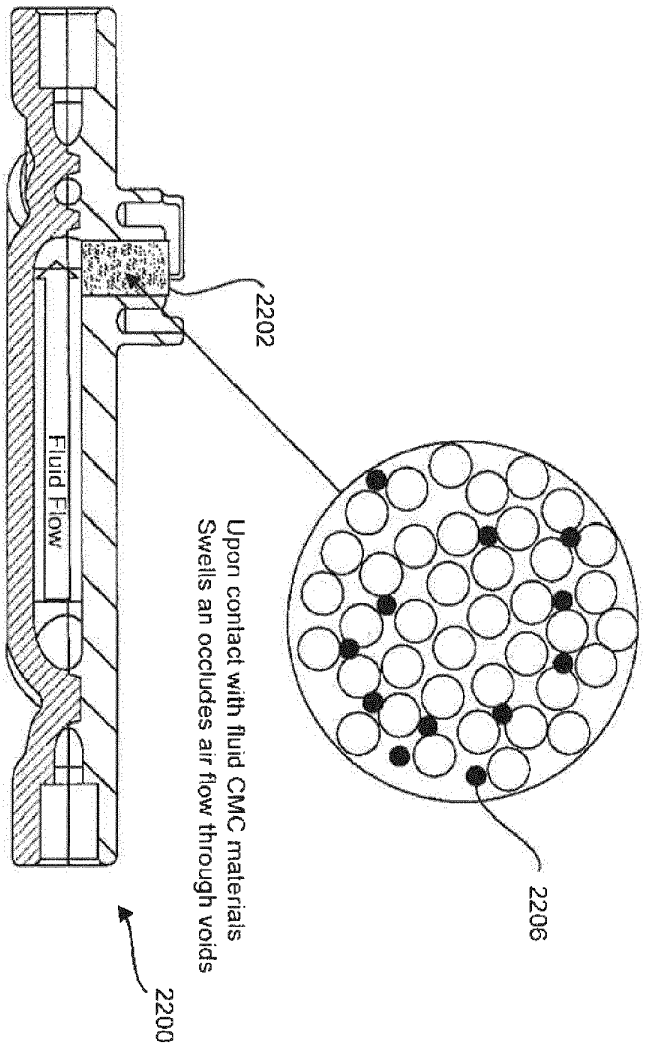

2202
Fluid Flow
Upon contact with fluid CMC materials
Swells an occludes air flow through voids
2206
2200

FIG. 22B

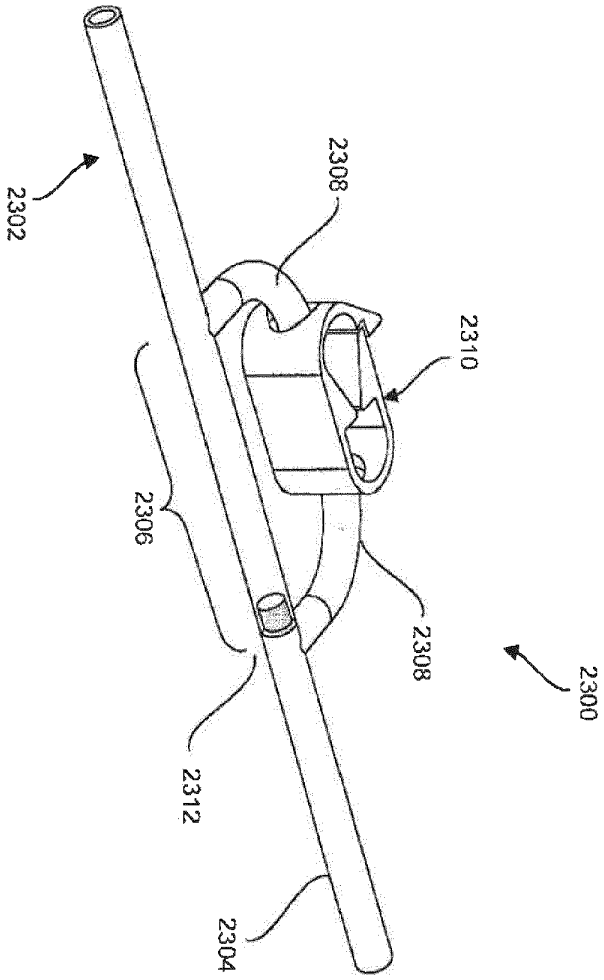


FIG. 23A

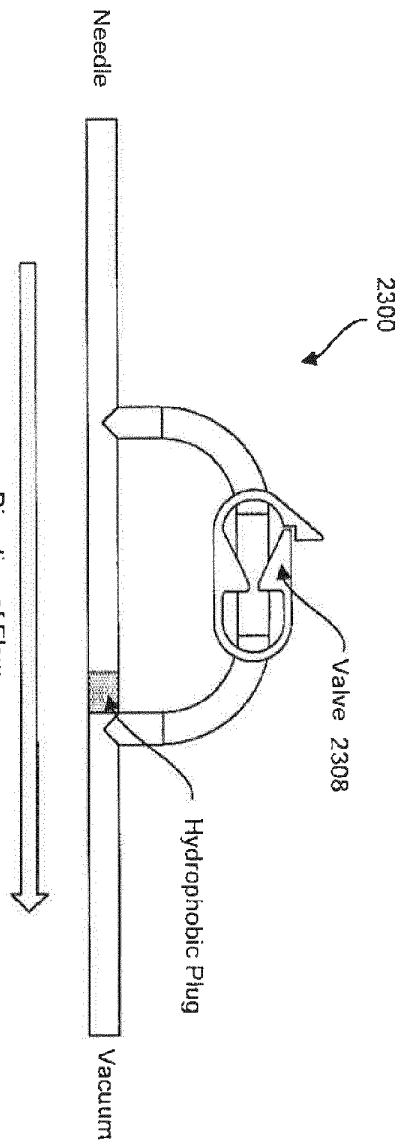

Needle
2300
Direction of Flow
Valve 2308
Hydrophobic Plug
Vacuum

FIG. 23B

Europäisches Patentamt
European Patent Office
Office européen des brevets

EUROPEAN SEARCH REPORT

Application Number
EP 19 20 0766

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)
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A	US 2009/227953 A1 (TAN CHEE LEONG [SG] ET AL) 10 September 2009 (2009-09-10) * the whole document *	1-14	
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The present search report has been drawn up for all claims

Place of search	Date of completion of the search	Examiner
Berlin	18 November 2019	Schultz, Ottmar

CATEGORY OF CITED DOCUMENTS

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EUROPEAN SEARCH REPORT

Application Number
EP 19 20 0766

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Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)
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TECHNICAL FIELDS SEARCHED (IPC)

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& : member of the same patent family, corresponding document

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ANNEX TO THE EUROPEAN SEARCH REPORT ON EUROPEAN PATENT APPLICATION NO. EP 19 20 0766

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Espacenet

Bibliographic data: WO2018125929 (A1) — 2018-07-05

BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE AND METHOD

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Applicant(s): KURIN INC [US] ± (KURIN, INC)

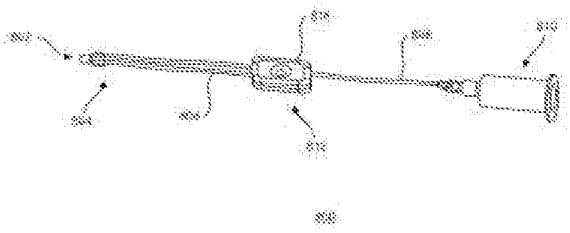
Classification: **- international:** ***A61B5/15; A61B5/153; A61B5/154; A61B5/157***
- cooperative: **A61B5/15003 (EP, US); A61B5/150213 (EP, US); A61B5/150221 (US); A61B5/150251 (EP, US); A61B5/150274 (EP, US); A61B5/150351 (US); A61B5/150755 (US); A61B5/150786 (US); A61B5/150946 (US); A61B5/150992 (EP, US); A61B5/1535 (EP, US); A61B5/1545 (EP, US);** A61B5/150389 (EP, US); A61B5/150488 (EP, US); A61B5/157 (EP, US)

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Abstract of WO2018125929 (A1)



Blood sample optimization systems and methods are described that reduce or eliminate contaminates in collected blood samples, which in turn reduces or eliminates false positive readings in blood cultures or other testing of collected blood samples. A blood sample optimization system can include a blood sequestration device located between a patient needle and a sample needle. The blood sequestration device can include a sequestration chamber for sequestering an initial, potentially contaminated aliquot of blood, and may further include a sampling channel that bypasses the sequestration chamber to convey likely uncontaminated blood between the patient needle and the sample needle after the initial aliquot of blood is sequestered in the sequestration chamber.

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(54) Title: BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE AND METHOD

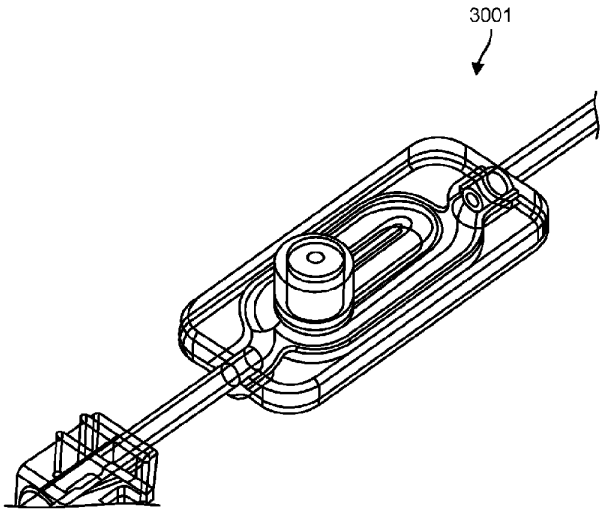


FIG. 30B

(57) Abstract: Blood sample optimization systems and methods are described that reduce or eliminate contaminates in collected blood samples, which in turn reduces or eliminates false positive readings in blood cultures or other testing of collected blood samples. A blood sample optimization system can include a blood sequestration device located between a patient needle and a sample needle. The blood sequestration device can include a sequestration chamber for sequestering an initial, potentially contaminated aliquot of blood, and may further include a sampling channel that bypasses the sequestration chamber to convey likely uncontaminated blood between the patient needle and the sample needle after the initial aliquot of blood is sequestered in the sequestration chamber.

[Continued on next page]

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BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE AND METHOD

BACKGROUND

[0001] Bacteraemia is the presence of microorganisms in the blood. Sepsis, on the other hand, is bacteraemia in the presence of clinical symptoms and signs such as fever, tachycardia, tachypnea and hypotension. Bacteraemia and sepsis are associated with a high mortality and an increased incidence and duration of hospital stay and associated costs. Many bacteraemias, sepsis, fungaemias and other pathogens actually occur within a hospital or other healthcare settings with catheters and venipunctures being a source of contamination as potential carriers of these pathogens.

[0002] Blood cultures are the standard test used to detect microbial pathogens related to bacteraemia and sepsis in a patient's blood. The term blood culture refers to a single venipuncture, either from a peripheral site or central or arterial line, with the blood inoculated into one or more blood culture bottles or containers. One bottle is considered a blood culture where two or more are considered a set. Multiple sets may be obtained from multiple venipunctures and are associated with different sites on the patient.

[0003] These methods allow for microbial identification and susceptibility testing to be performed, which is a critical component to managing sepsis, however the lack of rapid results and decreased sensitivity for fastidious pathogens has led to the development of improved systems and adjunctive molecular or proteomic testing.

[0004] Collection of blood samples for conducting blood cultures is a critical component of modern patient care and can either positively affect the patient outcome by providing an accurate diagnosis, or can adversely affect the outcome by prolonging unnecessary antimicrobial therapy, the length of hospital stays, and increasing costs.

[0005] One outcome of collection of blood cultures is contamination. Blood culture contamination can lead to a false positive culture result and/or significant increase in healthcare related costs. Sources of blood culture contamination include improper skin antisepsis, improper collection tube disinfection, and contamination of the initial blood draw which may then skew results.

[0006] Blood culture collection kits generally consist of a "butterfly" set, infusion set, or other type of venipuncture device as offered by companies like BD, Smiths, B. Braun and others, and aerobic and anaerobic blood culture bottles. Various different bottles are also available depending on the test requirements. These bottles are specifically designed to optimize recovery of both aerobic and anaerobic organisms. In conventional kits, a bottle used is known generally as a "Vacutainer," which is a blood collection tube formed of a sterile glass or plastic tube with a closure that is evacuated to create a vacuum inside the tube to facilitate the draw of a predetermined volume of liquid such as blood.

[0007] False positive blood cultures are typically a result of poor sampling techniques. They cause the use of antibiotics when not needed, increasing hospital costs and patient anxiety. Blood cultures are drawn from a needlestick into the skin, and then a Vacutainer is attached to capture a sample of blood. Contamination may occur from improper or incomplete disinfection of the skin area in and around the puncture site. It may also occur from the coring of the skin by the needle during insertion, with the cored skin cells and any associated contamination being pulled into the sample.

[0008] Blood flow through a hypodermic needle is laminar, and as such, a velocity gradient can be developed over the flow tube as a pressure drop is applied to the hypodermic needle. Either forceful aspiration of blood, or using a very small hypodermic needle, can cause lysis and a release of potassium from the red blood cells, thereby rendering the blood samples abnormal.

[0009] In other instances, some patients have delicate veins that can collapse under a pressure drop or vacuum, particularly as applied by a syringe's plunger that is drawn too quickly for the patient's condition. Since such condition is impossible to know beforehand, such vein collapses are a risk and very difficult to control.

[0010] Various strategies have been implemented to decrease blood culture contamination rates, e.g. training staff with regard to aseptic collection technique, feedback with regard to contamination rates and implementation of blood culture collection kits. Although skin antisepsis can reduce the burden of contamination, 20% or more of skin organisms are located deep within the dermis and are unaffected by

antisepsis. Changing needles before bottle inoculation is not advisable as it increases the risk to acquire needle stick injuries without decreasing contamination rates.

[0011] Some conventional systems and techniques for reducing blood culture contamination include discarding the initial aliquot of blood taken from central venous catheters, venipunctures, and other vascular access systems. However, these systems require the user to mechanically manipulate an intravascular device, or require a complex series of steps that are difficult to ensure being followed.

SUMMARY

[0012] This document presents systems and methods for reducing blood culture contamination, lysing of cells, and vein collapse. In some implementations, a system and method can eliminate user variability in disinfection, and also eliminate the risk of skin cells getting into the blood culture sample. The systems and methods disclosed herein do not require a change in existing clinical processes, other than to potentially indicate when a vacutainer or other blood collection device (i.e., syringe) should be attached for drawing contaminant-free blood samples.

[0013] In some implementations of the systems and methods disclosed herein the withdrawal of blood is accomplished passively by use of the patient's own blood pressure, thereby reducing the risk of vein collapse and eliminating any additional user steps over current practice. The systems and methods can be applied to accommodate short-path direct stick or butterfly venipuncture systems. They can also be used with samples drawn through a catheter.

[0014] In one aspect, a blood sequestration device is presented. The blood sequestration device includes an inlet port and an outlet port. The blood sequestration device further includes a sequestration chamber connected with the inlet port, the sequestration chamber having a vent comprising an air permeable blood barrier. The blood sequestration device further includes a sampling channel having a proximal end connected with the inlet port and a distal end connected with the outlet port.

[0015] In another aspect, a blood sequestration device connected with a blood sampling pathway is described. The blood sampling pathway has a patient needle and a sample collection device. The blood sequestration device includes an inlet port connected

with the patient needle, and a sequestration chamber connected with the inlet port, the sequestration chamber having a vent comprising an air permeable blood barrier. The blood sequestration device further includes a sampling channel having a proximal end connected with the inlet port, and an outlet port connected with a distal end of the sampling channel and with the sample collection device.

[0016] In yet another aspect, a blood sequestration device connected with a blood sampling system is described. The blood sampling system includes a patient needle for accessing a blood sample from a patient, and a sample needle that is sealed and adapted for receiving an evacuated blood collection tube. The blood sequestration device includes an inlet port connected with the patient needle to receive the blood sample from the patient. The blood sequestration device further includes a sequestration chamber connected with the inlet port and having a vent comprising an air permeable blood barrier, the sequestration chamber for receiving and sequestering a first portion of the blood sample prior to the sample needle being unsealed by the evacuated blood collection tube. The blood sequestration device further includes a sampling channel having a proximal end connected with the inlet port, the sampling channel for conveying a subsequent portion of the blood sample once the sample needle is unsealed by the evacuated blood collection tube. The blood sequestration device further includes an outlet port connected with a distal end of the sampling channel for conveying the subsequent portion of the blood sample to the sample needle.

[0017] In yet another aspect, a blood sample optimization system is disclosed and described. The blood sample optimization system includes a blood sampling system for accessing and acquiring one or more samples of a patient's blood, and a blood sequestration device for receiving and sequestering a first portion of the one or more samples of the patient's blood which might be contaminated by a venipuncture process and which could result in a false positive identification of a pathogen in the patient's blood.

[0018] The blood sampling system includes a patient needle configured for a venipuncture of a patient to access a sample of blood of a patient, a blood sampling pathway connected with the patient needle for conveying the sample of blood, and a sample needle configured for receiving an evacuated blood collection container to collect and contain a subsequent portion of the sample of blood.

[0019] In yet another aspect, a blood sequestration device is disclosed and described. In some implementations, the blood sequestration device can include an inlet port, an outlet port connected with the inlet port, and a sequestration chamber connected with the inlet port. The sequestration chamber can have a vent comprising an air permeable blood barrier.

[0020] The blood sequestration device, in one aspect can include an inlet port, an outlet port, a sequestration chamber connected with the inlet port via a junction, the sequestration chamber having a vent that includes an air permeable blood barrier, the vent being defined by an outer wall that at least partially circumscribes the air permeable blood barrier and includes one or more air vents, the vent further includes a cap that at least partially covers the wall and a one-way seal abutting the air permeable blood barrier that inhibits air from entering the sequestration chamber, and a sampling channel having a proximal end connected with the inlet port via the junction, and a distal end connected with the outlet port. In certain related aspects, the sequestration chamber, the sampling channel and the junction are sized and configured such that a first portion of blood flows into the sequestration chamber toward the air permeable blood barrier for sequestration therein, and a second portion of blood bypasses the sequestration chamber and the first portion of blood sequestered therein and is directed into the sampling channel toward the outlet port.

[0021] In another aspect, the sampling channel and the junction is sized and configured such that a first portion of blood flows into and fills the sequestration chamber to displace air therein through the vent, and such that a second portion of blood bypasses the sequestration chamber and the first portion of blood sequestered therein and is directed into the sampling channel toward the outlet port.

[0022] The blood sequestration and sampling system sequestration device, in certain aspects can include a blood sampling pathway having a patient needle on a proximal end and a sample collection device on a distal end; and a blood sequestration device attached on the blood sampling pathway between the proximal end and distal end of the blood sampling pathway. The blood sequestration device in one aspect can include an inlet port coupled with the blood sampling pathway toward the patient needle, an outlet port coupled with the blood sampling pathway toward the sample collection device, a sequestration chamber connected with the inlet port via a junction, which chamber has a

vent that includes an air permeable blood barrier, the vent being defined by an outer wall that at least partially circumscribes the air permeable blood barrier and includes one or more air vents, the vent further including a cap that at least partially covers the wall and a one-way seal abutting the air permeable blood barrier that inhibits air from entering the sequestration chamber; and a sampling channel having a proximal end connected with the inlet port via the junction, and a distal end connected with the outlet port. In a certain related aspect, the sequestration chamber, the sampling channel and the junction can be sized and configured such that a first portion of blood flows into the sequestration chamber toward the air permeable blood barrier for sequestration therein, and a second portion of blood bypasses the sequestration chamber and the first portion of blood sequestered therein and is directed into the sampling channel toward the outlet port.

[0023] The blood sequestration device is connected along the blood sampling pathway between the patient needle and the sample needle, and includes an inlet port for receiving the sample of blood. The blood sequestration device further includes a sequestration chamber connected with the inlet port for receiving a first amount of the sample of blood, the sequestration chamber having a vent comprising an air permeable blood barrier for sequestering at least a first portion of the first amount of the sample of blood. The blood sequestration device may further include a sampling channel having a proximal end connected with the inlet port, the sampling channel conveying a subsequent amount of the sample of blood to the evacuated blood collection container upon the sequestration chamber sequestering at least the first portion of the first amount of the sample of blood. The blood sequestration device further includes an outlet port connected with a distal end of the sampling channel, the outlet port for outputting the subsequent amount of the sample of blood.

[0024] The details of one or more embodiments are set forth in the accompanying drawings and the description below. Other features and advantages will be apparent from the description and drawings, and from the claims.

BRIEF DESCRIPTION OF THE DRAWINGS

[0025] These and other aspects will now be described in detail with reference to the following drawings.

[0026] FIG. 1 illustrates a blood sample optimization system.

[0027] FIG. 2 illustrates a blood sample optimization system in accordance with an alternative implementation.

[0028] FIG. 3 illustrates a blood sample optimization system in accordance with another alternative implementation.

[0029] FIG. 4 illustrates a blood sample optimization system in accordance with another alternative implementation.

[0030] FIG. 5 illustrates a blood sample optimization system in accordance with another alternative implementation.

[0031] FIG. 6 illustrates a blood sample optimization system in accordance with an alternative implementation.

[0032] FIG. 7 is a flowchart of a method for optimizing a quality of a blood culture.

[0033] FIGS. 8A – 8E illustrate a blood sequestration system for non-contaminated blood sampling, in accordance with some implementations.

[0034] FIG. 9 illustrates a pathway splitter for use in a blood sequestrations system.

[0035] FIGS. 10A – 10D illustrate a blood sequestration system for non-contaminated blood sampling, in accordance with alternative implementations.

[0036] FIGS. 11A – 11E illustrate a blood sequestration system for non-contaminated blood sampling, in accordance with other alternative implementations.

[0037] FIGS. 12A-12D illustrate a blood sample optimization system including a blood sequestration device in accordance with yet other alternative implementations.

[0038] FIGS. 13A-13D illustrate a blood sample optimization system 1300 in accordance with yet another alternative implementations.

[0039] FIGS. 14A-14E illustrate yet another implementation of a blood sampling system to sequester contaminates of an initial aliquot or sample to reduce false positives in blood cultures or tests performed on a patient's blood sample.

[0040] FIGS. 15A-15G illustrate a blood sequestration device and method of using the same, in accordance with yet another implementation.

[0041] FIGS. 16A-16D illustrate a blood sequestration device in accordance with yet another implementation.

[0042] FIGS. 17A – 17E illustrate a bottom member of a housing for a blood sequestration device.

[0043] FIGS. 18A – 18F illustrate a top member of a housing for a blood sequestration device.

[0044] FIGS. 19A and 19B illustrate a blood sequestration device having a top member mated with a bottom member.

[0045] FIG. 20 shows a blood sample optimization system including a blood sequestration device.

[0046] FIG. 21 illustrates a non-vented blood sequestration device using a wicking material chamber.

[0047] FIGS. 22A and 22B illustrate a material makeup of a filter for sequestering blood in a sequestration chamber of a blood sequestration device.

[0048] FIGS. 23A – 23E illustrate another implementation of a blood sequestration device that uses a vacuum force from a blood collection device.

[0049] FIGS. 24A – 24D illustrate another implementation of a blood optimization system and blood sequestration device.

[0050] FIGS. 25A – 25D illustrate another implementation of a blood optimization system and blood sequestration device.

[0051] FIGS. 26A – 26E illustrate another implementation of a blood optimization system and blood sequestration device.

[0052] FIGS. 27A – 27D illustrate another implementation of a blood optimization system and blood sequestration device.

[0053] FIGS. 28A – 28F illustrate another implementation of a blood optimization system and blood sequestration device.

[0054] FIGS. 29A – 29C illustrate another implementation of a blood optimization system and blood sequestration device.

[0055] FIGS. 30A – 30G illustrate another implementation of a blood optimization system and blood sequestration device.

[0056] Like reference symbols in the various drawings indicate like elements.

DETAILED DESCRIPTION

[0057] This document describes blood sample optimization systems and methods for reducing or eliminating contaminates in collected blood samples, which in turn reduces or eliminates false positive readings in blood cultures or other testing of collected blood samples. In some implementations, a blood sample optimization system includes a patient needle for vascular access to a patient's bloodstream, a sample needle for providing a blood sample to a blood collection container, such as an evacuated blood collection container or tube like a Vacutainer™ or the like, or other sampling device, and a blood sequestration device located between the patient needle and the sample needle. The blood sequestration device includes a sequestration chamber for sequestering an initial, potentially contaminated aliquot of blood, and may further include a sampling channel that bypasses the sequestration chamber to convey likely uncontaminated blood between the patient needle and the sample needle after the initial aliquot of blood is sequestered in the sequestration chamber.

[0058] FIG. 1 illustrates a blood sample optimization system in accordance with some implementations. The system includes a patient needle 1 to puncture the skin of a patient to access the patient's vein and blood therein. The system further includes a sample needle (i.e., a resealably closed needle for use with Vacutainers™ or the like) 5, which may be contained within and initially sealed by a resealable boot 10, a Luer activated valve, or another collection interface or device. The resealable boot 10 can be

pushed aside or around the sample needle 5 by application of a Vacutainer™ bottle (not shown) for drawing the patient's blood. The system can further include a low volume chamber 30 that leads to the sample needle 5, but also includes an orifice or one or more channels 45 that lead to a sequestration chamber 55 formed by a housing 50.

[0059] The sequestration chamber 55 is a chamber, channel, pathway, lock, or other structure for receiving and holding a first aliquot of the patient's blood, which may be in a predetermined or measured amount, depending on a volume of the sequestration chamber 55. The first draw of blood typically contains or is more susceptible to containing organisms that cause bacteraemia and sepsis or other pathogens than subsequent blood draws. The sequestration chamber 55 can be a vessel encased in a solid housing, formed in or defined by the housing itself, or can be implemented as tubing or a lumen. The sequestration chamber 55, regardless how formed and implemented, may have a predetermined volume. In some implementations, the predetermined volume may be based on a volume of the patient needle, i.e. ranging from less than the volume of the patient needle to any volume up to or greater than 20 times or more of the volume of the patient needle. The predetermined volume of the sequestration chamber 55 may also be established to economize or minimize an amount of blood to be sequestered and disposed of.

[0060] The sequestration chamber 55 can be formed, contained or housed in a chamber housing 50, and can be made of plastic, rubber, steel, aluminum or other suitable material. For example, the sequestration chamber 55 could be formed of flexible tubing or other elastomeric materials. The sequestration chamber 55 further includes an air permeable blood barrier 20 that allows air to exit the sequestration chamber 55. As used herein the term "air permeable blood barrier" means an air permeable but substantially blood impermeable substance, material, or structure. Examples may include hydrophobic membranes and coatings, a hydrophilic membrane or coating combined with a hydrophobic membrane or coating, mesh, a filter, a mechanical valve, antimicrobial material, or any other means of allowing air to be displaced from the sequestration chamber 55 as it is filled with blood. In various exemplary embodiments, an air permeable blood barrier may be formed by one or more materials that allow air to pass through until contacted by a liquid, such material then becomes completely or partially sealed to prevent or inhibit the passage of air and/or liquid. In other words, prior to contact with liquid, the material forms a barrier that is air permeable. After contact with a

liquid, the material substantially or completely prevents the further passage of air and/or liquid.

[0061] The orifice or channel 45 can be any desired length, cross-sectional shape or size, and/or can be formed to depart from the low volume chamber 30 at any desired angle or orientation. The orifice or channel 45 may also include a one-way flap or valve 60 that maintains an initial aliquot of blood sample within the sequestration chamber 55. In some specific implementations, the orifice or channel 45 can include a "duck bill" or flapper valve 60, or the like, for one-way flow of blood from low volume chamber 30 to the sequestration chamber 55. The air permeable blood barrier 20 can also be constructed of a material that allows air to exit but then seals upon contact with blood, thereby not allowing external air to enter sequestration chamber 55. This sealing would eliminate the need for a valve.

[0062] Valve 60 can be any type of valve or closing mechanism. Chamber 30 is designed to hold virtually no residual blood, and can be designed to be adapted to hold or allow pass-through of a particular volume or rate of blood into sequestration chamber 55. Likewise, sequestration chamber 55 may also include any type of coating, such as an anti-microbial coating, or a coating that aids identification and/or diagnosis of components of the first, sequestered blood draw.

[0063] Housing 50 and 40 can be formed of any suitable material, including plastic, such as acrylonitrile butadiene styrene (ABS) or other thermoplastic or polymeric material, rubber, steel, or aluminum. The air permeable blood barrier 20 can include a color-providing substance, or other signaling mechanism, that is activated upon contact with blood from the initial blood draw, or when air displacement is stopped, or any combination of events with blood in the sequestration chamber 55. The air permeable barrier may also include an outer layer such as a hydrophobic membrane or cover that inhibits or prevents the inadvertent or premature sealing of the filter by an external fluid source, splash etc. Sequestration chamber 55 can also be translucent or clear to enable a user to visually confirm the chamber is filled.

[0064] FIG. 2 illustrates a blood sample optimization system in accordance with some alternative implementations. In the implementation shown in FIG. 2, a sequestration chamber 55, or waste chamber, surrounds the patient needle 1, with an

open-ended cuff or housing connected with the waste chamber and encircling the sample needle housing base and housing. The patient needle 1 and sample needle 5 are connected together by a boot 56, which forms a continuous blood draw channel therethrough. The boot 56 includes a single orifice or channel leading from the blood draw channel into sequestration chamber 55. The device can include more than one single orifice or channel, in other implementations. Each orifice or channel can include a one-way valve, and can be sized and adapted for predetermined amount of blood flow.

[0065] The sequestration chamber 55 includes an air permeable blood barrier. The filter can further include a sensor or indicator to sense and/or indicate, respectively, when a predetermined volume of blood has been collected in the sequestration chamber 55. That indication will alert a user to attach an evacuated blood collection tube or bottle, such as a Vacutainer™ to the sample needle 5. The housing for the sequestration chamber 55 can be any size or shape, and can include any type of material to define an interior space or volume therein. The interior space is initially filled only with air, but can also be coated with an agent or substance, such as a decontaminate, solidifying agent, or the like. Once evacuated blood collection tube is attached to the sample needle 5, blood will flow automatically into the patient needle 1, through the blood draw channel and sample needle 5, and into the bottle. The sample needle 5 is covered by a resealable boot, coating or membrane that seals the sample needle when a blood collection bottle is not attached thereon or thereto.

[0066] FIG. 3 illustrates a blood sample optimization system in accordance with some alternative implementations. In the implementation shown, a sample needle 5 is surrounded by a resealable boot or membrane, and is further connected with a patient needle 1. A blood flow channel is formed through the sample needle and the patient needle. The connection between the sample needle and patient needle includes a "T" or "Y" connector 102, which includes a channel, port or aperture leading out from the main blood flow channel to a sequestration chamber 104.

[0067] The T or Y connector 102 may include a flap or one-way valve, and have an opening that is sized and adapted for a predetermined rate of flow of blood. The sequestration chamber 104 can be formed from tubing, or be formed by a solid housing, and is initially filled with air. The sequestration chamber 104 will receive blood that flows out of a patient automatically, i.e. under pressure from the patient's own blood

pressure. The sequestration chamber 104 includes an air permeable blood barrier 106, preferably at the distal end of tubing that forms the sequestration chamber 104, and which is connected at the proximal end to the T or Y connector 102. The T or Y connector 102 can branch off at any desired angle for most efficient blood flow, and can be formed so as to minimize an interface between the aperture and channel and the main blood flow channel, so as to minimize or eliminate mixing of the initial aliquot of blood with main blood draw samples.

[0068] In some alternative implementations, the sample needle may be affixed to a tubing of any length, as shown in FIG. 4, connecting at its opposite end to the T or Y connector 102. The sequestration chamber 104 can be any shape or volume so long as it will contain a predetermined amount of blood sample in the initial aliquot. The T or Y connector 102 may also include an opening or channel that is parallel to the main blood flow channel. The air permeable blood barrier may further include an indicator 107 or other mechanism to indicate when a predetermined amount of blood has been collected in the sequestration chamber, or when air being expelled reaches a certain threshold, i.e. to zero. The tubing can also include a clip 109 that can be used to pinch off and prevent fluid flow therethrough.

[0069] Once the air permeable blood barrier and primary chamber are sealed the initial aliquot of blood is trapped in the sequestration chamber 104, an evacuated blood collection tube, such as a Vacutainer™ bottle may be attached to the sample needle 5 to obtain the sample. The blood collection tube can be removed, and the sample needle 5 will be resealed. Any number of follow-on blood collection tubes can then be attached for further blood draws or samples. Upon completion of all blood draws, the system can be discarded, with the initial aliquot of blood remaining trapped in the sequestration chamber 104.

[0070] FIG. 5 illustrates a blood sample optimization system in accordance with some alternative implementations. In the implementation shown, a sample needle 5 is connected with a patient needle by tubing. A "T" or "Y" connector 120 is added along the tubing at any desired location, and includes an aperture, port or channel leading to a sequestration chamber 204, substantially as described above.

[0071] FIG. 6 illustrates a blood sample optimization system in accordance with some alternative implementations, in which a sequestration chamber 304, formed as a primary collection channel, receives an initial aliquot of blood, and is provided adjacent to the blood sampling channel. The sequestration chamber 304 can encircle the blood sampling channel, the patient needle 1, and/or the sample needle 5. The primary collection channel can include a T or Y connector 120, or other type of aperture or channel. The sequestration chamber 304 includes an air permeable blood barrier, which can also include an indicator of being contacted by a fluid such as blood, as described above.

[0072] In some implementations, either the patient needle 1 or the sample needle 5, or both, can be replaced by a Luer lock male or female connector. However, in various implementations, the connector at a sample needle end of the blood sample optimization system is initially sealed to permit the diversion of the initial aliquot of blood to the sequestration chamber, which is pressured at ambient air pressure and includes the air outlet of the air permeable blood barrier. In this way, the system passively and automatically uses a patient's own blood pressure to overcome the ambient air pressure of the sequestration chamber to push out air through the air permeable blood barrier and displace air in the sequestration chamber with blood.

[0073] FIG. 7 is a flowchart of an exemplary method for optimizing the quality of a blood culture. At 702, a clinician places a needle into a patient's vein. At 704, blood then flows into a sequestration chamber, pushing the air in the sequestration chamber out of the sequestration chamber through an air permeable blood barrier. In some implementations, the volume of the sequestration chamber is less than 0.1 to more than 5 cubic centimeters (cc's), or more. The sequestration chamber is sized and adapted to collect a first portion of a blood sample, which is more prone to contamination than secondary and other subsequent portion of the blood sample or subsequent draws. Since the sequestration chamber has an air-permeable blood barrier through which air can be displaced by blood pushed from the patient's vein, such blood will naturally and automatically flow into the sequestration chamber before it is drawn into or otherwise enters into a Vacutainer or other bottle for receiving and storing a blood sample.

[0074] When the sequestration chamber fills, the blood will gather at or otherwise make contact with the air permeable blood barrier, which will inhibit or prevent blood

from passing therethrough. At 706, when the blood comes into contact with the entire internal surface area of the air permeable blood barrier, the air permeable blood barrier is then closed and air no longer flows out or in. At 708, the clinician may be provided an indictor or can see the full chamber, to indicate the evacuated blood collection tube, such as a Vacutainer™ can be attached. The indicator can include visibility into the primary chamber to see whether it is full, the blood barrier changing color, for example, or other indicator. The fill time of the sequestration chamber may be substantially instantaneous, so such indicator, if present, may be only that the sequestration chamber is filled.

[0075] Prior to an evacuated blood collection tube being attached, communication between the needle, sampling channel, and the sequestration chamber is restricted by the sealing of the sequestration chamber blood barrier thereby not permitting air to reenter the system through the sequestration. Sealing the communication path could also be accomplished with a mechanical twist or other movement, a small orifice or tortuous pathway, eliminating the need for a separate valve or mechanical movement or operation by the clinician. At 710, once the evacuated blood collection tube is removed, the self-sealing membrane closes the sample needle, and at 712, additional subsequent evacuated blood collection tubes may be attached. Once samples have been taken, at 714 the device is removed from the patient and discarded.

[0076] FIGS. 8A – 8E illustrate an exemplary blood sample optimization system 800 for non-contaminated blood sampling, in accordance with some implementations. The blood sample optimization system 800 includes an inlet port 802 that can be connected to tubing, a patient needle (or both), or other vascular or venous access device, and a pathway splitter 804 having a first outlet to a sequestration chamber tubing 806 and a second outlet to sample collection tubing 808. One or both of the sequestration chamber tubing 806 and the sample collection tubing 808 can be formed of tubing. In some implementations, the sequestration chamber tubing 806 is sized so as to contain a particular volume of initial blood sample. The sample collection tubing 808 will receive a blood sample once the sequestration chamber tubing 806 is filled. The sample collection tubing 808 can be connected to a Vacutainer™ base or housing 810, or other blood sample collection device.

[0077] The blood sequestration system 800 further includes a blood sequestration device 812 which, as shown in more detail in FIGS. 8B – 8D, includes a housing 818 that

includes a sampling channel 820 defining a pathway for the non-contaminated sample collection tubing 808 or connected at either end to the non-contaminated sample collection tubing 808. The sampling channel 820 can be curved through the housing 818 so as to better affix and stabilize the housing 818 at a location along the non-contaminated sample collection tubing 808.

[0078] The blood sequestration device 812 further includes a sequestration chamber 822 connected with the sequestration chamber tubing 806 or other chamber. The sequestration chamber 822 terminates at an air permeable blood barrier 824. The air permeable blood barrier 824 can also include a coloring agent that turns a different color upon full contact with blood, as an indicator that the regular collection of blood samples (i.e. the non-contaminated blood samples) can be initiated. Other indicators may be used, such as a small light, a sound generation mechanism, or the like. In some implementations, the air permeable blood barrier is positioned at a right angle from the direction of sequestration chamber 822, but can be positioned at any distance or orientation in order to conserve space and materials used for the housing 818. The housing 818 and its contents can be formed of any rigid or semi-rigid material or set of materials.

[0079] FIG. 9 illustrates a pathway splitter 900 for use in a blood sequestrations system, such as those shown in FIGS. 8A – 8E, for example. The pathway splitter 900 includes an inlet port 902, a main line outlet port 904, and a sequestration channel outlet port 906. The inlet port 902 can be connected to main tubing that is in turn connected to a patient needle system, or directly to a patient needle. The main line outlet port 904 can be connected to main line tubing to a blood sampling system, such as a vacutainer base or housing, or directly to such blood sampling system. The sequestration channel outlet port 906 can be connected to sequestration tubing for receiving and sequestering a first sample of blood, up to a measured amount or predetermined threshold. Alternatively, the sequestration channel outlet port 906 can be connected to a sequestration chamber. The sequestration channel outlet port 906 is preferably 20-70 degrees angled from the main line outlet port 904, which in turn is preferably in-line with the inlet port 902. Once the predetermined amount of initial blood sample is sequestered in the sequestration tubing or chamber, in accordance with mechanisms and techniques described herein, follow-on blood samples will flow into the inlet port 902 and directly out the main line outlet port 904, without impedance.

[0080] FIGS. 10A – 10D illustrate a blood sequestration device 1000 in accordance with alternative implementations. The blood sequestration device 1000 includes an inlet port 1002, a main outlet port 1004, and a sequestration channel port 1006. The inlet port 1002 can be connected to a patient needle or related tubing. The main outlet port 1004 can be connected to a blood sample collection device such as a Vacutainer, associated tubing, or a Luer activated valve, or the like. The sequestration channel port 1006 splits off from the main outlet port 1004 to a sequestration chamber 1008. In some implementations, the sequestration chamber 1008 is formed as a helical channel within a housing or other container 1001.

[0081] The sequestration chamber 1008 is connected at the distal end to an air permeable blood barrier 1010, substantially as described above. Air in the sequestration chamber 1008 is displaced through the air permeable blood barrier 1010 by an initial aliquot of blood that is guided into the sequestration channel port 1006. Once the sequestration chamber 1008 is filled, further blood draws through the main outlet port 1004 can be accomplished, where these samples will be non-contaminated.

[0082] FIGS. 11A – 11E illustrate a blood sequestration device 1100 in accordance with other alternative implementations. The blood sequestration device 1100 includes an inlet port 1102, similar to the inlet ports described above, a main outlet port 1104, and a sequestration channel port 1106 that splits off from the main outlet port 1104 and inlet port 1102. The sequestration channel port is connected to a sequestration chamber 1108. In the implementation shown in FIGS. 11A – 11E, the blood sequestration device includes a base member 1101 having a channel therein, which functions as the sequestration chamber 1108. The channel can be formed as a tortuous path through the base member 1101, which is in turn shaped and formed to rest on a limb of a patient.

[0083] A portion of the sequestration chamber 1108 can protrude from the base member or near a top surface of the base member, just before exiting to an air permeable blood barrier 1110, to serve as a blood sequestration indicator 1109. The indicator 1109 can be formed of a clear material, or a material that changes color when in contact with blood.

[0084] In some implementations, the blood sequestration device 1100 can include a blood sampling device 1120 such as a normally closed needle, Vacutainer™ shield or other collection device. The blood sampling device 1120 can be manufactured and sold with the blood sequestration device 1100 for efficiency and convenience, so that a first aliquot of blood that may be contaminated by a patient needle insertion process can be sequestered. Thereafter, the blood sampling device 1120 can draw non-contaminated blood samples to reduce the risk of false positive testing and ensure a non-contaminated sample.

[0085] FIGS. 12A-12D illustrate a blood sample optimization system 1200 in accordance with yet other alternative implementations. The system 1200 includes a blood sequestration device 1202 for attaching to a blood sampling device 1204, such as a Vacutainer™ or other collection and sampling device. The blood sequestration device 1202 is configured and arranged to receive, prior to a Vacutainer™ container or vial being attached to a collection needle of the blood sampling device 1204, a first aliquot or amount of blood, and sequester that first aliquot or amount in a sequestration channel of the blood sequestration device 1202.

[0086] In some implementations, the blood sequestration device 1202 can include an inlet port 1212, a main outlet port, and a sequestration channel port. The inlet port 1212 can be connected to a patient needle or related tubing. The main outlet port 1214 can be connected to a normally closed needle or device to enable connection with an evacuated blood collection container or other collection device such as a Vacutainer™, associated tubing, luer connectors, syringe, a Luer activated valve, or the like. The sequestration channel port splits off from the main outlet port to a sequestration chamber 1218.

[0087] In some implementations, the sequestration chamber 1218 is formed as a channel within the body of a sequestration device 1202. The sequestration chamber 1218 can be a winding channel, such as a U-shaped channel, an S-shaped channel, a helical channel, or any other winding channel. The sequestration device 1202 can include a housing or other containing body, and one or more channels formed therein. As shown in FIGS. 12A and 12B, the sequestration device 1202 includes a main body 1206 and a cap 1208. The main body 1206 is formed with one or more cavities or channels, which are further formed with one or more arms 1210 that extend from the cap 1208, and which

abut the cavities or channels in the main body 1206 to form the primary collection port and main outlet port.

[0088] FIGS. 13A-13D illustrate a blood sample optimization system 1300 in accordance with yet other alternative implementations. The system 1300 includes a blood sequestration device 1302 for attaching to a blood sampling device 1304, such as a Vacutainer or other bodily fluid collection and sampling device. The blood sequestration device 1302 is configured and arranged to receive, prior to a Vacutainer container or vial being attached to a collection needle of the blood sampling device 1304, a first aliquot or amount of blood, and to sequester that first aliquot or amount of blood or other bodily fluid in a sequestration channel of the blood sequestration device 1302.

[0089] The blood sequestration device 1302 includes a housing 1301 having an inlet port 1314, a main outlet port 1312, and a sequestration channel port 1316. The inlet port 1314 can be connected to a patient needle or associated tubing. The main outlet port 1312 can be connected to a normally closed needle or device to enable connection with an evacuated blood collection container or other collection device such as a Vacutainer™, associated tubing, luer connectors, syringe, a Luer activated valve, or the like. The sequestration channel port 1316 splits off from the main inlet port 1314 to a sequestration chamber 1318.

[0090] In the implementation shown in FIGS. 13A-D, the sequestration chamber 1318 is formed as a cavity or chamber within housing 1301 or formed by walls that define housing 1301. The sequestration chamber 1318 can be a winding channel, such as a U-shaped channel, an S-shaped channel, a helical channel, or any other winding channel, that is defined by the cooperation and connection of housing 1301 with cap 1307 which cap 1307 can include a protrusion 1305 that provides one or more walls or directors for the winding channel in the sequestration chamber 1318. The protrusion 1305 from the cap 1307 can be straight or curved, and may have various channels, apertures or grooves embedded therein, and can extend from the cap 1307 any angle or orientation. When the cap 1307 is connected with the housing 1301 to complete the formation of the sequestration chamber 1318, the protrusion 1305 forms at least part of the winding channel to sequester a first aliquot or amount of blood or other bodily fluid in a sequestration channel formed in the sequestration chamber 1318 and by the winding channel.

[0091] The sequestration chamber 1318 includes an air permeable blood barrier 1310, substantially as described above. Air in the sequestration chamber 1318 is displaced through the air permeable blood barrier 1310 by an initial aliquot of blood that is provided into the sequestration chamber 1318 by the blood pressure of the patient. Once the sequestration chamber 1318 is filled and the air in the sequestration chamber 1318 displaced, the blood pressure of the patient will be insufficient to drive or provide further blood into the blood sequestration device 1302, and in particular the outlet port 1312, until a force such as a vacuum or other pressure, such as provided by the blood sample collection device like Vacutainer is provided to draw out a next aliquot or amount of blood or bodily fluid. Further blood draws through the main outlet port 1312 can be accomplished, where these samples will be non-contaminated since any contaminants would be sequestered in the sequestration chamber 1318 with the first aliquot of blood.

[0092] FIGS. 14A-14E illustrate yet another implementation of a blood sampling system 1400 to sequester contaminates of an initial aliquot or sample to reduce false positives in blood cultures or tests performed on a patient's blood sample. The blood sampling system 1400 includes a blood sequestration device 1401 that can be connected between a blood sample collection device 1403 and a patient needle (not shown). The blood sample collection device 1403 can be a Vacutainer or the like. The blood sequestration device 1401 includes an inlet port 1402 that can be connected with a patient needle that is inserted into a patient's vascular system for access to and withdrawing of a blood sample. The inlet port 1402 may also be connected with tubing or other conduit that is in turn connected with the patient needle.

[0093] The inlet port 1402 defines an opening into the blood sequestration device 1401, which opening can be the same cross sectional dimensions as tubing or other conduit connected with the patient needle or the patient needle itself. For instance, the opening can be circular with a diameter of approximately 0.045 inches, but can have a diameter of between 0.01 inches or less to 0.2 inches or more. The blood sequestration device 1401 further includes an outlet port 1404, which defines an opening out of the blood sequestration device 1401 and to the blood sample collection device 1403. The outlet port 1404 may also be connected with tubing or other conduit that is in turn connected with the blood sequestration device 1403. The outlet port 1404 can further include a connector device such as a threaded cap, a Luer connector (male or female), a

non threaded interference or glue joint fitting for attachment of various devices including but not limited to tubing, or the like.

[0094] The blood sequestration device 1401 further includes a sampling channel 1406 between the inlet port 1402 and the outlet port 1404, and which functions as a blood sample pathway once a first aliquot of blood has been sequestered. The sampling channel 1406 can be any sized, shaped or configured channel, or conduit. In some implementations, the sampling channel 1406 has a substantially similar cross sectional area as the opening of the inlet port 1402. In other implementations, the sampling channel 1406 can gradually widen from the inlet port 1402 to the outlet port 1404.

[0095] The blood sequestration device 1401 further includes a sequestration chamber 1408 that is connected to and split off or diverted from the sampling channel 1406 at any point between the inlet port 1402 and the outlet port 1404, but preferably from a proximal end of the sampling channel 1406 near the inlet port 1402. The sequestration chamber 1408 is at first maintained at atmospheric pressure, and includes an air outlet 1412 at or near a distal end of the sequestration chamber 1408 opposite the diversion point from the sampling channel 1406. The air outlet 1412 includes an air permeable blood barrier 1412. As shown in FIG. 14B, the air permeable blood barrier 1412 can be overlaid with a protective cover 1416. The protective cover 1416 can be sized and configured to inhibit a user from touching the air permeable blood barrier 1412 with their finger or other external implement, while still allowing air to exit the air permeable blood barrier 1412 as the air is displaced from the sequestration chamber 1408 by blood being forced into the sequestration chamber 1408 by a patient's own blood pressure. In addition the protective cover 1416 can be constructed to inhibit or prevent accidental exposure of the air permeable blood barrier to environmental fluids or splashes. This can be accomplished in a variety of mechanical ways including but not limited to the addition of a hydrophobic membrane to the protective cover.

[0096] As shown in FIGS. 14C and 14D, the sampling channel 1406 can be cylindrical or frusto-conical in shape, going from a smaller diameter to a larger diameter, to minimize a potential to lyse red blood cells. Likewise, the sampling channel 1406 is formed with a minimal amount of or no sharp turns or edges, which can also lyse red blood cells. The sampling channel 1406 splits off to the sequestration chamber 1408 near the inlet port 1402 via a diversion pathway 1409. The diversion pathway 1409 can have

any cross-sectional shape or size, but is preferably similar to the cross-sectional shape of at least part of the inlet port 1402.

[0097] In some implementations, the sampling channel 1406 and the sequestration chamber 1408 are formed by grooves, channels, locks or other pathways formed in housing 1414. The housing 1414 can be made of plastic, metal or other rigid or semi-rigid material. The housing 1414 can have a bottom member that sealably mates with a top member. One or both of the bottom member and the top member can include the sampling channel 1406 and the sequestration chamber 1408, as well as the diversion pathway 1409, the inlet port 1402, and the outlet port 1404. In some other implementations, one or more of the diversion pathway 1409, the inlet port 1402, and/or the outlet port 1404 can be at least partially formed by a cap member that is connected to either end of the housing 1414. In some implementations, the top member and the bottom member, as well as the cap member(s), can be coupled together by laser welding, heat sealing, gluing, snapping, screwing, bolting, or the like. In other implementations, some or all of the interior surface of the diversion pathway 1409 and/or sequestration chamber 1408 can be coated or loaded with an agent or substance, such as a decontaminate, solidifying agent, or the like. For instance, a solidifying agent can be provided at the diversion pathway 1409 such that when the sequestration chamber 1408 is filled and the initial aliquot of blood backs up to the diversion pathway 1409, that last amount of sequestered blood could solidify, creating a barrier between the sequestration chamber 1408 and the sampling channel 1406.

[0098] FIGS. 15A-15G illustrate a blood sequestration device 1500. The blood sequestration device 1500 can be connected to a normally closed needle or device to enable connection with an evacuated blood collection container or other collection device such as a Vacutainer™, associated tubing, luer connectors, syringe, a Luer activated valve, or the like.

[0099] The blood sequestration device 1500 includes an inlet port 1502 that can be connected with a patient needle that is inserted into a patient's vascular system for access to and withdrawing of a blood sample. The inlet port 1502 may also be connected with tubing or other conduit that is in turn connected with the patient needle. The inlet port 1502 defines an opening into the blood sequestration device 1500, which opening may be the same cross sectional dimensions as tubing or other conduit connected with the

patient needle or the patient needle itself. For instance, the opening can be circular with a diameter of approximately 0.045 inches, but can have a diameter of between 0.01 inches or less to 0.2 inches or more.

[00100] The inlet port 1502 can also include a sealing or fluid-tight connector or connection, such as threading or Luer fitting, or the like. In some implementations, tubing or other conduit associated with the patient needle can be integral with the inlet port 1502, such as by co-molding, gluing, laser weld, or thermally bonding the parts together. In this manner, the blood sequestration device 1500 can be fabricated and sold with the patient needle as a single unit, eliminating the need for connecting the patient needle to the blood sequestration device 1500 at the time of blood draw or sampling.

[00101] The blood sequestration device 1500 further includes an outlet port 1504, which defines an opening out of the blood sequestration device 1500 and to the blood sample collection device. The outlet port 1504 may also be connected with tubing or other conduit that is in turn connected with the blood sequestration device, and may also include a sealing or fluid-tight connector or connection, such as threading or Luer fitting, or the like. Accordingly, as discussed above, the blood sequestration device 1500 can be fabricated and sold with the patient needle and/or tubing and the blood sample collection device as a single unit, eliminating the need for connecting the patient needle and the blood sample collection device to the blood sequestration device 1500 at the time of blood draw or sampling.

[00102] The blood sequestration device 1500 further includes a sampling channel 1506 between the inlet port 1502 and the outlet port 1504, and which functions as a blood sample pathway once a first aliquot of blood has been sequestered. The sampling channel 1506 can be any sized, shaped or configured channel or conduit. In some implementations, the sampling channel 1506 has a substantially similar cross sectional area as the opening of the inlet port 1502. In other implementations, the sampling channel 1506 can gradually widen from the inlet port 1502 to the outlet port 1504.

[00103] The blood sequestration device 1500 further includes a sequestration chamber 1508 that is connected to and split off or diverted from the sampling channel 1506 at any point between the inlet port 1502 and the outlet port 1504, but preferably from a proximal end of the sampling channel 1506 near the inlet port 1502. In some

implementations, the diversion includes a Y-shaped junction. The sequestration chamber 1508 is preferably maintained at atmospheric pressure, and includes a vent 1510 at or near a distal end of the sequestration chamber 1508. The vent 1510 includes an air permeable blood barrier 1512. FIG. 15C illustrates the blood sequestration device 1500 with the sequestration chamber 1508 filled with a first aliquot or sample of blood from the patient.

[00104] The air permeable blood barrier 1512 can be covered with a protective cover 1516. The protective cover 1516 can be sized and configured to inhibit a user from touching the air permeable blood barrier 1512 with their finger or other external implement, while still allowing air to exit the air permeable blood barrier 1512 as the air is displaced from the sequestration chamber 1508 by blood being forced into the sequestration chamber 1508 by a patient's own blood pressure. The protective cover 1516 can be constructed to inhibit or prevent accidental exposure of the filter to environmental fluids or splashes. This can be accomplished in a variety of mechanical ways including but not limited to the addition of a hydrophobic membrane to the protective cover.

[00105] FIG. 15B is a perspective view of the blood sequestration device 1500 from the outlet port 1504 and top side of a housing 1501 of the blood sequestration device 1500 that includes the vent 1510, and illustrating an initial aliquot of blood filling sequestration chamber 1508 while the sampling channel 1506 is empty, before a sample collection device is activated. FIG. 15G is a perspective view of the blood sequestration device 1500 from the outlet port 1504 and bottom side of the housing 1501 of the blood sequestration device 1500, and illustrating the initial aliquot of blood filling sequestration chamber 1508 while the sampling channel 1506 is empty, before the sample collection device is activated. FIG. 15C is another perspective view of the blood sequestration device 1500 from the inlet port 1502 and top side of a housing 1501 of the blood sequestration device 1500 that includes the vent 1510, and illustrating blood now being drawn through sampling channel 1506 while the sequestered blood remains substantially in the sequestration chamber 1508.

[00106] FIG. 15D is a cross section of the blood sequestration device 1500 in accordance with some implementations, showing the housing 1501 that defines the sampling channel 1506 and the sequestration chamber 1508. FIGS. 15E and 15F

illustrate various form factors of a housing for a blood sequestration device, in accordance with one or more implementations described herein.

[00107] The sequestration chamber 1508 can have a larger cross-sectional area than the sampling channel 1506, and the cross-sectional area and length can be configured for a predetermined or specific volume of blood to be sequestered or locked. The sampling channel 1506 can be sized to be compatible with tubing for either or both of the patient needle tubing or the blood collection device tubing.

[00108] The housing 1501 can be formed of multiple parts or a single, unitary part. In some implementations, and as illustrated in FIG. 15D, the housing 1501 includes a top member 1520 and a bottom member 1522 that are mated together, one or both of which having grooves, channels, locks, conduits or other pathways pre-formed therein, such as by an injection molding process or by etching, cutting, drilling, etc. The top member 1520 can be connected with the bottom member 1522 by any mating or connection mechanism, such as by laser welding, thermal bonding, ultrasonic welding, gluing, using screws, rivets, bolts, or the like, or by other mating mechanisms such as latches, grooves, tongues, pins, flanges, or the like.

[00109] In some implementations, such as shown in FIG. 15D, the top member 1520 can include the grooves, channels, locks, conduits or other pathways, while the bottom member 1522 can include a protrusion 1524 that is sized and adapted to fit into at least one of the grooves, channels, locks or other pathways of the top member 1520. The protrusion 1524 can provide a surface feature, such as a partial groove or channel, for instance, to complete the formation of either the sampling channel 1506 and/or the sequestration chamber 1508. In some implementations, the protrusion 1524 can be formed with one or more angled sides or surfaces for a tighter fit within the corresponding groove, channel, lock or other pathway. In yet other implementations, both the top member 1520 and the bottom member can include grooves, channels, locks or other pathways, as well as one or more protrusions 1524.

[00110] In some implementations, the sampling channel 1506 and the sequestration chamber 1508 are formed by grooves, channels, locks or other pathways formed in housing 1501. The housing 1501 can be made of any suitable material, including rubber, plastic, metal or other material. The housing 1501 can be formed of a clear or translucent

material, or of an opaque or non-translucent material. In other implementations, the housing 1501 can be mostly opaque or non-translucent, while the housing surface directly adjacent to the sampling channel 1506 and/or the sequestration chamber 1508 is clear or translucent, giving a practitioner a visual cue or sign that the sequestration chamber 1508 is first filled to the extent necessary or desired, and/or then a visual cue or sign that the sequestered blood remains sequestered while a clean sample of blood is drawn through the sampling channel 1506. Other visual cues or signs of the sequestration can include, without limitation: the air permeable blood barrier 1512 turning a different color upon contact, saturation, or partial saturation with blood; a color-coded tab or indicator at any point along or adjacent to the sequestration chamber; an audible signal; a vibratory signal; or other signal.

[00111] After a venipuncture by a patient needle of a patient (not shown), which could gather a number of pathogens from the patient's skin, a first amount of the patient's blood with those pathogens will make its way into the inlet port 1502 blood sequestration device 1500 and flow into the sequestration chamber 1508 by following the path of least resistance, as the patient's own blood pressure overcomes the atmospheric pressure in the sequestration chamber 1508 to displace air therein through the air permeable blood barrier 1512. The patient's blood pressure will not be sufficient to overcome the air pressure that builds up in the sealed sampling channel 1506. Eventually, the sequestration chamber 1508, which has a predetermined volume, is filled with blood that displaces air through the air permeable blood barrier 1512. Once the blood hits the air permeable blood barrier, the blood interacts with the air permeable blood barrier 1512 material to completely or partially seal the vent 1510. A signal or indication may be provided that the practitioner can now utilize the Vacutainer capsule or other blood sample collection device to acquire a next amount of the patient's blood for sampling. The blood in the sequestration chamber 1508 is now effectively sequestered in the sequestration chamber.

[00112] Upon filling the blood sequestration pathway 1508 but prior to use of the Vacutainer or other blood sample collection device, the patient's blood pressure may drive compression of the air in the sampling channel 1506, possibly resulting in a small amount of blood moving past the diversion point to the sequestration chamber 1508 and into the sampling channel 1506, queuing up the uncontaminated blood to be drawn through the sampling channel 1506.

[00113] In some instances, as shown in FIG. 15H, an inlet port 1532 can include a male luer connector for connecting to a removable patient needle, and an outlet port 11534 can include a female luer connector for connecting with a syringe. This implementation of the inlet port and outlet port can be used with any device described herein, for avoiding a propensity of a Vacutainer-type device collapsing a patient's vein. In this implementation, a clinician can use the syringe in a modulated fashion to obtain a blood sample. In operation, the syringe is attached to the outlet port 1004, and the needle is attached to the inlet port 1002. A venipuncture is performed with the needle, and without the clinician pulling on the syringe. An initial aliquot of blood fills a sequestration chamber, and then the syringe can be used to draw a sample of blood through the collection channel, bypassing the sequestered blood in the sequestration chamber.

[00114] FIGS. 16-19 illustrate yet another implementation of a blood sequestration device. FIGS. 16A-16D illustrate a blood sequestration device 1600 that can be connected between a blood sample collection device, such as an evacuated blood collection container like a Vacutainer™ (not shown), and a patient needle (not shown) and/or associated tubing. FIG. 17 illustrates a bottom member of the blood sequestration device, and FIG. 18 illustrates a top member of the blood sequestration device, which top member and bottom member can be mated together to form an inlet port, and outlet port, a sequestration chamber and a sampling channel, as explained more fully below. FIGS. 19A and B show the top member and bottom member mated together. It should be understood that FIGS. 16-19 illustrate one exemplary manner of constructing a blood sequestration device as described herein, and other forms of construction are possible.

[00115] Referring to FIGS. 16A – D, the blood sequestration device 1600 includes an inlet port 1602 that can be connected with a patient needle that is inserted into a patient's vascular system for access to and withdrawing of a blood sample. The inlet port 1602 may also be connected with tubing or other conduit that is in turn connected with the patient needle. The inlet port 1602 defines an opening into the blood sequestration device 1600, which opening can be the same cross sectional dimensions as tubing or other conduit connected with the patient needle or the patient needle itself. For instance, the opening can be circular with a diameter of approximately 0.045 inches, but can have a diameter of between 0.01 inches or less to 0.2 inches or more.

[00116] The inlet port 1602 can also include a sealing or fluid-tight connector or connection, such as threading or Luer fitting, or the like. In some implementations, tubing or other conduit associated with the patient needle can be integral with the inlet port 1602, such as by co-molding, gluing, laser weld, or thermally bonding the parts together. In this manner, the blood sequestration device 1600 can be fabricated and sold with the patient needle and/or tubing as a single unit, eliminating the need for connecting the patient needle to the blood sequestration device 1600 at the time of blood draw or sampling.

[00117] The blood sequestration device 1600 further includes an outlet port 1604, which defines an opening out of the blood sequestration device 1600 and to the blood sample collection device. The outlet port 1604 may also be connected with tubing or other conduit that is in turn connected with the blood sequestration device, and may also include a sealing or fluid-tight connector or connection, such as threading or Luer fitting, or the like. Accordingly, as discussed above, the blood sequestration device 1600 can be fabricated and sold with the patient needle and/or tubing and the blood sample collection device as a single unit, eliminating the need for connecting the patient needle and the blood sample collection device to the blood sequestration device 1600 at the time of blood draw or sampling.

[00118] The blood sequestration device 1600 further includes a sampling channel 1606 between the inlet port 1602 and the outlet port 1604, and a sequestration chamber 1608 that is connected to and split off or diverted from the sampling channel 1606 at any point between the inlet port 1602 and the outlet port 1604. The sampling channel 1606 functions as a blood sampling pathway once a first aliquot of blood has been sequestered in the sequestration chamber 1608. The sampling channel 1606 can be any sized, shaped or configured channel, or conduit. In some implementations, the sampling channel 1606 has a substantially similar cross sectional area as the opening of the inlet port 1602. In other implementations, the sampling channel 1606 can gradually widen from the inlet port 1602 to the outlet port 1604. The sequestration chamber 1608 may have a larger cross section to form a big reservoir toward the sequestration channel path so that the blood will want to enter the reservoir first versus entering a smaller diameter on the sampling channel 1606, as is shown more fully in FIGS. 17 and 19.

[00119] In some exemplary implementations, the diversion between the sampling channel 1606 and the sequestration chamber 1608 is by diverter junction 1607. Diverter junction 1607 may be a substantially Y-shaped, T-shaped, or U-shaped. In some preferred exemplary implementations, and as shown in FIG. 17A – 17B, the diverter junction 1607 is configured such that the flow out of the inlet port 1602 is preferentially directed toward the sequestration chamber 1608. The sequestration chamber 1608 may also include or form a curve or ramp to direct the initial blood flow toward and into the sequestration chamber 1608.

[00120] The sequestration chamber 1608 is preferably maintained at atmospheric pressure, and includes a vent 1610 at or near a distal end of the sequestration chamber 1608. The vent 1610 may include an air permeable blood barrier 1612 as described above.

[00121] The blood sequestration device 1600 can include a housing 1601 that can be formed of multiple parts or a single, unitary part. In some implementations, and as illustrated in FIGS. 17A – 17E and FIGS. 18A – 18F, the housing 1601 includes a top member 1620 and a bottom member 1622 that are mated together. The blood sequestration device 1600 can also include a gasket or other sealing member (not shown) so that when the top member 1620 is mechanically attached with the bottom member 1622, the interface between the two is sealed by the gasket or sealing member. The FIGS. 17A – 17E illustrate a bottom member 1622 of a housing for a blood sequestration device 1600. The bottom member 1622 can include grooves, channels, locks, conduits or other pathways pre-formed therein, such as by an injection molding process or by etching, cutting, drilling, etc., to form the sampling channel 1606, the sequestration chamber 1608, and diverter junction 1607.

[00122] The sequestration chamber 1608 may have a larger cross section than the sampling channel 1606 so that the blood will preferentially move into the sequestration chamber first versus entering a smaller diameter on the sampling channel 1606.

[00123] FIGS. 18A – 18F illustrate the top member 1620, which can be connected with the bottom member 1622 by any mating or connection mechanism, such as by laser welding, thermal bonding, gluing, using screws, rivets, bolts, or the like, or by other mating mechanisms such as latches, grooves, tongues, pins, flanges, or the like. The top

member 1620 can include some or all of the grooves, channels, locks, conduits or other pathways to form the sampling channel 1606, the sequestration chamber 1608, and the diverter junction 1607. In yet other implementations, both the top member 1620 and the bottom member 1622 can include the grooves, channels, locks or other pathways.

[00124] In some implementations, the sampling channel 1606 and the sequestration chamber 1608 are formed by grooves, channels, locks or other pathways formed in housing 1601. The housing 1601 can be made of rubber, plastic, metal or any other suitable material. The housing 1601 can be formed of a clear or translucent material, or of an opaque or non-translucent material. In other implementations, the housing 1601 can be mostly opaque or non-translucent, while the housing surface directly adjacent to the sampling channel 1606 and/or the sequestration chamber 1608 may be clear or translucent, giving a practitioner a visual cue or sign that the sequestration chamber 1608 is first filled to the extent necessary or desired, and/or then a visual cue or sign that the sequestered blood remains sequestered while a clean sample of blood is drawn through the sampling channel 1606. Other visual cues or signs of the sequestration can include, without limitation: the air permeable blood barrier 1612 turning a different color upon contact, saturation, or partial saturation with blood; a color-coded tab or indicator at any point along or adjacent to the sequestration chamber; an audible signal; a vibratory signal; or other signal.

[00125] As shown in FIGS. 18A – 18F, the air permeable blood barrier 1612 can be covered with, or surrounded by, a protective member 1616. The protective member 1616 can be sized and configured to inhibit a user from touching the air permeable blood barrier 1612 with their finger or other external implement, while still allowing air to exit the air permeable blood barrier 1612 as the air is displaced from the sequestration chamber 1608. In some implementations, the protective member 1616 includes a protrusion that extends up from a top surface of the top member 1620 and around the air permeable blood barrier 1612. The protective member 1616 can be constructed to inhibit or prevent accidental exposure of the filter to environmental fluids or splashes. This can be accomplished in a variety of mechanical ways including but not limited to the addition of a hydrophobic membrane to the protective cover.

[00126] In use, the blood sequestration device 1600 includes a sampling channel 1606 and a sequestration chamber 1608. Both pathways are initially air-filled at

atmospheric pressure, but the sampling channel 1606 is directed to an outlet port 1604 that will be initially sealed by a Vacutainer or other such sealed blood sampling device, and the sequestration chamber 1608 terminates at a vent 1610 to atmosphere that includes an air permeable blood barrier 1612.

[00127] After a venipuncture by a patient needle of a patient (not shown), which could gather a number of pathogens from the patient's skin, a first amount of the patient's blood with those pathogens will pass through inlet port 1602 of blood sequestration device 1600. This initial volume of potentially contaminated blood will preferentially flow into the sequestration chamber 1608 by finding the path of least resistance. The patient's own blood pressure overcomes the atmospheric pressure in the vented sequestration chamber 1608 to displace air therein through the air permeable blood barrier 1612, but is not sufficient to overcome the air pressure that builds up in the sealed sampling channel 1606. In various exemplary embodiments, the sequestration chamber 1608 and sampling channel 1606 can be configured such that the force generated by the patient's blood pressure is sufficient to overcome any effect of gravity, regardless of the blood sequestration device's orientation.

[00128] Eventually, the sequestration chamber 1608 fills with blood that displaces air through the air permeable blood barrier 1612. Once the blood contacts the air permeable blood barrier, the blood interacts with the air permeable blood barrier 1612 material to completely or partially seal the vent 1610. A signal or indication may be provided that the practitioner can now utilize the Vacutainer or other blood sampling device.

[00129] Upon filling the blood sequestration pathway 1608 but prior to use of the Vacutainer or other blood sample collection device, the patient's blood pressure may drive compression of the air in the sampling channel 1606, possibly resulting in a small amount of blood moving past the diversion point into the sampling channel 1606, queuing up the uncontaminated blood to be drawn through the sampling channel 1606.

[00130] FIG. 19A is a side view, and FIG. 19B is a cross-sectional view, of the blood sequestration device 1600, illustrating the top member 1620 mated with the bottom member 1622.

[00131] FIG. 20 shows a blood sample optimization system 2000 that includes a patient needle 2002 for vascular access to a patient's bloodstream, a blood sample collection device 2004 to facilitate the collecting of one or more blood samples, and a conduit 2006 providing a fluid connection between the patient needle 2002 and the blood sample collection device 2004. In some implementations, the blood sample collection device 2004 includes a protective shield that includes a sealed collection needle on which a sealed vacuum-loaded container is placed, which, once pierced by the collection needle, draws in a blood sample under vacuum pressure or force through the conduit 2006 from the patient needle 2002.

[00132] The blood sample optimization system 2000 further includes a blood sequestration device 2008, located at any point on the conduit 2006 between the patient needle 2002 and the blood sample collection device 2004 as described herein.

[00133] FIG. 21 illustrates a non-vented blood sequestration device 2100 using a wicking material chamber. The blood sequestration device 2100 includes a housing 2101 that has a sampling channel 2104 that is at least partially surrounded or abutted by a sequestration chamber 2102 that is filled with a wicking material. An initial aliquot of blood is drawn in from the patient needle into the sampling channel 2104 where it is immediately wicked into the wicking material of the sequestration chamber 2102. The wicking material and/or sequestration chamber 2102 is sized and adapted to receive and hold a predetermined amount of blood, such that follow-on or later blood draws pass by the wicking material and flow straight through the sampling channel 2104 to a sampling device such as a Vacutainer. The wicking material can include a substance such as a solidifier, a decontaminate, or other additive.

[00134] As described herein, an air permeable blood barrier may be created using a wide variety of different structures and materials. As shown in FIGS. 22A and B, an air permeable blood barrier 2202 of a blood sequestration device 2200 can include a polymer bead matrix 2204, in which at least some beads are treated to make them hydrophilic. The air permeable blood barrier 2202 further includes a self-sealing material 2206, such as carboxymethyl cellulose (CMC) or cellulose gum, or other sealing material. The air permeable blood barrier 2202 can further include voids 2208 that permit air flow before contact or during partial contact with a fluid such as blood. As shown in FIG. 22B,

contact with a fluid causes the self-sealing material 2206 to swell and close off the voids 2208, occluding air flow through the voids 2208 and creating a complete or partial seal.

[00135] FIGS. 23A and B illustrate yet another implementation of a blood sequestration device 2300, having an inlet port 2302 to connect with a patient needle, an outlet port 2304 to connect with a blood sample collection device, a sequestration chamber 2306, and a sampling channel 2308 that bypasses the sequestration chamber 2306 once the sequestration chamber is filled to an initial aliquot of potentially contaminated blood to be sequestered. The sequestration chamber 2306 includes a hydrophobic plug 2312 at a distal end of the sequestration chamber 2306 that is farthest from the inlet port 2302. A vacuum or other drawing force applied from the outlet port 2304, such as from a Vacutainer or the like, draws in blood into the inlet port 2302 and directly into the sequestration chamber 2306, where the initial aliquot of blood will contact the hydrophobic plug 2312 and cause the initial aliquot of blood to back up into the sequestration chamber 2306 and be sequestered there. A small amount of blood may make its way into the sampling channel 2308, which is initially closed off by valve 2308. Upon release of the valve 2308, and under further force of the vacuum or other force, follow-on amounts of blood will flow into inlet port 2302, bypass the sequestration chamber 2306, and flow into and through sampling channel 2308 toward the outlet port 2304 and to the collection device.

[00136] The sampling channel 2308 can have any suitable geometry and can be formed of plastic tubing or any other suitable material. Valve 2308 can be a clip or other enclosing device to pinch, shunt, bend or otherwise close off the sampling channel 2308 before the initial aliquot of blood is sequestered in the sequestration chamber 2306. For instance, valve 2308 can also be formed as a flap, door or closable window or barrier within the sampling channel 2308.

[00137] FIGS. 23C – 23E illustrate an alternative implementation of the blood sequestration device 2300', in which a sequestration chamber 2320 branches off from a main collection channel 2322 between an inlet port 2316 to connect with a patient needle and an outlet port 2318 to connect with a blood sample collection device, such as a Vacutainer, a syringe, or the like. The sequestration chamber 2320 includes an air-permeable, blood impermeable blood barrier 2324, such as a hydrophobic plug of material, or a filter formed of one or more layers, for example. A valve 2324 closes off

and opens the collection channel 2322, and the device 2300' can be used similarly as described above.

[00138] FIG. 24A – 24D illustrate a blood sample optimization system 2400 that includes a patient needle 2402 for vascular access to a patient's bloodstream, a blood sample collection device 2404 to facilitate the collecting of one or more blood samples for blood testing or blood cultures, and a conduit 2406 providing a fluid connection between the patient needle 2402 and the blood sample collection device 2404. In some implementations, the blood sample collection device 2404 includes a protective shield that includes a sealed collection needle on which a sealed vacuum-loaded container is placed, which, once pierced by the collection needle, draws in a blood sample under vacuum pressure or force through the conduit 2006 from the patient needle 2402.

[00139] The blood sample optimization system 2400 further includes a blood sequestration device 2408, located at any point on the conduit 2406 between the patient needle 2402 and the blood sample collection device 2404. The location of the blood sequestration device 2408 can be based on a length of the conduit between the blood sequestration device 2408 and the patient needle 2402, and the associated volume that length provides.

[00140] The blood sequestration device 2408 includes an inlet port 2412 for being connected to the conduit 2406 toward the patient needle 2402, and an outlet port 2414 for being connected to the conduit 2406 toward the blood sample collection device 2404, and a housing 2416. The housing 2416 can be any shape, although it is shown in FIGS. 24A – D as being substantially cylindrical, and includes the inlet port 2412 and outlet port 2414, which can be located anywhere on the housing although shown as being located on opposite ends of the housing 2416.

[00141] The blood sequestration device 2408 further includes a blood sequestration chamber 2418 connected with the inlet port 2412. The blood sequestration chamber 2418 is defined by an inner chamber housing 2419 that is movable from a first position to receive and sequester a first aliquot of blood, to a second position to expose one or more apertures 2424 at a proximal end of the inner chamber housing 2419 to allow blood to bypass and/or flow around the inner chamber housing 2419 and through a blood sample channel 2422 defined by the outer surface of the inner chamber housing 2419 and the

inner surface of the housing 2416. The blood sequestration chamber 2418 includes an air permeable blood barrier 2420 at a distal end of the blood sequestration chamber 2418.

[00142] In operation, the inner chamber housing 2419 is in the first position toward the inlet port 2412, such that the one or more apertures 2424 are closed, and the blood sequestration chamber 2418 is in a direct path from the patient needle. Upon venipuncture of a patient, and drawing of blood by way of a syringe or Vacutainer, or other blood collection device 2404, the initial aliquot of blood flows into the blood sequestration chamber 2418. As the initial aliquot of blood flows into the blood sequestration chamber, it displaces air therein and eventually the blood contacts the blood barrier 2420, forcing the inner chamber housing to the second position. The inner chamber housing 2419 and/or housing 2416 can include a locking mechanism of one or more small tabs, grooves, detents, bumps, ridges, or the like, to maintain the inner chamber housing 2419 in the first position until the blood sequestration chamber 2418 is filled, providing force to overcome the locking mechanism to enable movement of the inner chamber housing 2419 to the second position. Once in the second position, the initial aliquot of blood is sequestered in the blood sequestration chamber 2418 and the one or more apertures 2424 are opened to create a pathway from the inlet port 2412 to the blood sampling channel 2422, bypassing and/or flowing around the blood sequestration chamber 2418.

[00143] As described above, the housing 2416 and/or inner chamber housing 2419 can be formed as cylindrical and concentric, but can be any shape, such as squared, rectangular, elliptical, oval, or other cross-sectional shape. The outer surface of the distal end of the inner chamber housing 2419 can have one or more outwardly projecting tangs 2421with gaps therebetween. The tangs 2421 contact the inner surface of the housing 2416 to help define the blood sampling channel 2422 therebetween, and to help stop the inner chamber housing 2419 in the second position. The gaps between the tangs 2421 enable blood to flow through the blood sampling channel 2422 and to the outlet port 2414. When the inner chamber housing 2419 is in the second position and the blood sequestration chamber 2418 is filled with the first aliquot of blood, further blood samples will automatically flow through the inlet port 2412, through the one or more apertures 2424, through the blood sampling channel 2422, through the gaps between the tangs 2421, and ultimately through the outlet port 2414 to be collected by a blood sampling device 2404.