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THE UNITED STATES OF AMERICA

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UNITED STATES DEPARTMENT OF COMMERCE

United States Patent and Trademark Office

September 23, 2025

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APPLICATION NUMBER: ***18/494,622***
FILING DATE: ***October 25, 2023***
PATENT NUMBER: ***12357209***
ISSUE DATE: ***July 15, 2025***

Certified by

DIRECTOR OF THE UNITED STATES PATENT AND TRADEMARK OFFICE

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PATENT AND TRADEMARK OFFICE

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ELECTRONIC ACKNOWLEDGEMENT RECEIPT

APPLICATION #	RECEIPT DATE / TIME	ATTORNEY DOCKET #
18/494,622	**10/25/2023 06:55:02 PM ET**	**069366-0577657_KUR2C05US**

Title of Invention

BLOOD SAMPLE OPTIMIZATION DEVICE

Application Information

APPLICATION TYPE	Utility - Nonprovisional Application under 35 USC 111(a)	PATENT #	-
CONFIRMATION #	9839	FILED BY	Trent Tercenio
PATENT CENTER #	63081424	FILING DATE	-
CUSTOMER #	27500	FIRST NAMED INVENTOR	Bobby E. ROGERS
CORRESPONDENCE ADDRESS	-	AUTHORIZED BY	Benjamin Hudson

Documents

TOTAL DOCUMENTS: 3

DOCUMENT	PAGES	DESCRIPTION	SIZE (KB)
069366-0577657_KUR2C05US_ADS.pdf	9	Application Data Sheet	2174 KB
069366-0577657_KUR2C05US_Specification-APP.TEXT.docx	34	Application body structured text document	61 KB

Warning: The margins of the attached document do not meet USPTO rules. This may cause processing errors or delays. All artifacts (SmartArt, Drawings, Charts, etc) have been replaced with images. Bookmarks were found and have been removed. The abstract contains more than one paragraph. Please review and revise if necessary.

069366-0577657_KUR2C05US_Draw	50	Drawings-only black and white line drawings	831 KB

ings.pdf

Digest

DOCUMENT	MESSAGE DIGEST(SHA-512)
069366-0577657_KUR2C05US_ADS.pdf	1E90CD1562B598ABB08D3E0A34B3E57C7AAB2F43051C5A9FBF9B7DE40D5BB157C98CCB2F209C3A4EF97CD9C8325091689AA30EDBA4944EB748272D4BBBAFEB82
069366-0577657_KUR2C05US_Specification-APP.TEXT.docx	8DFBC3EEAF3C3C71AED18B4593BBF9EF7DAD1A77E3AEC466A20F91AEA1D71C74443B55384EA0108F516E77E77B9497D9CB892BDAFCC8B106ECA1871B3A77554C
069366-0577657_KUR2C05US_Drawings.pdf	E54DB584FCE190D4B315ECC791E834408F57E39D532001631F4D8FCECFC84BB62957C2C365B0684BB35959027B82D27908A4590BD083C4A43F35B9B6DA5C9535

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 Data Sheet 37 CFR 1.76	Attorney Docket Number	069366-0577657_KUR2C05US
	Application Number	
Title of Invention	BLOOD SAMPLE OPTIMIZATION DEVICE	

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	c/o Kurin, Inc.

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	c/o Kurin, Inc.

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

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Application Data Sheet 37 CFR 1.76	Attorney Docket Number	069366-0577657_KUR2C05US
	Application Number	
Title of Invention	BLOOD SAMPLE OPTIMIZATION DEVICE	

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 DEVICE		
Attorney Docket Number	069366-0577657_KUR2C05US	**Small Entity Status Claimed**	☒
Application Type	Nonprovisional		
Subject Matter	Utility		
Total Number of Drawing Sheets (if any)	50	**Suggested Figure for Publication (if any)**	1

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.

Application Data Sheet 37 CFR 1.76	Attorney Docket Number	069366-0577657_KUR2C05US
	Application Number	
Title of Invention	BLOOD SAMPLE OPTIMIZATION DEVICE	

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	18113710	2023-02-24
Prior Application Status	Pending		Remove
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)
18113710	Continuation of	17538990	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

Application Data Sheet 37 CFR 1.76	Attorney Docket Number	069366-0577657_KUR2C05US
	Application Number	
Title of Invention	BLOOD SAMPLE OPTIMIZATION DEVICE	

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
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	069366-0577657_KUR2C05US
	Application Number	
Title of Invention	BLOOD SAMPLE OPTIMIZATION DEVICE	

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 Data Sheet 37 CFR 1.76	Attorney Docket Number	069366-0577657_KUR2C05US
	Application Number	
Title of Invention	BLOOD SAMPLE OPTIMIZATION DEVICE	

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. [X]

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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Application Data Sheet 37 CFR 1.76	Attorney Docket Number	069366-0577657_KUR2C05US
	Application Number	
Title of Invention	BLOOD SAMPLE OPTIMIZATION DEVICE	

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)	2023-10-25
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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U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
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	069366-0577657_KUR2C05US
	Application Number	
Title of Invention	BLOOD SAMPLE OPTIMIZATION DEVICE	

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.

BLOOD SAMPLE OPTIMIZATION DEVICE

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application is a Continuation of U.S. Application No. 18/113,710 filed February 24, 2023, entitled "BLOOD SAMPLE OPTIMIZATION DEVICE," which is a continuation of U.S. Application No. 17/538,990 filed November 11, 2021, entitled "BLOOD SAMPLE OPTIMIZATION DEVICE," 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.

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.

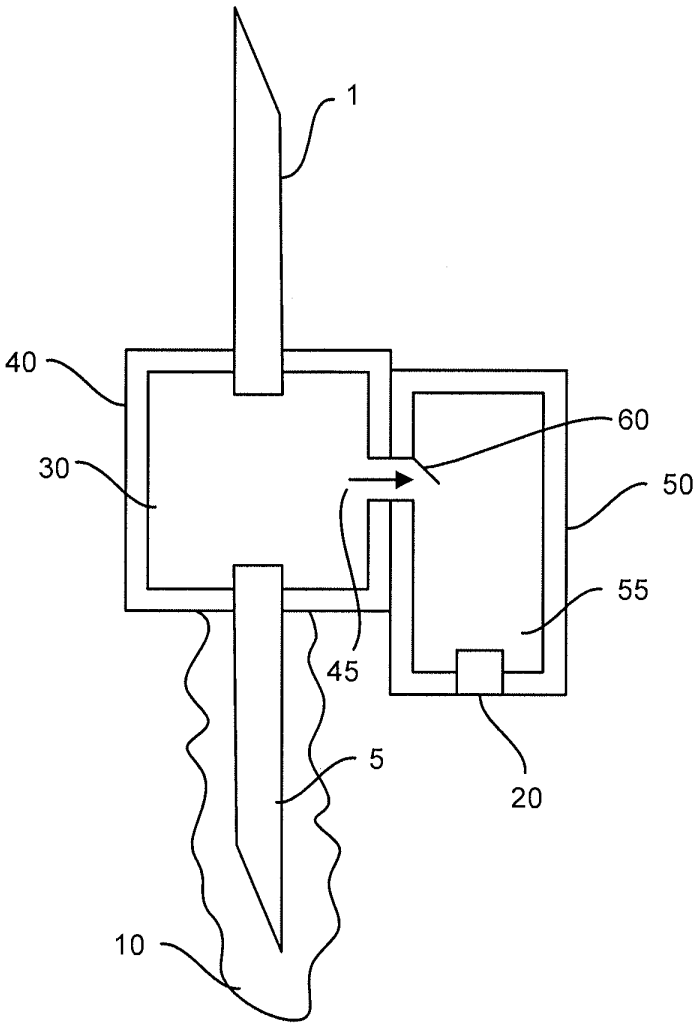


FIG. 1

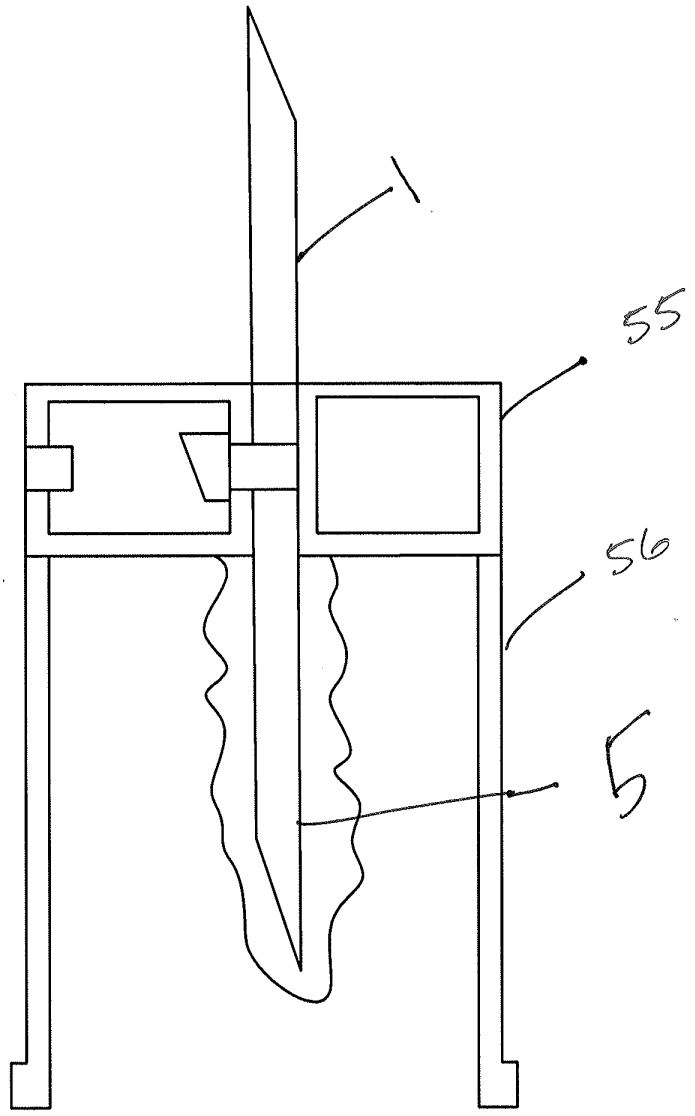


FIG. 2

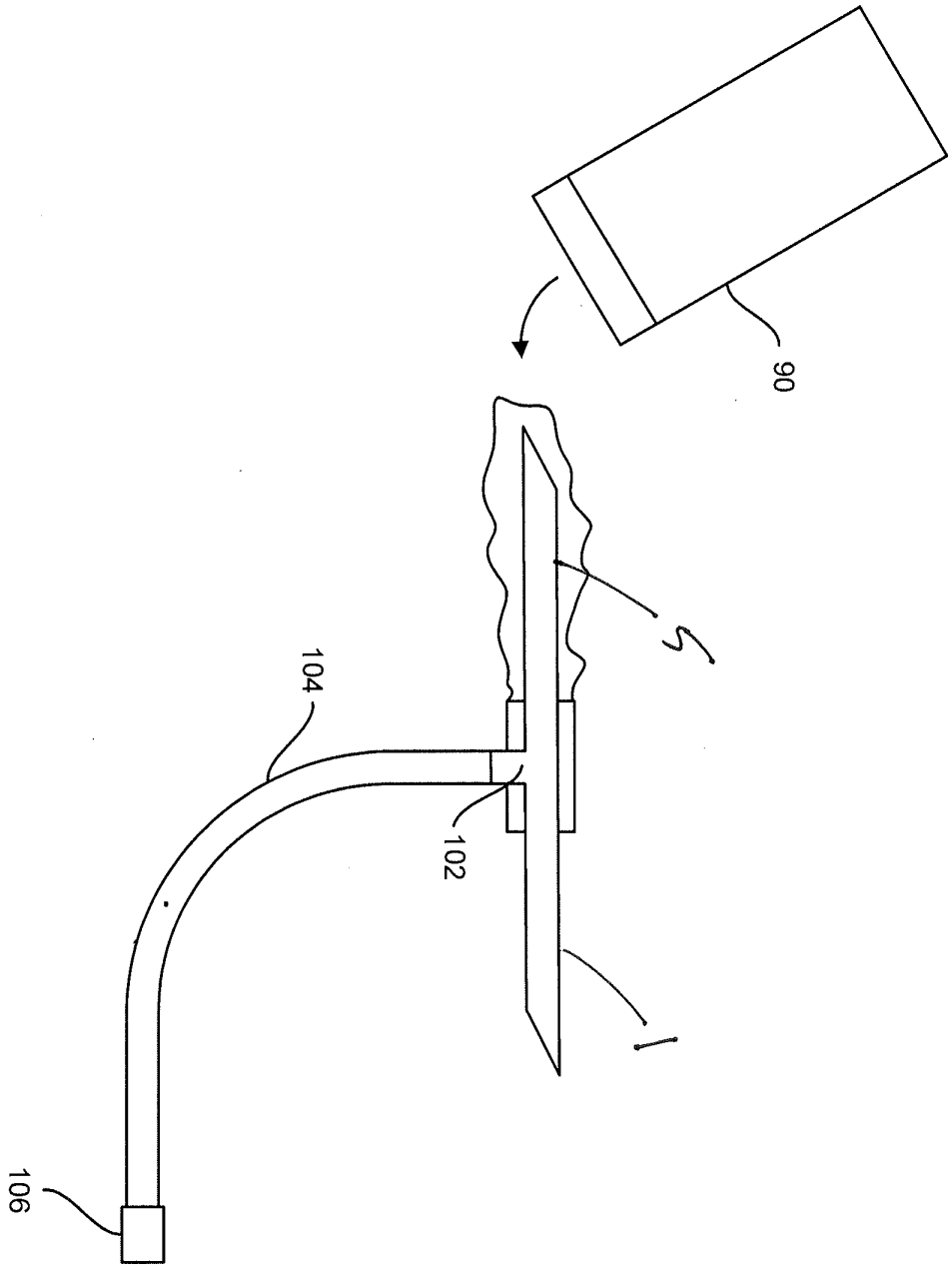


FIG. 3

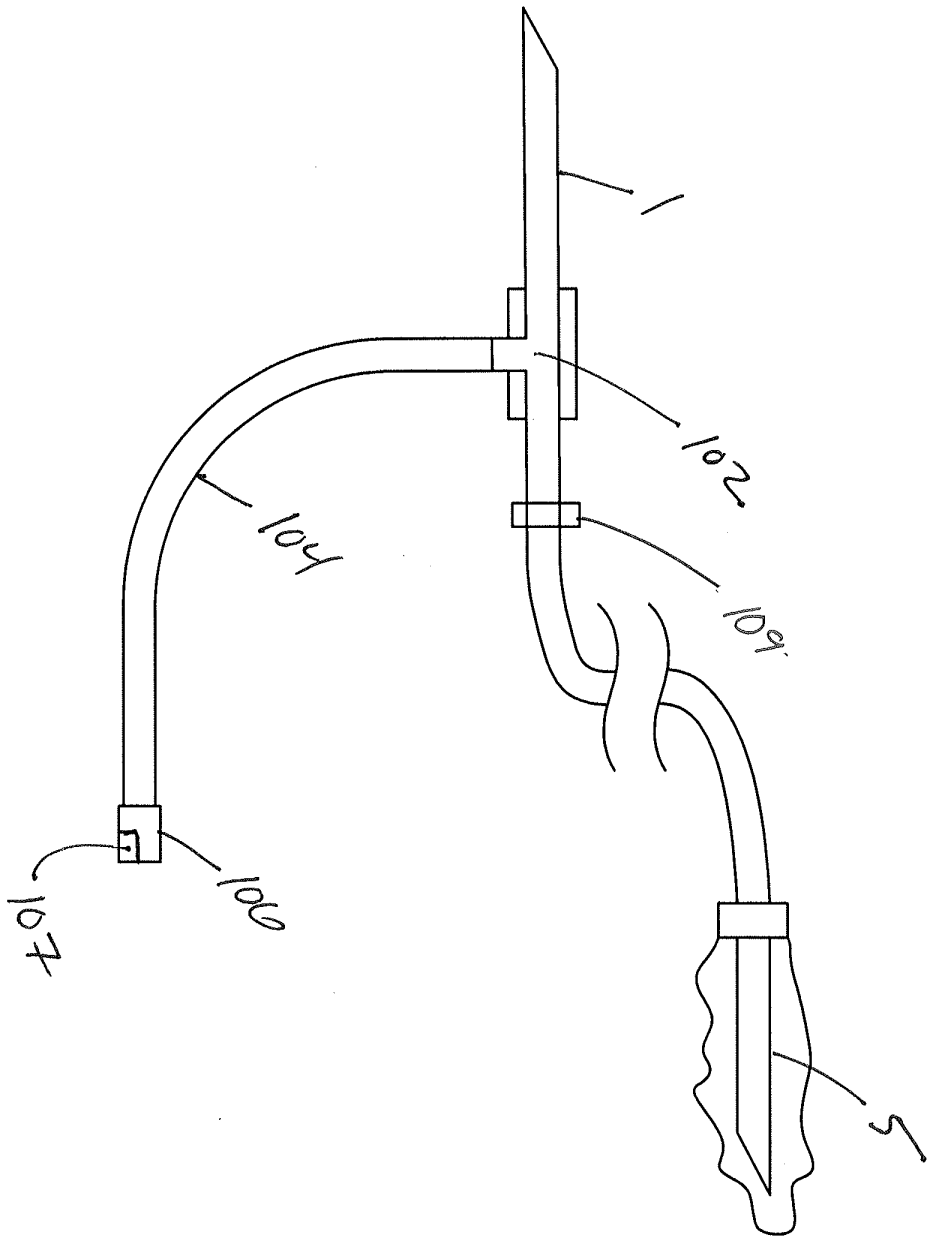


FIG. 4

FIG. 5

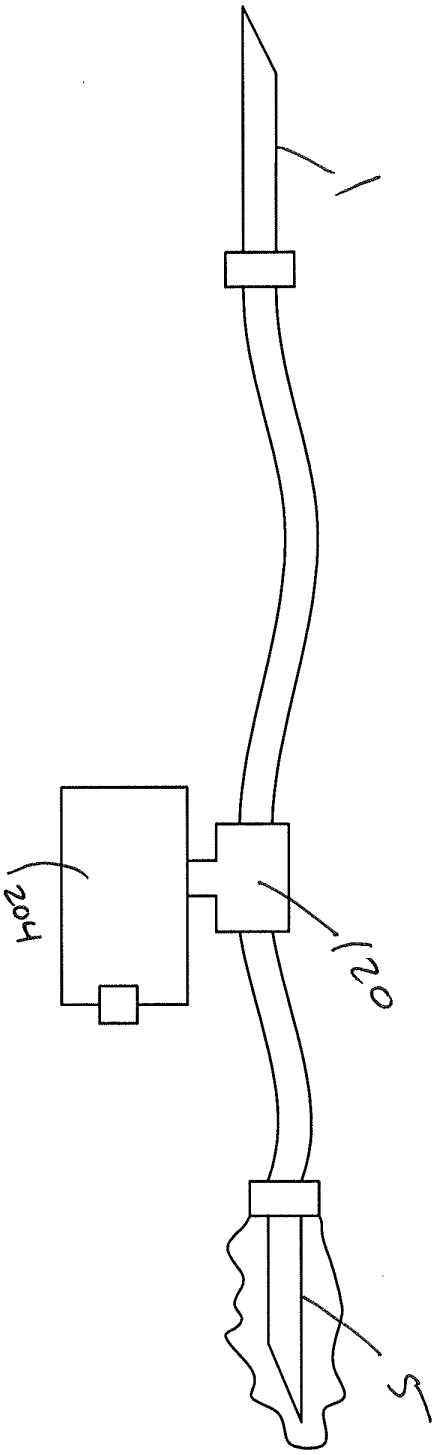
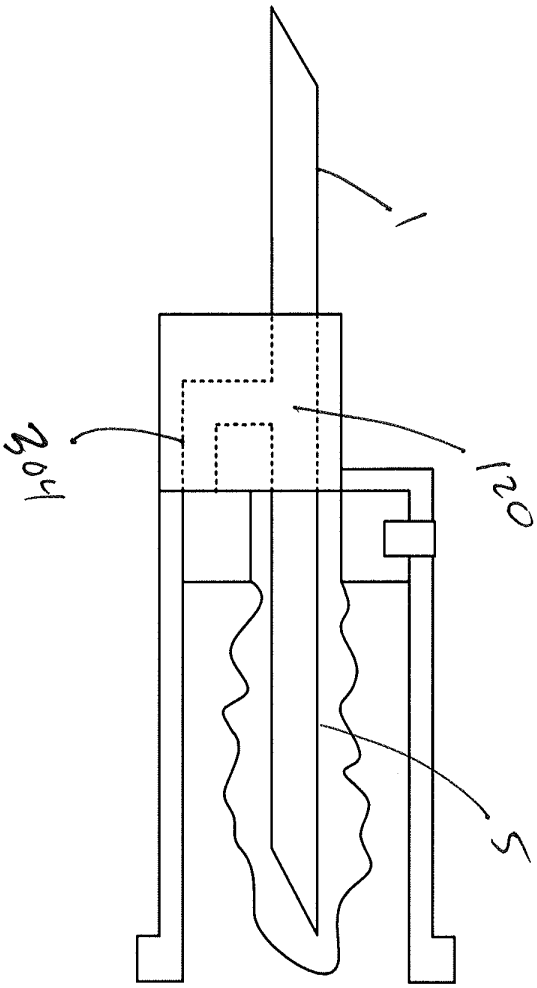


FIG. 6



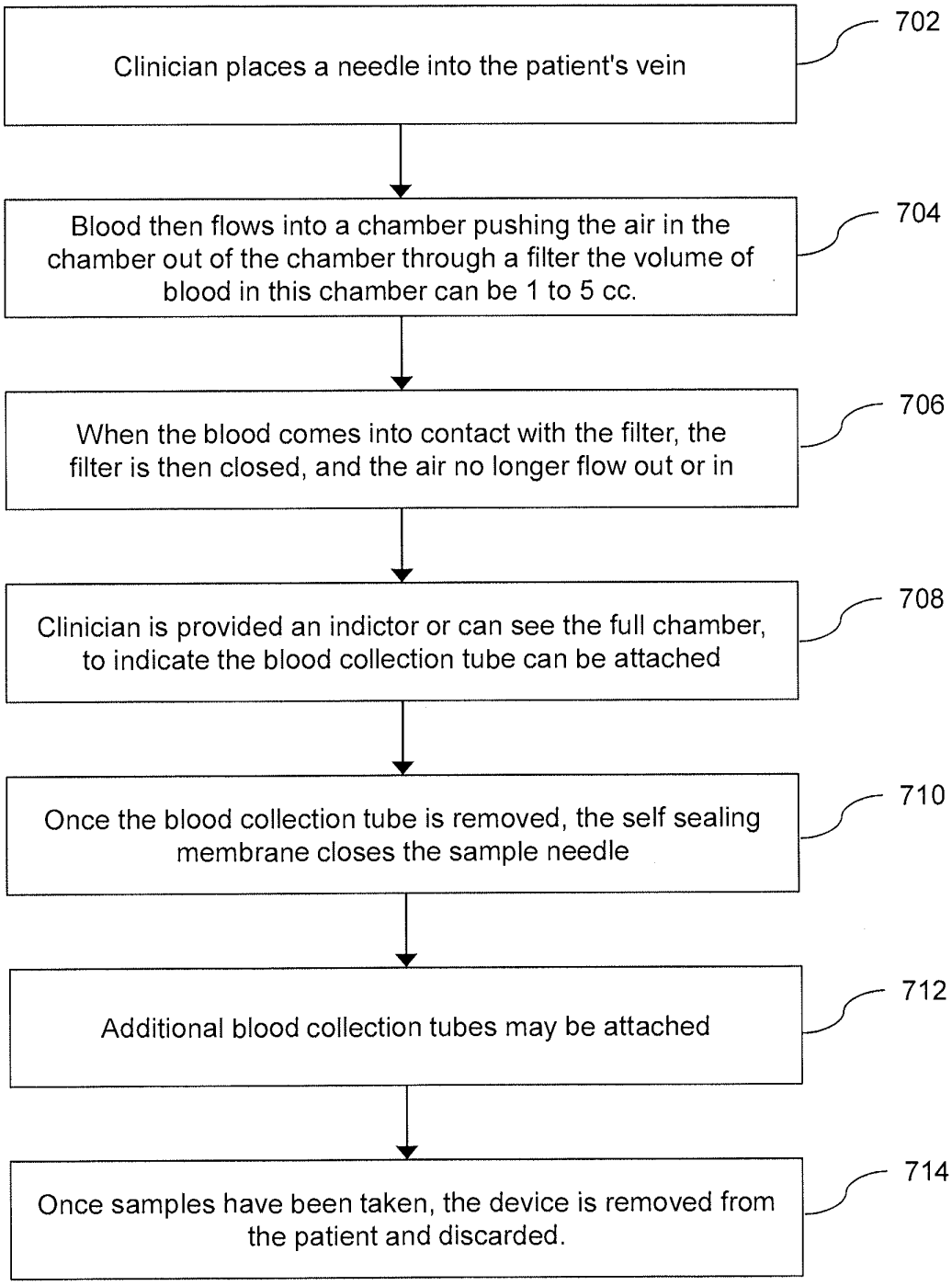
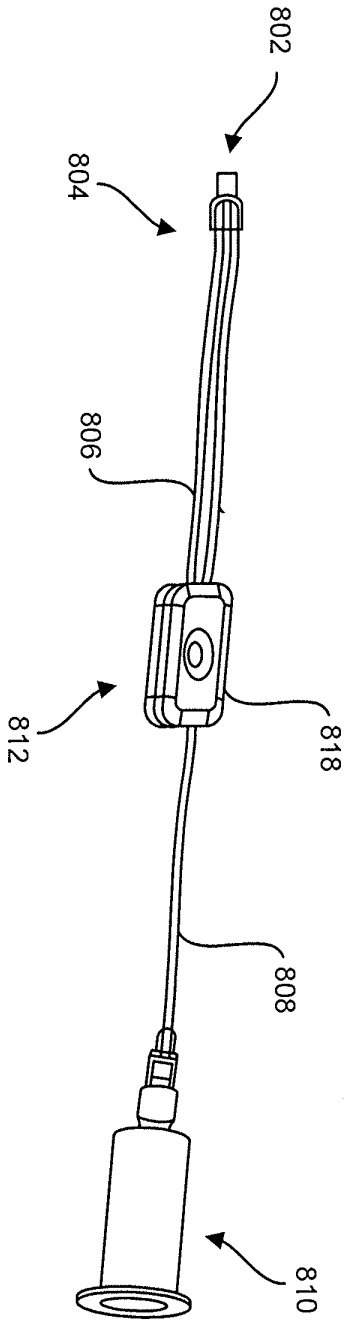

Clinician places a needle into the patient's vein
702
Blood then flows into a chamber pushing the air in the chamber out of the chamber through a filter the volume of blood in this chamber can be 1 to 5 cc.
704
When the blood comes into contact with the filter, the filter is then closed, and the air 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



800

FIG. 8A

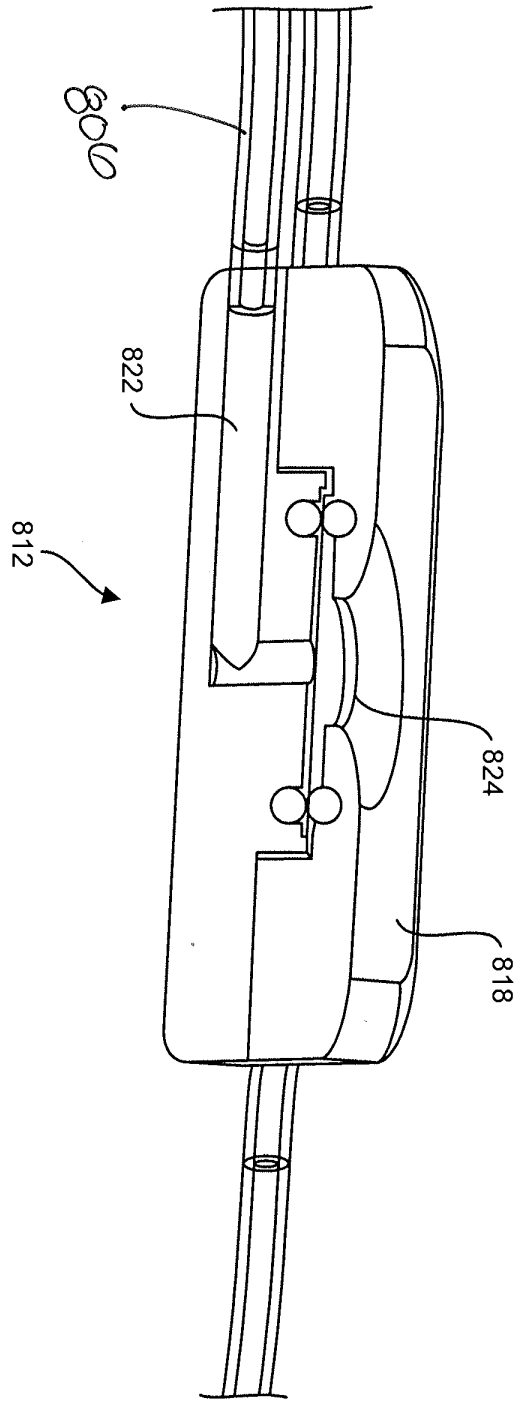


FIG. 8B

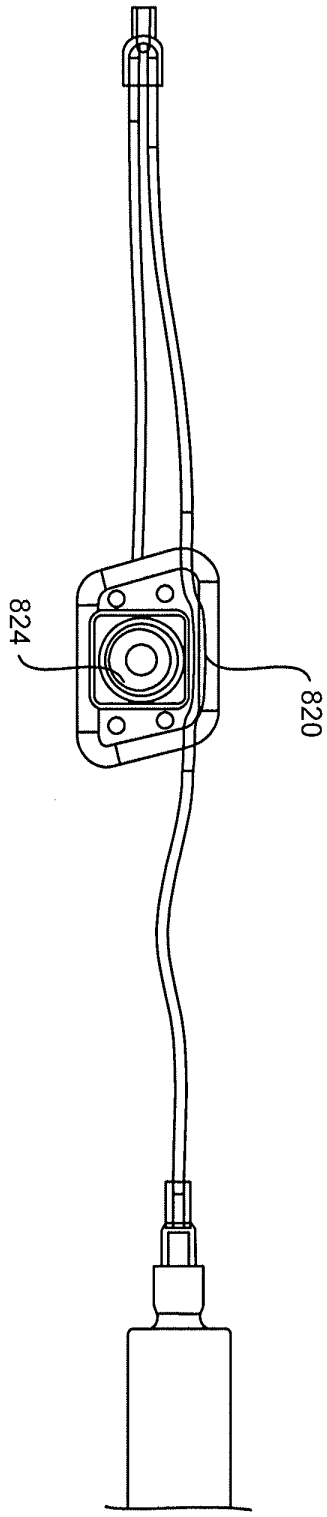


FIG. 8C

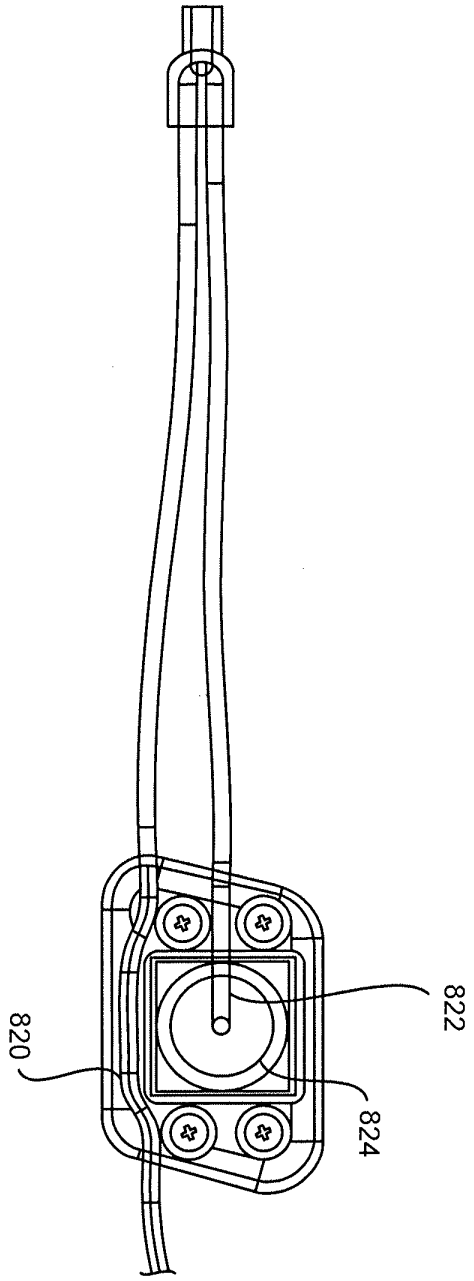


FIG. 8D

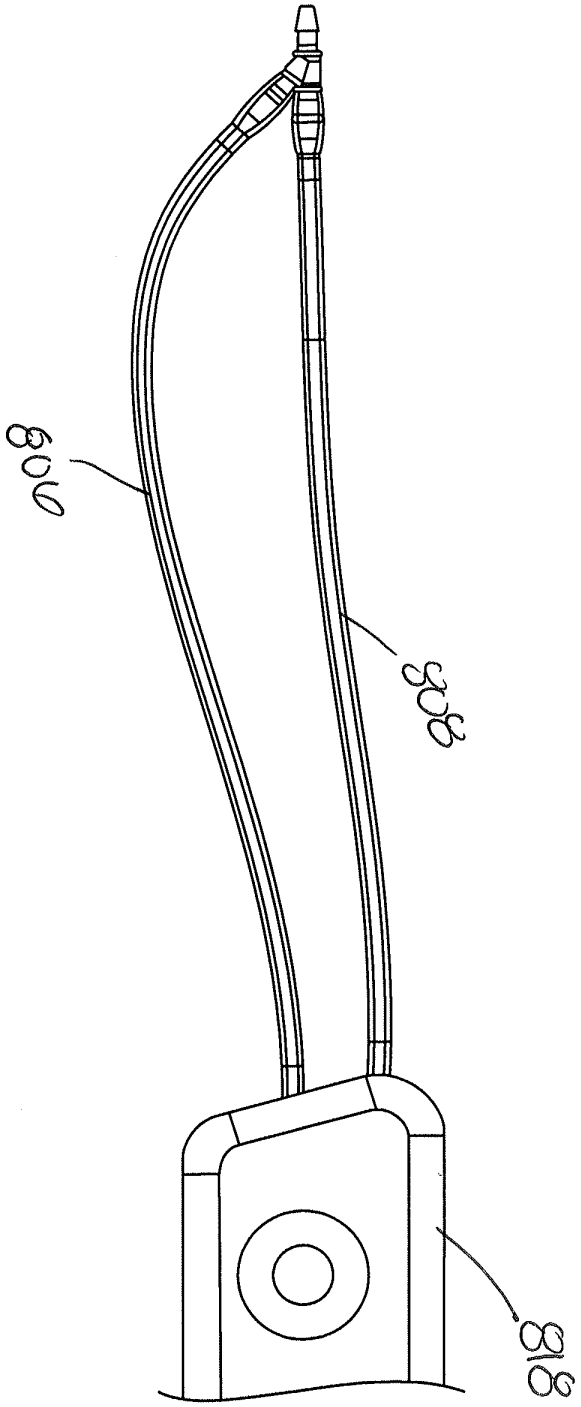
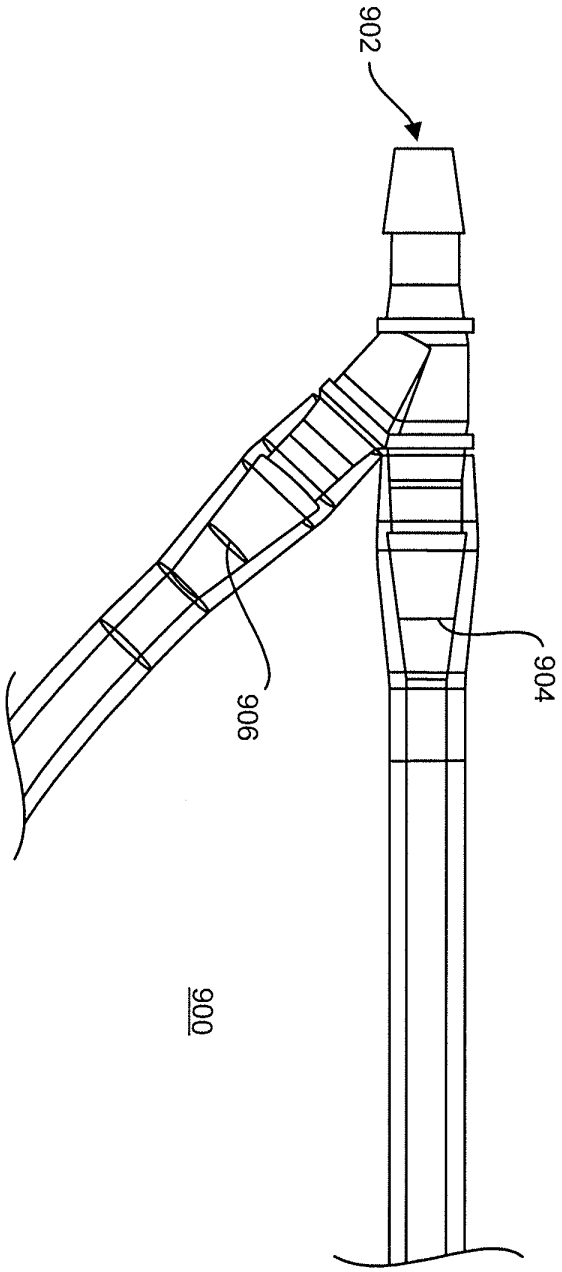


FIG. 8E

FIG. 9



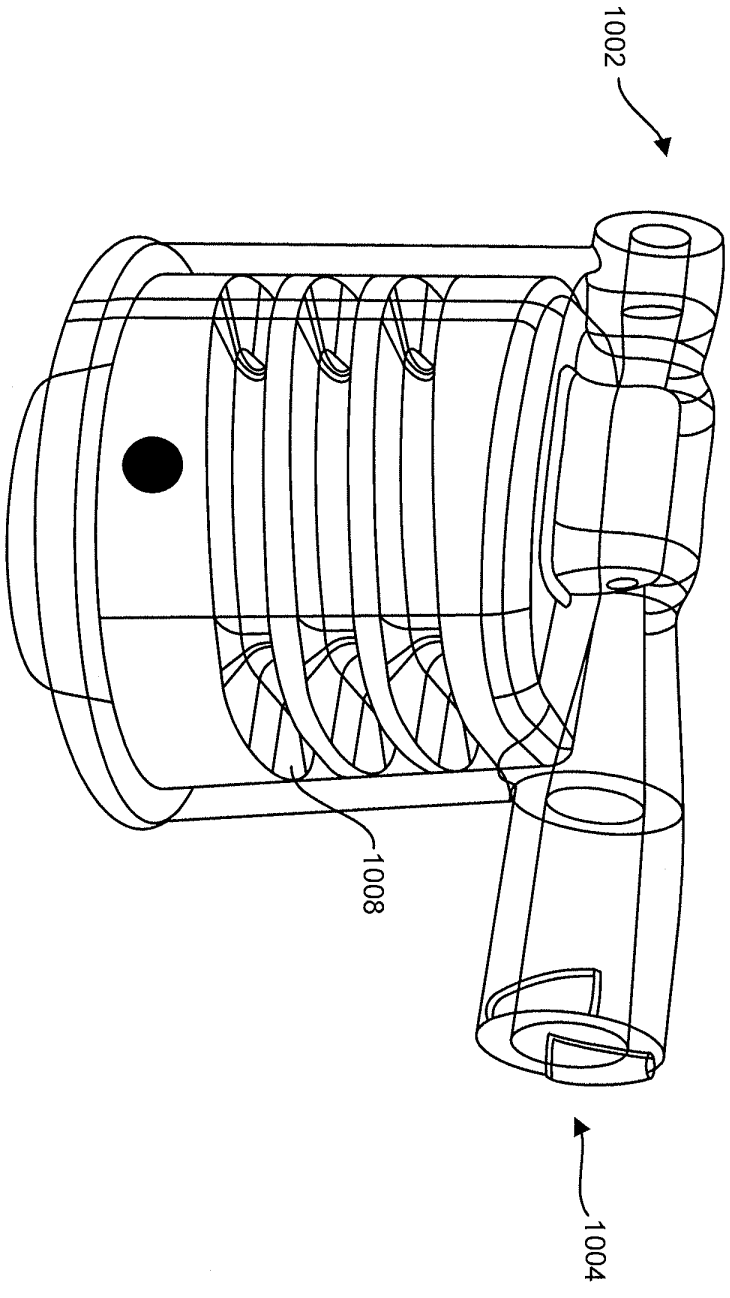


FIG. 10A

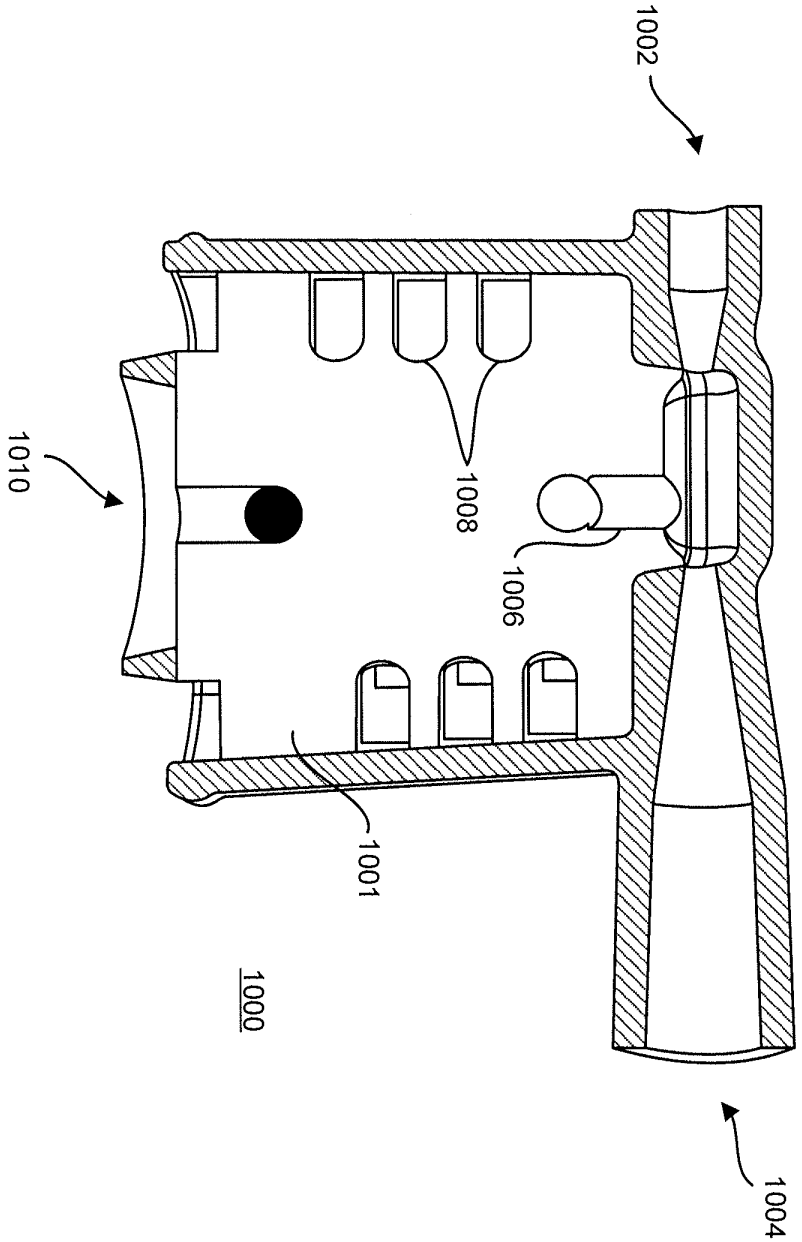


FIG. 10B

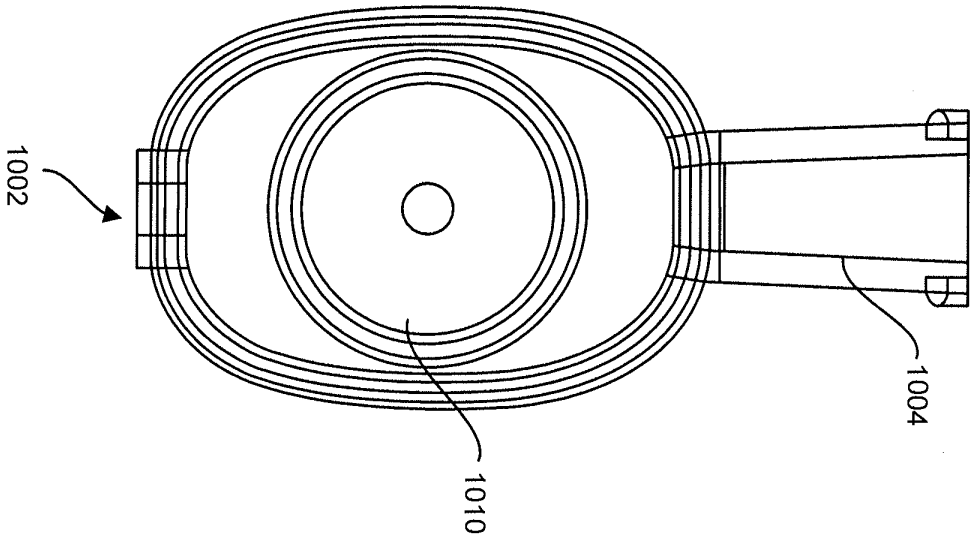
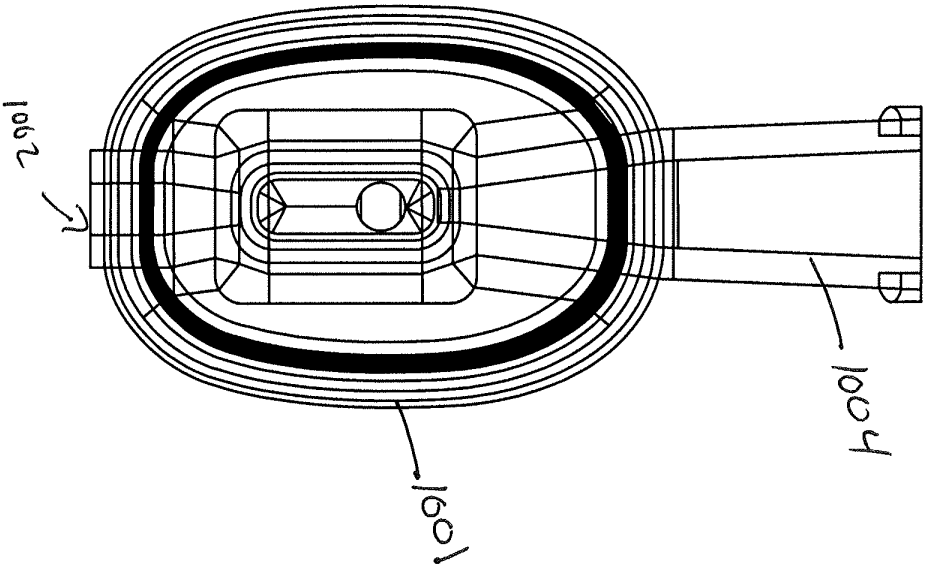


FIG. 10C

FIG. 10D



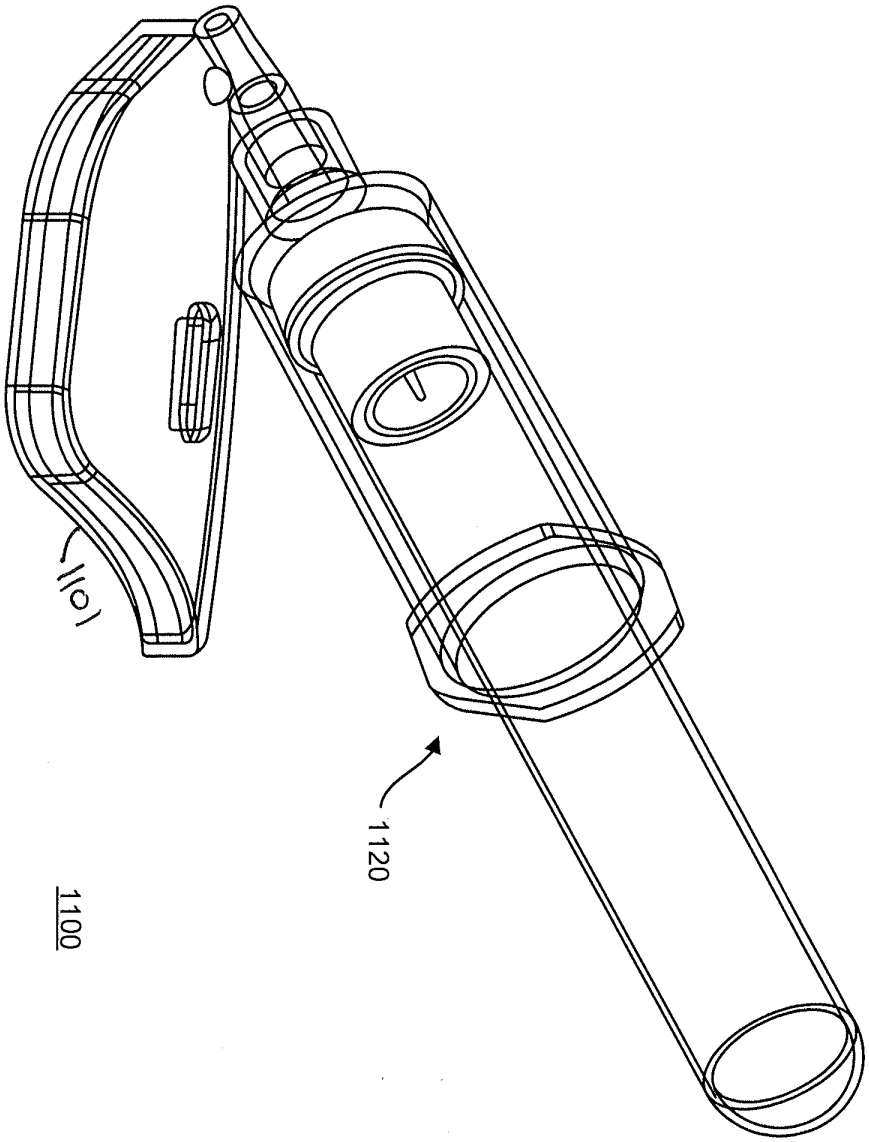


FIG. 11A

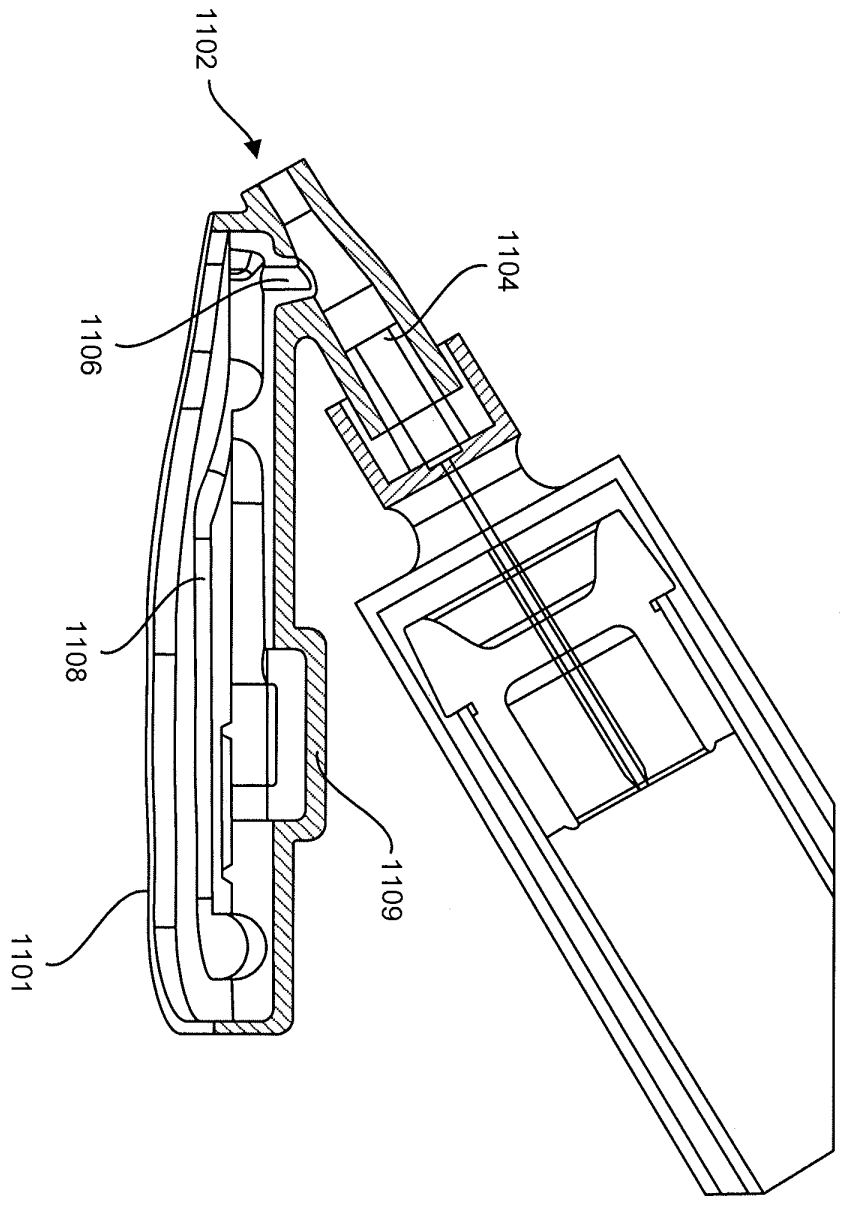


FIG. 11B

FIG. 11C

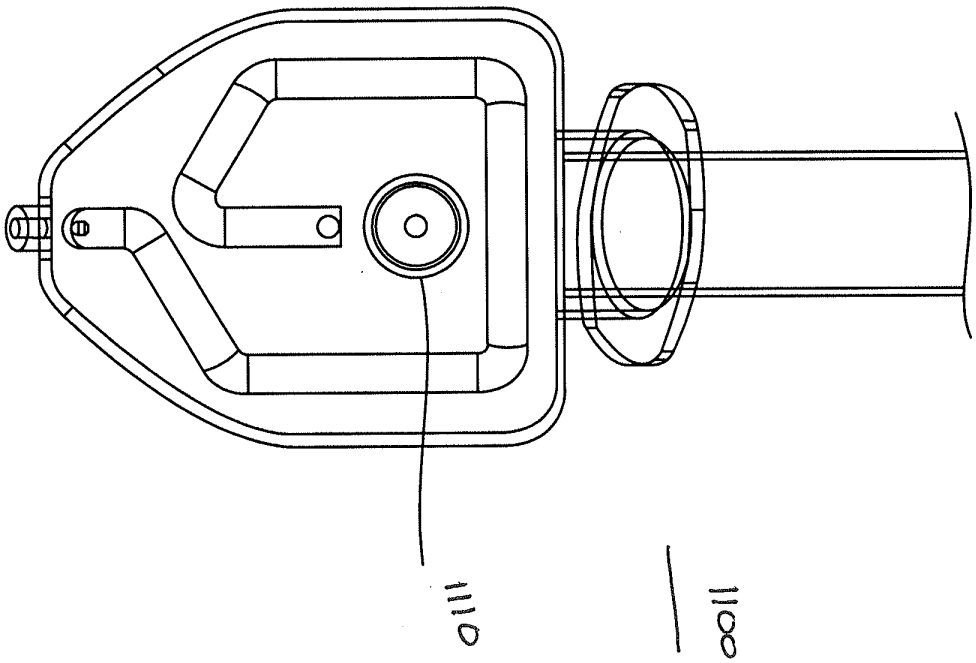
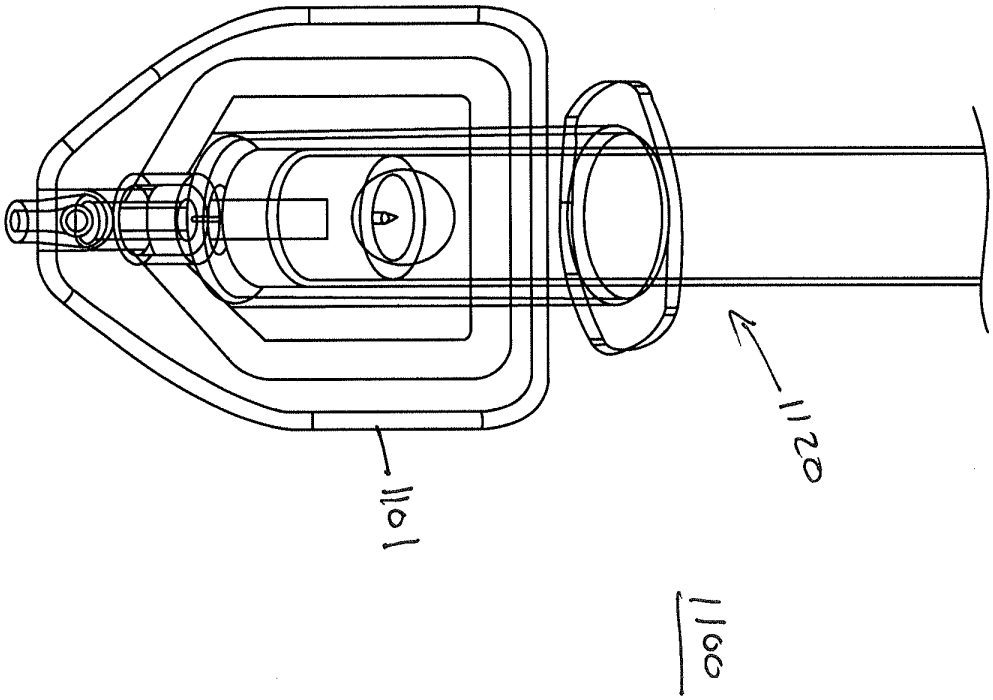


FIG. 11D



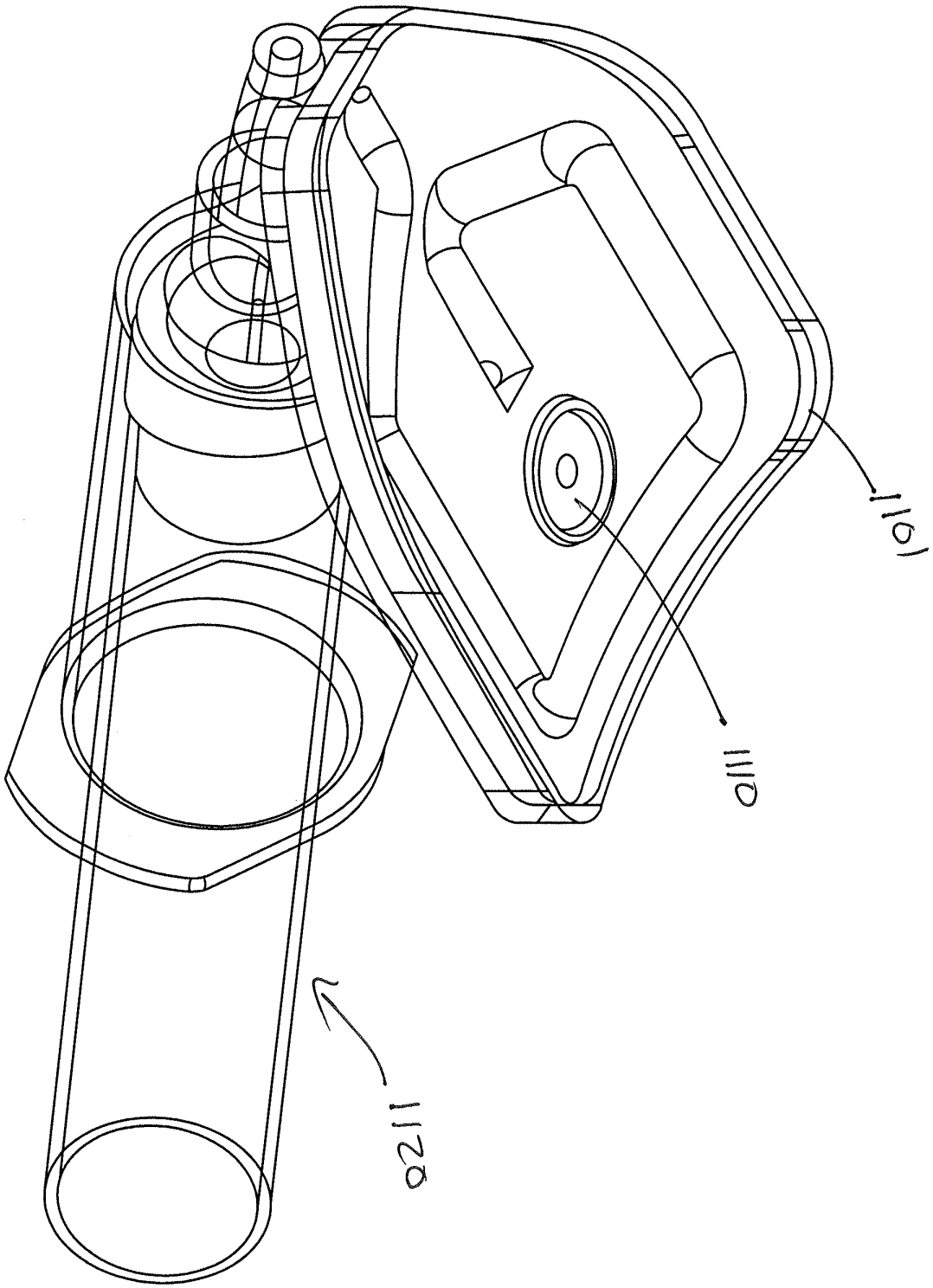


FIG. 11E

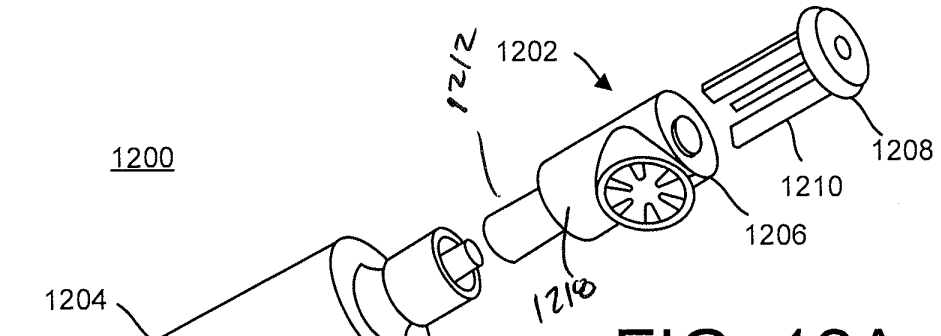


FIG. 12A

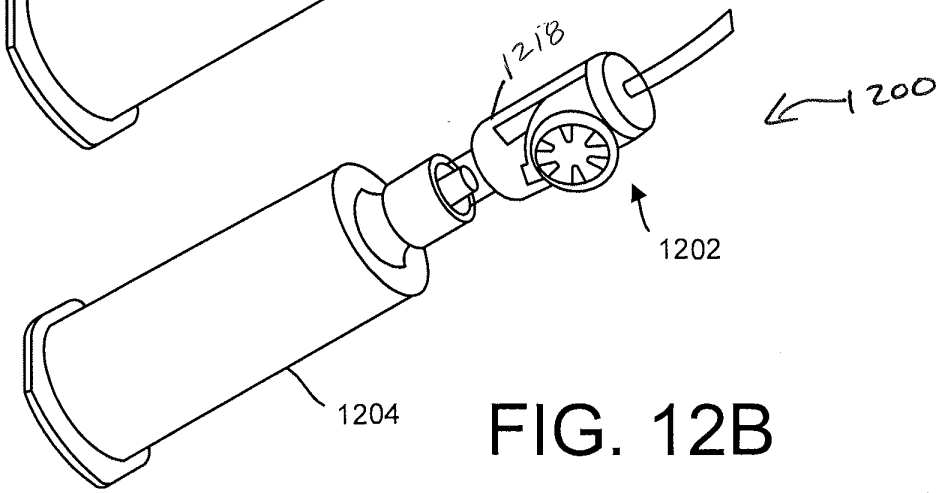


FIG. 12B

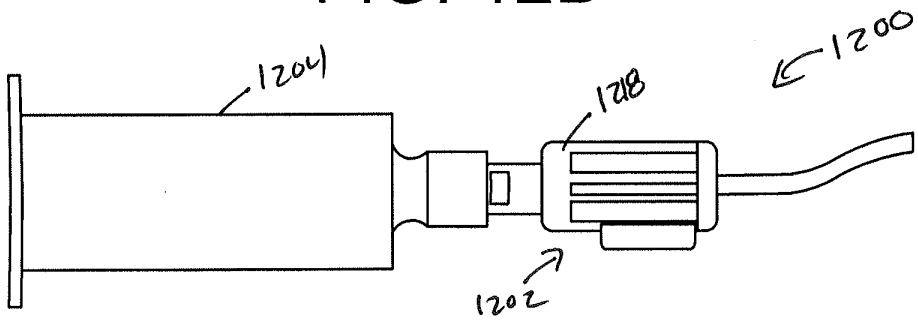


FIG. 12C

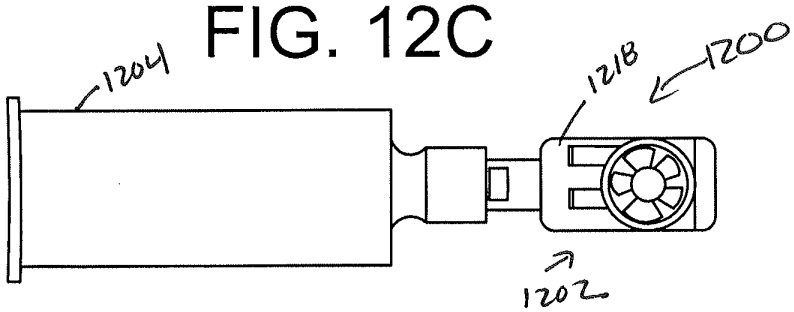


FIG. 12D

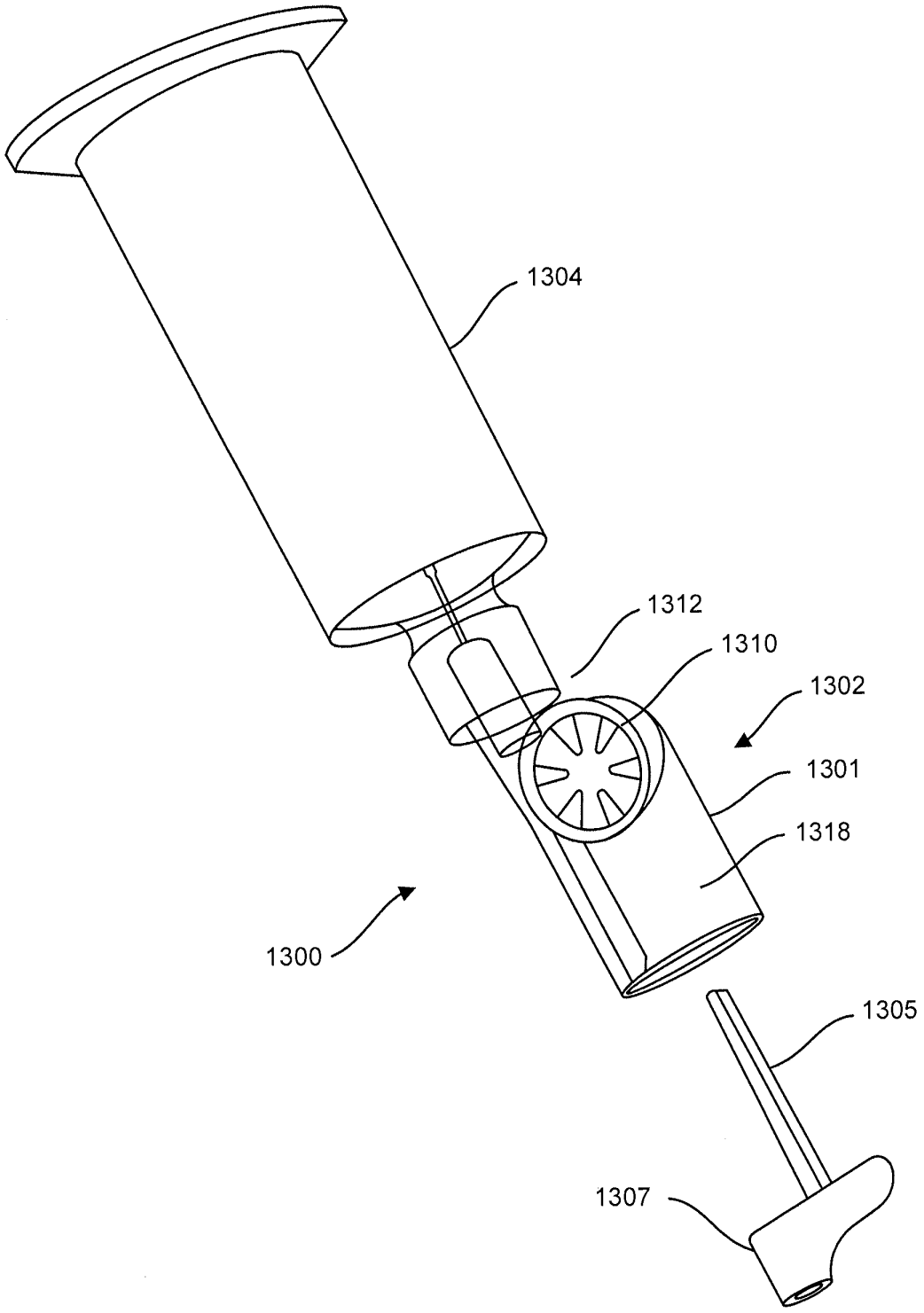


FIG. 13A

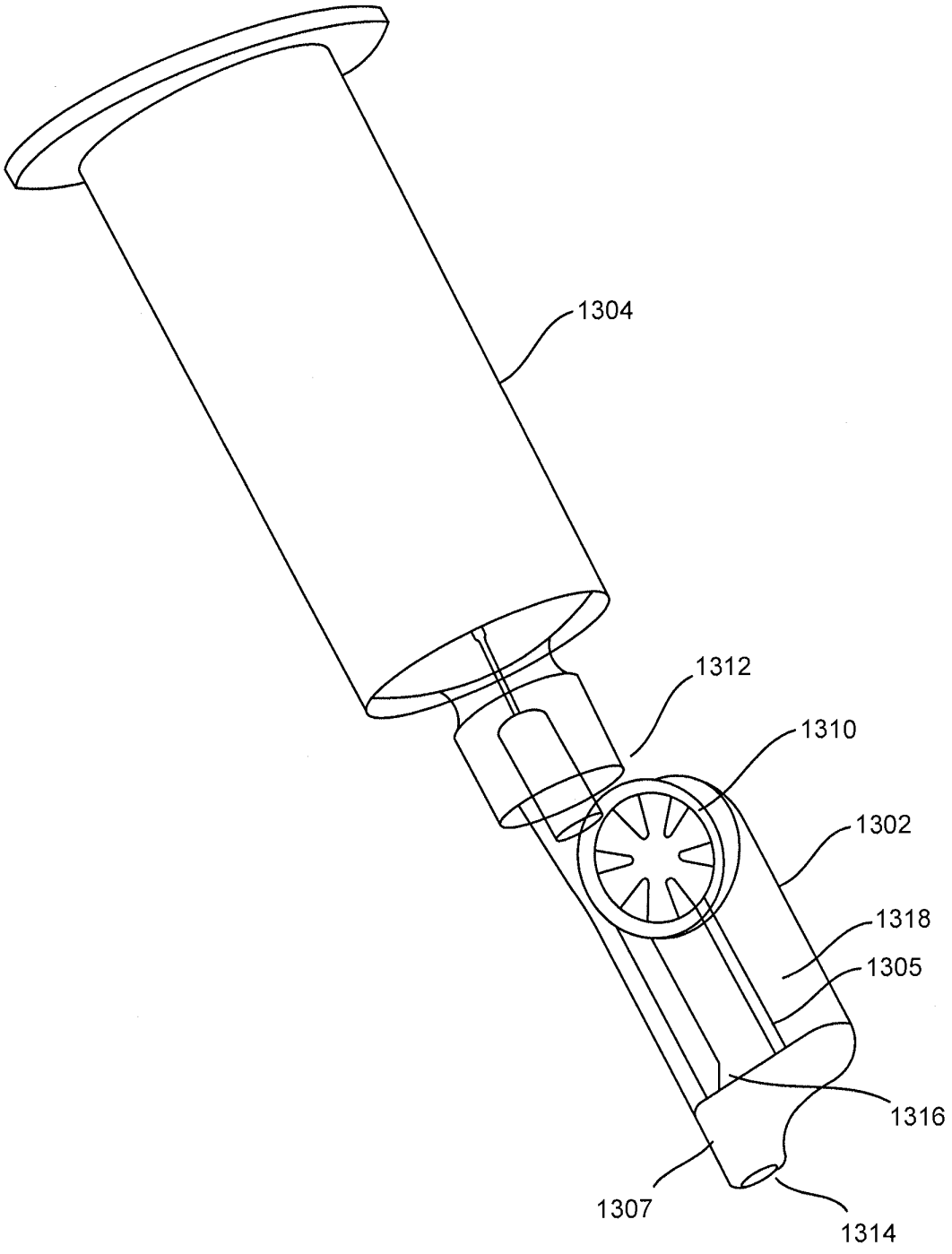


FIG. 13B

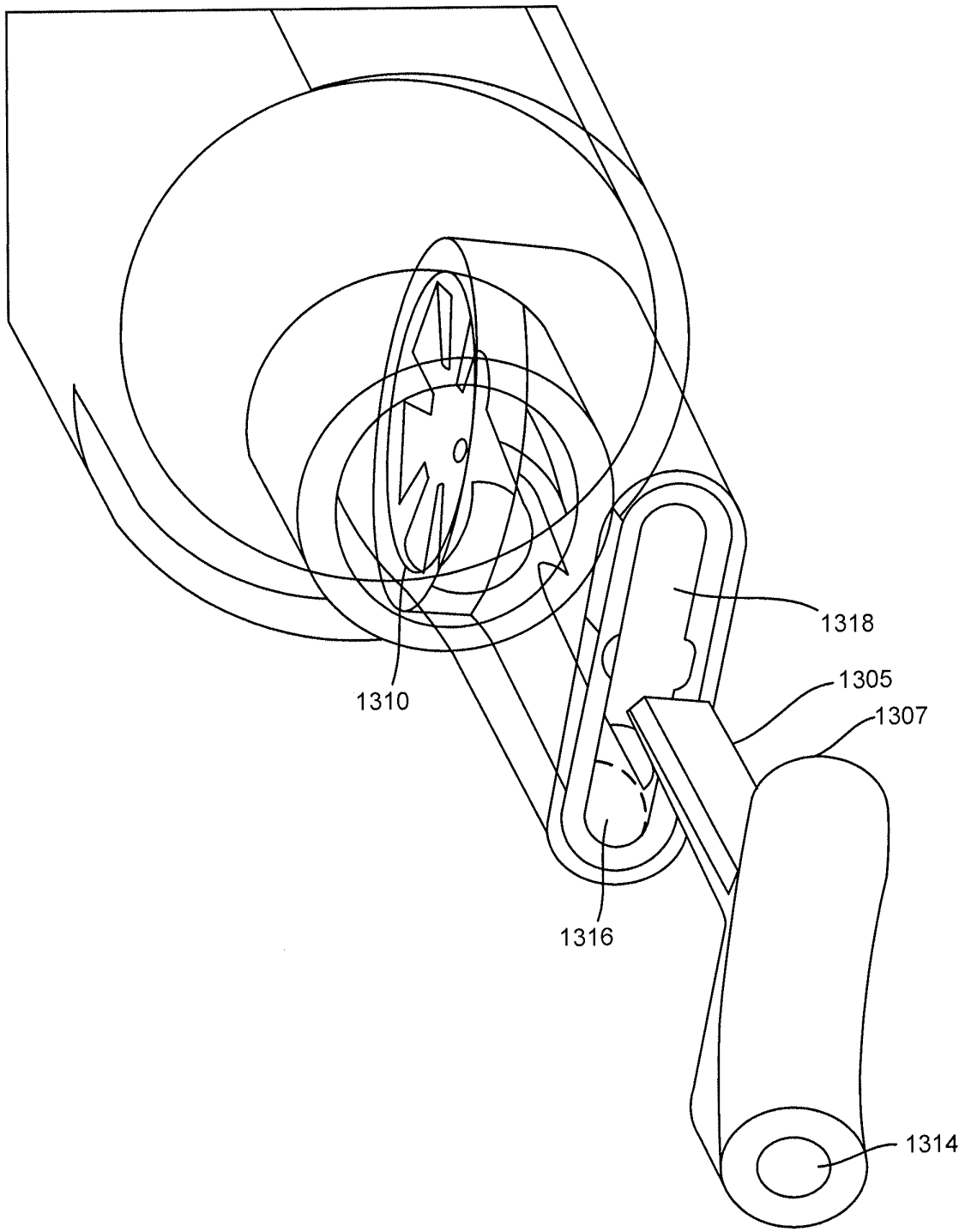


FIG. 13C

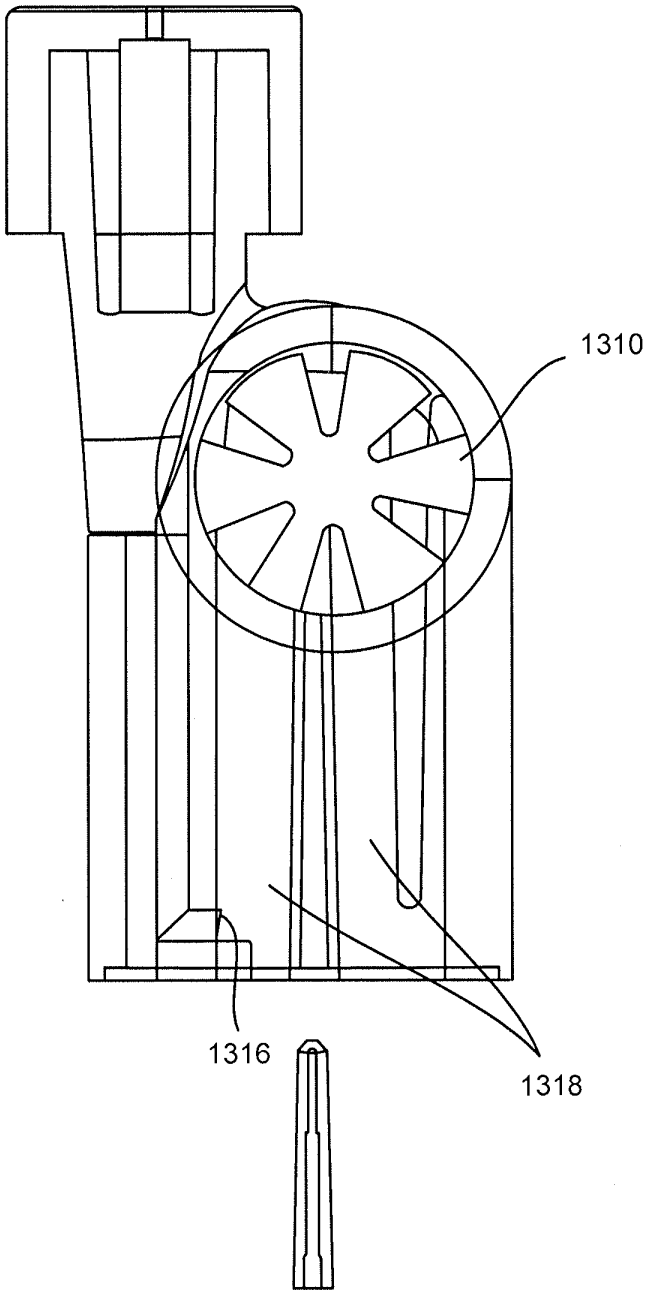


FIG. 13D

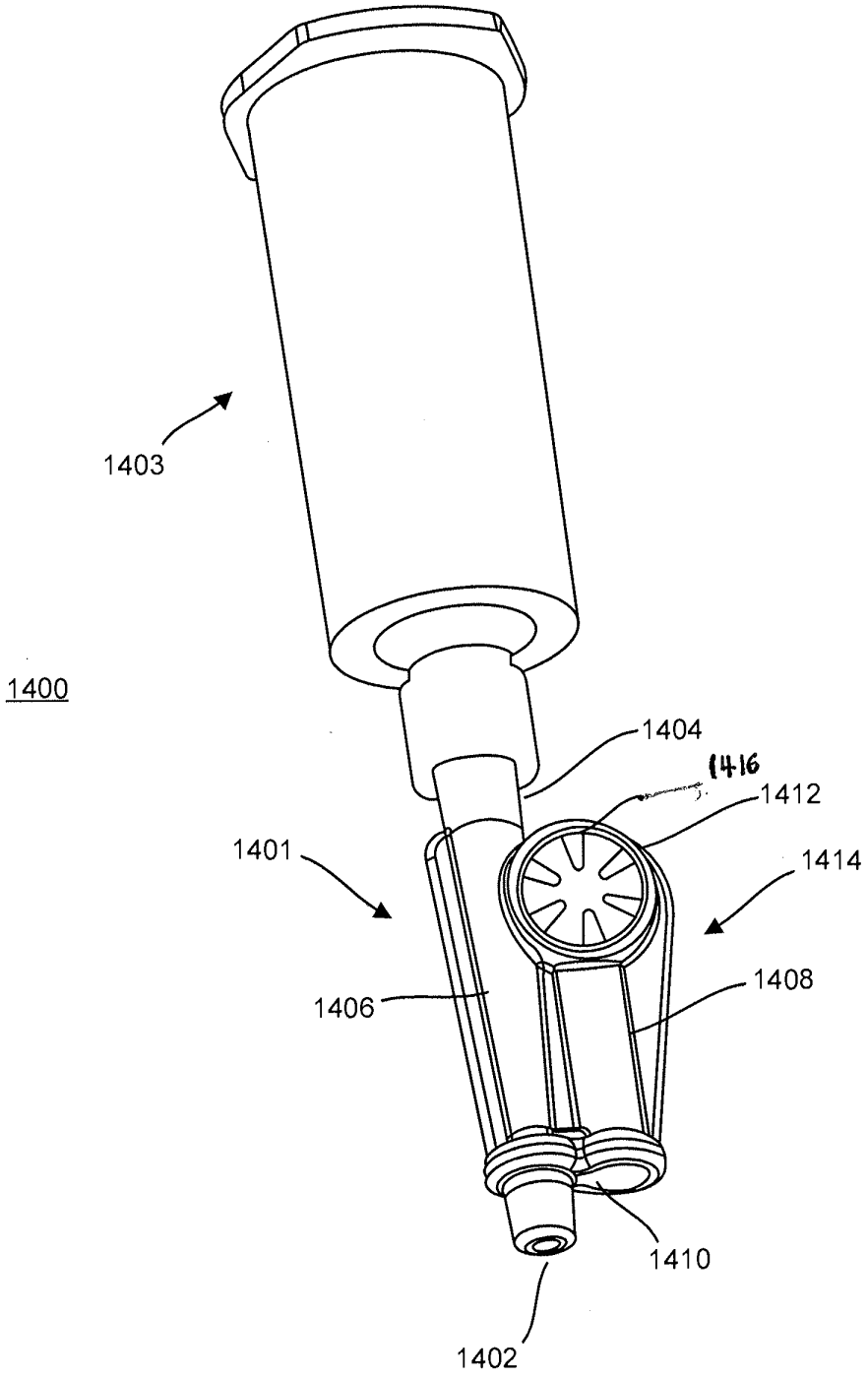


FIG. 14A

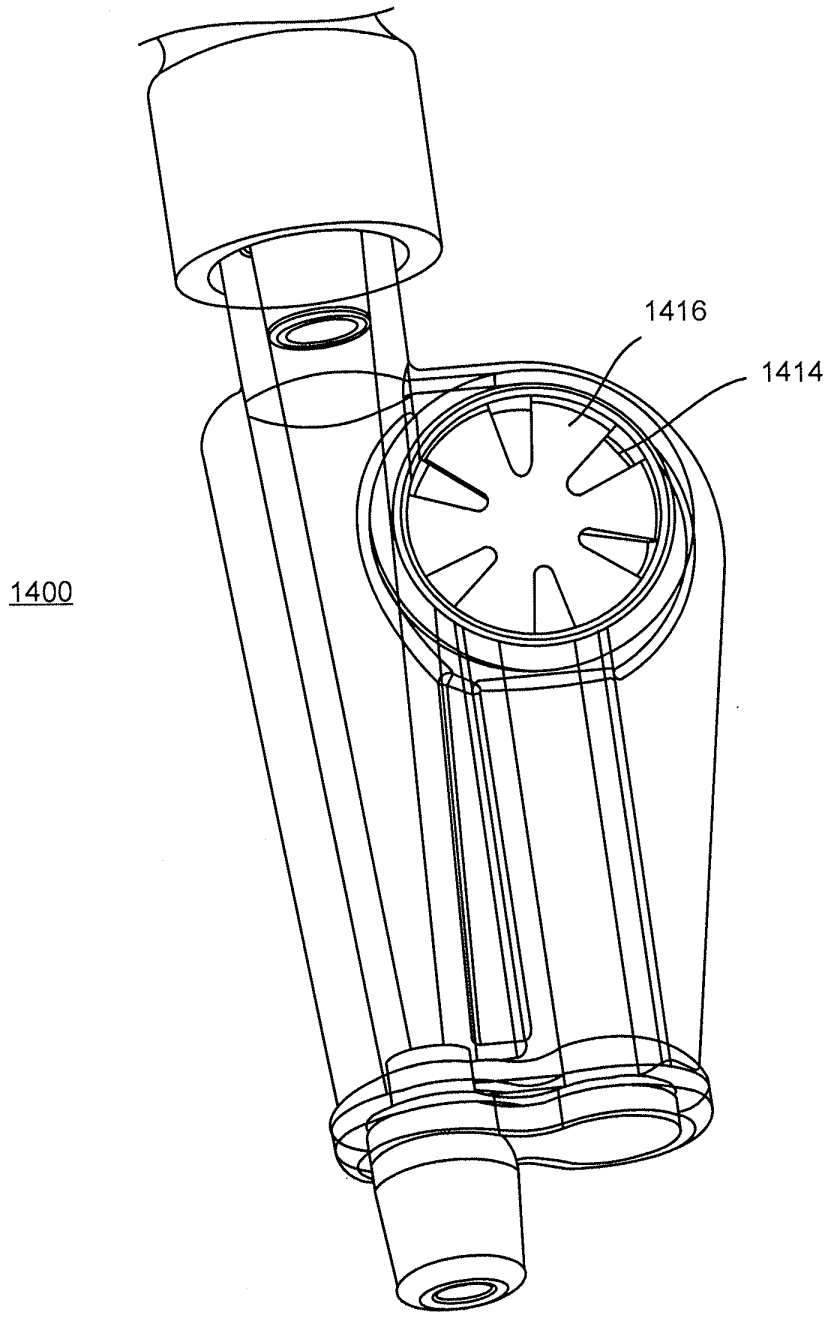


FIG. 14B

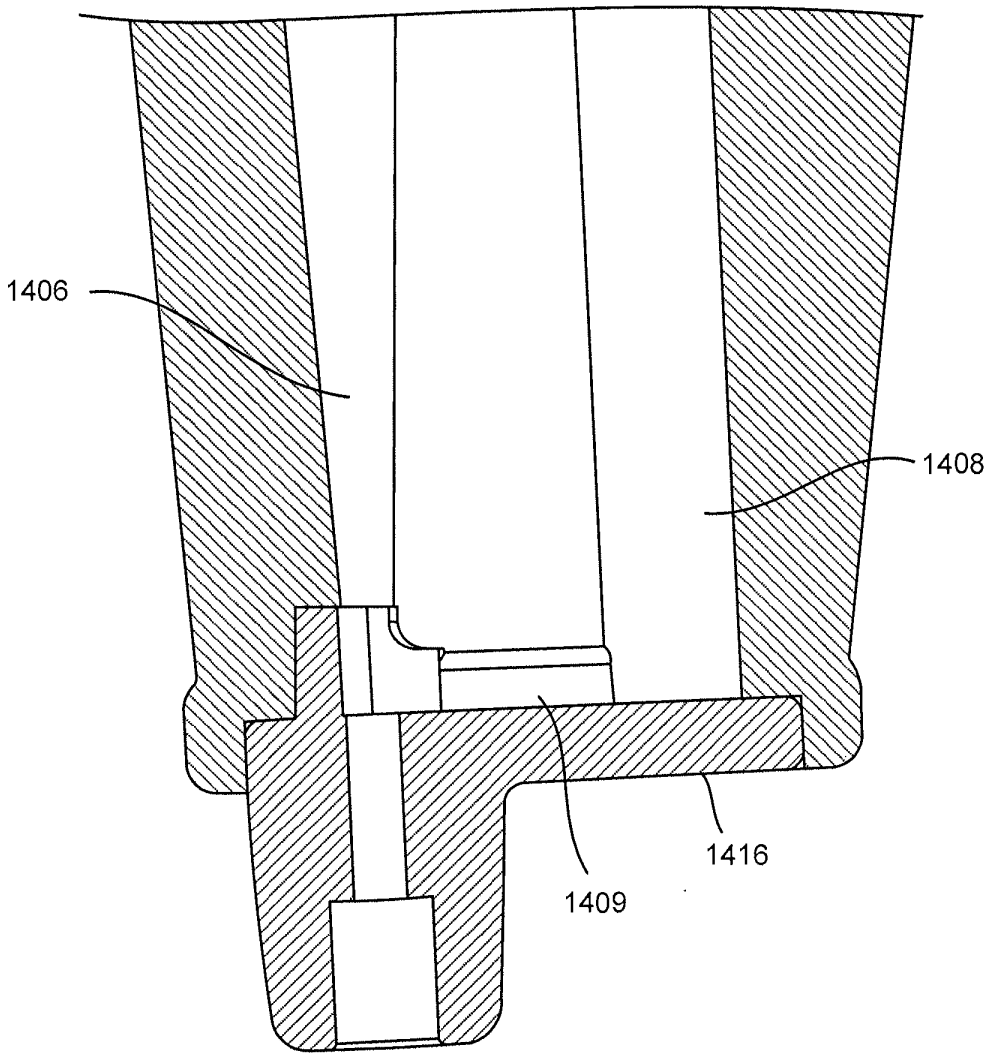


FIG. 14C

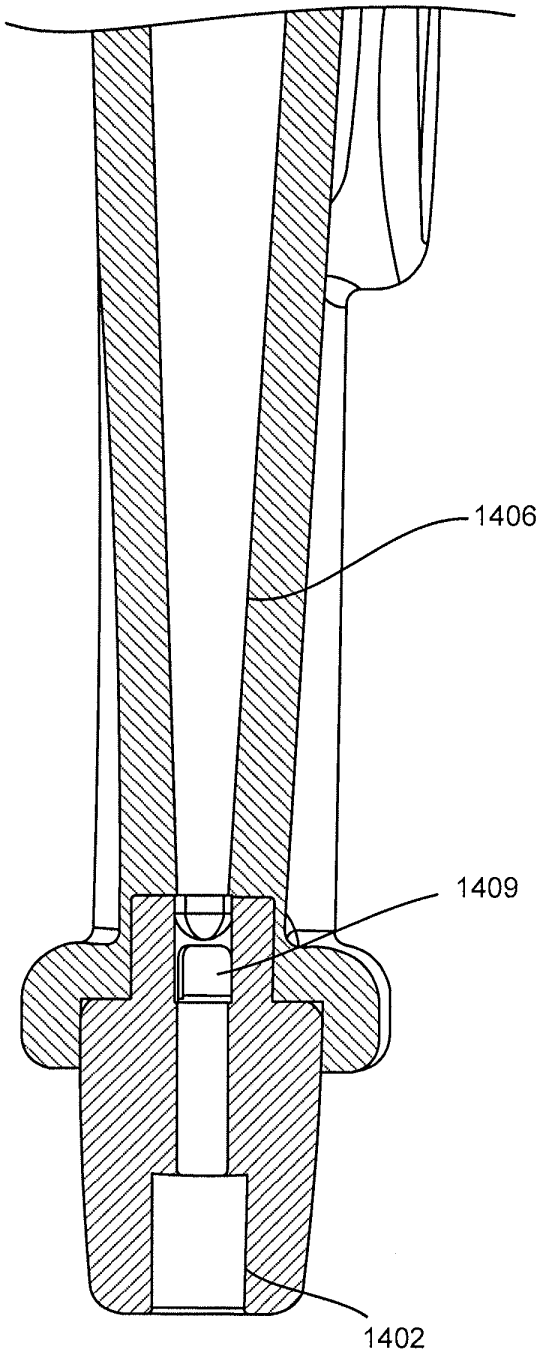


FIG. 14D

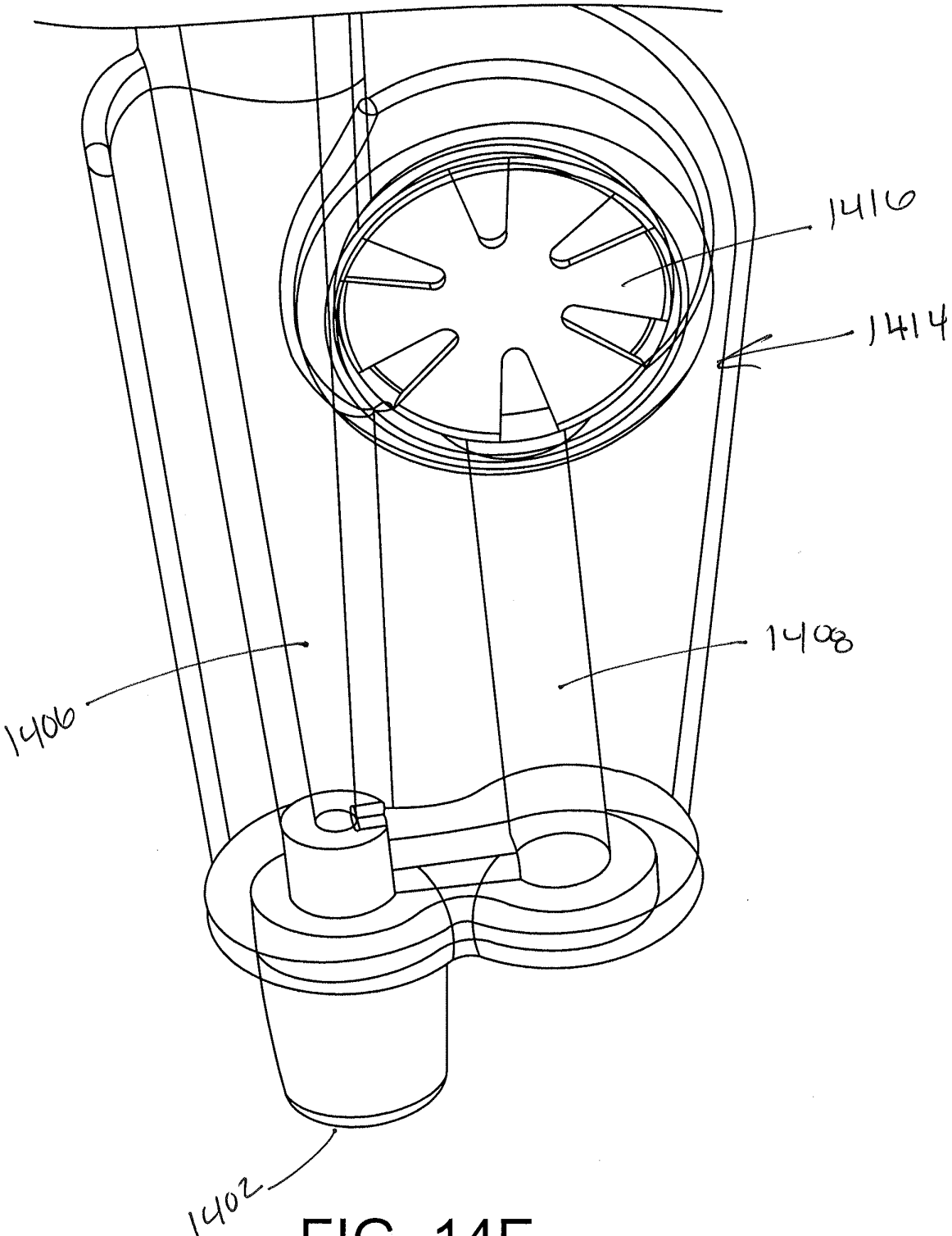


FIG. 14E

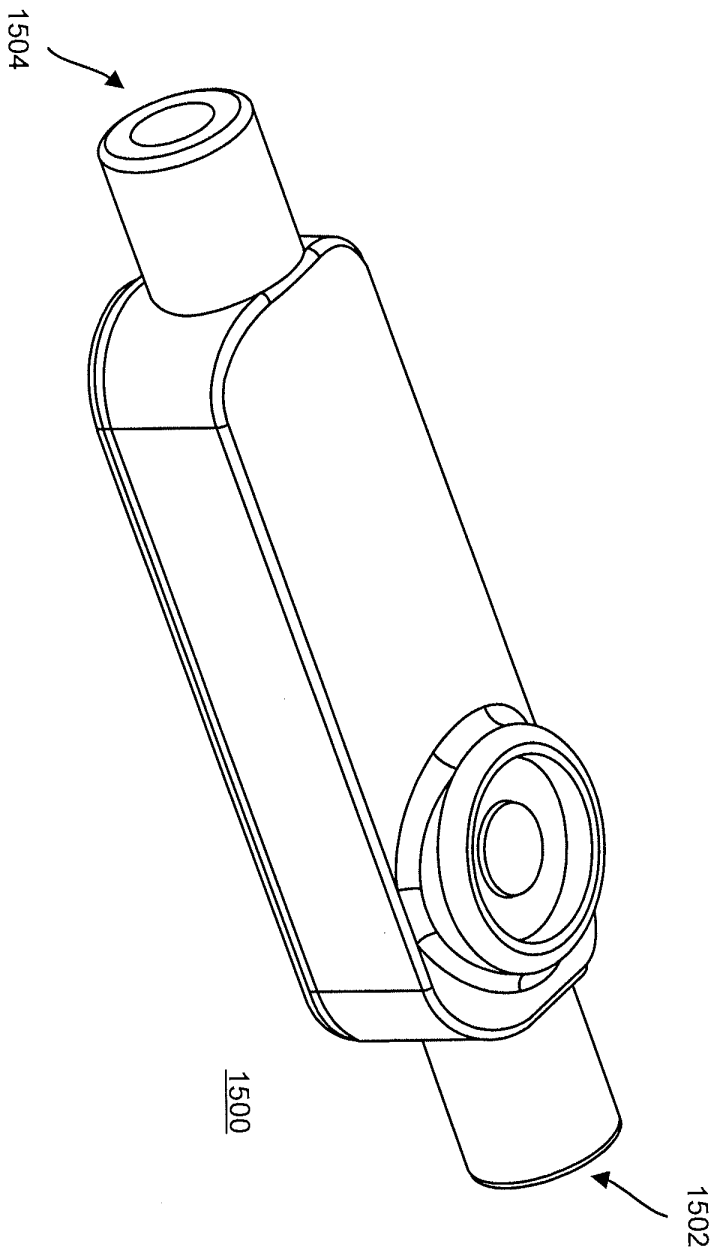


FIG. 15A

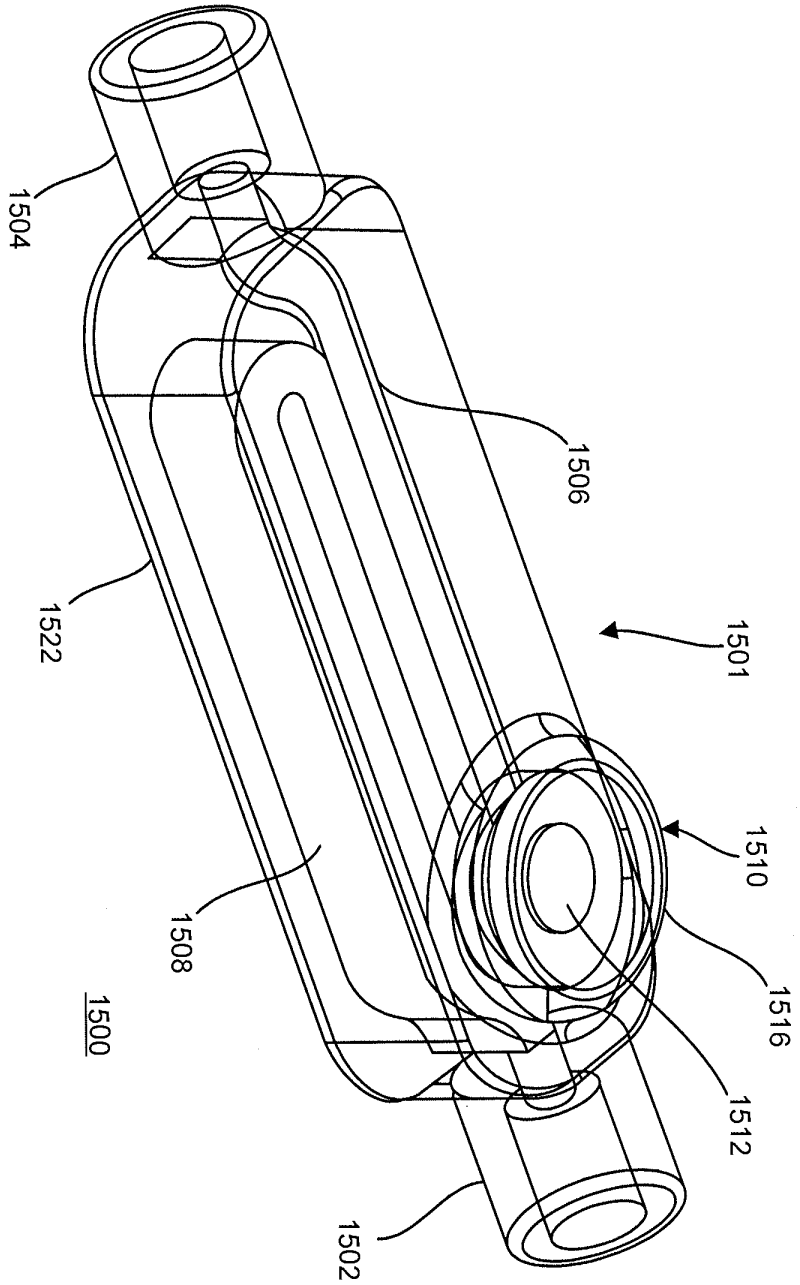


FIG. 15B

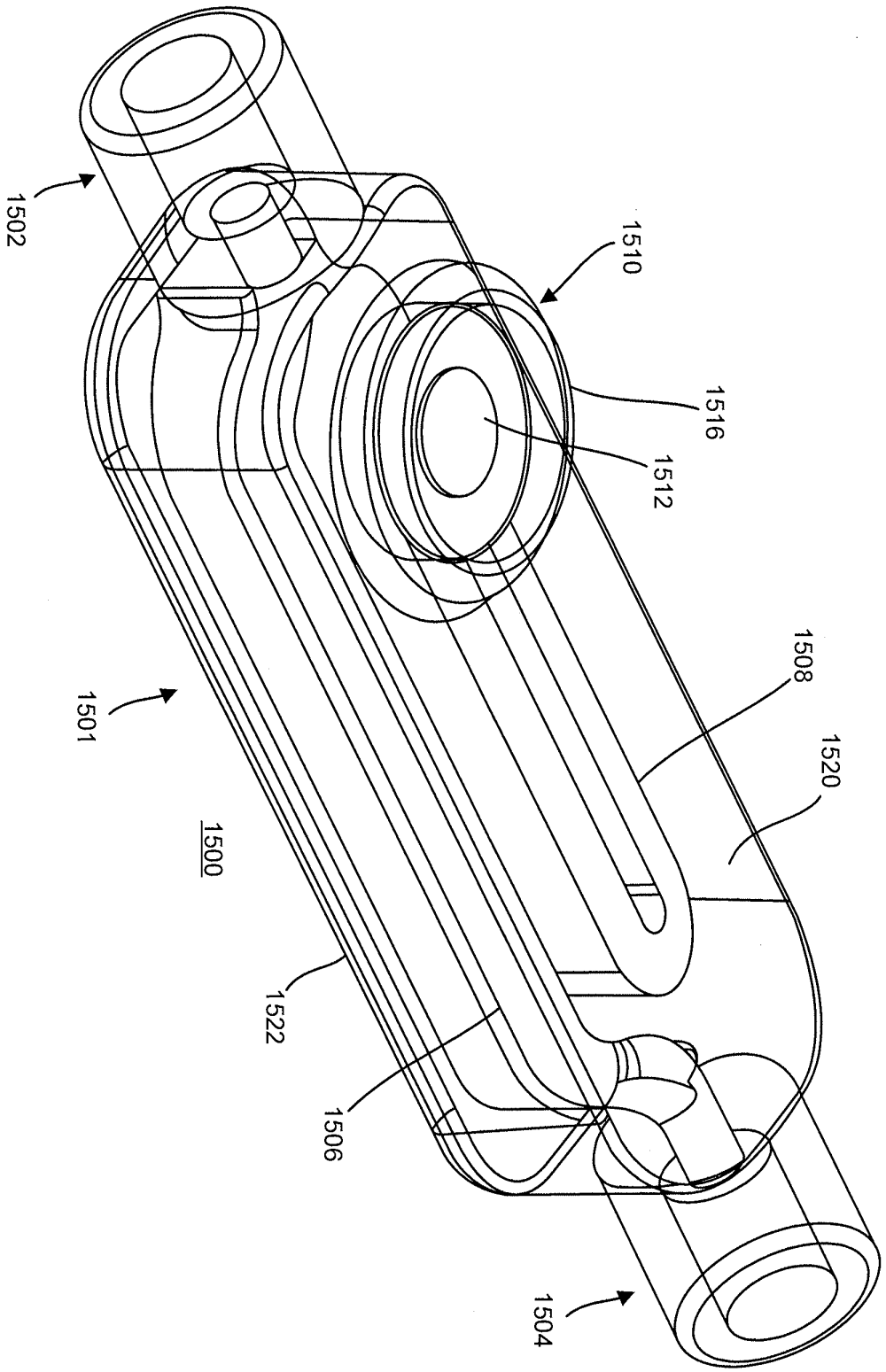


FIG. 15C

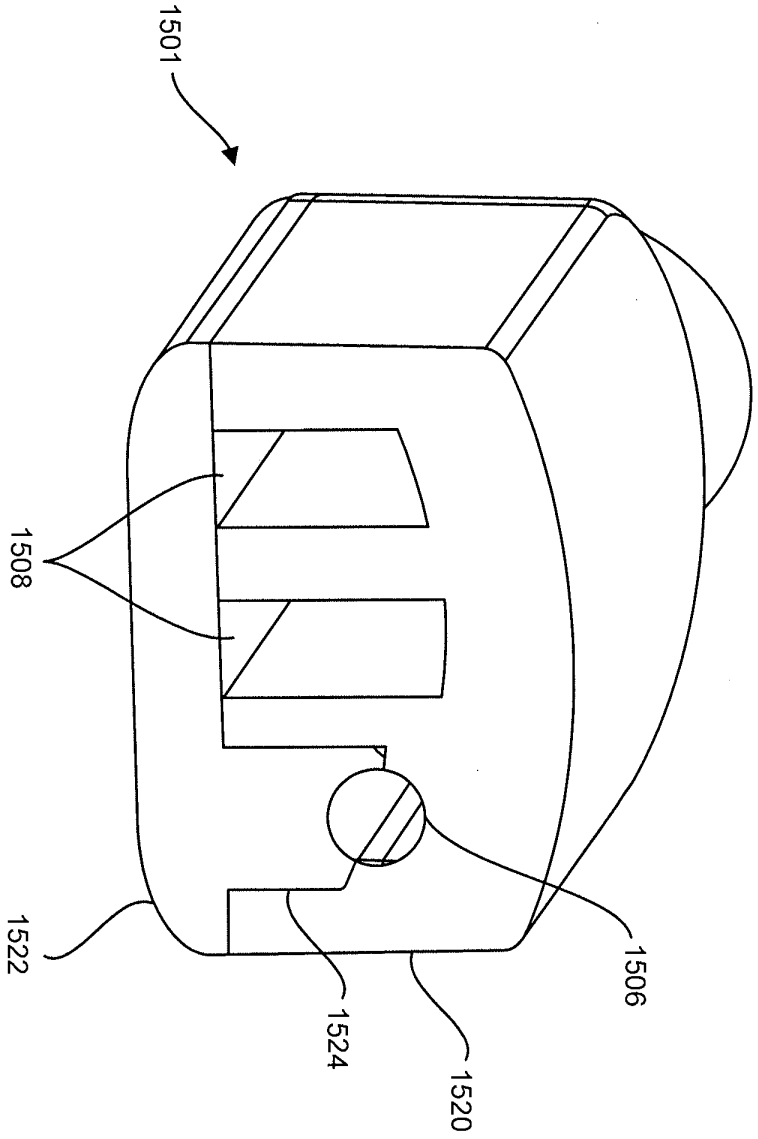


FIG. 15D

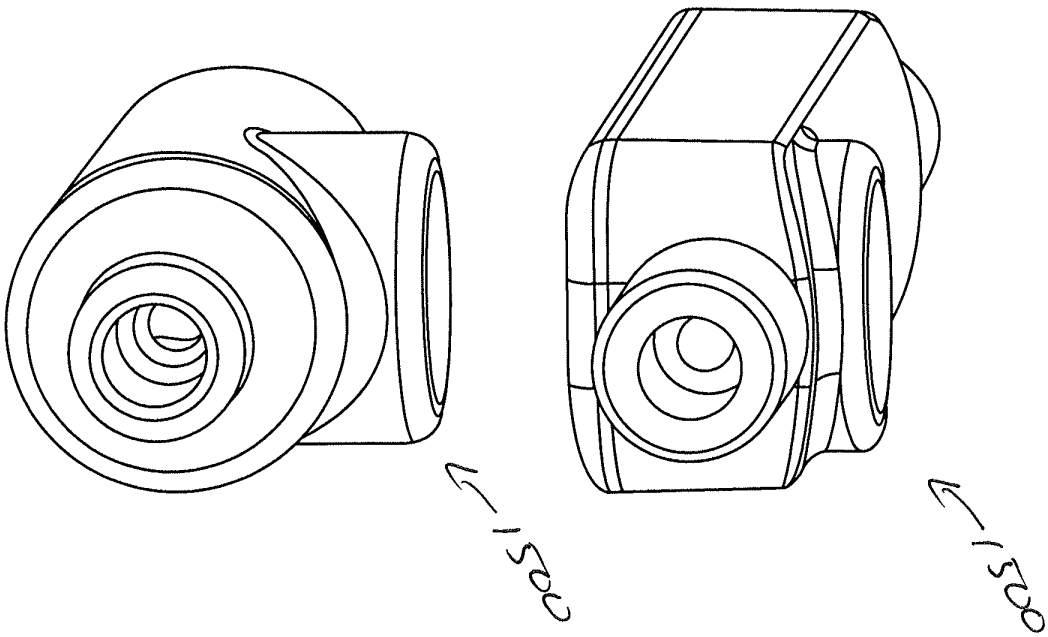


FIG. 15E

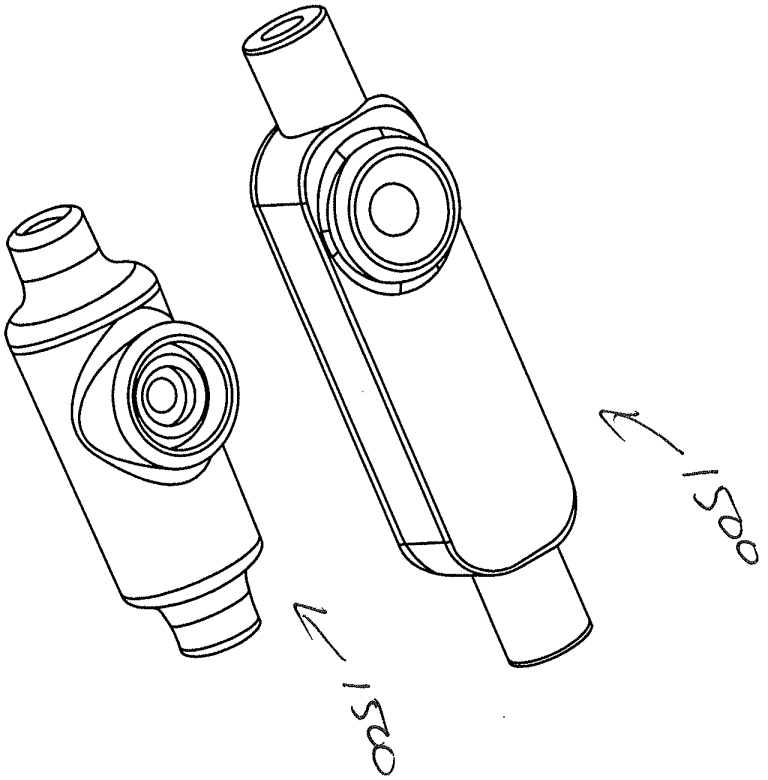


FIG. 15F

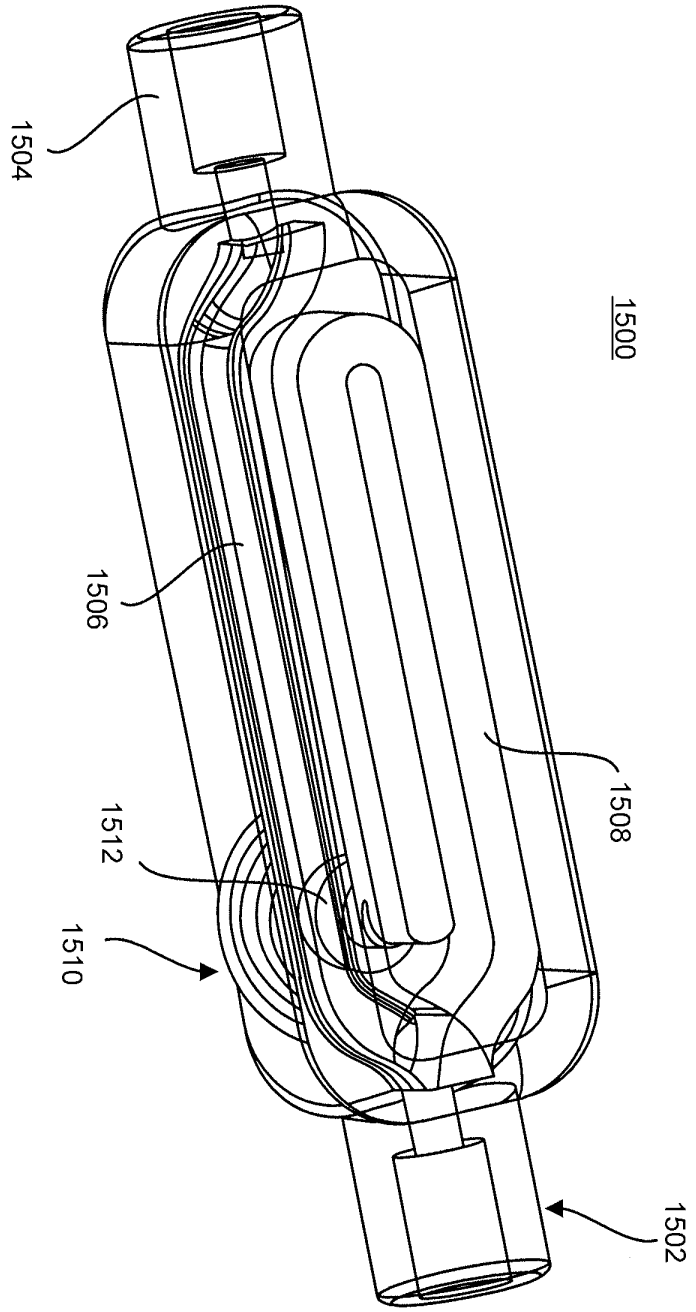


FIG. 15G

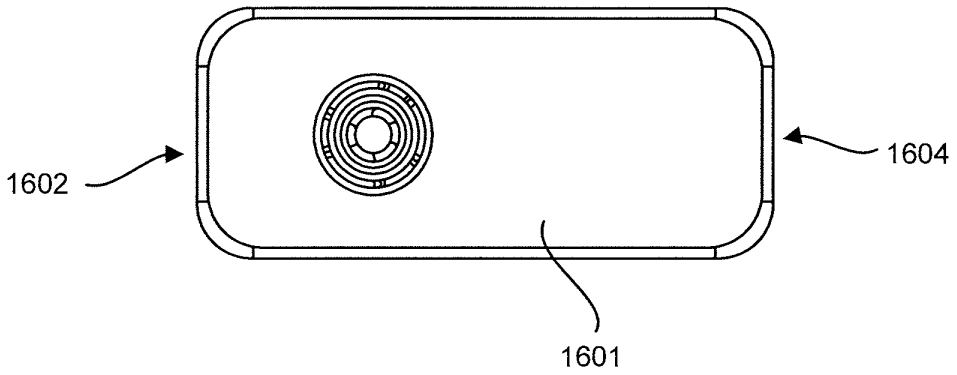


FIG. 16A

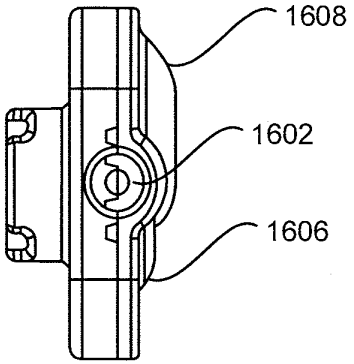


FIG. 16C

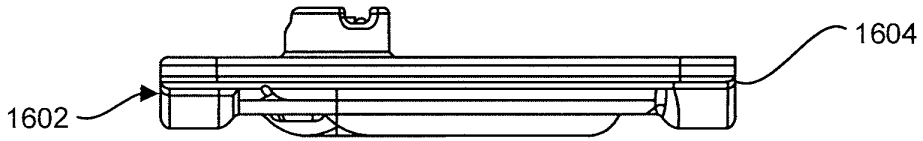


FIG. 16B

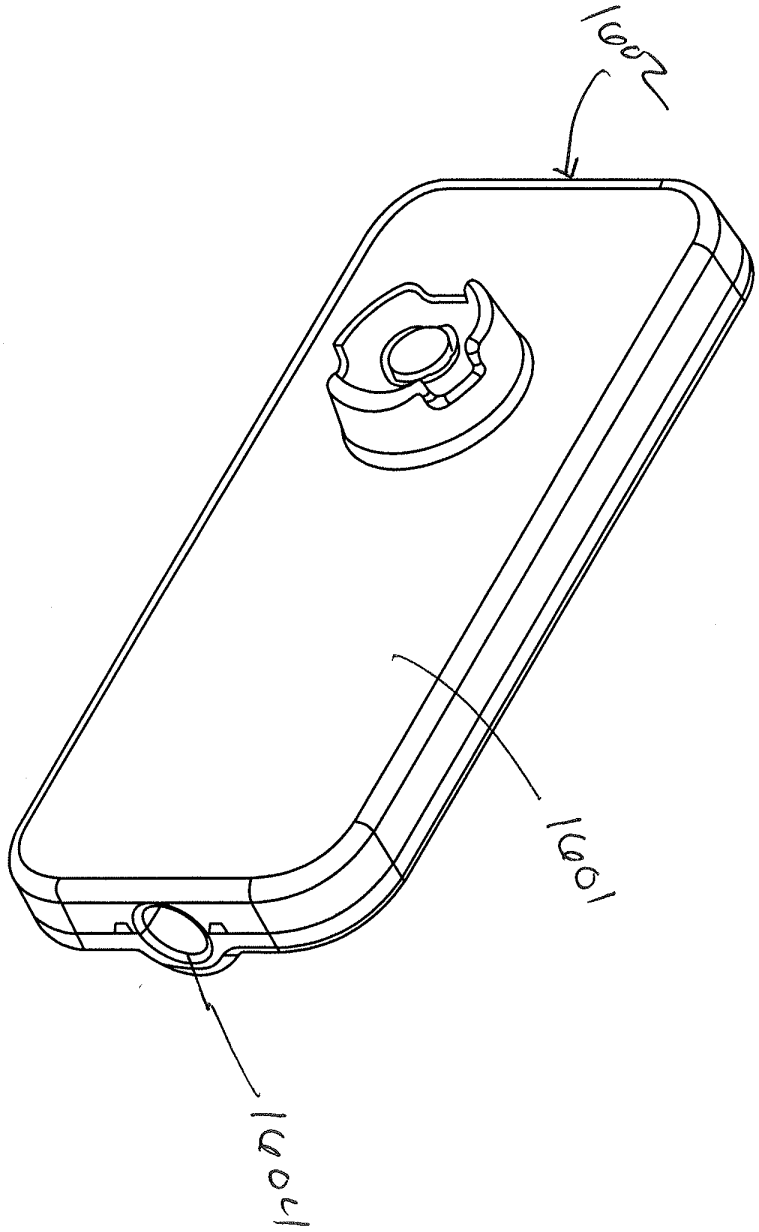


FIG. 16D

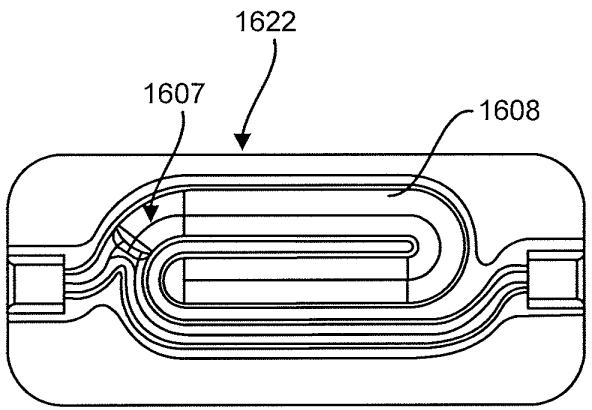


FIG. 17A

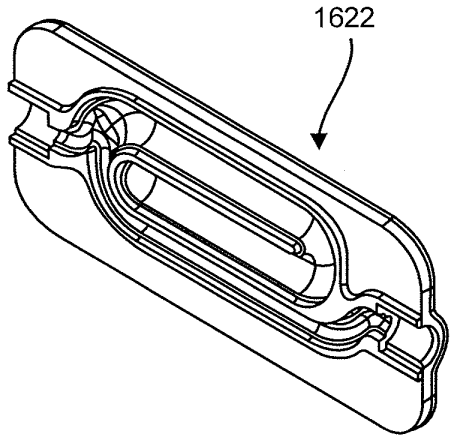


FIG. 17B

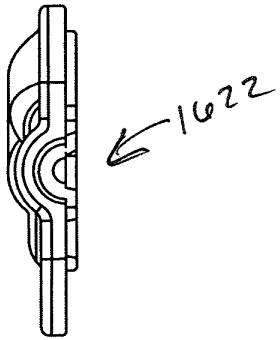


FIG. 17C

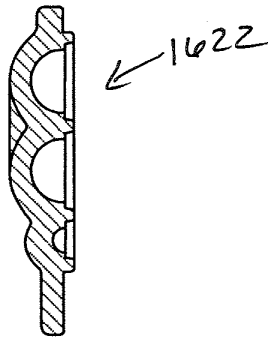


FIG. 17D

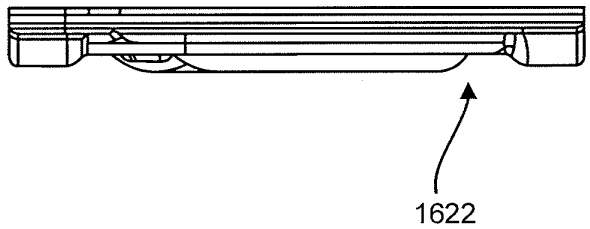


FIG. 17E

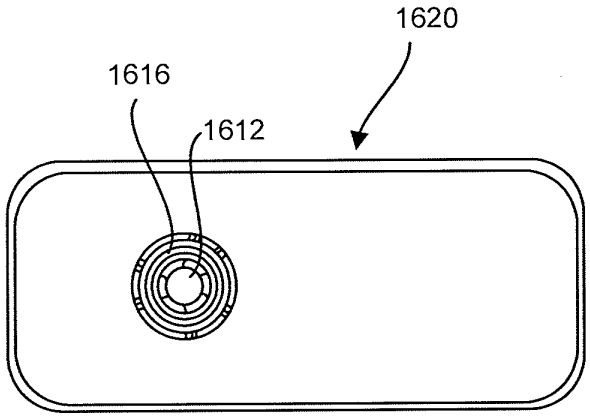


FIG. 18A

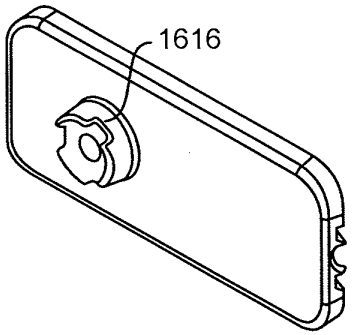


FIG. 18B

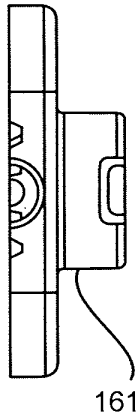


FIG. 18C

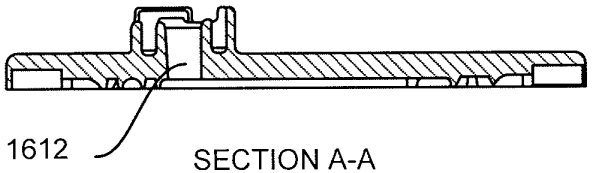


FIG. 18D

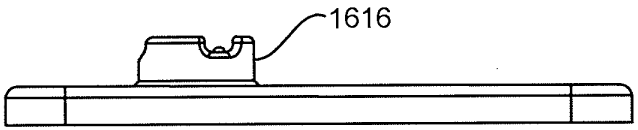


FIG. 18E

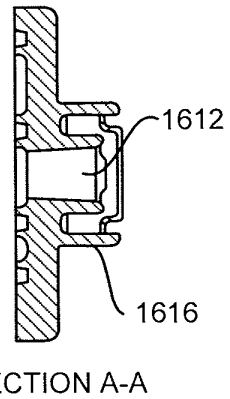


FIG. 18F

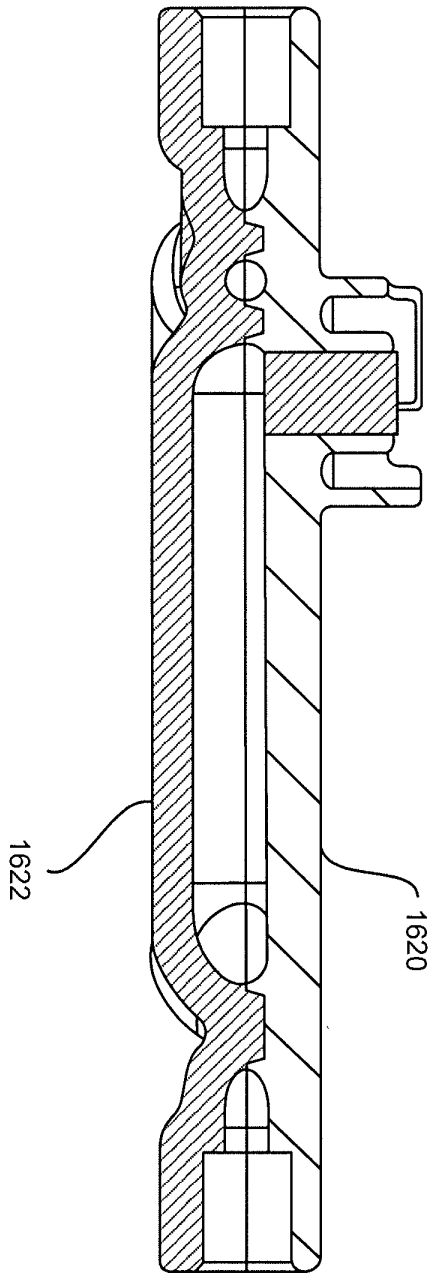


FIG. 19A

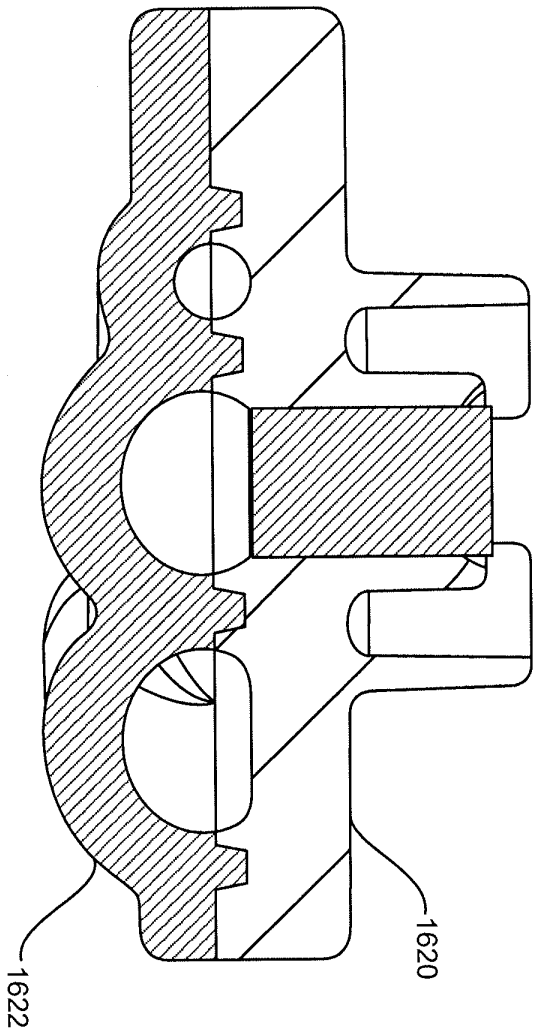


FIG. 19B

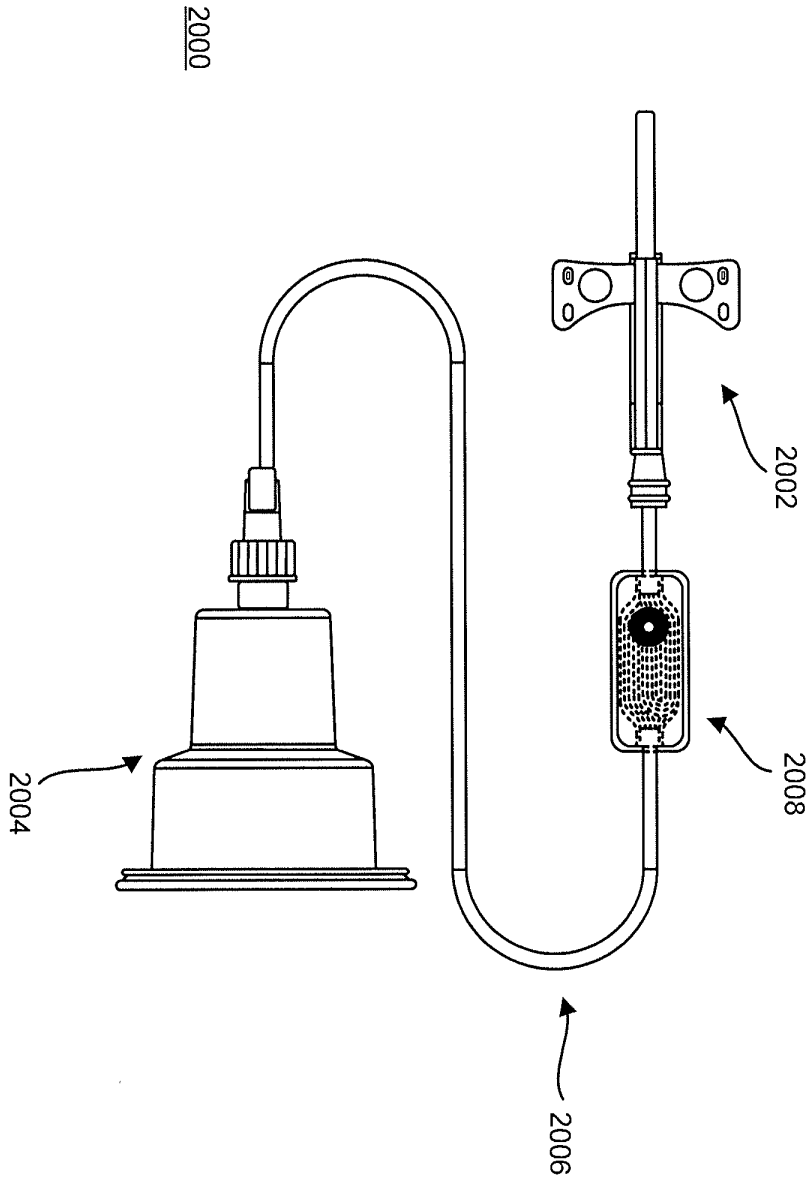


FIG. 20

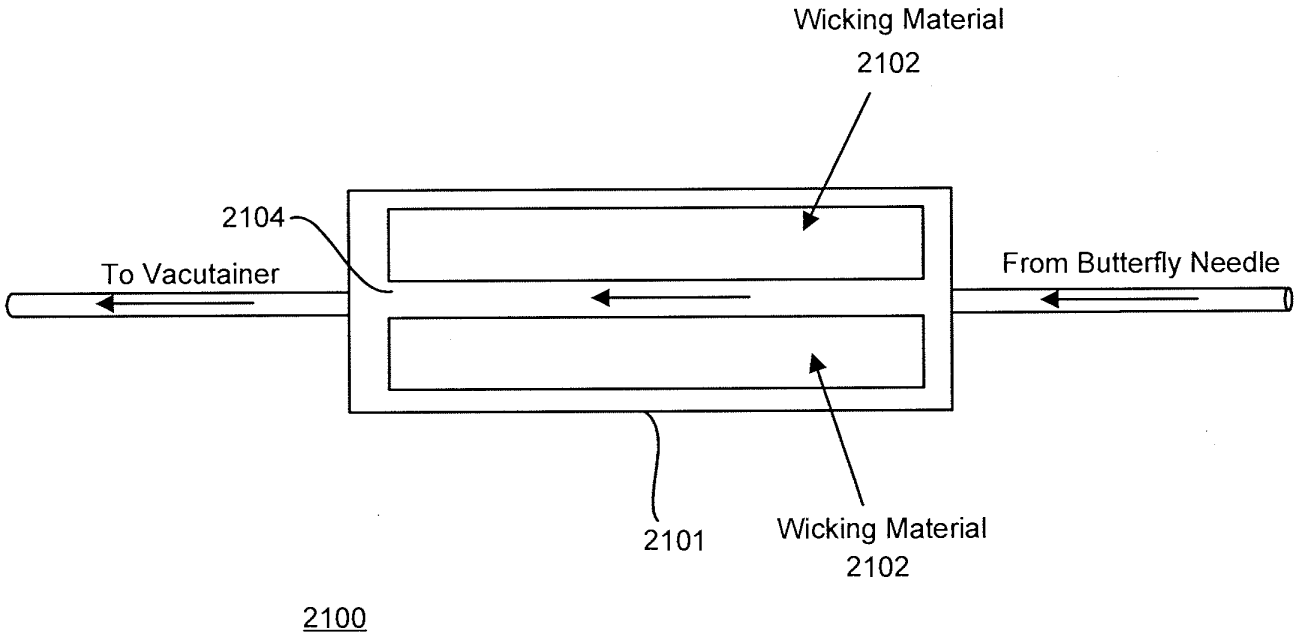

Wicking Material
2102
2104
To Vacutainer
From Butterfly Needle
2101
Wicking Material
2102
2100

FIG. 21

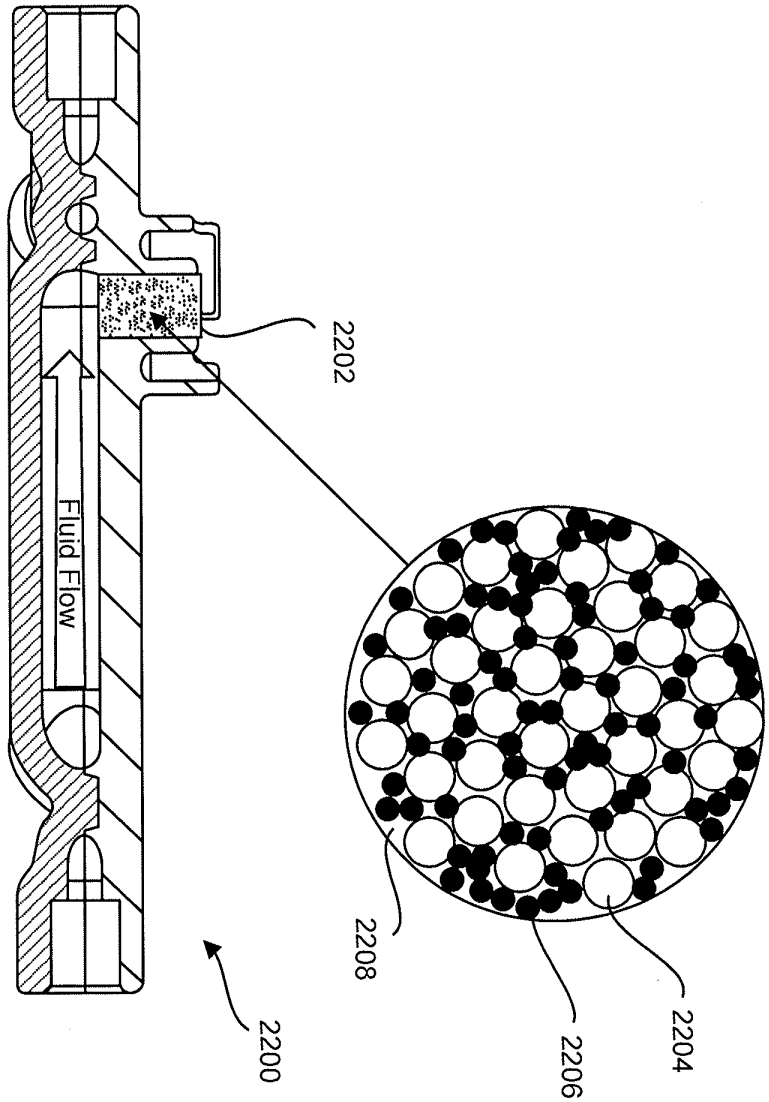


FIG. 22A

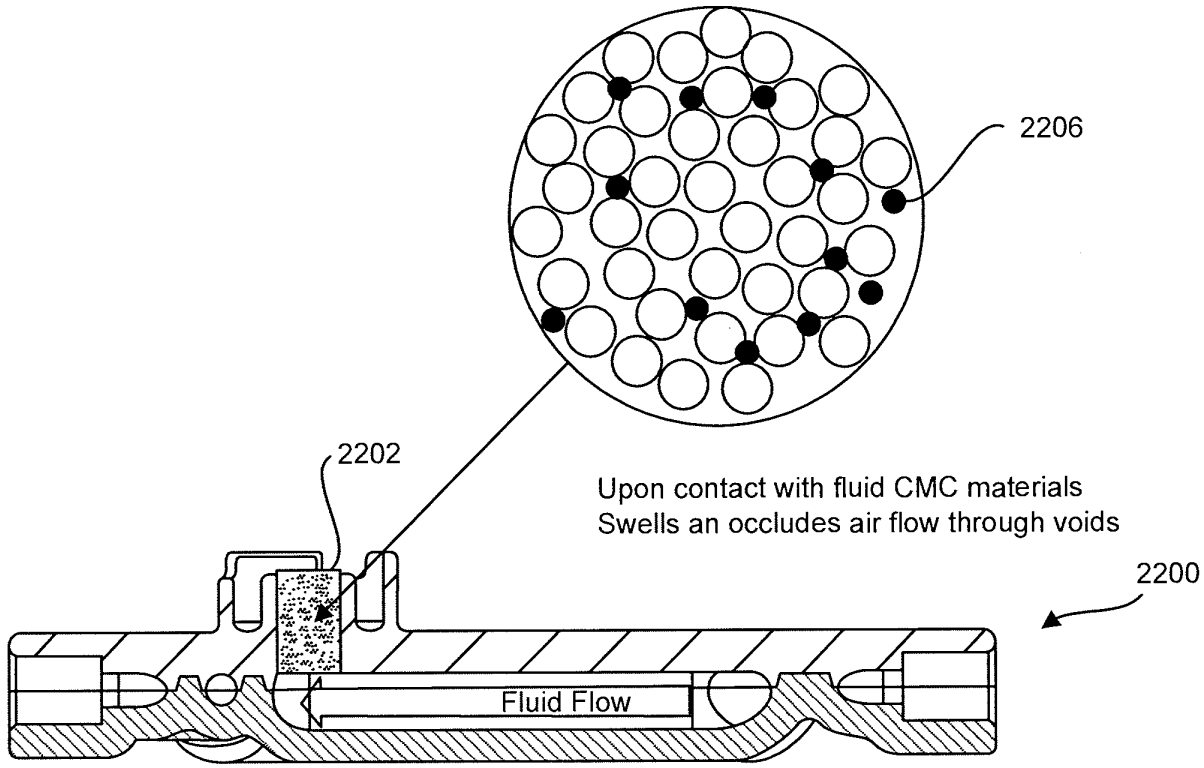

2206
2202
Upon contact with fluid CMC materials
Swells an occludes air flow through voids
2200
Fluid Flow

FIG. 22B

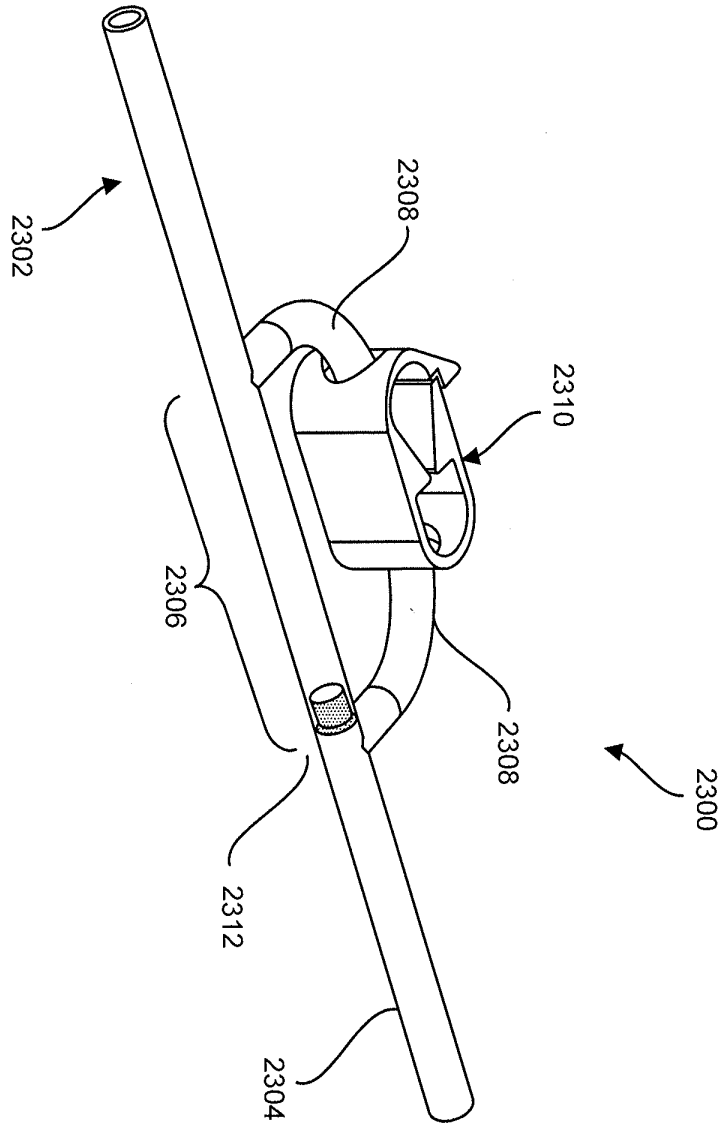


FIG. 23A

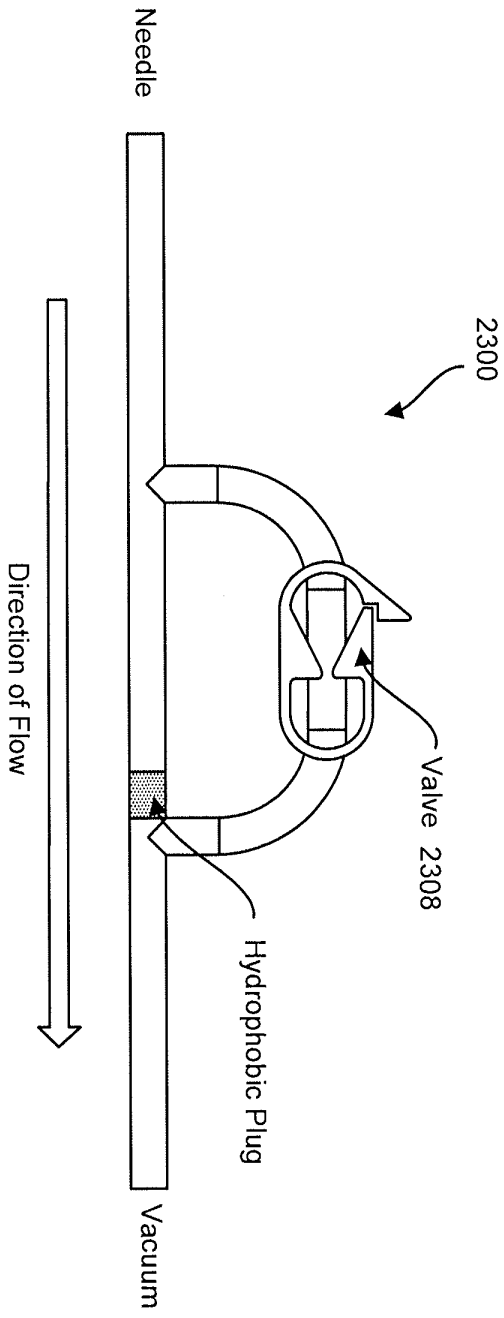

2300
Needle
Valve 2308
Hydrophobic Plug
Vacuum
Direction of Flow

FIG. 23B

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APPLICATION NUMBER	FILING or 371(c) DATE	GRP ART UNIT	FIL FEE REC'D	ATTY.DOCKET.NO	TOT CLAIMS	IND CLAIMS
18/494,622	10/25/2023		0	069366-0577657_KUR2C05US	1	1

CONFIRMATION NO. 9839

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

FILING RECEIPT

OC000000064303076

Date Mailed: 11/08/2023

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: None

Domestic Priority data as claimed by applicant

This application is a CON of 18/113,710 02/24/2023
which 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

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: 11/07/2023

The country code and number of your priority application, to be used for filing abroad under the Paris Convention, is **US 18/494,622**

Projected Publication Date: To Be Determined - pending completion of Missing Parts.

Non-Publication Request: No

Early Publication Request: No
**** SMALL ENTITY ****
Title

BLOOD SAMPLE OPTIMIZATION DEVICE

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.

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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).

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Title 37, Code of Federal Regulations, 5.11 & 5.15

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PATENT APPLICATION FEE DETERMINATION RECORD

Substitute for Form PTO-875

Application or Docket Number: 18/494,622

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))	1 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

AMENDMENT A

	(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($)	OTHER THAN SMALL ENTITY ADDITIONAL FEE($)
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	

AMENDMENT B

	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	RATE($)	ADDITIONAL FEE($)	OR	RATE($)	ADDITIONAL FEE($)
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.

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APPLICATION NUMBER	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
18/494,622	10/25/2023	Bobby E. ROGERS	069366-0577657_KUR2C05US

CONFIRMATION NO. 9839

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

FORMALITIES LETTER

OC00000000643031 19

Date Mailed: 11/08/2023

NOTICE TO FILE MISSING PARTS OF NONPROVISIONAL APPLICATION

FILED UNDER 37 CFR 1.53(b)

Filing Date Granted

An application number and filing date have been accorded to the above-identified nonprovisional application. The item(s) indicated below, however, are missing. Applicant is given **TWO MONTHS** from the date of this Notice within which to file all required items below to avoid abandonment. Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 CFR 1.136(a).

- The statutory basic filing fee has not been received.
- The application search fee must be submitted.
- The application examination fee must be submitted.
- Surcharge as set forth in 37 CFR 1.16(f) has not been received.

  The surcharge is due for any one of:
  - late submission of the basic filing fee, search fee, or examination fee,
  - late submission of inventor's oath or declaration,
  - filing an application that does not contain at least one claim on filing, or
  - submission of an application filed by reference to a previously filed application.

SUMMARY OF FEES DUE:

The fee(s) required (including the fees noted above) are as follows. Small entity discount is in effect. If applicant is qualified for micro entity status, an acceptable Certification of Micro Entity Status must be submitted to establish micro entity status. (See 37 CFR 1.29 and forms PTO/SB/15A and 15B.)

- $**64** basic filing fee.
- $**64** surcharge.
- $**280** search fee.
- $**320** examination fee.
- $(**0**) previous unapplied payment amount.
- $**728** TOTAL FEE BALANCE DUE.

Applicant is notified that the above-identified application contains the deficiencies noted below. No period for reply is set forth in this Notice for correction of these deficiencies. However, if a deficiency relates to the inventor's

oath or declaration, the applicant must file an oath or declaration in compliance with 37 CFR 1.63, or a substitute statement in compliance with 37 CFR 1.64, executed by or with respect to each actual inventor no later than the expiration of the time period set in the "Notice of Allowability" to avoid abandonment. See 37 CFR 1.53(f).

Items Required To Avoid Processing Delays:

The deficiencies indicated below should be addressed promptly to avoid further processing delays.

- A properly executed inventor's oath or declaration has not been received for the following inventor(s):

  Bobby E. ROGERS
  Gino KANG
  John DETLOFF

  An inventor's oath or declaration in compliance with 37 CFR 1.63 or 1.64 executed by or with respect to each inventor must be submitted no later than the date on which the issue fee is paid in response to a notice requiring such fee. See 37 CFR 1.53(f).

Replies must be received in the USPTO within the set time period or must include a proper Certificate of Mailing or Transmission under 37 CFR 1.8 with a mailing or transmission date within the set time period. For more information and a suggested format, see Form PTO/SB/92 and MPEP 512.

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Mail Stop Missing Parts
Commissioner for Patents
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Alexandria VA 22313-1450

REPLY VIA ELECTRONIC FILING

A reply may be submitted via electronic filing only by registered users of the appropriate USPTO patent electronic filing system and must include:

- A separate document having the document description, "**Applicant response to Pre-Exam Formalities Notice**"; and
- the item(s) for which a reply period is set forth above.

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NOTE: If the reply is not being submitted electronically, a copy of this notice must be included.

Questions about the contents of this notice and the requirements it sets forth should be directed to the Office of Data Management, Application Assistance Unit, at **(571) 272-4000** or **(571) 272-4200** or **1-888-786-0101**.

/agizaw/

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Kathi Vidal

Kathi Vidal
Under Secretary of Commerce for Intellectual Property and
Director of the United States Patent and Trademark Office

Derrick Brent
Deputy Under Secretary of Commerce for Intellectual Property and
Deputy Director of the United States Patent and Trademark Office

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

Wed Nov 08 05:10:52 EST 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.

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Application	Document	Mailroom Date	Attorney Docket No.
18494622	APP.FILE.REC	11/08/2023	069366-0577657_KUR2C05US
18494622	NTC.MISS.PRT	11/08/2023	069366-0577657_KUR2C05US
18494622	WELCOME.LET	11/08/2023	069366-0577657_KUR2C05US

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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.

Please do not reply to this email as it was sent from an unmonitored mailbox.

Sincerely,

The Patent Center Team

PATENT ASSIGNMENT COVER SHEET

Electronic Version v1.1
Stylesheet Version v1.2

Assignment ID: PATI115625

SUBMISSION TYPE:	NEW ASSIGNMENT
NATURE OF CONVEYANCE:	ASSIGNMENT

CONVEYING PARTY DATA

Name	Execution Date
Bobby E. Rogers	01/22/2018
Gino Kang	01/22/2018
John Detloff	01/23/2018

RECEIVING PARTY DATA

Company Name:	Kurin, Inc.
Street Address:	10755 Scripps Poway Parkway #257
City:	San Diego
State/Country:	CALIFORNIA
Postal Code:	92131

PROPERTY NUMBERS Total: 1

Property Type	Number
Application Number:	18494622

CORRESPONDENCE DATA

Fax Number:

Correspondence will be sent to the e-mail address first; if that is unsuccessful, it will be sent using a fax number, if provided; if that is unsuccessful, it will be sent via US Mail.

Phone: 8585094000
Email: Docket_ip@pillsburylaw.com
Correspondent Name: Trent A. Tercenio
Address Line 1: P.O. BOX 10500
Address Line 4: MCLEAN, VIRGINIA 22102

ATTORNEY DOCKET NUMBER:	069366-0577657_KUR2C05US
NAME OF SUBMITTER:	Trent Tercenio
SIGNATURE:	Trent Tercenio
DATE SIGNED:	03/22/2024
	This document serves as an Oath/Declaration (37 CFR 1.63).

Total Attachments: 3
source=069366-0577657_KUR2C05US_ASSIGNMENT 4876-1358-5746 v.2#page1.tif
source=069366-0577657_KUR2C05US_ASSIGNMENT 4876-1358-5746 v.2#page2.tif
source=069366-0577657_KUR2C05US_ASSIGNMENT 4876-1358-5746 v.2#page3.tif

ASSIGNMENT OF INVENTIONS & PATENT APPLICATIONS

WHEREAS, we, **Bobby E. Rogers, Gino Kang,** and **John Detloff** (collectively, "ASSIGNOR"), have invented certain improvements and inventions in a **BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE AND METHOD** for which a U.S. provisional patent application was filed on July 24, 2015 and assigned Serial No. 62/196,797; a U.S. provisional patent application was filed on October 7, 2015 and assigned Serial No. 62/238,636; a U.S. provisional patent application was filed on April 4, 2016 and assigned Serial No. 62/318,194; a U.S. patent application was filed on April 27, 2016 and assigned Serial No. 15/140,448; and whereas other related patent applications may be filed in the United States and elsewhere (all of said applications collectively referred to as "Application"), and whereas

KURIN, INC.
10755 Scripps Poway Parkway #257
San Diego, CA 92131
USA

("ASSIGNEE") desires to purchase all the rights in same;

NOW THEREFORE, in consideration of good and valuable considerations by the said ASSIGNEE, the receipt and sufficiency of which are hereby acknowledged, ASSIGNOR has and by these presents does hereby assign, transfer and convey unto said ASSIGNEE the full, exclusive and entire right, title, and interest in and to said Application, including in and to any provisional, conventional, division, continuation, continuation-in-part, substitution, reissue, renewal, reexam, continued prosecution application ("CPA"), or request for continued examination ("RCE") thereof, and in and to all inventions and improvements thereon (herein collectively referred to as "Related US Applications"), preparatory to obtaining Letters Patent of the United States therefor; and ASSIGNOR hereby requests the Commissioner of Patents and Trademarks to issue any and all Letters Patent of the United States resulting from said Application and Related US Applications, to ASSIGNEE, for its interest and for the sole use and benefit of ASSIGNEE and its assigns and legal representatives.

For the same consideration, ASSIGNOR, by these presents does assign and transfer to ASSIGNEE the full, exclusive, and entire right, title and interest in and to any foreign and international applications related to and/or seeking benefit of said Application and Related US Applications and in and to all inventions and improvements thereon (herein collectively referred to as "Related Foreign Applications"), in and to any Letters Patent and similar protective rights granted on said Related Foreign Applications, and in and to the right to claim any applicable priority rights arising from or required for said Related Foreign Applications under the terms of any applicable conventions, treaties, statutes, or regulations, said Related Foreign Applications to be filed and issued in the name of ASSIGNEE or its designee, insofar as permitted by applicable law.

For the same consideration, ASSIGNOR agrees, without charge to ASSIGNEE, but at ASSIGNEE'S expense, to sign all lawful papers, execute said Application, Related US Applications and Related Foreign Applications, make all assignments and rightful oaths, assist in prosecution of said Application, Related US Applications and Related Foreign Applications, assist in prosecution of legal proceedings, and generally do everything reasonably possible to aid ASSIGNEE its successors,

assigns, and nominees, to obtain and enforce proper protection for all said inventions and improvements in all countries throughout the world.

AND, for the same consideration, ASSIGNOR also hereby sells, assigns and transfers unto ASSIGNEE all rights and claims to sue for damages and other remedies with respect to any and all past infringement of all said Application, Related US Applications, and Related Foreign Applications, including said inventions and improvements which may have occurred before the date of this Assignment.

Assignment to KURIN, INC.:

Date: 1/22/18

Bobby E. Rogers

Date: 1/22/2018

Gino Kang

Date: 1-23-2018

John Detloff

ACCEPTANCE BY ASSIGNEE

Assignee hereby accepts from Assignor the sale, assignment, transfer and conveyance unto said Assignee of the full, exclusive and entire right, title, and interest in and to said Application, Related US Applications and Related Foreign Applications, by its duly authorized officer.

KURIN, INC.
(Assignee)

Date: 1/23/18

By: [signature]

Name: Bobby Rogers

Title: CEO

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
18/494,622	10/25/2023		0	069366-0577657_KUR2C05US	1	1

CONFIRMATION NO. 9839

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

FILING RECEIPT

OC000000070333377

Date Mailed: 03/28/2024

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: None

Domestic Priority data as claimed by applicant

This application is a CON of 18/113,710 02/24/2023 PAT 11,832,944
which 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

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: 11/07/2023

The country code and number of your priority application, to be used for filing abroad under the Paris Convention, is **US 18/494,622**

Projected Publication Date: PEAR

Non-Publication Request: No

Early Publication Request: No
**** SMALL ENTITY ****
Title

BLOOD SAMPLE OPTIMIZATION DEVICE

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.

The grant of a license does not in any way lessen the responsibility of a licensee for the security of the subject matter as imposed by any Government contract or the provisions of existing laws relating to espionage and the national security or the export of technical data. Licensees should apprise themselves of current regulations especially with respect to certain countries, of other agencies, particularly the Office of Defense Trade Controls, Department of State (with respect to Arms, Munitions and Implements of War (22 CFR 121-128)); the Bureau of Industry and Security, Department of Commerce (15 CFR parts 730-774); the Office of Foreign AssetsControl, Department of Treasury (31 CFR Parts 500+) and the Department of Energy.

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: 18/494,622

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))	1 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($)	ADDITIONAL FEE($)		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.

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	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
18/494,622	10/25/2023	Bobby E. ROGERS	069366-0577657_KUR2C05US

CONFIRMATION NO. 9839

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

FORMALITIES LETTER

OC00000007033337

Date Mailed: 03/28/2024

NOTICE OF INCOMPLETE REPLY (NONPROVISIONAL)

Filing Date Granted

The U.S. Patent and Trademark Office received your reply on 03/22/2024 to the NOTICE TO FILE MISSING PARTS OF NONPROVISIONAL APPLICATION (Notice) mailed 11/08/2023 and it has been entered into the application. The reply, however, is not a complete reply because all of the items required by the NOTICE TO FILE MISSING PARTS OF NONPROVISIONAL APPLICATION have not been received. See "Items Required to Avoid Abandonment" section below. A complete reply must be timely filed to prevent ABANDONMENT of the above-identified application.

The period for reply continues to run from the date of the NOTICE TO FILE MISSING PARTS OF NONPROVISIONAL APPLICATION mailed 11/08/2023. Applicant must submit all required items and pay any fees required below to avoid abandonment. Extensions of time may be obtained by filing a petition accompanied by the appropriate extension fee under the provisions of 37 CFR 1.136(a). See "Time Period for Reply" section below.

Applicant's reply to the NOTICE TO FILE MISSING PARTS OF NONPROVISIONAL APPLICATION mailed 11/08/2023 was received in the U.S. Patent and Trademark Office on 03/22/2024, after the expiration of the two month period for reply set forth in the Notice. The application will become abandoned unless applicant obtains an extension of the period for reply, as above. The petition for extension of time must be accompanied by the appropriate fee as set forth in 37 CFR 1.17 (see "Time Period for Reply" section below). The date on which the reply, the petition for extension of time, and the fee are filed is the date for purposes of determining the period of extension and the corresponding amount of the fee due. The amount of fee paid determines the expiration of the time period for reply. Applicant is advised that extensions may not be granted under 37 CFR 1.136(a) for more than FIVE MONTHS beyond the time period set in the Notice.

Items Required to Avoid Abandonment:

The required items noted below SHOULD be filed along with any items required above.

- The statutory basic filing fee has not been received.
- The application search fee has not been received.
- The application examination fee has not been received.
- Surcharge as set forth in 37 CFR 1.16(f) has not been received.

  The surcharge is due for any one of:
  - late submission of the basic filing fee, search fee, or examination fee,

- late submission of inventor's oath or declaration,
- filing an application that does not contain at least one claim on filing, or
- submission of an application filed by reference to a previously filed application.

SUMMARY OF FEES DUE:

The fee(s) required (including the fees noted above) are as follows. Small entity discount is in effect. If applicant is qualified for micro entity status, an acceptable Certification of Micro Entity Status must be submitted to establish micro entity status. (See 37 CFR 1.29 and forms PTO/SB/15A and 15B.)

- $**64** basic filing fee.
- $**64** surcharge.
- $**280** search fee.
- $**320** examination fee.
- $(**0**) previous unapplied payment amount.
- $**728** TOTAL FEE BALANCE DUE.

Time Period for Reply:

Mail date of Notice: 11/08/2023

Last date that extension may be obtained: (Note: The petition and fee must be received by this date, or include a proper certificate of mailing under 37 CFR 1.8 with a date on or before this date, and extend the time to include this date.) 06/10/2024

The following table sets forth the possible extensions of time available, depending on when the reply and corresponding extension of time fee are received.

Length of Extension of Time	Fee under 37 CFR 1.17(a) effective March 19, 2013		
(response due on or before)	Undiscounted	Small Entity	Micro Entity
Three Months (04/08/2024)	$1480	$592	$296
Four Months (05/08/2024)	$2320	$928	$464
Five Months (06/10/2024)	$3160	$1264	$632

Replies must be received in the USPTO within the set time period or must include a proper Certificate of Mailing or Transmission under 37 CFR 1.8 with a mailing or transmission date within the set time period. For more information and a suggested format, see Form PTO/SB/92 and MPEP 512.

Replies should be addressed to:

Mail Stop Missing Parts
Commissioner for Patents
P.O. Box 1450
Alexandria VA 22313-1450

REPLY VIA ELECTRONIC FILING

A reply may be submitted via electronic filing only by registered users of the appropriate USPTO patent electronic filing system and must include:

- A separate document having the document description, "**Applicant response to Pre-Exam Formalities Notice**"; and
- the item(s) for which a reply period is set forth above.

For more information about electronic filing, contact the Patent Electronic Business Center (EBC) 1-866-217-9197 or visit https://www.uspto.gov/ebc

NOTE: If the reply is not being submitted electronically, a copy of this notice must be included.

Questions about the contents of this notice and the requirements it sets forth should be directed to the Office of Data Management, Application Assistance Unit, at **(571) 272-4000** or **(571) 272-4200** or **1-888-786-0101**.

/snguyen/

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 Mar 28 07:28:22 EDT 2024

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.
18494622	APP.FILE.REC	03/28/2024	069366-0577657_KUR2C05US
18494622	NT.INC.REPLY	03/28/2024	069366-0577657_KUR2C05US

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.

Please do not reply to this email as it was sent from an unmonitored mailbox.

Sincerely,

The Patent Center Team

UNITED STATES
PATENT AND TRADEMARK OFFICE

P.O. Box 1450
Alexandria, VA 22313 - 1450
www.uspto.gov

ELECTRONIC PAYMENT RECEIPT

APPLICATION #	RECEIPT DATE / TIME	ATTORNEY DOCKET #
18/494,622	04/08/2024 06:14:19 PM Z ET	069366-0577657_KUR2C05US

Title of Invention

BLOOD SAMPLE OPTIMIZATION DEVICE

Application Information

APPLICATION TYPE	Utility - Nonprovisional Application under 35 USC 111(a)	PATENT #	-
CONFIRMATION #	9639	FILED BY	Trent Tercenio
PATENT CENTER #	65010472	AUTHORIZED BY	Benjamin Hudson
CUSTOMER #	27500	FILING DATE	10/25/2023
CORRESPONDENCE ADDRESS	-	FIRST NAMED INVENTOR	Bobby E. ROGERS

Payment Information

PAYMENT METHOD	PAYMENT TRANSACTION ID	PAYMENT AUTHORIZED BY
DA / 033975	E202448114535934	Trent Tercenio

FEE CODE	DESCRIPTION	ITEM PRICE($)	QUANTITY	ITEM TOTAL($)
2051	SURCHARGE- LATE FILING FEE, SEARCH FEE, EXAMINATION FEE, INVENTOR'S OATH OR DECLARATION, OR APPLICATION FILED WITHOUT AT LEAST ONE CLAIM OR BY REFERENCE	64.00	1	64.00
2111	UTILITY PATENT APPL. SEARCH FEE	280.00	1	280.00
4011	BASIC FILING FEE- UTILITY	64.00	1	64.00
2311	EXAMINATION OF ORIGINAL PATENT APPLICATION	320.00	1	320.00

2253	EXTENSION FOR RESPONSE WITHIN THIRD MONTH -	592.00	1	592.00

TOTAL AMOUNT: **$1,320.00**

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.

UNITED STATES
PATENT AND TRADEMARK OFFICE

P.O. Box 1450
Alexandria, VA 22313 - 1450
www.uspto.gov

ELECTRONIC ACKNOWLEDGEMENT RECEIPT

APPLICATION #	RECEIPT DATE / TIME	ATTORNEY DOCKET #
18/494,622	**04/08/2024 06:14:19 PM Z ET**	**069366-0577657_KUR2C05US**

Title of Invention

BLOOD SAMPLE OPTIMIZATION DEVICE

Application Information

APPLICATION TYPE	Utility - Nonprovisional Application under 35 USC 111(a)	PATENT #	-
CONFIRMATION #	9839	FILED BY	Trent Tercenio
PATENT CENTER #	65010472	FILING DATE	10/25/2023
CUSTOMER #	27500	FIRST NAMED INVENTOR	Bobby E. ROGERS
CORRESPONDENCE ADDRESS	-	AUTHORIZED BY	Benjamin Hudson

Documents

TOTAL DOCUMENTS: 0

DOCUMENT	PAGES	DESCRIPTION	SIZE (KB)

Digest

DOCUMENT	MESSAGE DIGEST(SHA-512)

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.

Received 6.24.05 | Revisions Received 7.26.05 | Accepted 7.27.05

Bacterial Contamination of Platelets for Transfusion: Recent Advances and Issues

Chelsea A. Sheppard, MD, Cassandra D. Josephson, MD, Christopher D. Hillyer, MD

(Transfusion Medicine Program, Department of Pathology and Laboratory Medicine, Emory University School of Medicine, Atlanta, GA)

DOI: 10.1309/16794BJY25TMY611

- Bacterial contamination of blood products has emerged as a serious problem in transfusion medicine in the past 20 years and is second only to ABO-mismatch in causing transfusion-associated death.
- Data from 1985 - 1999 showed that 11% (77/694) of transfusion-associated fatalities reported to the FDA were caused by bacterially contaminated products leading to sepsis.
- As platelets are stored at room temperature, and in a large volume of plasma and a bag that allows oxygen diffusion, it is platelet products that are the most frequently implicated in transfusion-associated fatalities due to bacterial contamination.

The transfusion medicine community has attempted to reduce the amount of bacterial contamination in the blood supply by several methods including improved skin disinfection prior to donation, removal of the skin plug with diversion of the first 10 cc of the collection, ongoing donor screening, and analysis/culture of the donated product. Even with these measures in place, several fatalities due to septic reactions associated with transfusion have occurred and been reported. At the time of this writing, the exact "residual risk" of bacterial contamination is not known.

While packed red blood cell units can be contaminated by bacteria, the fact that they are *not* stored at room temperature and are not in a medium containing a large amount of plasma, leads the incidence of sepsis following transfusion of these units to be much less frequent. For a discussion of pRBC bacterial contamination, the first 3 references are recommended to the reader.[1-3] Below, the authors focus on the risks, strategies, and regulations regarding bacterial contamination of platelet products and its mitigation.

Estimates of Prevalence and Incidence

Prior to routine culturing of platelet units, which became universal following implementation AABB Standard 5.1.5.1 (discussed in more detail below), the estimated numbers of bacterially contaminated units, transfusion-associated septic reactions and deaths were usually made retrospectively based on reported or published reactions and sequelae.

By 2000, it was generally held that between 1:1,000 and 1:4,000 units[3-8] were contaminated with bacteria; the estimate of 1:2,000 to 3,000 became commonly accepted. Sepsis due to bacterial contamination was less common and estimated to occur in 1:20,000 to 1:85,000 units.[8] Estimates at the number of deaths due to this transfusion related complication were more difficult to elucidate.

In 2001, Yomtovian and colleagues estimated that 500 to 750 "severe and possibly fatal" events occurred annually.[4] Other estimates of this figure are more on the order of 100 to 150 deaths per year.[9,10] (The estimated risk of bacterially contaminated red cell units was significantly lower (approximately 1:500,000)[11] and approximately 10 to 1,000 times greater than the combined risk of transfusing HIV, HBV, HCV, and HTLV.[11]

Sources of Bacterial Contamination

Occult donor bacteremia and contamination of the product during collection have been the main avenues for entry of bacteria and have been the focus of prevention efforts. Gram-positive skin flora, introduced to the unit during collection, are the most common contaminates identified in retrospective analysis of platelet units.[12] Three reporting systems have suggested that 70% of contaminates isolated were gram-positive bacteria, while 80% of fatalities due to transfusion-related sepsis were caused by gram-negative organisms.[13-15] This finding was also observed in a recent review of the American Red Cross (ARC) experience with pretransfusion culturing of apheresis-derived platelets (ADP) between March and December 2004 (discussed in detail below).[16] This data showed that gram-positive organisms are implicated in approximately 4/5 of the cases. Gram-negative bacteria comprise the other 20%; however, they account for 40% of deaths due to septic transfusion reactions. Burns and colleagues recently published an extensive list of primary reports of clinically significant sepsis attributed to platelet transfusion from a PubMed literature search of all published cases.[17]

Due to the clinical significance of bacterial contamination, much effort has been made over the years to improve disinfection of skin at the phlebotomy site including the discontinuation of "green soap." Additionally, diversion of the skin plug produced by the needle as it passes through the skin, away from the bag into a pouch used for other viral testing, has been instituted nationwide in the United States. Despite these efforts, bacterial contamination of products continued(s) to be observed and skin flora continued(s) to be the most frequently cultured organisms.

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Asymptomatic donor bacteremia is the reason seemingly healthy volunteers may be allowed to donate while infectious, leading to bacterial contamination of blood products. In this case, even stringent donor screening will not catch this potential source of bacterial contamination. There are many examples of donors who unknowingly donate blood while bacteremic. For example, a case of transfusion associated *Staphylococcus aureus* platelet contamination has been reported in a blood donor who had undergone a tooth extraction 3 hours prior to donation, and was likely the result of transient bacteremia.[12] Haimowitz and colleagues discovered *Streptococcus bovis* at 11.4 hours after incubation of a platelet product donated by an asymptomatic female. After being informed of the result and despite negative follow up blood cultures, she underwent colonoscopy and a 3 cm mass was noted and removed.[18] Jafari and colleagues reported a case of *Salmonella* sepsis transmitted via platelet transfusion to 2 recipients from an asymptomatic donor who upon retrospective questioning reported that he had fever, abdominal pain, diarrhea, and hematochezia 13 days *prior* to donation. The donor owned a pet boa constrictor. The snake was thought to have been colonized with *Salmonella* and the original source of the infection.[19] Finally, there have been several cases of pRBC transfusion-associated *Yersinia enterolitica* septicemia in which many of the donors retrospectively reported diarrhea in the days preceding donation.[20]

An Open Letter to the Blood Community and AABB Standard 5.1.5.1

Physicians concerned that the risk from infected units was too high and that there were technologies that could address the issue at least in part wrote an "open letter" to the transfusion medicine community urging implementation of a method to stem this complication.[21] In 2003, AABB Standard 5.1.5.1 was released after considerable discussion, debate, and a public comment period. To be implemented within 1 year, the Standard read, "The blood bank or transfusion service shall have methods to limit and detect bacterial contamination in all platelet components."

At that time and presently, there were no FDA-approved tests for unit-by-unit bacteria screening at the time and point of transfusion. In addition, it was known that more than 15 tests *could* be used but none met "optimal" criteria including sensitivity and specificity, cost:efficacy, and logistical considerations affecting product supply and outdating. Thus, AABB was in an unenviable position of introducing a standard without guidance (at that time) as to *how* to implement it. **Table 1** below (adapted from reference 22) lists the tests capable of detecting bacteria and some comments regarding each.

Clinical Relevance

Typically at the time of collection, the level of contamination is relatively low (between 1 to 10 colony forming units (CFU)/mL.[23] However, once the product is inoculated, the bacteria can proliferate to levels of 10^6/mL or greater.[3] This amount of bacteria transfused during a short period of time can cause bacteremia, fever, chills, hypotension, nausea, vomiting, diarrhea, and oliguria, which may progress to sepsis and ultimately multi-system organ failure and death. Alternatively, the transfusion of contaminated cellular blood products may produce no symptoms or long-term clinical consequences. The severity of the reaction depends on: 1) the species of bacteria present, 2) the inoculum, 3) the rate of bacterial propagation, and 4) underlying disease, leukocyte count, the status of the immune system, and receipt of concomitant antibiotics in the recipient.[3] Gram-negative bacteria tend to cause more severe reactions due to the presence of endotoxin produced by these organisms. While causing only one-fifth of the cases, gram-negative bacteria have been reported to account for 40% of deaths due to septic transfusion reactions.[12,16]

Table 1_Description of Tests Capable of Detecting Bacteria

Methodology	Comments
Culture-based methodology: BacT/ALERT 3D Automated Microbial Detection System (bioMérieux, Durham, NC)	Detects CO_2 production by bacteria; FDA approved for quality control; Semi-closed system; Detects 5-10 CFU/mL (12-26 hr incubation);4 mL required
Culture-based methodology: (Pall eBDS, Pall Corporation, East Hills, NY)	Measures O_2 consumption by bacteria; FDA approved for quality control; Completely closed system; Requires 5-6 mL (concentrated to 2-3 mL)
DNA/RNA-based amplification and non-amplification, Chemiluminescence systems	Highly sensitive and specific; Requires highly conserved target by all bacteria or multiple primers and large inoculum; In experimental use only
Tests detecting changes in metabolic parameters or physical elements (glucose concentration, pH, platelet swirling)	Low sensitivity and specificity; Platelet concentration of the sample can affect results; Can be used at point of issue; Validation and QC difficult
Flow or static cytometry: (Scansystem, Hemosystem, Marseilles, France [laser-based, solid-phase cytometry])	Recently approved in Europe; Rapid (30 hr incubation and 90 min test time); Acceptable sensitivity and specificity; Requires reagent antibody to highly conserved common antigen or multiple reagent antibodies; 3 mL required
Bacterial cell wall component detection systems: (Platelet PGD test, Verax Biomedical, Worcester, MA)	Rapid (20 minutes); Lateral flow format; Sensitivity (10^3 to 10^4) in preliminary trial; 0.5 mL required; In experimental use only
Dielectrophoretic method: (Cell Analysis, Slough, United Kingdom)	Recently approved in Europe; Rapid (30 min); Sensitivity (10^3 to 10^5) in preliminary trial; 1 mL required
Gram stain	Requires a high level of contamination; Low sensitivity at lower concentrations; Can be used at point of issue; Validation and QC difficult
Endotoxin detection	Requires a high level of contamination; Low sensitivity at lower concentrations

Adapted from Reference 22.

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Strategies for the Mitigation of Contaminated Blood Products

As previously stated, detection strategies show variable sensitivity and specificity. Measuring abnormal glucose concentrations, low pH, microscopic examination of gram-stained specimens, and platelet swirling characteristics have been less useful due to low sensitivity and specificity. However, these methods have the advantage of being able to be used at the time and point of transfusion, are less expensive and use equipment commonly available.

Automated culture-based systems used for years in the hospital setting for detection of bacteremia in blood cultures obtained from patients were implemented by many of the nation's blood collection systems. Principally, they detect CO_2 generation or O_2 consumption by bacteria. Some of the limitations of culture-based systems are relatively insensitive at low levels of bacterial contamination causing false negative results, long incubation times for slow-growing bacteria, false positive results, high cost and the need for capital investment.[24-26] Holme and colleagues have recently shown that modifications to the Pall eBDS system have attempted to minimize these limitations.[29] While feasible for apheresis-derived platelets (ADP), culture based methods are not considered feasible for each whole blood-derived platelet (WBP) unit at the time of collection because of the high cost. Thus, those centers and services that used ADP could comply more easily and effectively with the new standard than those who used WBP, and converting entire systems from ADP to WBP was in-and-of-itself costly and met with resistance due to standard of care, cost, and availability concerns.

Apheresis Derived (ADP) Versus Whole Blood Derived Platelets (WBP)

Even before the implementation of Standard 5.1.5.1, the use of ADP had increased (52% to 99% of total transfused products per Ness and colleagues from 1987-1998) likely in part due to concern by some authorities about bacterial contamination.[8] Indeed, Ness and colleagues concluded that the rate of septic transfusion reactions due to WBP was 5.39 times higher than ADP (95% CI, 1.89, 12.9). Dykstra and colleagues found that the rate of bacterial contamination in ADP and WBP was identical (P=1.0); however, when platelet concentrates were pooled, the risk increased by 5 fold.[7]

Despite the apparent advantages of using ADP, maintaining adequate inventories and simultaneously providing adequate bacterial contamination testing is still a challenge due to the time it takes for the culture. Many experts have considered the effect and possibility of extending the expiration date to 7 days. In order to have a licensed 7 day ADP, clinical tests of the platelets, storage and medium will be required as will demonstration of bacteria detection and an acceptable rate of "residual risk." In order to allow the use of WBP with cost effective and optimal bacterial detection performance, 2 alternatives can be considered, but both are in clinical development and thus are not available. These include: 1) a 5 or 7 day "pooled and stored" WBP where a culture-based system could be used as a single test on a pre-storage pooled product, and 2) the approval of a effective test that could be used at the point and time of transfusion and which would be rapid enough for most clinical situations.

Residual Risk in "Tested" Components

Despite the strategies described above, bacterial contamination continues to be observed, although markedly reduced, and fatal consequences have been reported. As there was no standardized or required system in place to determine the true incidence of the morbidity and mortality caused by septic platelet units prior to the implementation of AABB Standard 5.1.5.1, it is impossible to determine with accuracy the effect of the standard in terms of percent improvement or reduction in adverse events. Some relevant data are available however.

From March 1, 2004 through December 31, 2004, approximately 350,000 units from 87,000 voluntary donors at 36 regional centers were cultured by the American Red Cross. Two hundred nineteen were initially positive, 67 were confirmed on re-sampling for an overall confirmed positive rate of 0.019% or 1:5,234 as compared to published reports of 1:2,000 to 3,000. Initially, 4 to 5 mL from each unit was transferred through a sterile docking device at least 24 hours after collection and used to inoculate BacT/ALERT BPA aerobic culture bottles. Confirmation of a positive blood culture bottle was performed by taking a new sample from product, inoculating a new BacT/ALERT aerobic culture bottle and if positive, performing bacterial isolation and identification. Eighty percent of the confirmed positive cases were gram-positive bacteria, mainly *Staphylococcus* (46.3%) and *Streptococcus* (26.9%) species. Serratia was the most commonly isolated gram-negative bacteria (n=4). Seventy-two percent of gram-negative organisms were identified within the first 12 hours of inoculation (personal communication; ARC). No patient transfused with an unconfirmed positive product had a septic transfusion reaction.

Three fatal cases and 2 non-fatal cases of transfusion-associated sepsis in platelet recipients have occurred since the standard was adopted. The first 2 cases were reported in MMWR.[27] The first case was that of a 74-year-old man who received 1 pool of 5 platelet concentrates. The pooled unit was tested by a pH method and found to be acceptable. After a hypotensive reaction, *S. aureus* was cultured from both the patient's blood and the platelet bag and by pulsed-field gel electrophoresis (PFGE) were identical. The second case was a 79-year-old man who was transfused a single platelet pheresis unit. The unit was tested by an automated culture system using a standard method. One hour after transfusion the patient had shortness of breath, chills, and fever. *S. lugdenensis* was cultured from both the patient's blood and the platelet bag and by PFGE were identical. The final case of fatality [presented to the Advisory Committee on Blood Safety (1/25/2005)] was a premature infant who received 2 doses of a single platelet pheresis. The unit was tested by a manual culture. The patient had symptoms consistent with sepsis. The platelet unit was then recultured and found to be growing *Serratia marcescens*. The patient's cultures were negative, but the cultures were taken after antibiotic therapy was initiated. One of the non-fatal cases was a BacT/ALERT failure of an apheresis platelet unit.[16]

Using numbers that are estimates only, and recognizing the limitations therein, a residual risk figure may be on the order of 3 to 6 fatal cases per year following the administration of approximately 2 million platelet doses per year (*The reader is asked to note that the true number of transfused platelet doses per year in the United States has not been established with certainty. While as many as 9 million units are given, the proportion of ADP vs. WBP is not known, nor is the number of WBP pooled into a dose*). Therefore, an incidence figure of approximately 1 fatality per approximately 500,000 tested doses may be posited. This is

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likely to be grossly inaccurate due to the lack of validated data, suboptimal test methods for WBP, and reporting and assumptions used. If one uses the figures given earlier in this report of 100 to 150 deaths annually (pre-standard implementation) and a residual as high as 6, then the improvement has been about 95%. Again, this number is a gross estimate, which will likely be revised with the collection of additional data. Though the "improvement rate" seems excellent, a residual risk of fatality incidence of 1:500,000 may be judged unacceptable by some, and thus other means of improving upon this complication may be warranted.

Pathogen Reduction (Inactivation)

Pathogen reduction is the term given to a number of technologies that prevent pathogens from replicating and thus prevent them from causing disease following transfusion. Methods under investigation (some are in use in Europe) use a variety of compounds including methylene blue, riboflavin and solvent-detergent treatment. In addition, a number of photodynamic processes use psoralen-based chemicals followed by ultraviolet light to inactivate bacteria and viruses by preventing replication and transcription of nucleic acids. This latter method has been extensively tested for bacterial reduction in platelet products. Gram-positive and gram-negative bacteria have been shown in three preclinical trials to be sensitive to pathogen inactivation (reviewed in reference 28). The main disadvantage of pathogen inactivation is that no method is equally effective for all organisms and these methods may be especially ineffective for spore-forming organisms.[28] The advantage is that this is a proactive method for bacterial reduction and has the potential to be as effective for known pathogens as it is for emerging pathogens.

Ongoing Issues

Bacterial contamination of blood products was, and may continue to be, a serious health risk to transfusion recipients. While we believe substantial improvement has been made, though difficult to accurately quantify, some level of residual risk appears to exist. Systems to help quantify this residual risk need to be implemented and/or strengthened. In addition, there is some evidence to suggest that the implementation of Standard 5.1.5.1 has caused a significant reduction in platelet availability, delay in their release to hospital transfusion services, and/or a declination in WBP use which may have added to the overall cost of platelet provision and transfusion. In order to address these issues, rapid and cost-effective tests need to be developed and approved for use at the time and point of transfusion. Alternatively, and with the use of a validated bacterial detection test, prestorage pooling may be "allowed" and thus lead to a state of equipoise between ADP and WBP safety and therefore use. An effective method or methods for bacterial detection and limitation will likely allow the extension of either ADP or pooled and stored WBP to 7 or perhaps even 8 days, thus likely improving the logistical and availability issues currently surrounding this valuable human resource. Finally, the adoption of pathogen reduction technologies in Europe and their approval in the United States may abrogate any residual or evolving risk.

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JOURNAL OF CLINICAL MICROBIOLOGY, Mar. 1998, p. 657–661 Vol. 36, No. 3
0095-1137/98/$04.00+0
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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

R. ZIEGLER,[1] I. JOHNSCHER,[1] P. MARTUS,[2] D. LENHARDT,[1] AND H.-M. JUST[1]*

Institut für Klinikhygiene, Medizinische Mikrobiologie und Klinische Infektiologie, Klinikum Nürnberg, 90419 Nürnberg,[1] and Institut für Medizinische Statistik und Dokumentation, Universität Erlangen-Nürnberg, 91054 Erlangen,[2] Germany

Received 2 September 1997/Returned for modification 14 October 1997/Accepted 24 November 1997

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

* Corresponding author. Mailing address: Institut für Klinikhygiene, Medizinische Mikrobiologie und Klinische Infektiologie, Klinikum Nürnberg, Flurstr. 17, 90419 Nürnberg, Germany. Phone: (49) 911 398 2522. Fax: (49) 911 398 3266.

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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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ACKNOWLEDGMENTS

This study was supported in part by grants from Becton Dickinson and Organon Teknika.

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(19) Europäisches Patentamt
European Patent Office
Office européen des brevets

(11) EP 3 622 890 A1

(12) EUROPEAN PATENT APPLICATION

(43) Date of publication:
18.03.2020 Bulletin 2020/12

(51) Int Cl.:
A61B 5/15 *(2006.01)* ***A61B 5/153*** *(2006.01)*
A61B 5/154 *(2006.01)*

(21) Application number: **19200766.4**

(22) Date of filing: **22.07.2016**

(84) Designated 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

(30) Priority: **24.07.2015 US 201562196797 P**
07.10.2015 US 201562238636 P
04.04.2016 US 201662318194 P
27.04.2016 US 201615140448
27.04.2016 US 201615140443

(62) Document number(s) of the earlier application(s) in accordance with Art. 76 EPC:
16747682.9 / 3 324 845

(71) Applicant: **Kurin, Inc.**
San Diego, California 92131 (US)

(72) Inventors:
- **Rogers, Bobby**
  San Diego, CA 92131 (US)
- **Kang, Gino**
  San Diego, CA 92131 (US)
- **Detloff, John**
  San Diego, CA 92131 (US)

(74) Representative: **Thum, Bernhard**
Wuesthoff & Wuesthoff
Patentanwälte PartG mbB
Schweigerstraße 2
81541 München (DE)

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.

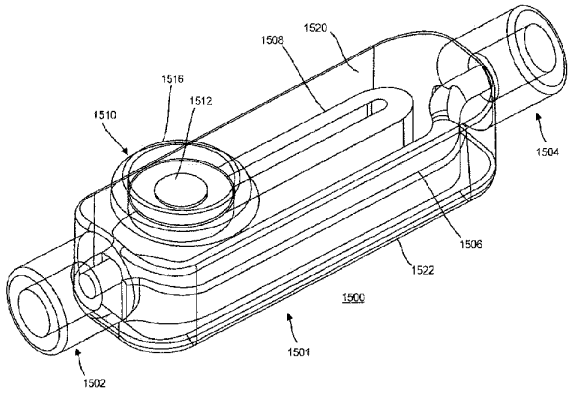


FIG. 15C

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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).

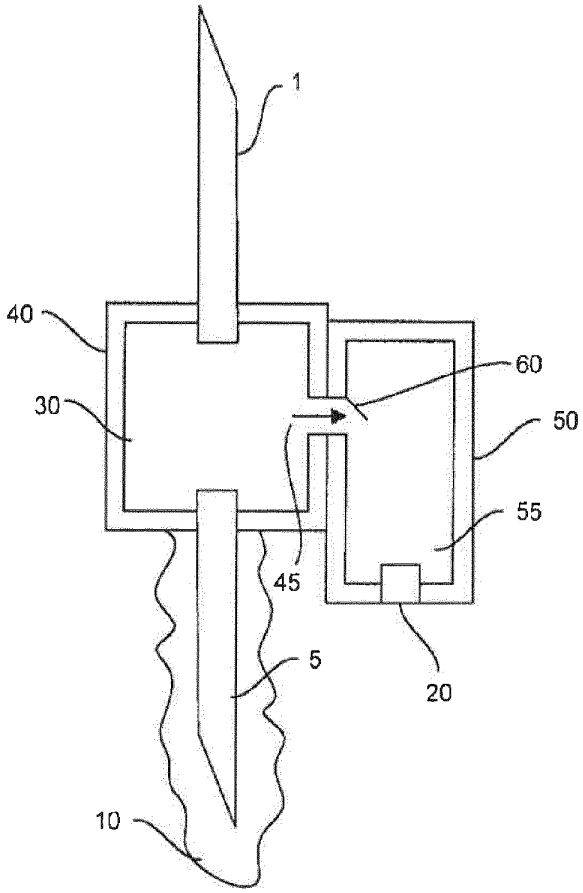


FIG. 1

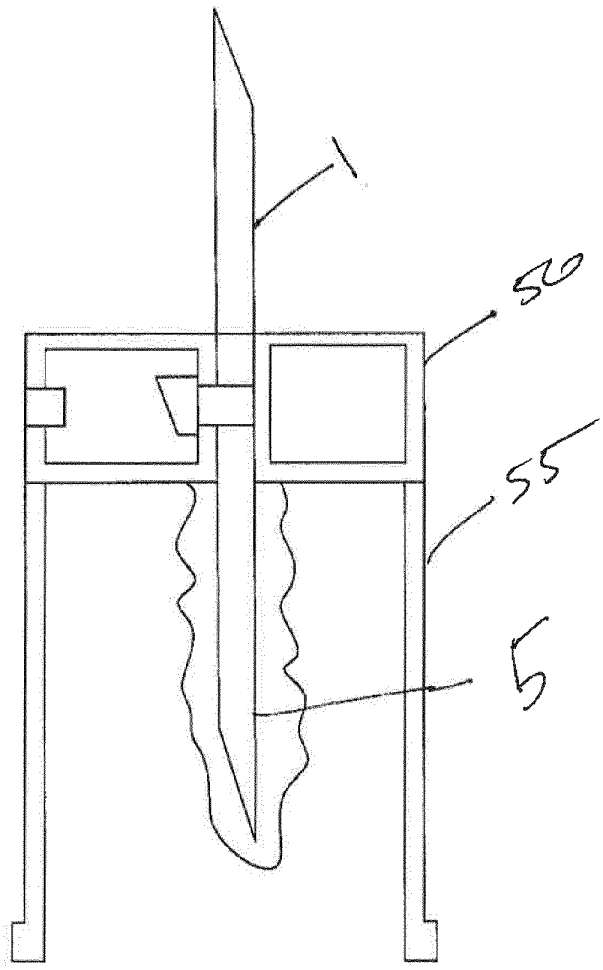


FIG. 2

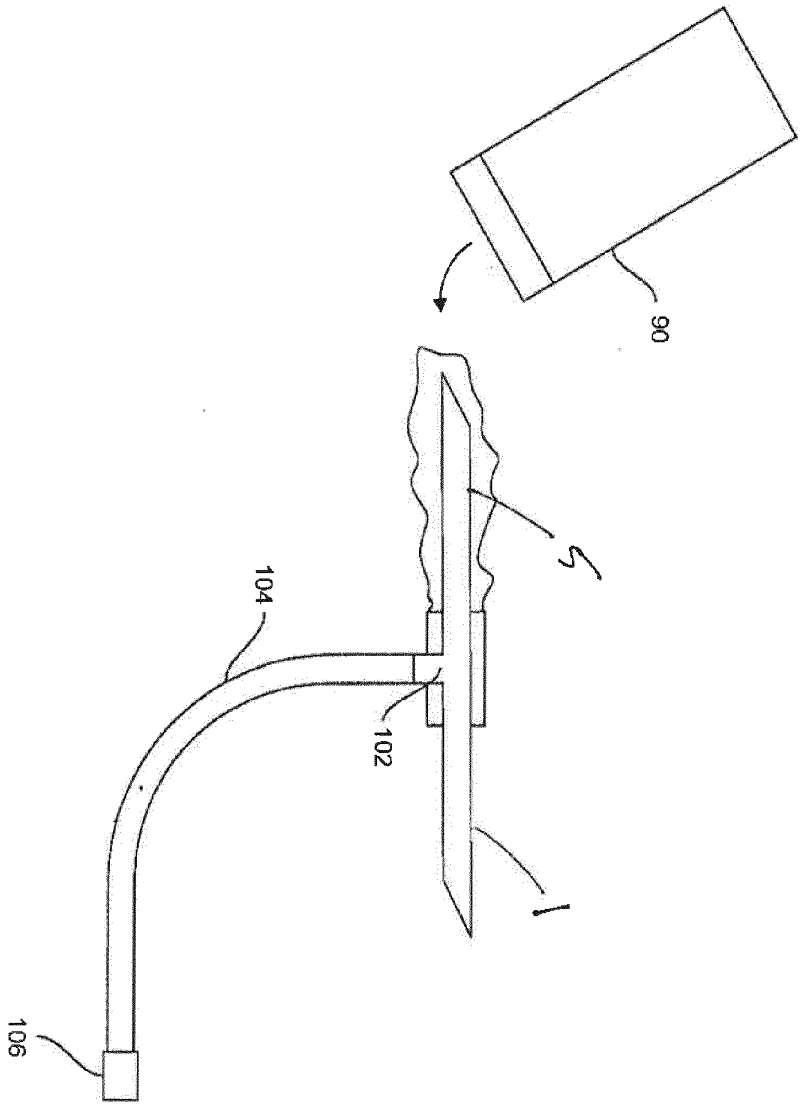


FIG. 3

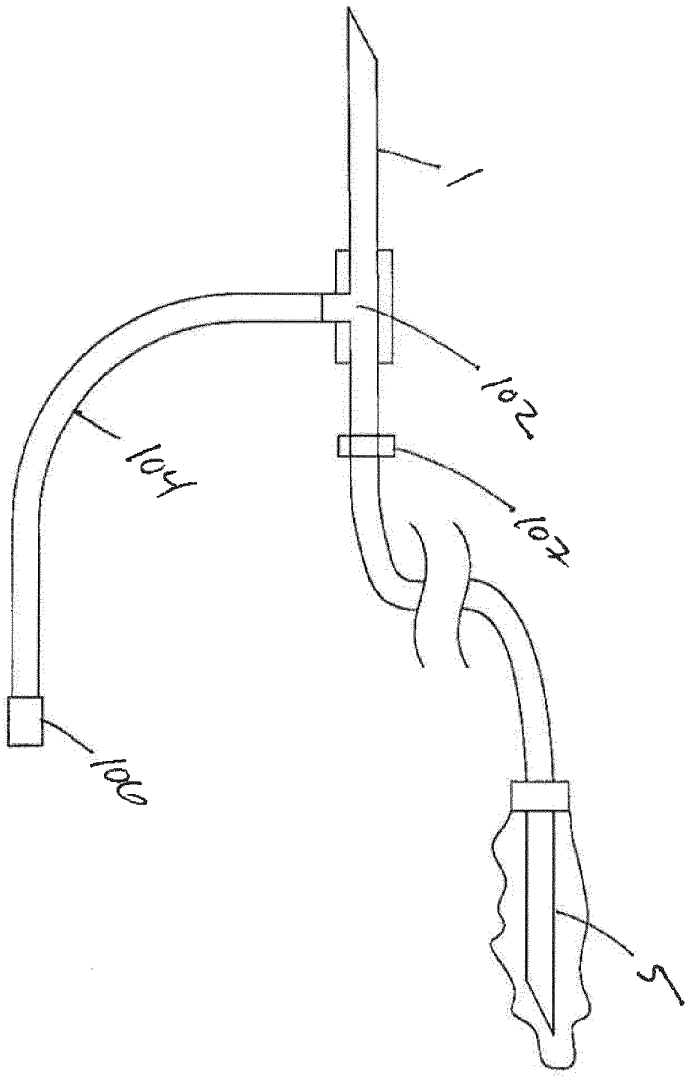


FIG. 4

FIG. 5

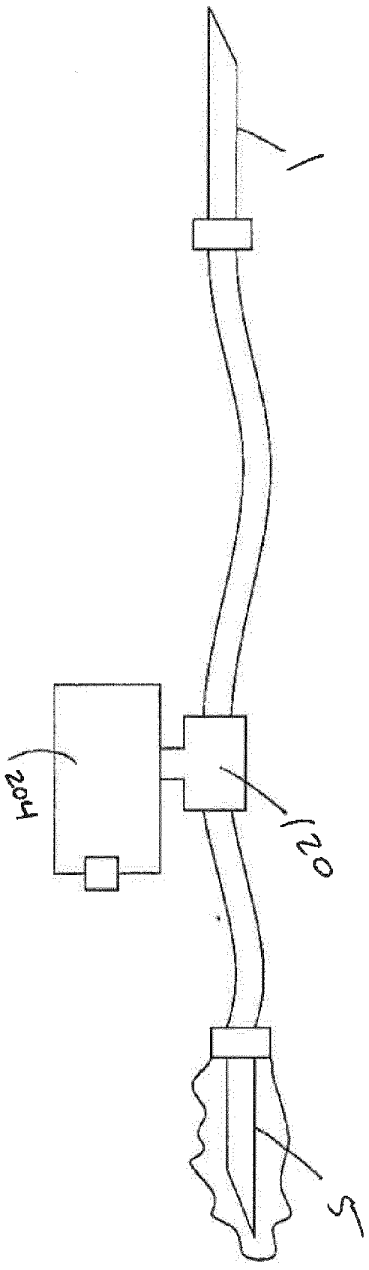
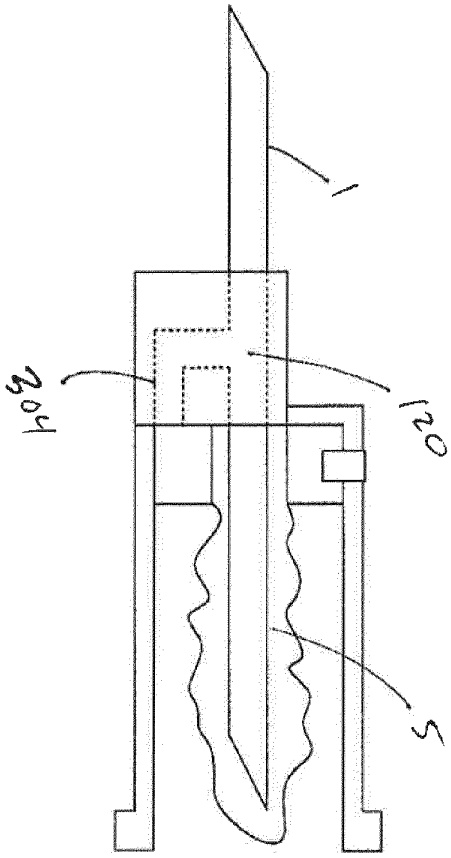


FIG. 6



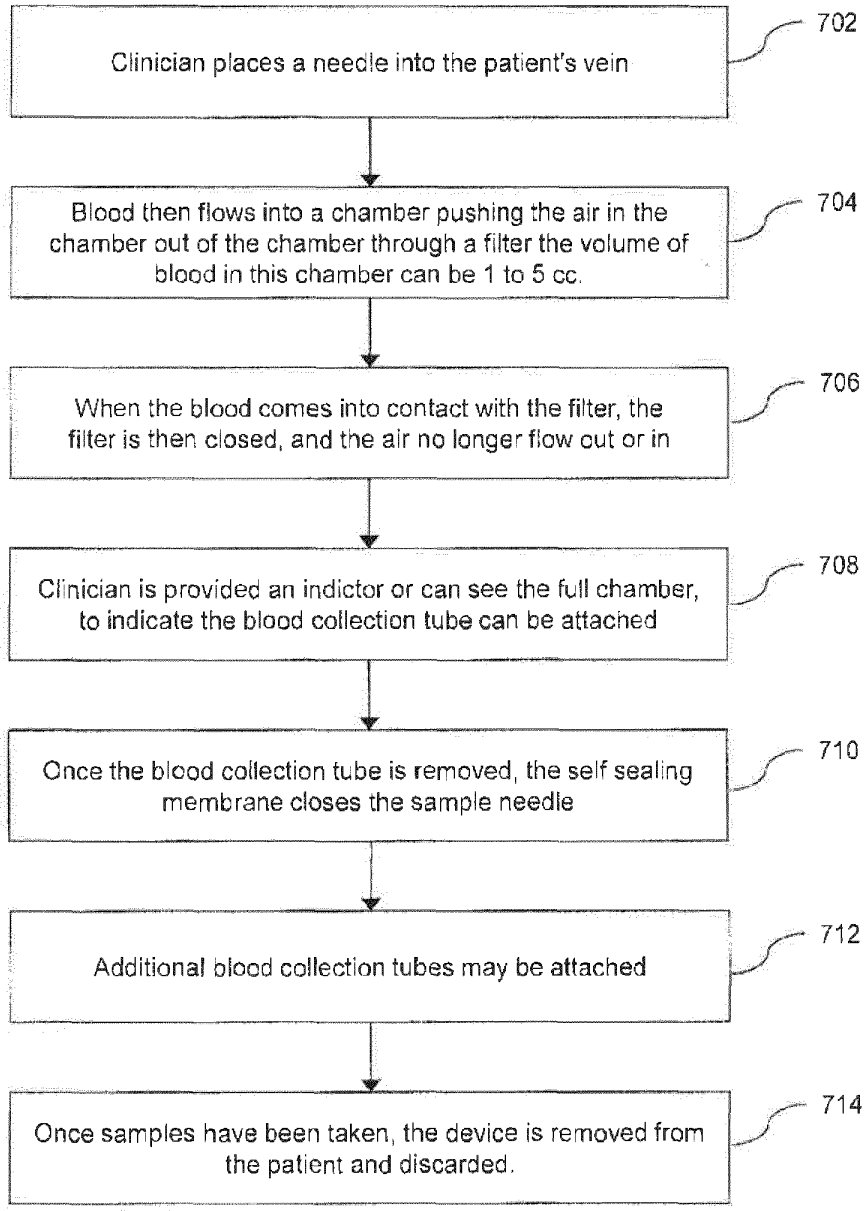

Clinician places a needle into the patient's vein
702
Blood then flows into a chamber pushing the air in the chamber out of the chamber through a filter the volume of blood in this chamber can be 1 to 5 cc.
704
When the blood comes into contact with the filter, the filter is then closed, and the air 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

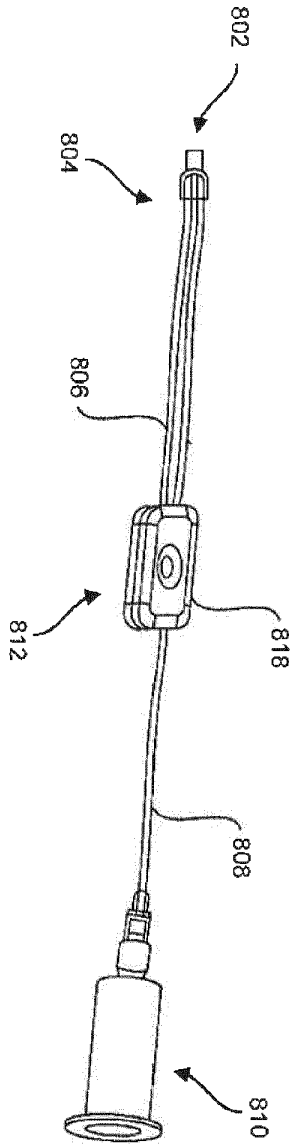


FIG. 8A

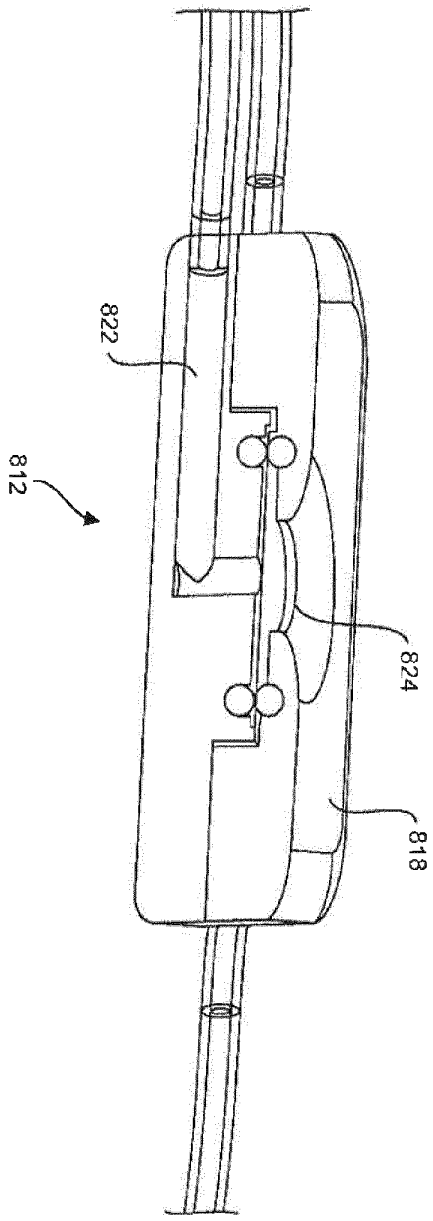


FIG. 8B

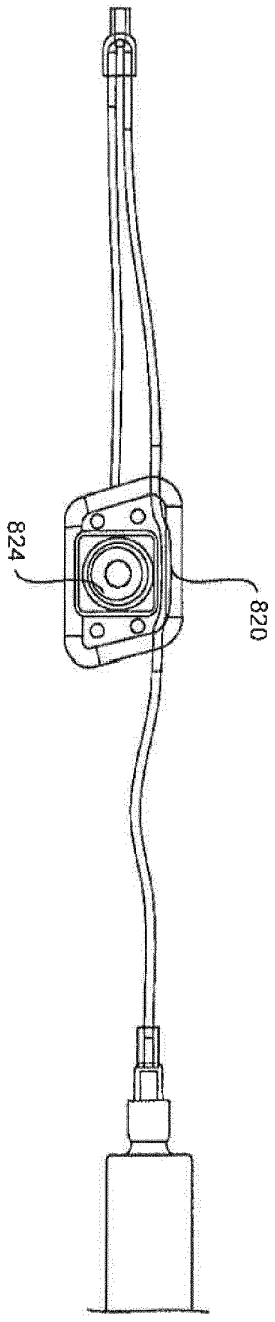


FIG. 8C

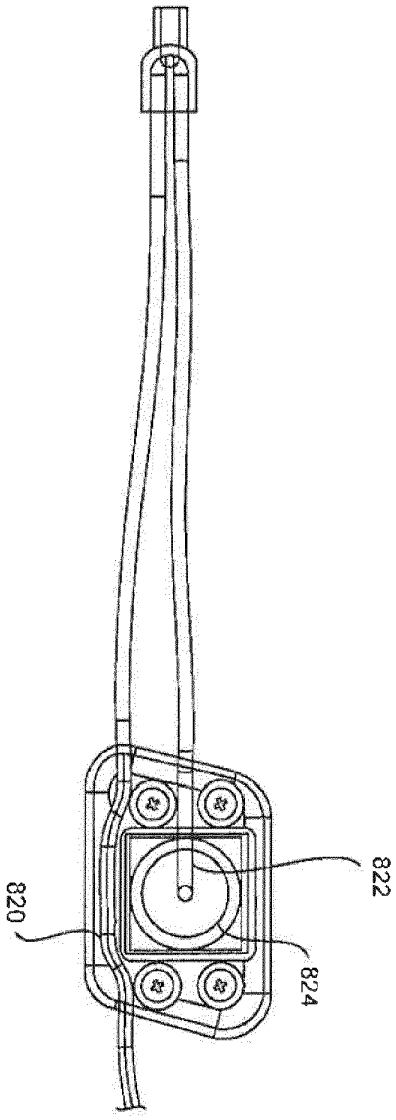


FIG. 8D

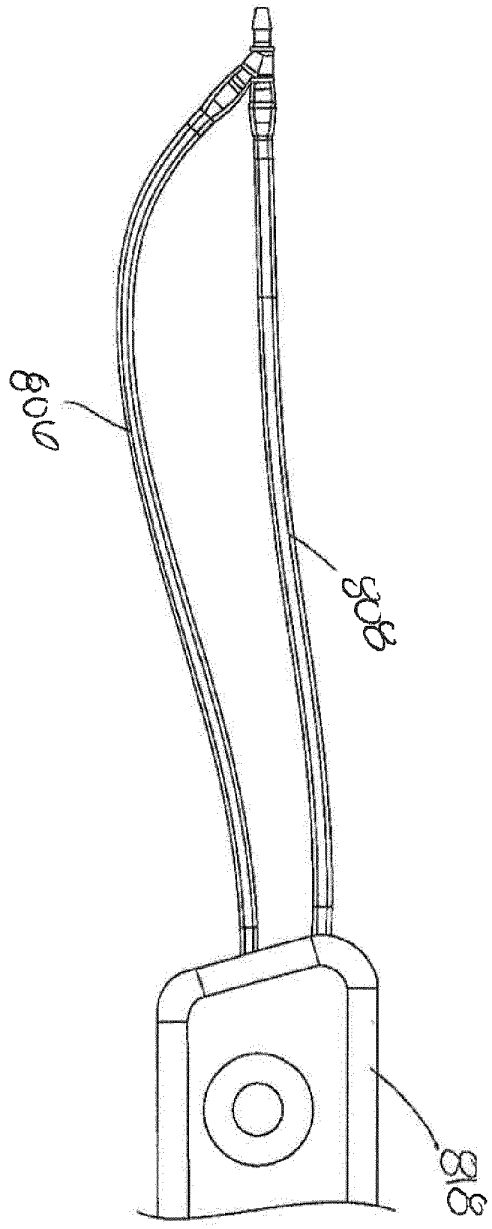


FIG. 8E

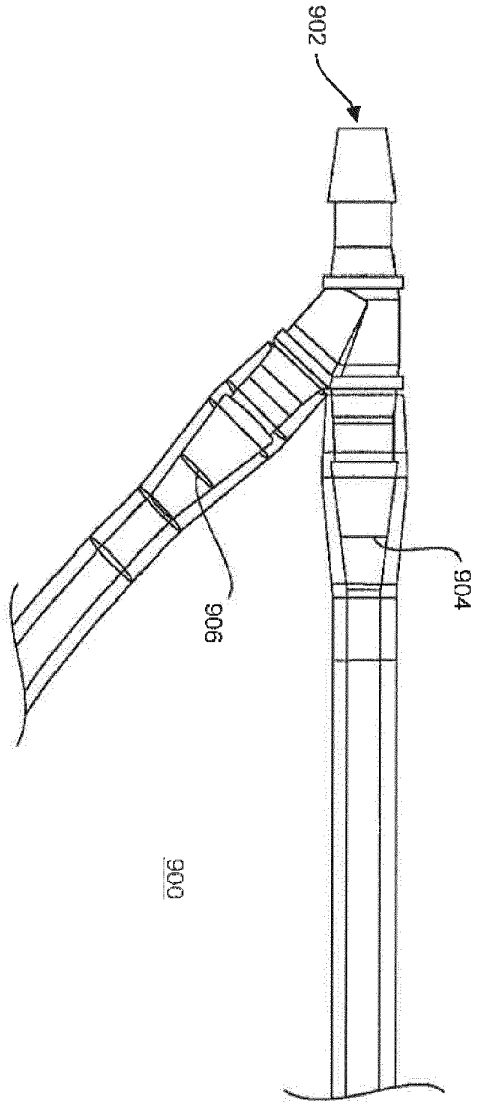


FIG. 9

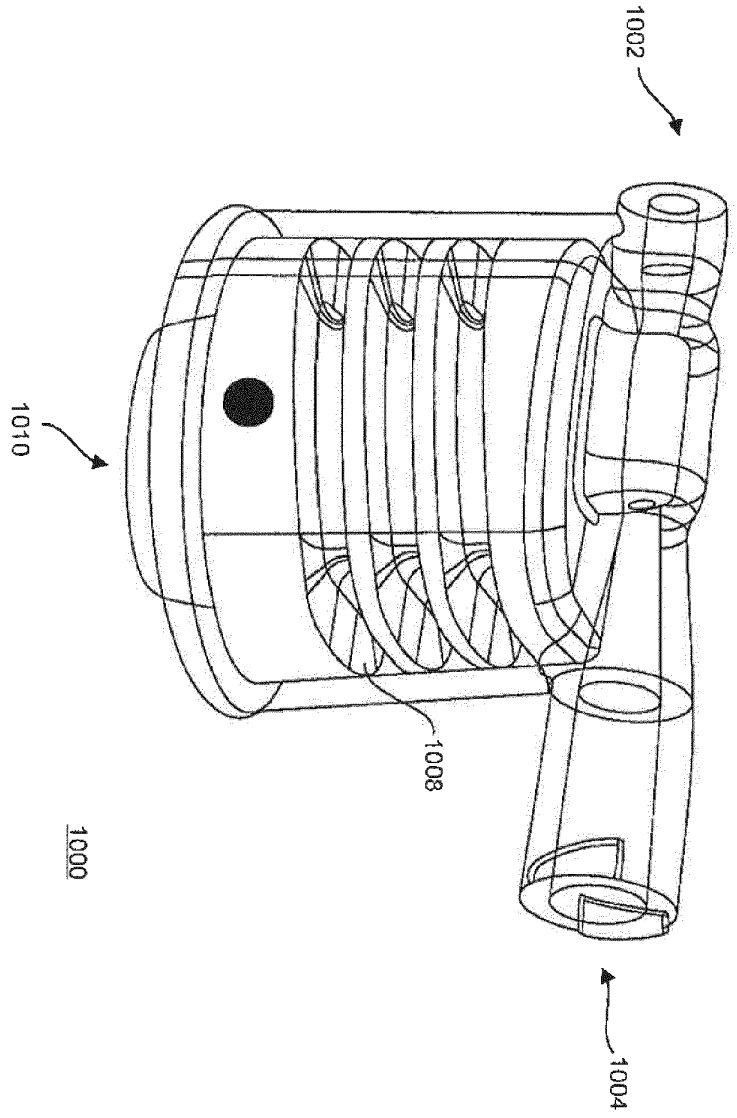


FIG. 10A

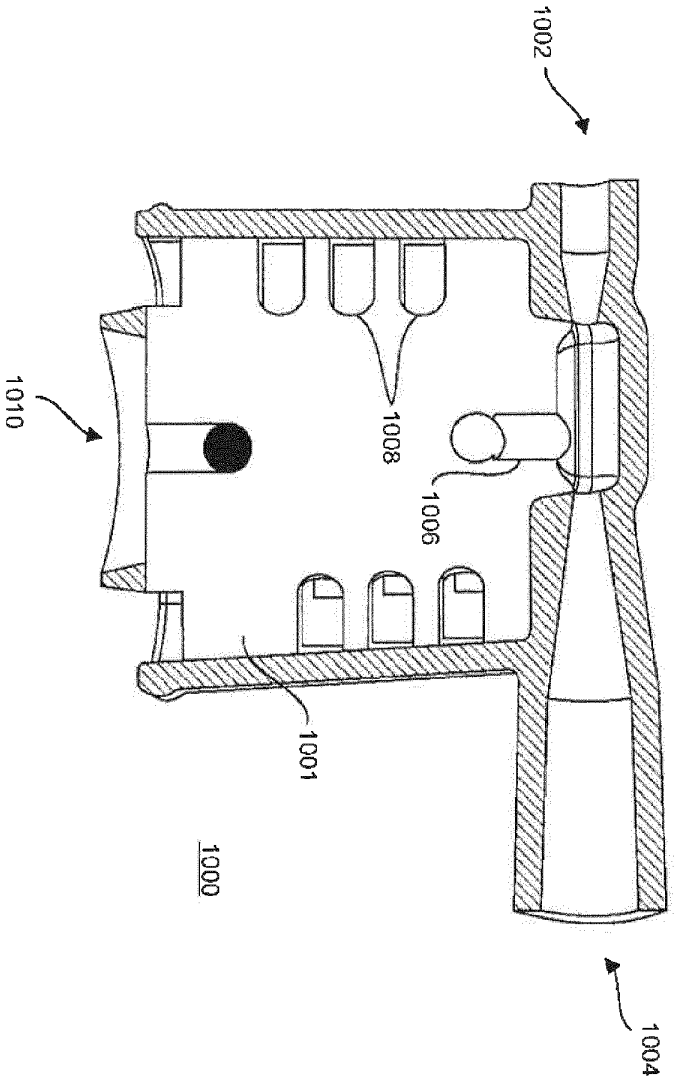


FIG. 10B

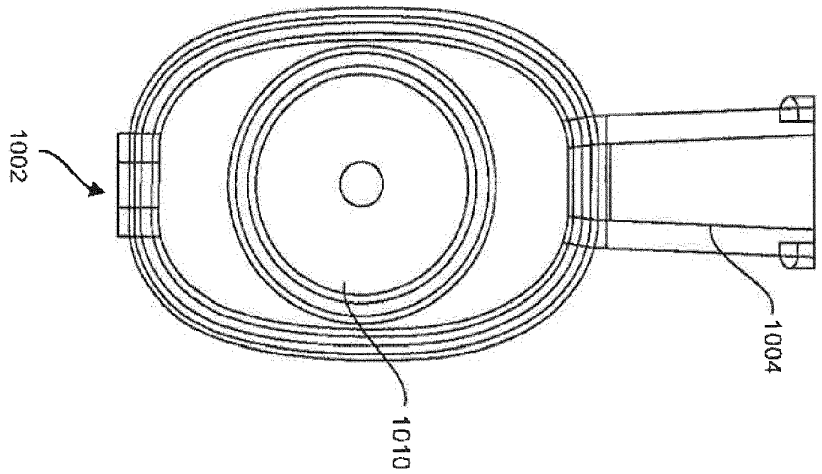


FIG. 10C

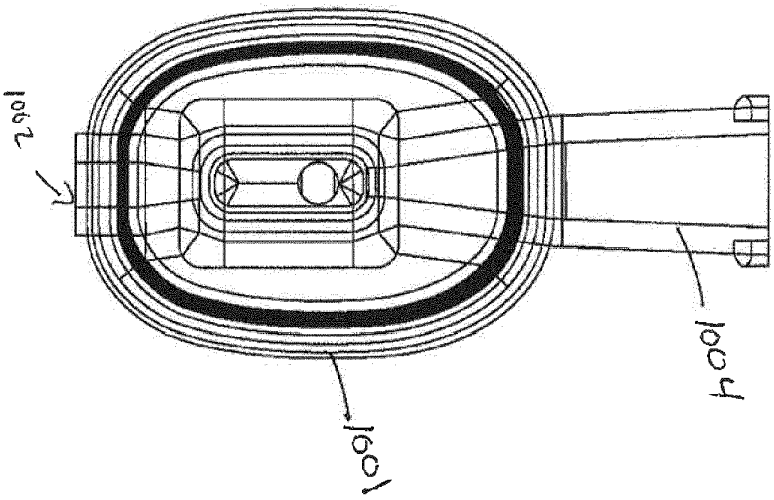
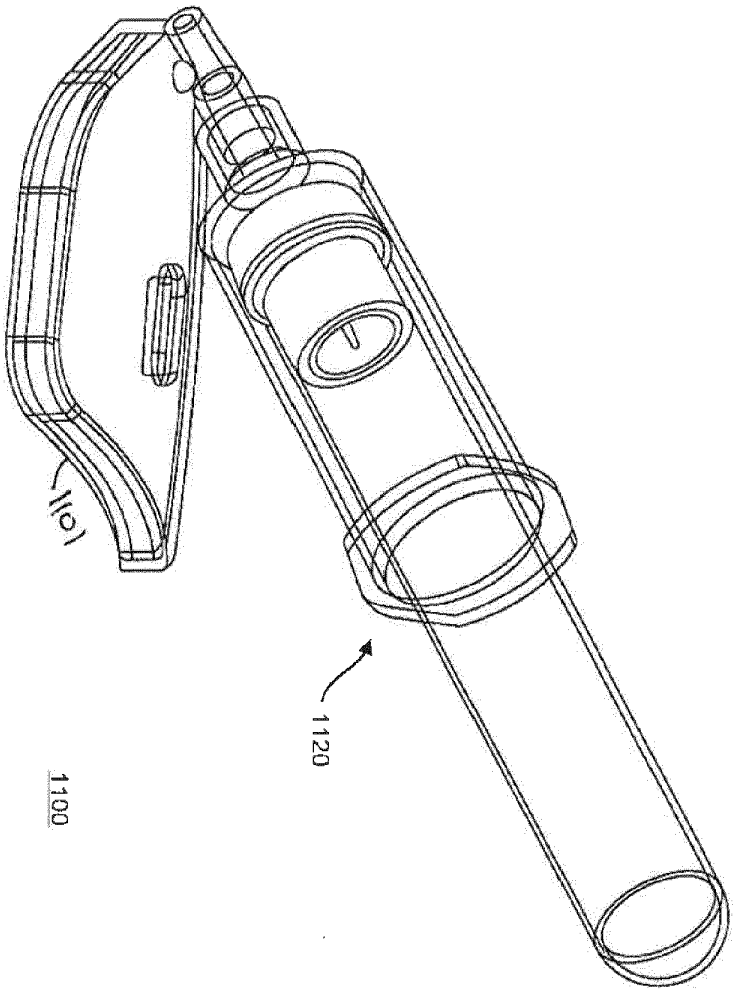


FIG. 10D

FIG. 11A



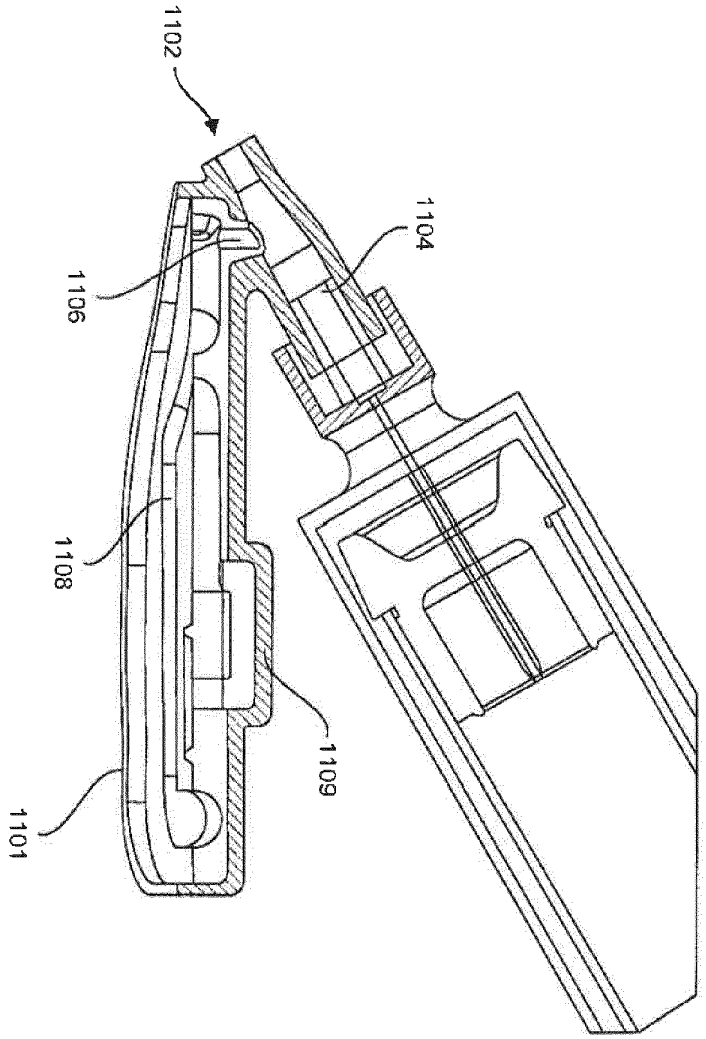


FIG. 11B

FIG. 11C

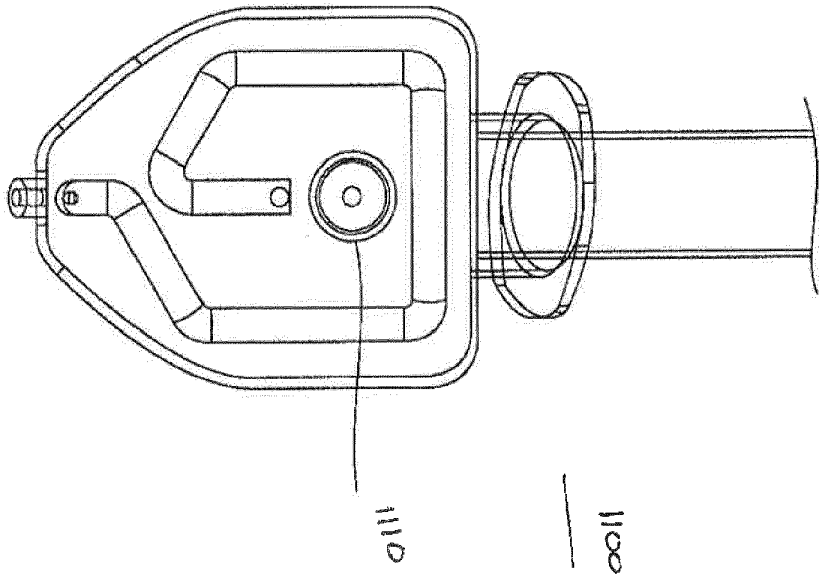
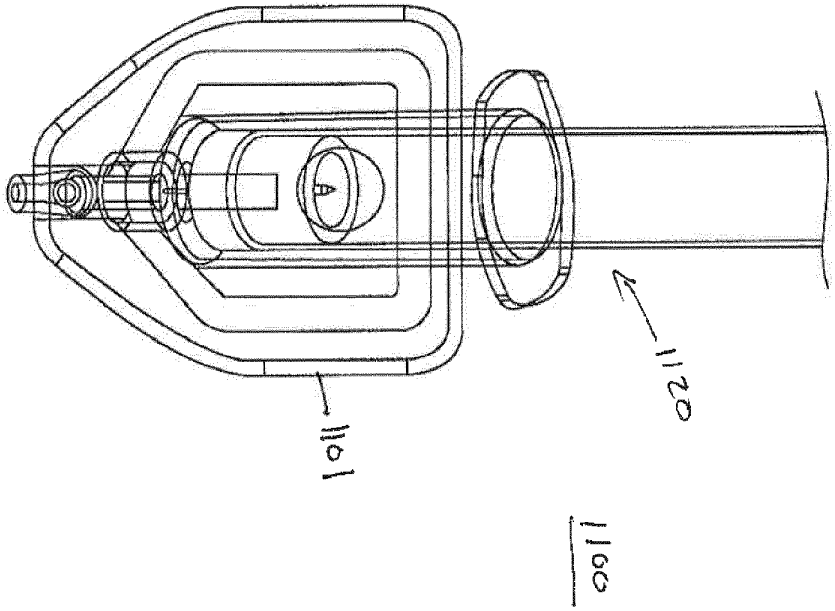


FIG. 11D



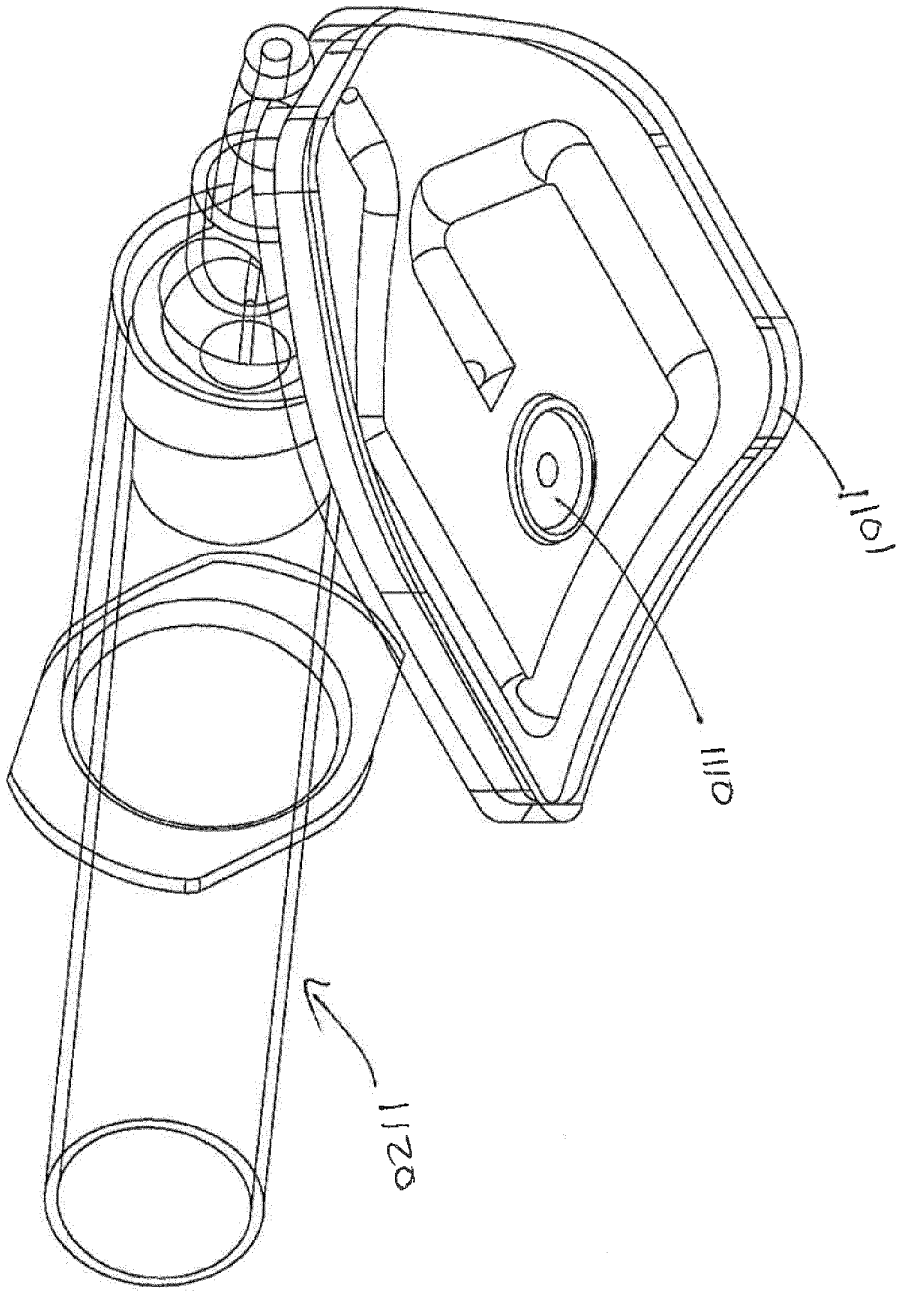


FIG. 11E

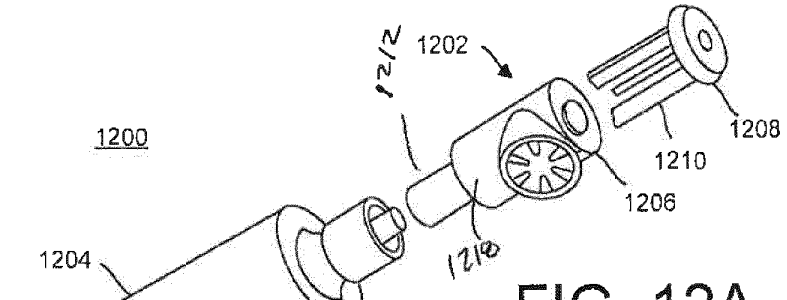


FIG. 12A

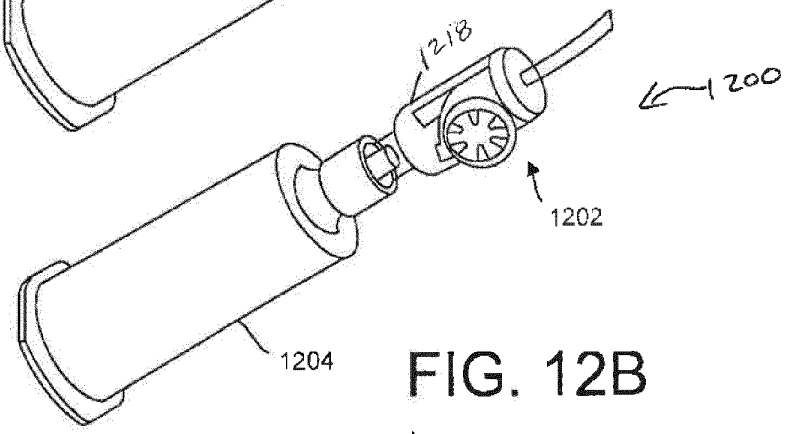


FIG. 12B

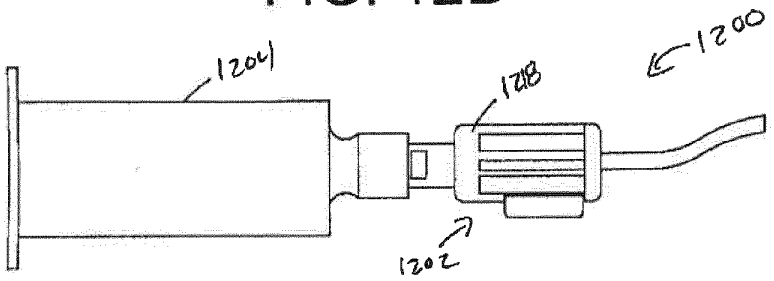


FIG. 12C

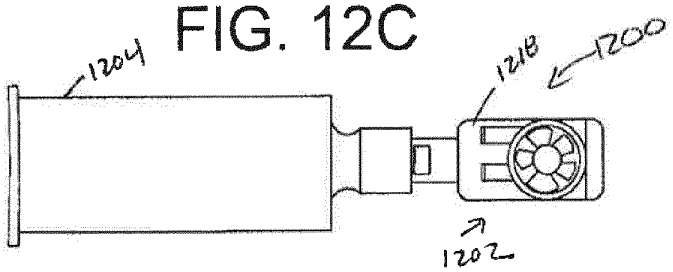


FIG. 12D

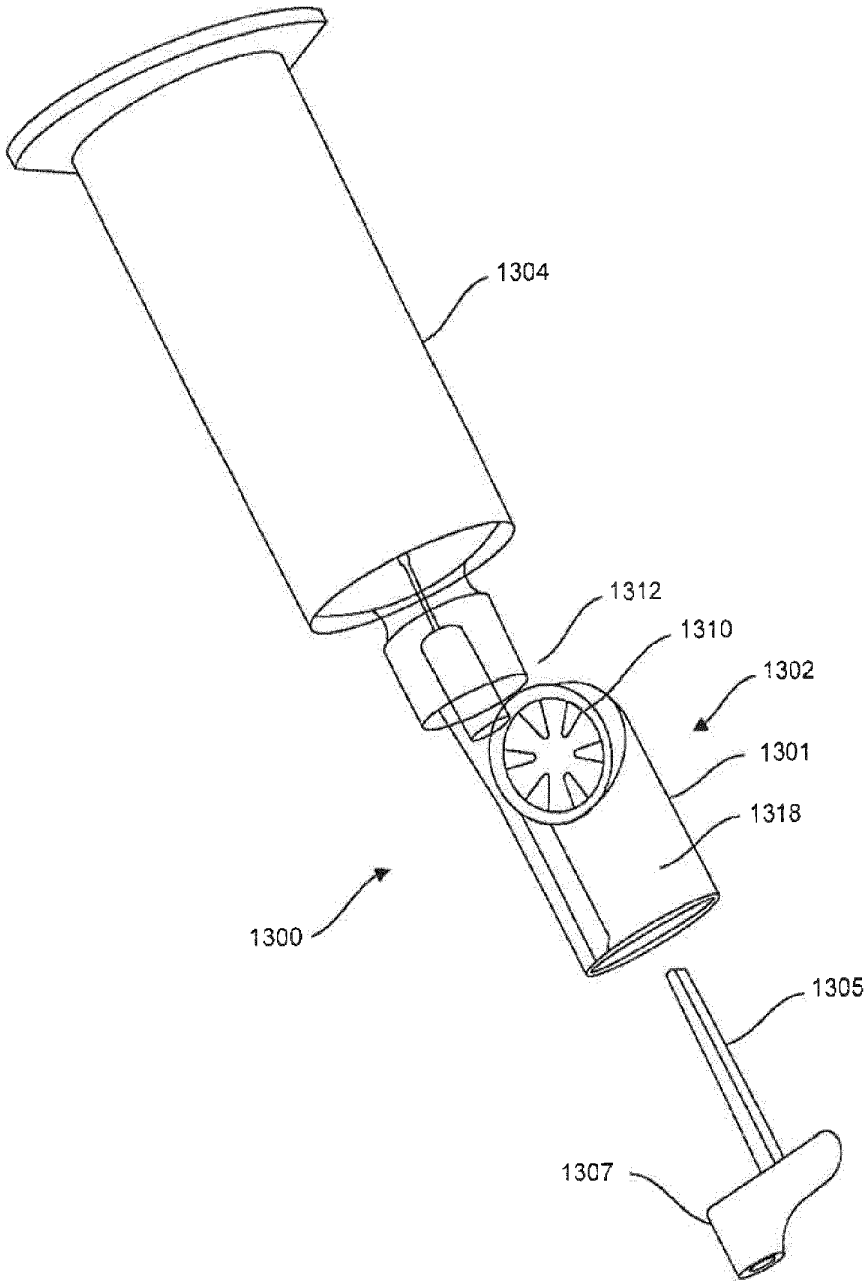


FIG. 13A

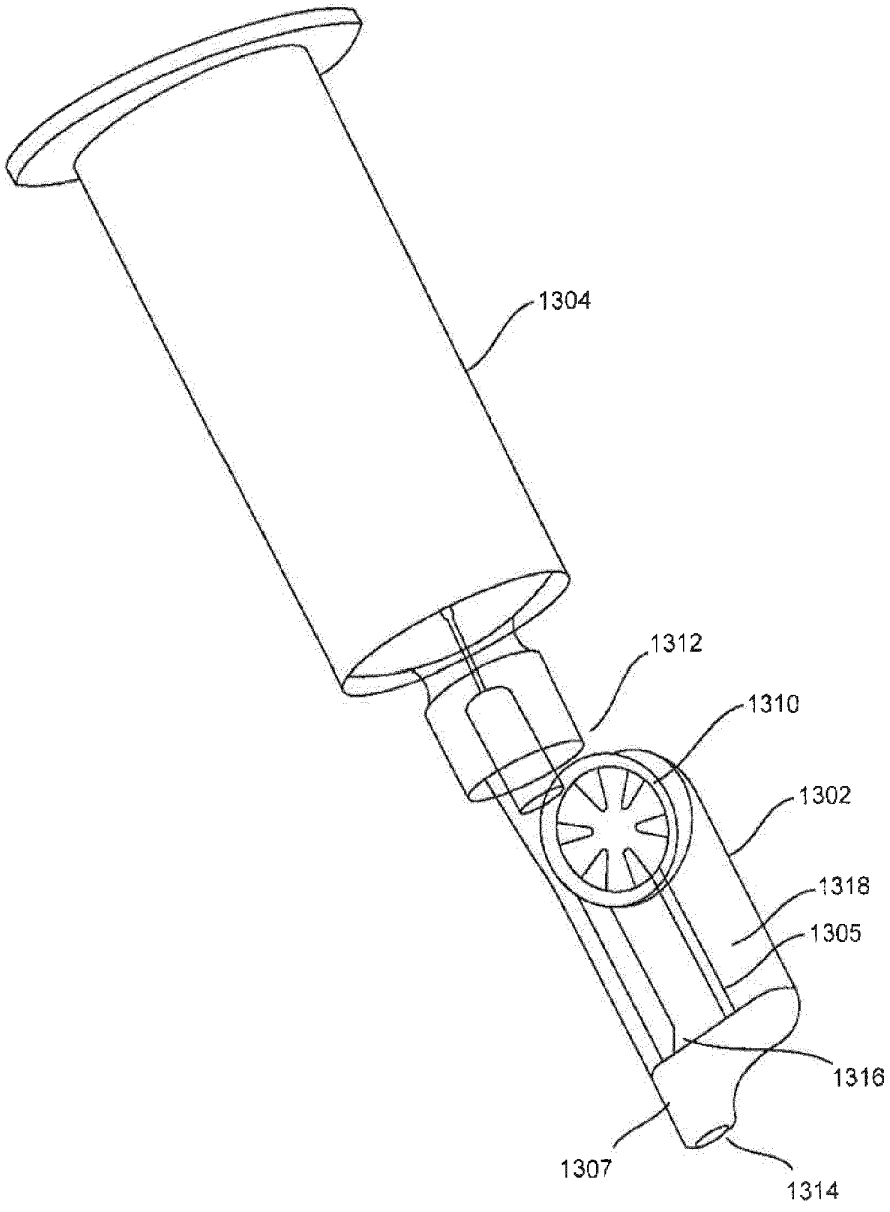


FIG. 13B

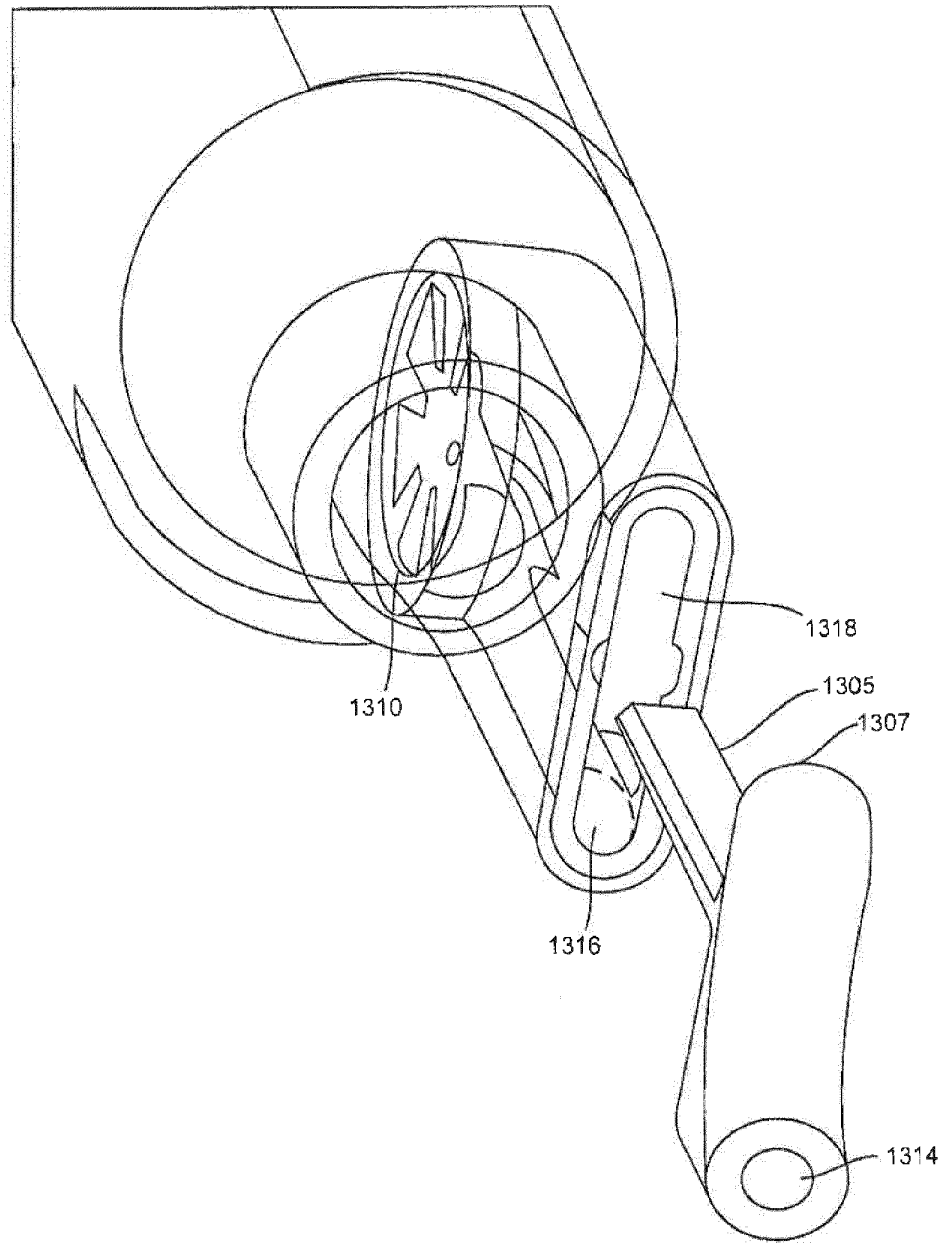


FIG. 13C

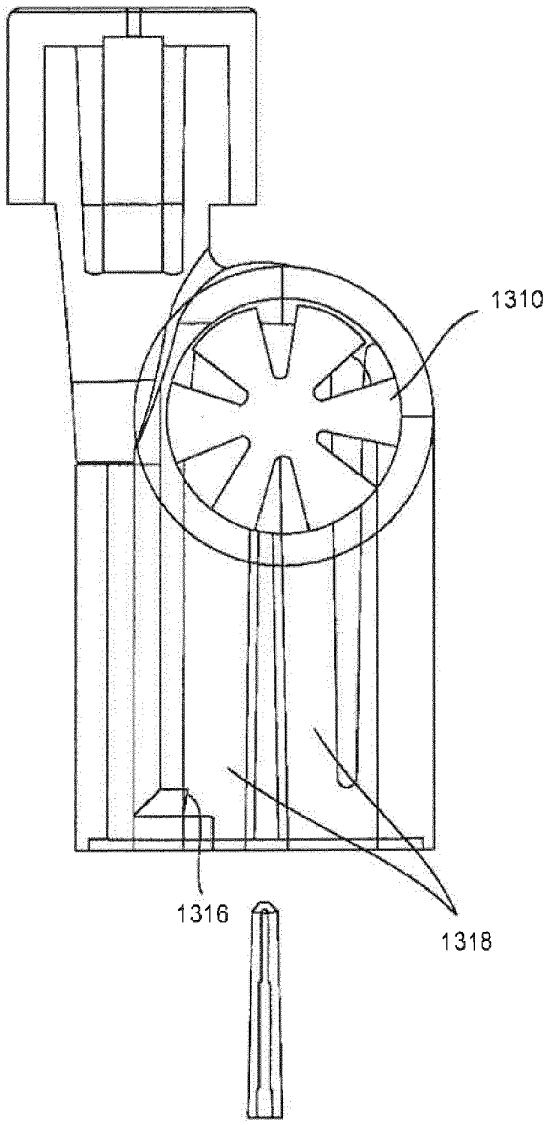


FIG. 13D

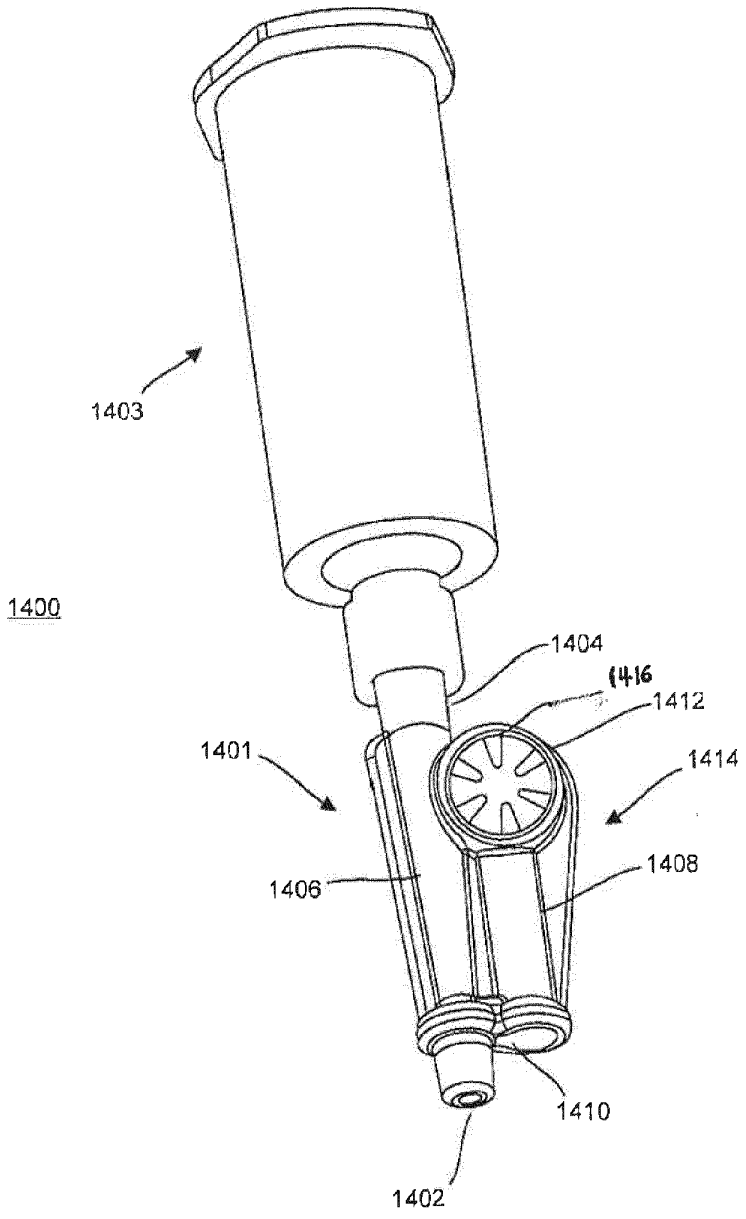


FIG. 14A

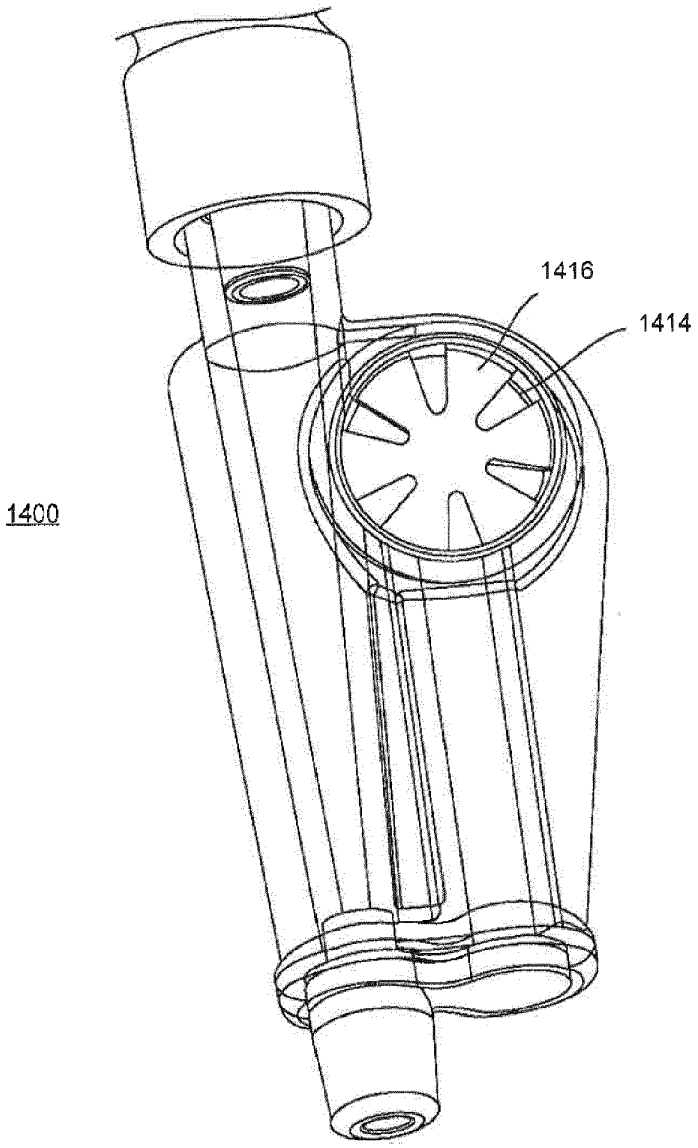


FIG. 14B

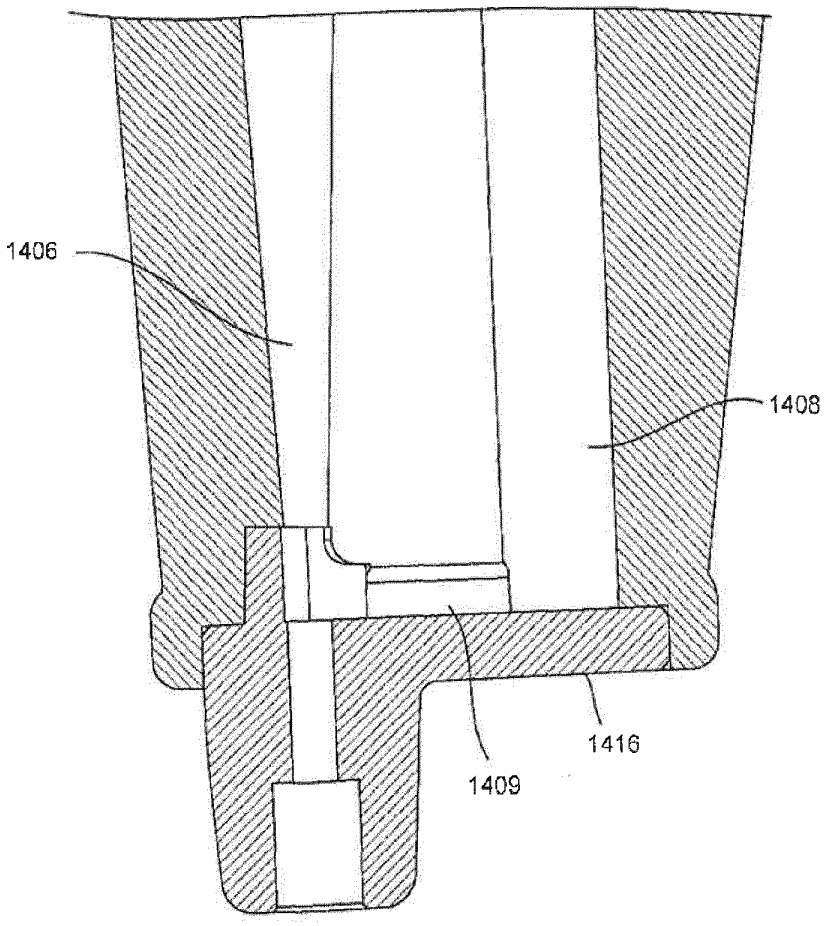


FIG. 14C

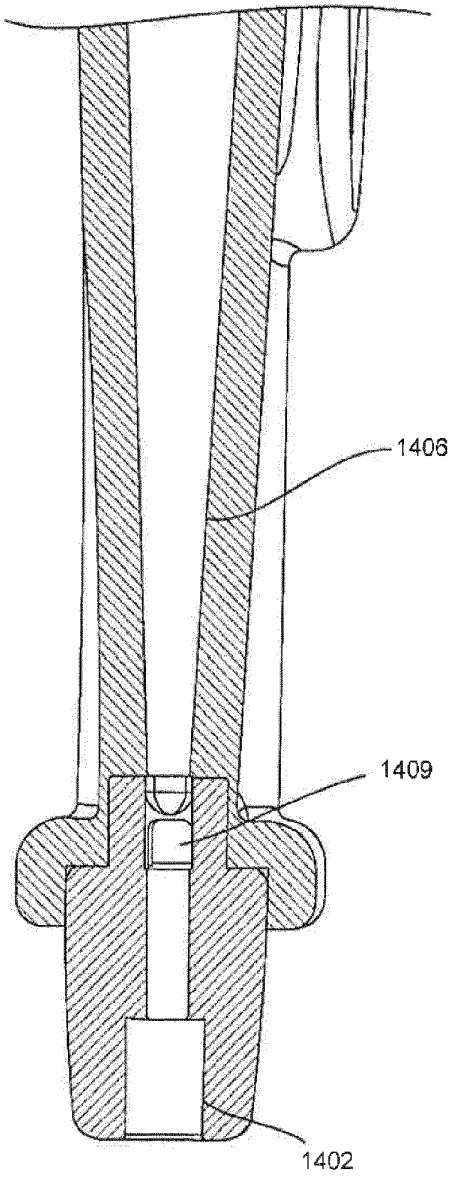


FIG. 14D

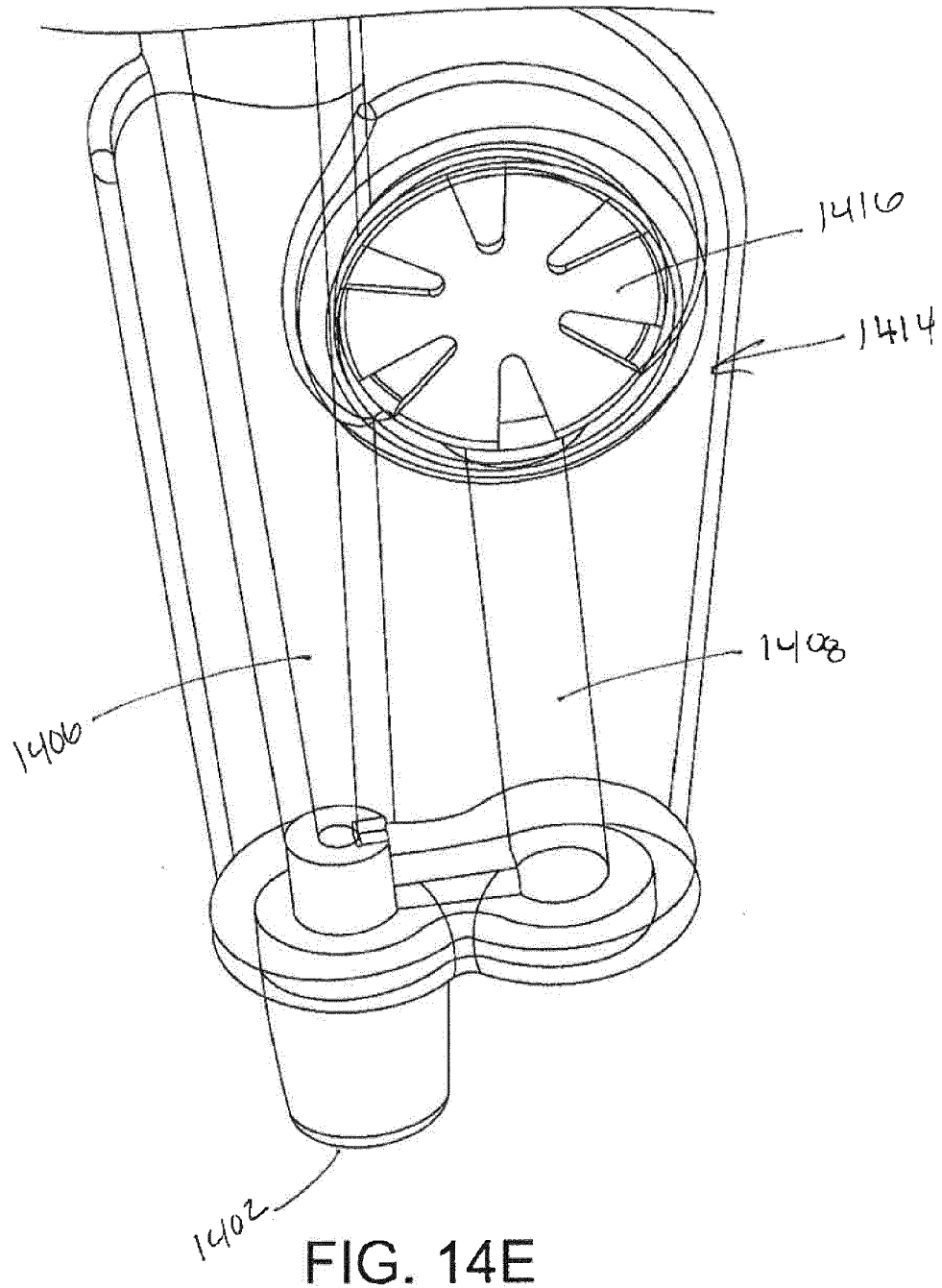


FIG. 14E

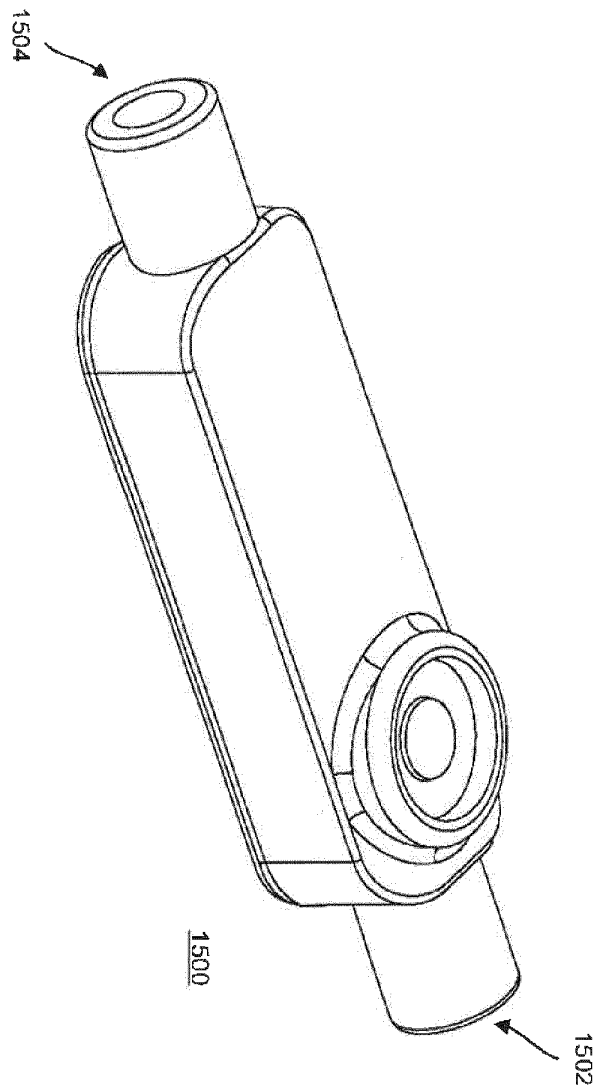


FIG. 15A

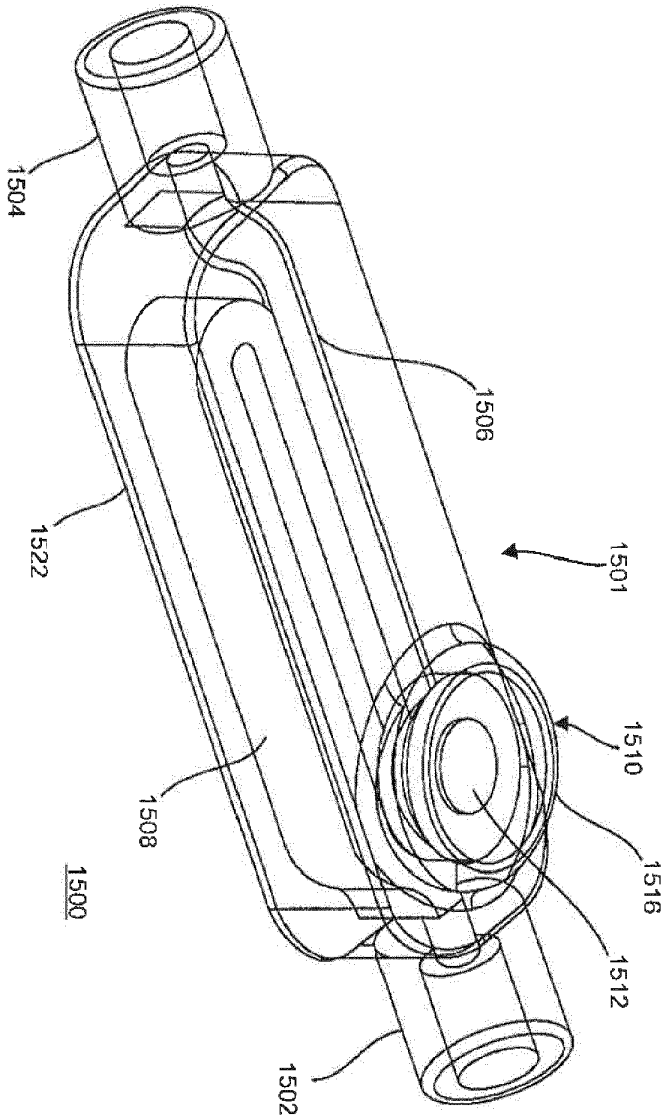


FIG. 15B

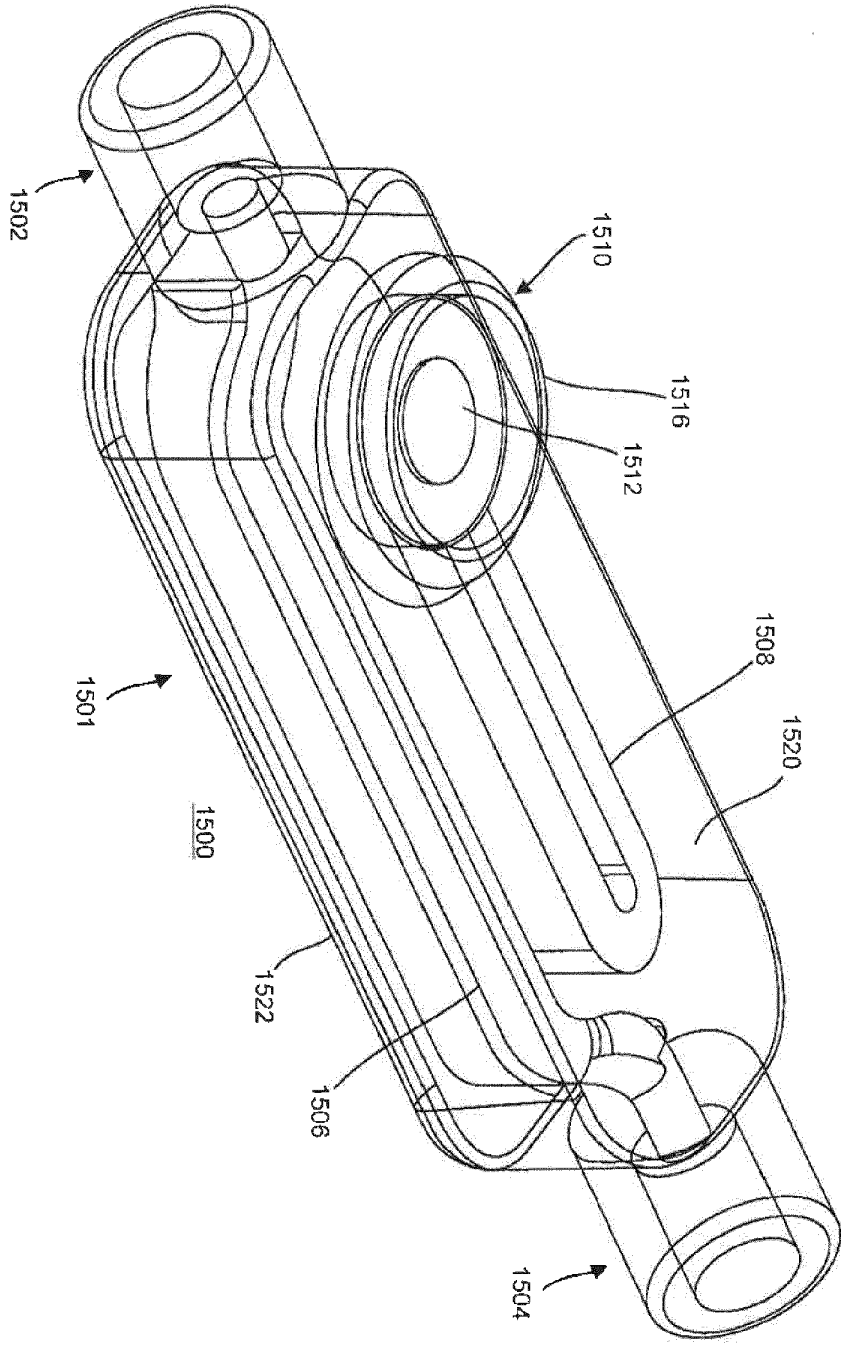


FIG. 15C

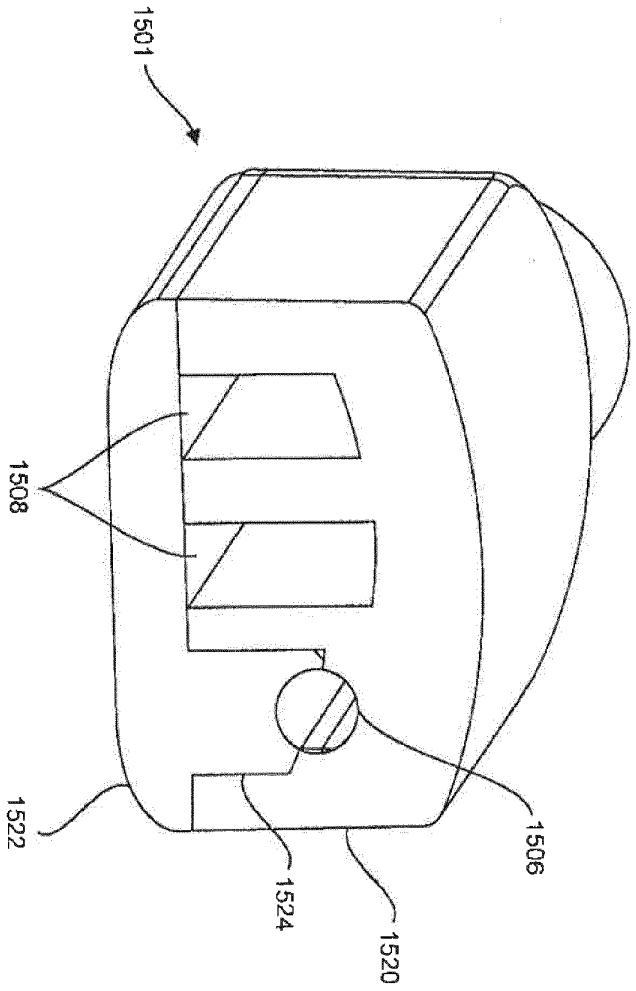


FIG. 15D

FIG. 15E

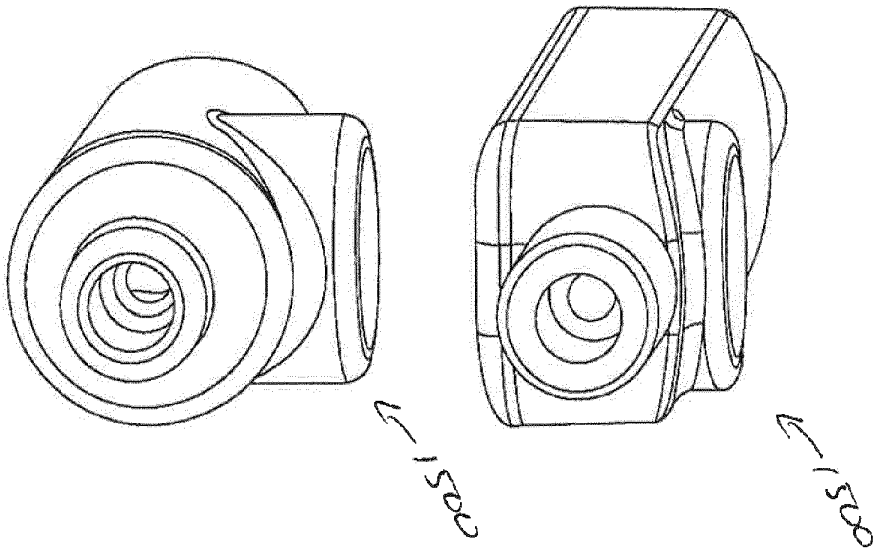
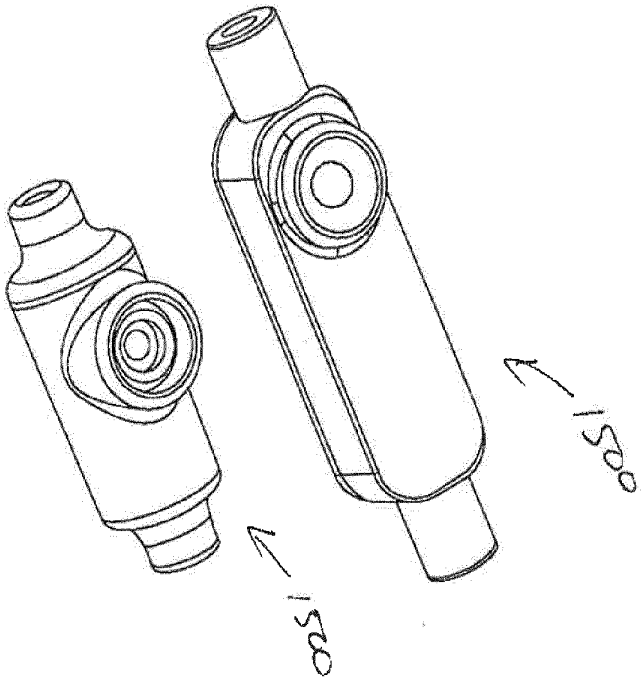


FIG. 15F



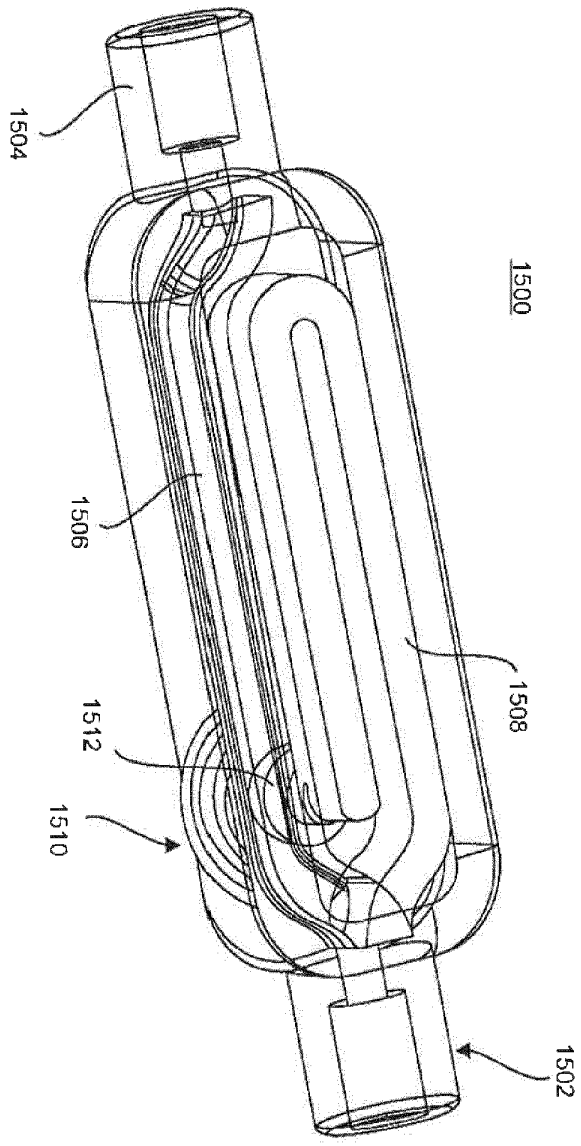


FIG. 15G

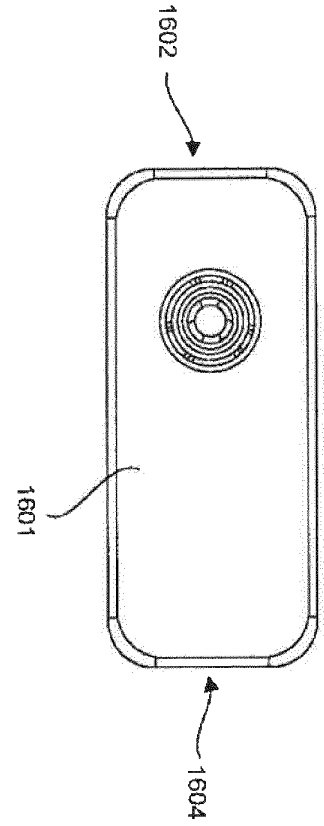


FIG. 16A

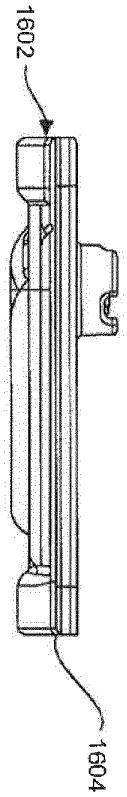


FIG. 16B

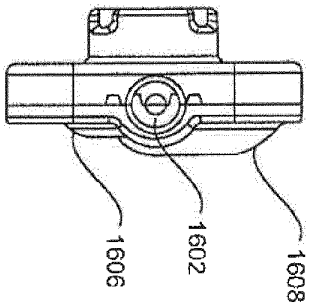


FIG. 16C

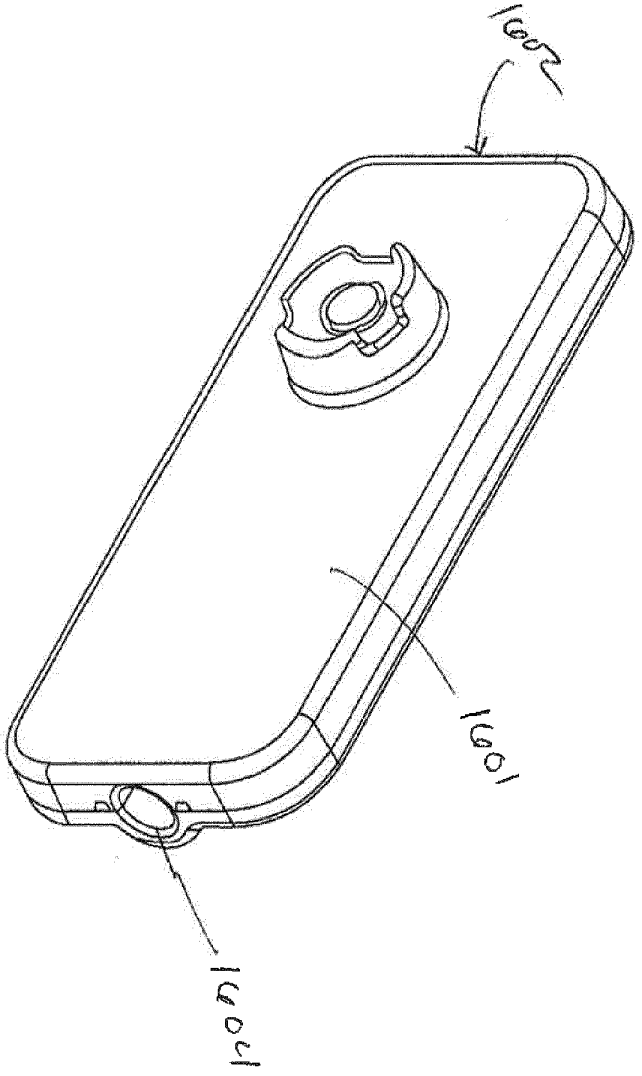


FIG. 16D

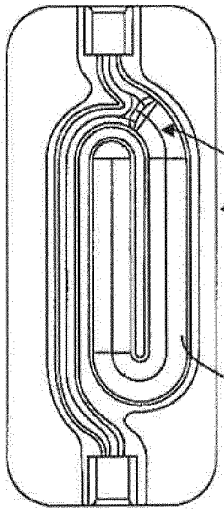


FIG. 17A

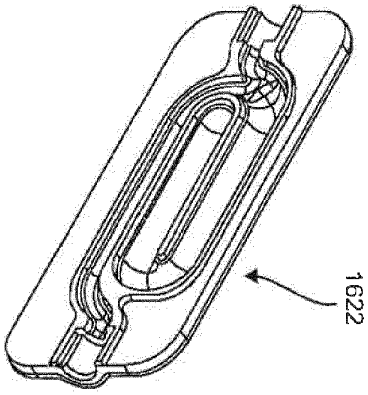


FIG. 17B

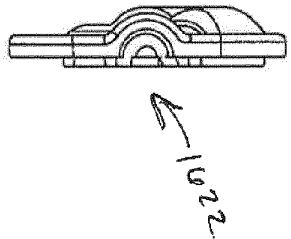


FIG. 17C

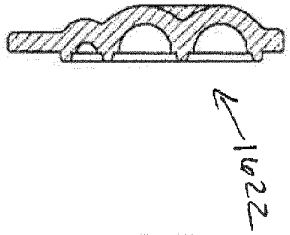


FIG. 17D

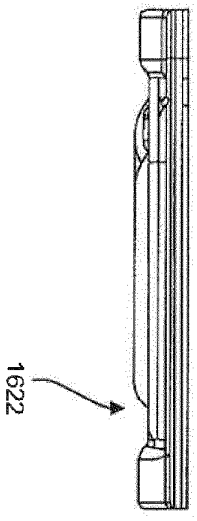


FIG. 17E

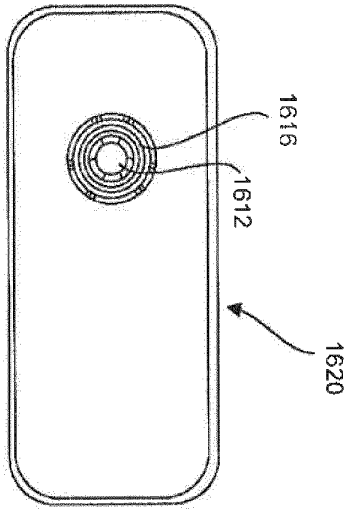


FIG. 18A

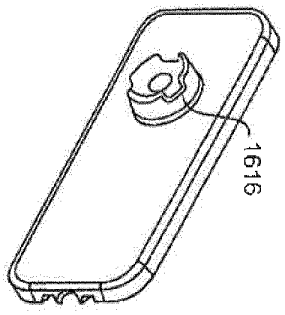


FIG. 18B

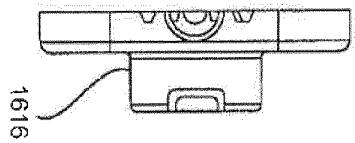


FIG. 18C

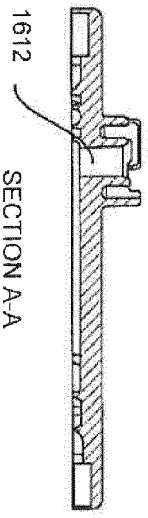


FIG. 18D

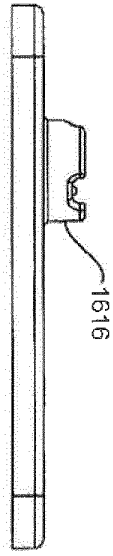


FIG. 18E

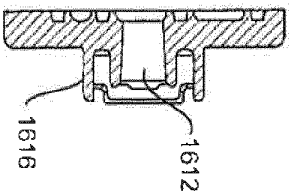


FIG. 18F

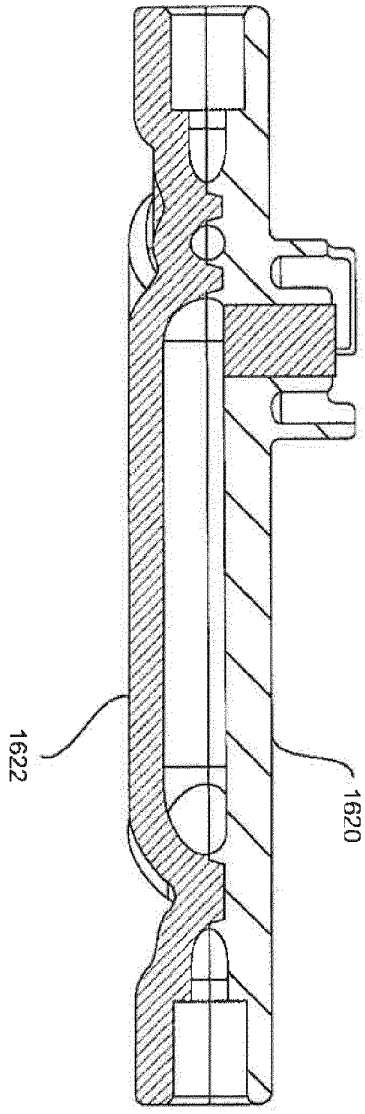


FIG. 19A

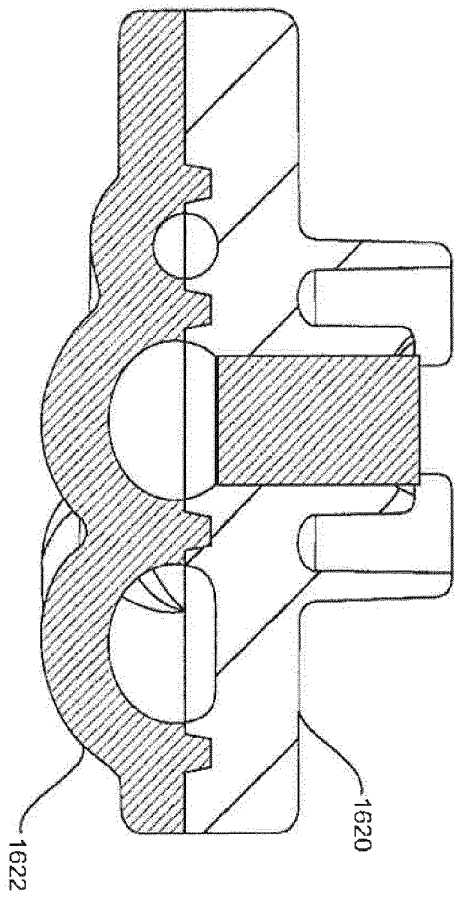


FIG. 19B

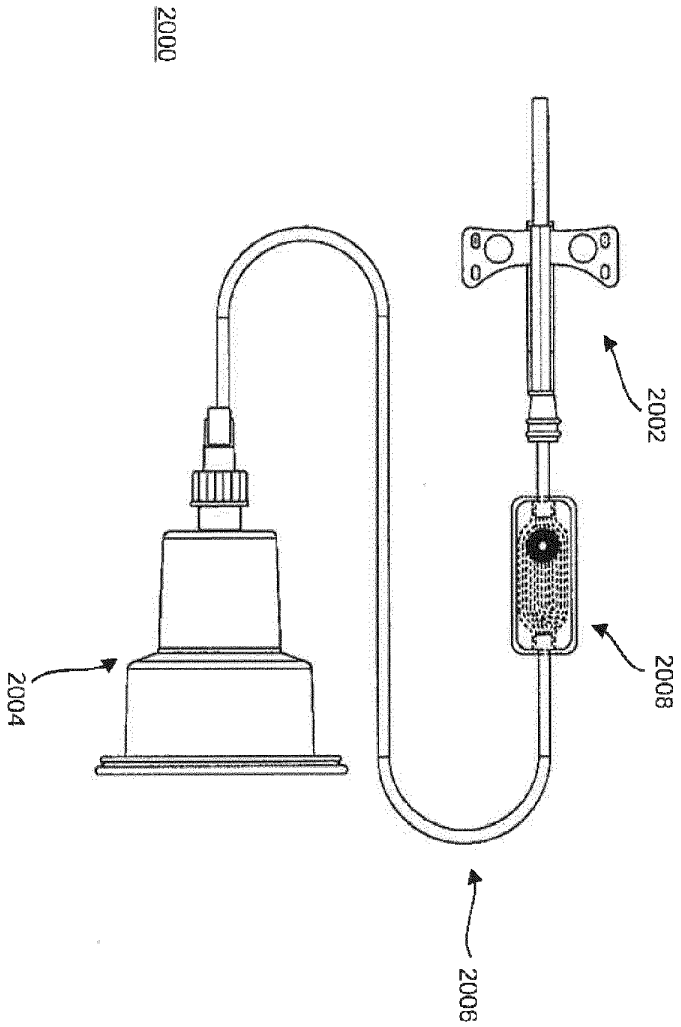


FIG. 20

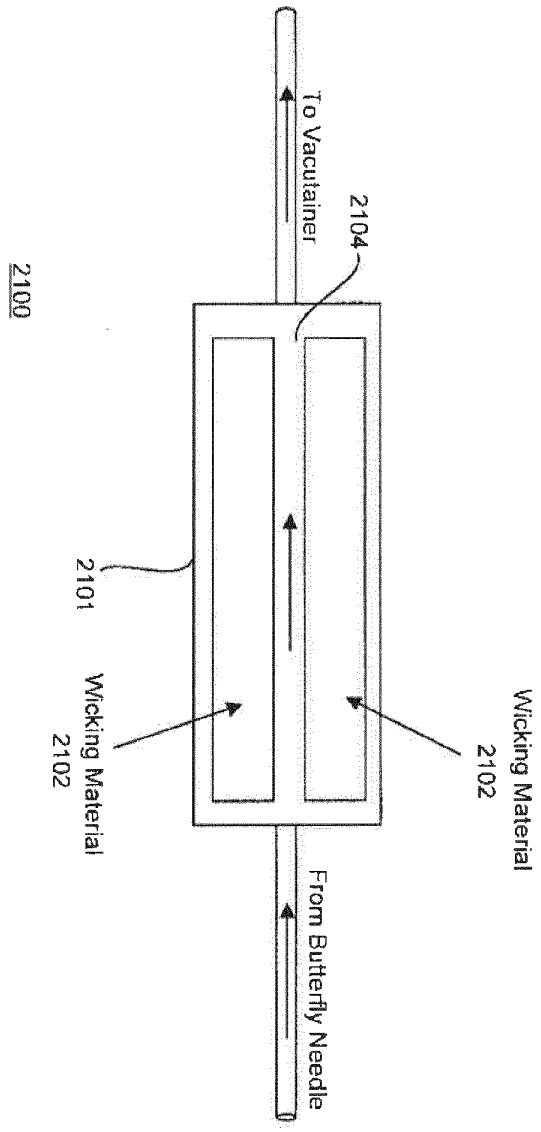

2100
To Vacutainer
2104
2101
Wicking Material
2102
Wicking Material
2102
From Butterfly Needle

FIG. 21

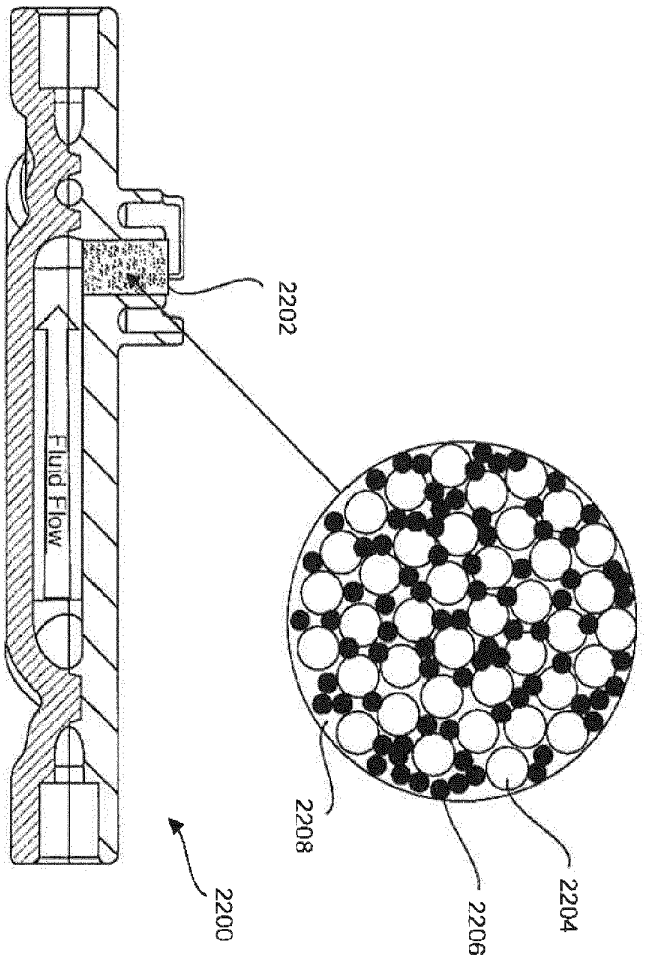


FIG. 22A

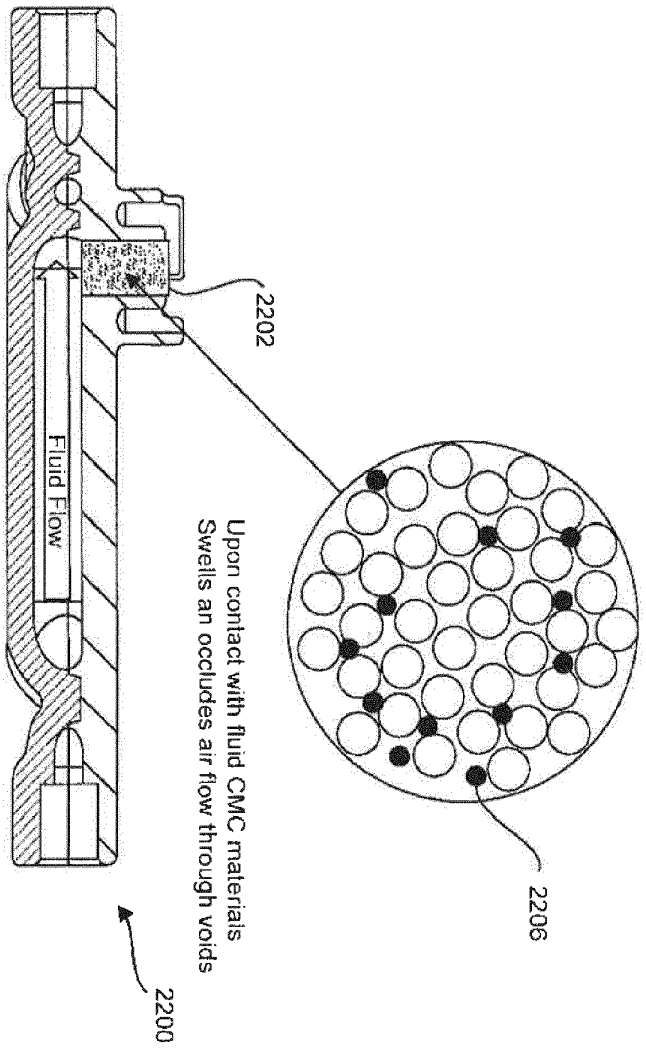

2202
Fluid Flow
Upon contact with fluid CMC materials
Swells an occludes air flow through voids
2206
2200

FIG. 22B

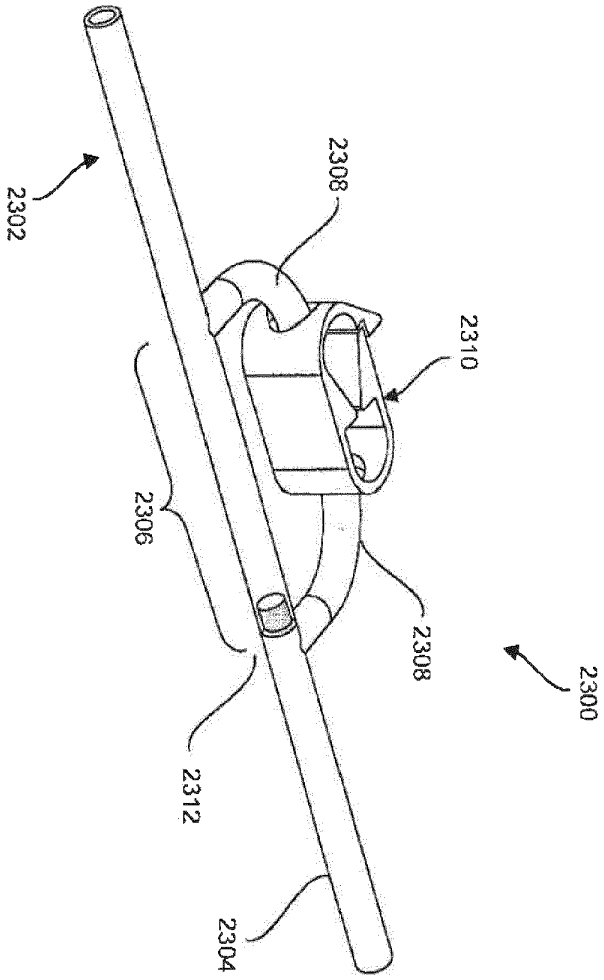


FIG. 23A

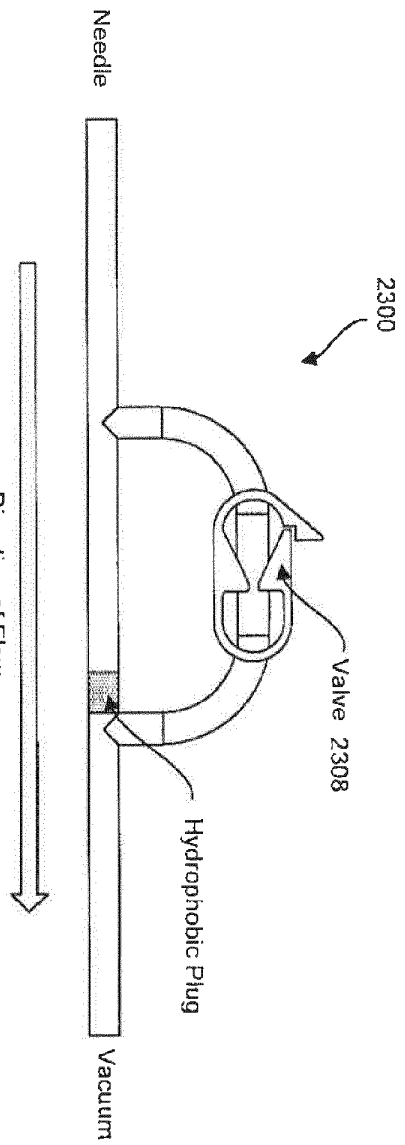

Needle
2300
Direction of Flow
Valve 2308
Hydrophobic Plug
Vacuum

FIG. 23B

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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)
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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

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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)

Europäisches Patentamt
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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
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L : document cited for other reasons

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ANNEX TO THE EUROPEAN SEARCH REPORT ON EUROPEAN PATENT APPLICATION NO. EP 19 20 0766

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18-11-2019

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For more details about this annex : see Official Journal of the European Patent Office, No. 12/82

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- US 62196797 **[0001]**
- US 62238636 **[0001]**
- US 62318194 **[0001]**

Original Article

Quality of Processed Blood for Autotransfusion

Gerald Shulman, MD

University of Texas Medical Branch, Galveston, Texas

Keywords: red cell mass flow rate, speed, plasma washout, quality

Presented at the American Society of Extra-Corporeal Technology 37th International Conference, April 8–11, 1999, New Orleans, Louisiana

ABSTRACT

Centrifugal red blood cell washers for intraoperative autotransfusion process shed blood during surgery. In this study, the quality of processed fresh, human bank blood was assessed in a standardized laboratory setting during standard, medium, and high flow processing. Red cell recovery rates and plasma washout efficiencies were compared using three different devices. The accurate parameters measuring effectiveness and product quality were red cell mass (RCM) flow rate and the plasma washout efficiency. Cobe BRAT 2, a system with discontinuous flow (DF) and a cylindrical centrifuge bowl, permitted processing in standard and medium flow of 26 and 35 mL RCM/min, respectively, with washout of residual plasma albumin of 93.2 and 91.2%. The Medtronic Sequestra 1000, a DF system with a conical centrifuge bowl processed blood at 15 and 23 mL RCM/min and eliminated plasma albumin with 98.4 and 96.8% washout during standard and medium flow, respectively, with significant red cell loss occurring during medium flow. The respective speeds of high-flow programs with BRAT 2 and Sequestra 1000 were 15 and 22 mL RCM/min, related to a hematocrit in the holding bag, less than that of the incoming blood from the reservoir. Washout was 58.2 and 58.3%, respectively. Fresenius CATS, a continuous flow (CF) device, produced flow rates of 19, 24, and 43 mL RCM/min and plasma albumin elimination of 97.8, 94.4, and 93.3% in standard, medium, and high-flow, respectively. Holding bag hematocrits with CF exceeded that of DF. Standard, medium, and high-flow programs of CATS may be used without restriction.

Address correspondence to:
Gerald Shulman, MD
Blood Bank Division
Department of Pathology and Laboratory Medicine
Emory University School of Medicine
1364 Clifton Road NE
Atlanta, GA 30322

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INTRODUCTION

The red blood cell recovery rate and washing efficiency of centrifugal devices used for intraoperative autologous transfusion (IAT) have an impact on the safety, purity, and potency of the processed product. Standard programs of most IAT devices have shown satisfactory performance during vascular surgery (1), cardiothoracic surgery (2), and major orthopedic surgery (3–7). However, accurate data on processing at high speeds are limited. The operating principles of centrifugal equipment are based either on discontinuous (DF) or continuous flow (CF). DF devices employ conical or cylindrical bowl geometries, which may affect results of the washing procedures. Manufacturers provide defined preprogrammed washing procedures with various washing speeds. In addition, operator-defined options are available, allowing for alteration of processing parameters of centrifuge speed and flow rates. Although changes that may affect the characteristics of the blood product are indicated, no exact data are provided.

The goal of this study is to perform a well-defined laboratory comparison of the processing speed and quality of the washed red cell product of three autotransfusion devices, each with operating principles based on different technology. Three speeds were studied in standard, medium, and high flow programs using nondistributable donor red cells reconstituted with compatible plasma and at three dilutions with saline, simulating conditions in the operating room.

MATERIALS AND METHODS

Washing programs were based on an ordinary requirement (standard flow), rapid (medium flow), and a very rapid (high flow), each representative of routine, rapidly processed, and emergency methods, respectively. The Cobe BRAT 2[a], the Fresenius CATS[b], and the Medtronic Sequestra 1000[c] were employed during this study. Manufacturer-specified programs for DF using Sequestra 1000 with a conical centrifuge bowl and CATS with CF were selected as corresponding standard, medium, and high flow programs. The programs for comparable function on BRAT 2 with DF and a cylindrical centrifuge bowl were the standard flow program as specified by the manufacturer, medium and high flow are available as operator-defined procedures (Table 1).

Compatible fresh frozen plasma and nondistributable donor packed red cells, less than 5 days from the time of collection, were pooled to achieve an hematocrit (HCT) of approximately 40%. To simulate blood collected from a surgical field, an adjustment was made with normal saline to dilute pools with target HCT of approximately 30, 20, and 10%, each confirmed before processing. After thorough mixing, the pool was divided into separate bags and used as blood reservoirs. The devices were used with the same disposable sets for each respective instrument in the three corresponding programs. Variability between individual lots are not expected to influence test results significantly because of the known high reproducibility of the manufacturing process involved. A fresh portion of the identical blood pool was processed on each device in three separate consecutive runs in the automatic modes. The processing times using the 250-mL bowl with BRAT 2 and the 225-mL bowl with Sequestra 1000 were recorded each for one completely filled bowl until the system stopped automatically; residual packed red blood cells in the emptying lines to the holding bags were transferred by activating the "Empty" routine twice more. The processing time with CATS was measured during accumulation of an equivalent volume of 225 mL packed red cells in the holding bag as measured by digital display on the instrument's control panel. To be consistent, the residual red cell volume in the emptying line to the holding bag was retained in the line. Volumes of blood from the reservoir and packed red cells in the holding bag were calculated from weights before and after processing. The weight differences were divided by densities according to measured HCT levels (8), respectively, to calculate volumes of blood drawn from reservoirs and packed red cells collected into holding bags. Volumes of five mL blood each were sampled from the reservoirs before and from holding bags after processing for CBC with the MAXM[d] blood cell counter and tested within 2 hours. Similarly, separate samples were collected, the centrifuged supernatant separated and frozen at −30°C, pending batch analysis of plasma albumin measured immunochemically with the Behring BN Laser Nephelometer[e] as the indicator for plasma washout.

Processing speeds, red cell recovery, rates of albumin elimination, and residual albumin transfusion were calculated as follows:

$$\text{blood flow rate from reservoir (mL/min)} = \frac{\text{blood volume processed}}{\text{processing time}}$$

$$\text{PRBC flow rate into holding bag (mL/min)} = \frac{\text{Volume of PRBC}}{\text{processing time}}$$

$$\text{RCM flow rate into holding bag (mL/min)} = \frac{\text{Volume PRBC} * \text{HCT}_{\text{PRBC}}}{\text{processing time}}$$

$$\text{RBC recovery rate in the holding bag (efficiency \%)} = \frac{\text{PRBC volume} * \text{HCT}_{\text{PRBC}}}{\text{Blood volume} * \text{HCT}_{\text{blood}}} * 100$$

[a] Cobe Laboratories, Inc., Arvada, CO 80004
[b] Medtronic Inc., Parker, CO 80134
[c] Fresenius Hemotechnology, Inc., Concord, CA 94520
[d] Coulter, Miami, FL
[e] Dade-Behring, Deerfield, IL

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Table 1. Processing parameters of three autotransfusion devices tested in three different programs with reconstituted human bank whole blood in three saline dilutions

Program	Parameter	BRAT 2	CATS	Sequestra 1000
Standard flow	Fill speed (mL/min)	400	35 mL/min*	300
	Wash speed (mL/min)	800	WF = 5**	300
	Empty speed (mL/min)	600		300
	Wash volume (mL)	1000		1000
Medium flow	Fill speed (mL/min)	700	50 mL/min*	500
	Wash speed (mL/min)	1000	WF = 3**	500
	Empty speed (mL/min)	1000		500
	Wash volume(mL)	1000		1000
High flow	Fill speed (mL/min)	1300	100 mL/min*	1000
	Wash speed (mL/min)	1300	WF = 1**	1000
	Empty speed(mL/min)	1300		1000
	Wash volume(mL)	1000		750

*Default blood flow to holding bag (packed red blood cells).
**WF = wash factor = mL saline/mL packed red blood cells.

Table 2. Hematocrits (mean ± standard deviation %) of blood in the holding bags for three autotransfusion devices using three programs at reservoir hematocrits of 10, 20, and 30% and three replicate procedures in each

	Cobe BRAT 2			Fresenius CATS			Medtronic Sequestra		
Reservoir Hematocrit	Stand	Med	High	Stand	Med	High	Stand	Med	High
10% $N = 3$	49 ± 1	47 ± 1	9 ± 0.0	58 ± 0.0	54 ± 0.0	63 ± 0.0	55 ± 0.0	53 ± 1	5 ± 0.0
20% $N = 3$	45 ± 0.0	41 ± 1	16 ± 0.0	58 ± 1	54 ± 1	58 ± 0.0	53 ± 1	49 ± 2	11 ± 1
30% $N = 3$	44 ± 0.0	39 ± 0.0	24 ± 0.0	54 ± 0.0	53 ± 1	58 ± 0.0	52 ± 2	45 ± 1	18 ± 0.0
Average All $N = 9$	46 ± 2 °|	42 ± 3 °|	16 ± 6 °	57 ± 2 °*	54 ± 5 °*	59 ± 3 °*	53 ± 2 *|	49 ± 3 *|	11 ± 5 *

Average All = means of all hematocrits; °*| = $p < .05$ between corresponding programs.

$$\text{Albumin elimination rate (\%)} = \left[\left| - \frac{\text{Total Albumin}_{\text{PRBC}}}{\text{Total Albumin}_{\text{blood}}} \right| \right] * 100$$

$$= \left[\left| - \frac{\text{Volume PRBC}* (1 - \text{HCT}_{\text{PRBC}})*\text{Albumin}_{\text{PRBC}}}{\text{Volume Blood} * (1 - \text{HCT}_{\text{blood}})*\text{Albumin}_{\text{blood}}} \right| \right] * 100$$

$$\text{Residual Albumin transfusion rate (mg/dL RCM)} = \frac{\text{Albumin}_{\text{PRBC}} * (1 - \text{HCT}_{\text{PRBC}})}{\text{HCT}_{\text{PRBC}}}$$

Mean values and standard deviations were calculated for three replicates of each parameter and program based on three runs each using blood with a HCT of 10, 20, and 30% ($N = 9$). This represented the range of applications encountered clinically.

STATISTICS

Student's *t*-test for unpaired data was used and probability of $p < .05$ was considered significant. Statistically significant differences are indicated by the symbols °*| in the tables and figures for corresponding programs.

RESULTS

The differences between DF and CF are shown in Figure 1. In CF, blood from the reservoir was pumped into a rotating horizontal wash chamber, C-shaped like a spiral, hollow band. First, the red blood cells were concentrated on the outer aspect of the channel, then became resuspended in saline, reconcentrated on the outer aspect, and then transferred to the holding bag in a continuous flow of blood through the system. Plasma and saline wash waste were diverted to the waste bag.

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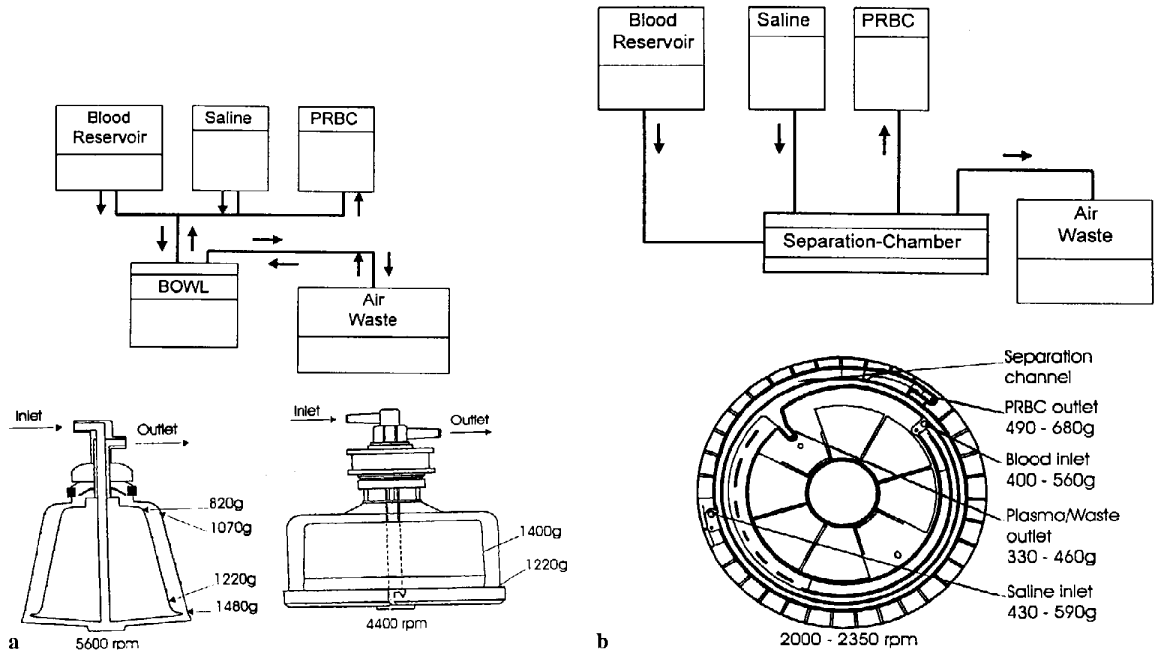


Figure 1: Diagrammatic representations of the flow in systems devised for intraoperative autologous transfusion in (a) discontinuous and (b) continuous flow procedures.

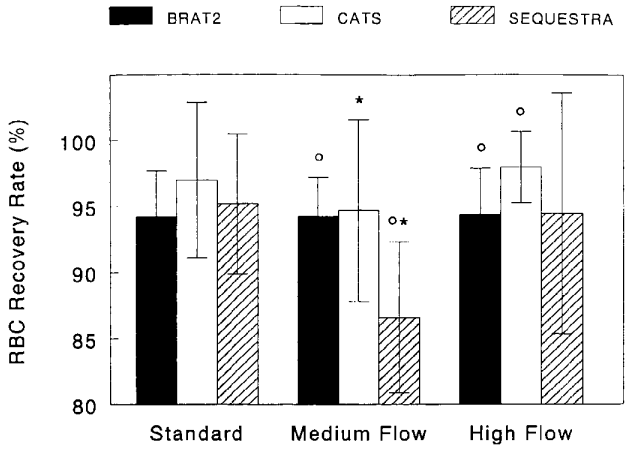


Figure 2: Mean red blood cell recovery rates ± standard deviations for three replicate processing runs using three autotransfusion devices in three programs; ° * = $p < .05$; $N = 9$.

HCT of the processed packed red cells was found to be consistently greatest in all CF (CATS) programs as compared with values obtained with the cylindrical DF (BRAT2) or the conical DF (Sequestra 1000) bowl systems. This was independent of the processing speed and HCT of the incoming blood. In DF, the HCT of packed red cells in the holding bag decreased progressively with greater processing speeds and with a greater HCT of the incoming blood (Table 2). High flow with BRAT 2 and Sequestra 1000 resulted in HCT even less than that of the blood in the reservoir before processing. As the speed was increased during processing with both BRAT 2 and Sequestra 1000, the volume of saline used per mL RCM became increased because of an insufficient red cell content in the bowls. However, with CATS, the volume of saline used per mL RCM decreased significantly (Table 3).

Apart from the medium flow program of Sequestra 1000, the range of red blood cell recovery rates was between 94 and 98% using all devices in all programs (Figure 2). During medium flow on Sequestra 1000, visible red cell loss to waste occurred with a diminished recovery rate of 86%. This was because of formation of an inverted saucer-shaped layer of red cells at the level of the rotating seal (Figure 3), caused by pressure diversion from the inlet port directly to the waste outlet. Red cell flow bypassed separation in the centrifugal field because of pressure buildup from force developed by rapid pump speeds once the bowl capacity was filled to about one-third.

In DF, processing reservoir samples with different HCT levels resulted in variation of the red cell mass flow rate into the holding bags (Table 4). Apart from incoming blood from the reservoir with high flow and an HCT of 10%, the red cell mass flow rate with CATS was found to be constant. The red cell mass flow rate into the holding bag increased progressively for all three devices from standard to medium flow. However, CATS high flow continued to show further increase in red cell mass flow rate, but both DF instruments showed a marked decline ($p < .0001$). The flow rates with high flow for both BRAT 2 and Sequestra 1000 were less than those of standard

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Table 3. Saline volumes per red cell mass processed (mean ± standard deviation; mL saline/mL RCM processed) for three autotransfusion devices using three programs with three replicate procedures in each

Reservoir Hematocrit	Cobe BRAT 2			Fresenius CATS			Medtronic Sequestra		
	Stand	Med	High	Stand	Med	High	Stand	Med	High
Average All	8.9 ± 0.4	9.8 ± 0.8	30.1 ± 12.5	9.6 ± 0.5	6.4 ± 0.2	2.6 ± 0.8	8.7 ± 0.4	9.4 ± 0.6	36.8 ± 18.9
$N = 9$	○	○	○*	○*	○*	○*	*	*	*

○*| = $p < .05$ between corresponding programs.

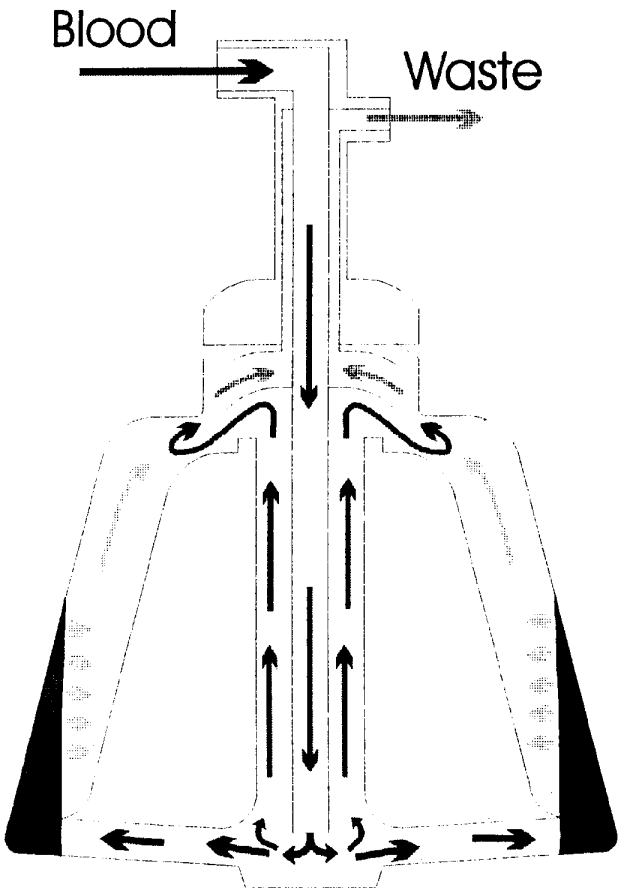


Figure 3: Processing with the conical centrifuge bowl at high flow rates showing red cell loss to waste, presumably due to pressure buildup.

flow because of premature triggering of the optical sensors by unseparated red blood cells. Wash cycles were initiated before filling the bowl properly, and the red cells were diluted further with saline wash solution. The CATS red cell mass high flow was 23% greater than the fastest program with the BRAT 2 (medium flow) and 87% greater than the fastest program of Sequestra 1000 (medium flow). Packed red blood cell flow rates proved to be misleading and erroneously indicated the greatest processing speed with DF in the high-flow programs (Table 5).

There was no visible hemolysis on naked eye examination of the supernatants; however, samples from the BRAT 2 with its cylindrical centrifuge bowl had a pale yellow color consistent with residual plasma. The depth of color increased with greater processing speeds. The washout efficiency was evaluated by comparing initial plasma albumin contents of the reservoir blood supernatant volumes before processing with those of corresponding packed red blood cells in the holding bags after processing. The supernatant residual albumin concentrations of samples taken from the holding bags after processing (packed red cells) are summarized in Table 6. Residual albumin concentration of supernatants in the holding bags increased progressively with greater processing speeds using all devices. Residual albumin concentrations using BRAT 2 was greatest in all three flow programs. In standard flow, comparison of the average albumin elimination rate with CATS and Sequestra 1000 showed no difference (Table 7). Both were greater than those of BRAT 2 ($p < .05$). In medium flow, the average albumin elimination rate with BRAT 2 was less than Sequestra 1000 ($p < .05$). In high flow, CATS was greater than both Sequestra 1000 and BRAT 2 ($p < .0001$). In all systems and programs, the albumin elimination rate decreased with an increase in HCT of the incoming blood. The mean albumin transfusion rates (Figure 4) in standard, medium, and high flow, respectively, with BRAT 2 were 447 ± 340 mg/dL, 604 ± 514 mg/dL, and 2,738 ± 167 mg/dL; with CATS were 90 ± 44 mg/dL, 337 ± 284 mg/dL, and 346 ± 357 mg/dL; and with Sequestra 1000 were 69 ± 36 mg/dL, 217 ± 125 mg/dL, and 2,277 ± 253 mg/dL. Compared with CATS and Sequestra 1000, residual albumin transfusion rates for BRAT 2 ranged up to six times greater in standard flow programs ($p < .01$) and up to three times greater in medium flow ($p < .01$). In high flow, the albumin transfusion rate of BRAT 2 and Sequestra 1000 were up to eight times greater as compared to CATS ($p < .0001$).

DISCUSSION

In confirmation of the value of intraoperative autologous transfusion practice, post-transfusion survival of salvaged red

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Table 4. Red cell mass (RCM) flow rates to the holding bags (mean ± standard deviation; mL/min) for three autotransfusion devices using three programs at reservoir hematocrits of 10, 20, and 30% as well as the means for all hematocrits

Reservoir Hematocrit	Cobe BRAT 2			Fresenius CATS			Medtronic Sequestra		
	Stand	Med	High	Stand	Med	High	Stand	Med	High
10% $N = 3$	19 ± 0.8	29 ± 1.2	12 ± 0.6	18 ± 0.3	23 ± 0.1	28 ± 0.4	11 ± 0.2	19 ± 0.7	7 ± 0.4
20% $N = 3$	27 ± 0.5	37 ± 0.8	22 ± 0.0	19 ± 0.3	25 ± 0.7	49 ± 3.5	17 ± 0.4	24 ± 1.2	14 ± 1.2
30% $N = 3$	32 ± 0.6	40 ± 0.3	34 ± 0.1	19 ± 1.4	24 ± 0.4	53 ± 1.7	18 ± 0.8	26 ± 2.8	24 ± 9.6
Average All $N = 9$	26 ± 5.6 °*	35 ± 4.5 °*	22 ± 9.0 °*	19 ± 1.0 °|	24 ± 0.9 °	43 ± 11.3 °|	15 ± 3.0 *°	23 ± 2.9 *	15 ± 7.0 *

Average All = three replicate procedures in each program; °*| = $p < .05$ between corresponding programs.

Table 5. Packed red blood cell (PRBC) processing rate (mean ± standard deviation; mL/min) for three autotransfusion devices using three replicate procedures in three programs

Reservoir Hematocrit	Cobe BRAT 2			Fresenius CATS			Medtronic Sequestra		
	Stand	Med	High	Stand	Med	High	Stand	Med	High
Average All $N = 9$	58 ± 15 °*	85 ± 17 °*	136 ± 6 °*	33 ± 2 °|	47 ± 5 °|	74 ± 21 °|	29 ± 5 *|	48 ± 7 *|	128 ± 6 *|

Average all = means of all reservoir hematocrits; °*| = $p < .05$ between corresponding programs.

Table 6. Washed packed red blood cell supernatant albumin concentrations (mean ± standard deviation; mg/dL) for three autotransfusion devices using three programs

Reservoir Hematocrit	Cobe BRAT 2			Fresenius CATS			Medtronic Sequestra		
	Stand	Med	High	Stand	Med	High	Stand	Med	High
Average All $N = 9$	358 ± 258 °*	395 ± 310	558 ± 265 °	114 ± 50 *	306 ± 212	474 ± 299	82 ± 45 °	194 ± 94	297 ± 152 °

Average All = means of all programs with three replicates in each; °*| = $p < .05$ between corresponding programs.

blood cells shed during surgery was studied; the radio-labeled chromium half-lives of shed red cells were reported previously to be comparable with normal values (9). In this report, quality of processed blood shed during surgery was evaluated in a defined environment using a single pool of donor banked blood to minimize variation for comparing test results. Red cells, suspended in freshly thawed, compatible frozen donor plasma were used to simulate operating room conditions in terms of blood viscosity and hemoglobin level. Comparable programs for each of the three systems were evaluated by using the same pool of blood with triplicate testing, showing close reproducibility within each program. Of the parameters studied, processing speed was the greatest factor influencing HCT, red cell recovery, and washout quality. Progressively greater processing speeds with DF devices led to decreased HCT of the packed red cells (PRBC) collected into the holding bag, and removal rates of plasma were reduced with all the devices to a varying degree.

Processed RBC must be prepared with a suitable HCT to affect a proper post-transfusion increment. The standard flow program of BRAT 2 and the standard and medium flow programs of Sequestra 1000 achieved a satisfactory HCT. HCT of the red cell products was inversely related to filling rates and the HCT of shed blood. The medium flow of BRAT 2 and high flow of both BRAT 2 and Sequestra 1000 yielded products with unacceptably low HCT. Because the separation capacity, defined by the radius of the bowl and centrifuge rotations per minute, is constant in all DF washing programs, a slower filling

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Table 7. Albumin elimination rates (mean ± standard deviation %) for three autotransfusion devices using three programs and three replicate procedures in each at 10, 20, 30%

Reservoir	Cobe BRAT 2			Fresenius CATS			Medtronic Sequestra		
Hematocrit	Stand	Med	High	Stand	Med	High	Stand	Med	High
10% $N = 3$	98.7 ± 0.4	98.4 ± 0.3	59 ± 0.4	99.4 ± 0.2	98.5 ± 0.5	98.3 ± 0.5	99.5 ± 0.04	98.6 ± 0.2	57.5 ± 2.9
20% $N = 3$	96.4 ± 2.5	96.1 ± 2.8	74.3 ± 18.2	98.3 ± 0.8	96.8 ± 0.2	94.7 ± 0.9	98.5 ± 0.5	98.0 ± 1.4	61.2 ± 2.0
30% $N = 3$	84.5 ± 0.7	79.3 ± 0.5	54.9 ± 2.8	96.2 ± 0.3	92.6 ± 1.2	86.8 ± 0.2	96.6 ± 0.1	93.3 ± 0.1	56.4 ± 1.0
Average All $N = 9$	93.2 ± 6.4 °*	91.2 ± 8.7 °	62.8 ± 3.5 °	97.8 ± 1.4 °	94.4 ± 4.6	93.3 ± 4.8 °*	98.4 ± 1.2 *	96.8 ± 2.3 °	58.3 ± 2.9 *

Average all = means for all hematocrits; °*| = $p < .05$ between corresponding programs.

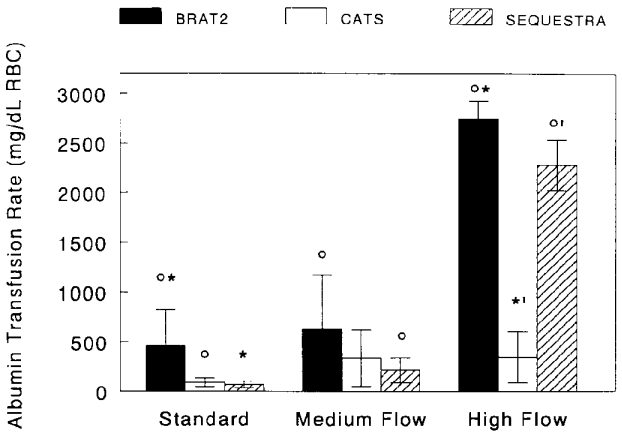


Figure 4: Mean holding bag supernatant albumin transfusion rates ± standard deviations (mg/dL/RCM) for three replicate processing runs using three autotransfusion devices in three programs; ° * = $p < .05$; $N = 9$.

rate increases the time that the red blood cells settle in the centrifuge bowl, facilitating more concentration. With increased flow and increased HCT, packing of red blood cells is reduced and, at even greater flow, poorly separated red blood cells may trigger optical sensors, falsely detecting the appropriate PRBC filling level in the bowl and initiating a premature wash cycle. Residual air in the bowl is replaced with saline wash, further diluting red cell mass. Improper red blood cell sedimentation in respective centrifuge bowls of DF devices permits excess saline retention, leading to errors with false packed red blood cell flow rates and albumin concentration measurements.

HCT was maintained at a high level during progressively increased processing speeds with CATS (54–59%). As shown in previous clinical studies at standard flow, HCT using CATS was consistently greater than a variety of DF systems (1, 5, 7, 10). HCT was between 55 and 78% using the high flow wash (2–4, 11), also confirmed in the author's operating room experience. While clinical experience with most DF equipment documented HCT results between 44 and 56% using standard flow (1, 5, 7, 10), no published data were found on the use of medium and high flow.

All laboratory and clinical data reviewed (1, 2, 5, 6) revealed no significant differences in RBC recovery using DF and CATS with standard flow programs. In medium flow of Sequestra 1000, diminished red cell recovery from red cell loss to waste was noted in the effluent line from the bowl, and was also noted in the author's operating room experience at flow rates higher than 500 mL/min; at 1000 mL/min there was almost complete red cell loss to waste. This observation was not seen with BRAT 2 and may be related to the design of the conical centrifuge bowl.

This study describes the importance of accuracy in reporting the data for red blood cell processing speeds. Packed red blood cell flow rates are invalid because of variability of HCT of samples from the holding bag. A system yielding packed red blood cells with a lower HCT seems to process blood more rapidly, but the RCM flow rate is low, and a salvaged red cell unit of inadequate potency results. The RCM flow rate is the accurate measurement. Although RCM flow increased significantly from standard to medium flow using all three systems evaluated, increased pump speeds with high flow actually failed to compensate for progressive decline in HCT of the packed red blood cells in DF systems. This was attributable to inadequate separation of red cells in the bowl of DF. Using CATS, there was progressive increase in RCM flow rates with greater processing speeds; in contrast the high flow programs of BRAT 2 and Sequestra 1000 showed markedly decreased RCM flow rates. The manufacturers of CATS claim that a constant packed red blood cell flow rate and HCT is related to preprogrammed specification of the various programs. This is substantiated in this study, even with high flow, as in the emergency wash procedure. In CATS, the RCM flow rate to the holding bag remains constant because of automatic varia-

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tion of incoming blood flow resulting from instrument adaptation to HCT of the blood from the reservoir. The processing speed with CATS may be modified during operation by selecting a processing program deemed more applicable while good product quality is maintained. In contrast, parameters of DF devices, including blood and saline flow, wash volume, and centrifuge speed, independently may be modified by the operator to increase processing speed. As shown in this study, this may lead to poor PRBC quality, even if used within permissible ranges that are recommended by the manufacturers. Changing processing parameters of DF during operation on quality may necessitate more stringent manufacturer limitations for the ranges of adjustable parameters to prevent transfusion of PRBC with questionable potency and purity.

As an indicator of plasma washout, plasma albumin endogenous in the samples proved to be a suitable analyte, because sampling or hemolysis did not interfere. Immunochemical analysis is relatively inexpensive, readily available in most clinical laboratories, and may be deferred while samples of red cell supernatant are maintained in appropriately frozen storage. Although used by many (1–3, 6–8, 11–13), potassium concentration is unreliable as a marker for washout because of spurious concentration increases from hemolysis or delay in separating supernatant from red cells. In addition, because measurement with the potassium ion selective electrode is optimized for testing in a plasma or serum medium, reproducibility was poor when measuring saline supernatants. Flame photometry, the appropriate analytical method, is very seldom used in clinical laboratories. Free hemoglobin and heparin measurements were also used by many (1–6, 12) but, because of very high dilution requirements for measurement, these methods may be too insensitive for levels encountered in shed blood. Fibrinogen and activated factor XII also were used (6) but may be unreliable markers, because erratic changes in concentration may be associated with incomplete anticoagulation.

All systems showed decreased washing efficiency with greater processing speeds. In contrast with the supernatant albumin concentration, which increased only slightly with greater flow rates, the albumin elimination rates decreased, and residual albumin transfusion rates increased very significantly. This observation was characteristic of DF systems, especially when comparing standard and high flow programs. These findings indicate that contaminating plasma proteins, including activated clotting factors, are transfused in relatively high amounts and could be significant in patients enduring estimated blood losses of one liter and more. The albumin concentration of supernatant in the holding bags is misleading; the albumin elimination and transfusion rates also reflect the variation in HCT of the packed red blood cells and are the proper parameters of quality control. Using DF devices reduced plasma washout with progressively greater processing speed related to a decreased HCT of the packed red blood cells, which reflected improper filling of the bowls. In DF, the phase of major elimination of plasma during red cell processing is when the plasma is separated to waste in a bowl that is filled properly. A respective separation of the plasma effluent during the filling cycle and the wash solution during the wash cycle into separate receptacles confirmed that 75% of plasma-free hemoglobin from shed blood was recovered in the separated plasma, and only 13% was found in the wash waste (9). Thus, the effect of the wash procedure in DF at the higher flow rates is minor and cannot compensate for insufficient plasma separation when bowls are filled incompletely.

The standard and medium flow programs of Sequestra 1000 may result in a satisfactory plasma protein elimination rate from shed blood in all surgical procedures. Using BRAT 2 with standard flow and parameters defined by the manufacturer, elimination of plasma is significantly less, and, in situations with poor blood quality, orthopedic surgery for example, using BRAT 2 may be questionable. In high-flow programs of the DF devices tested, the HCT and elimination of plasma are unacceptably low, and use of DF equipment is discouraged. All programs of CATS consistently yielded red cell products with preferred purity and potency. CATS provided red cell units with the greatest HCT, at the fastest processing speed and with the most elimination of plasma constituents, even when using high flow and may be recommended in all emergency situations without restriction. IAT is recommended as a viable transfusion option in a changing environment where autologous blood transfusion is accepted to be immunologically superior to allogeneic blood products and where costs and problems with the availability of blood products are increasing constantly.

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KUR-MAG-DE005197

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)

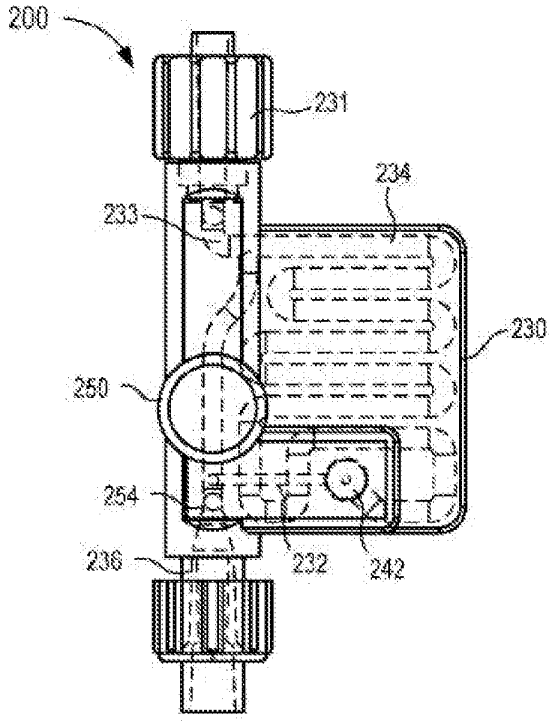
Application number: WO2018US50621 20180912 Global Dossier

Priority number(s): US201762557530P 20170912 ; US201862634569P 20180223 ; US201862678632P 20180531

Also published as: AU2018334138 (A1) CA3074105 (A1) CN111212597 (A) EP3681384 (A1) EP3681384 (A4) more

Abstract of WO2019055487 (A1)

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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(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
21 March 2019 (21.03.2019)

WIPO | PCT

(10) International Publication Number
WO 2019/055487 A1

(51) International Patent Classification:
A61B 5/00 (2006.01) *A61M 1/00* (2006.01)
A61B 17/00 (2006.01) *A61M 39/00* (2006.01)

(21) International Application Number:
PCT/US2018/050621

(22) International Filing Date:
12 September 2018 (12.09.2018)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
62/557,530 12 September 2017 (12.09.2017) US
62/634,569 23 February 2018 (23.02.2018) US
62/678,632 31 May 2018 (31.05.2018) US

(71) Applicant: **MAGNOLIA MEDICAL TECHNOLOGIES, INC.** [US/US]; 200 W Mercer St., Suite 500, Seattle, Washington 98119 (US).

(72) Inventors: **BULLINGTON, Gregory J.**; 2121 6th Avenue S1713, Seattle, Washington 98121 (US). **MIAZGA, Jay M.**; 2251 Goss Ridge Rd., Freeland, Washington 98249 (US). **GAW, Shan E.**; 4027 Sunnyside Ave. N, Seattle, Washington 98103 (US). **RAMSEY, Timothy F.**; 518 N 70th St., Seattle, Washington 98103 (US).

(74) Agent: **WESTON, Scott B.** et al.; COOLEY LLP, 1299 Pennsylvania Avenue NW, Suite 700, Washington, District of Columbia 20004-2400 (US).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JO, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

(54) Title: FLUID CONTROL DEVICES AND METHODS OF USING THE SAME

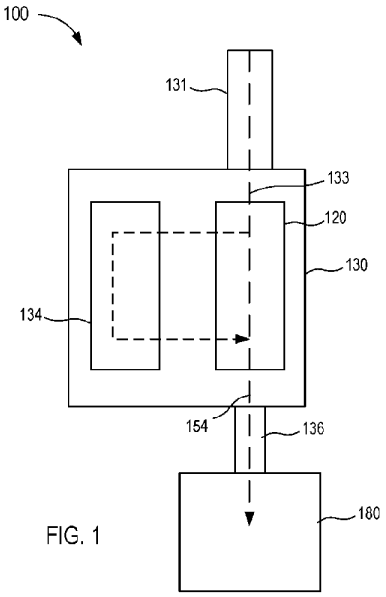


FIG. 1

(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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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

[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.

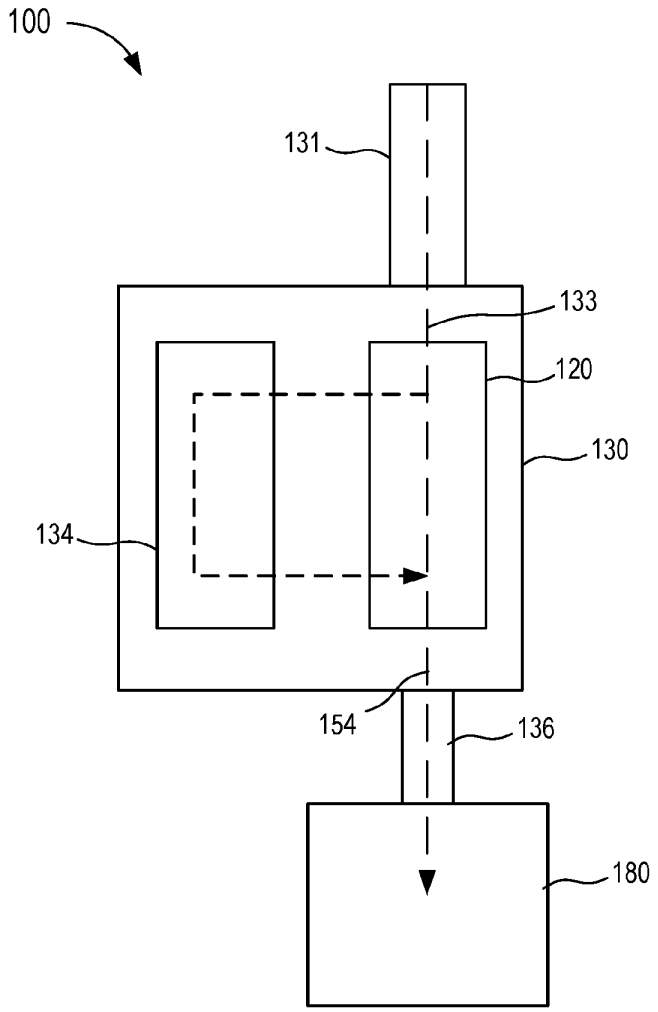


FIG. 1

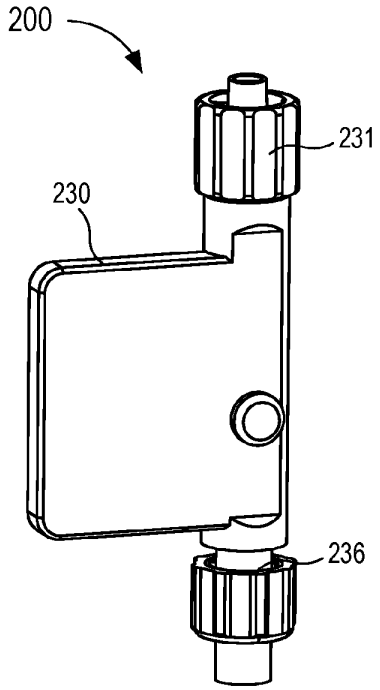


FIG. 2

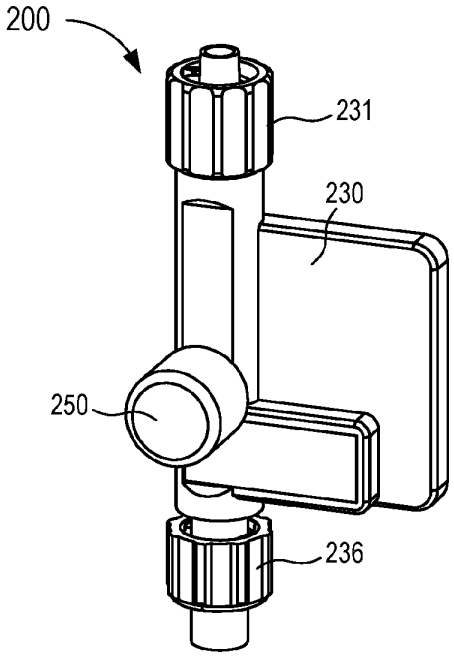


FIG. 3

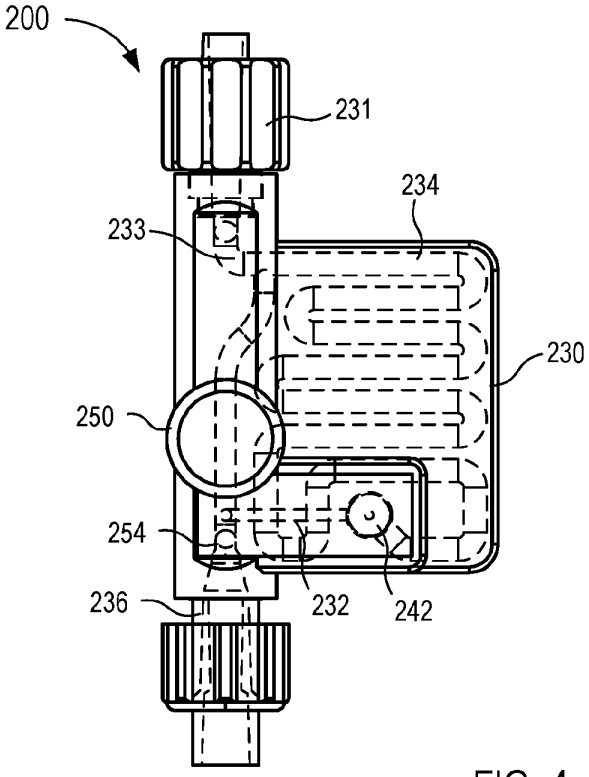


FIG. 4

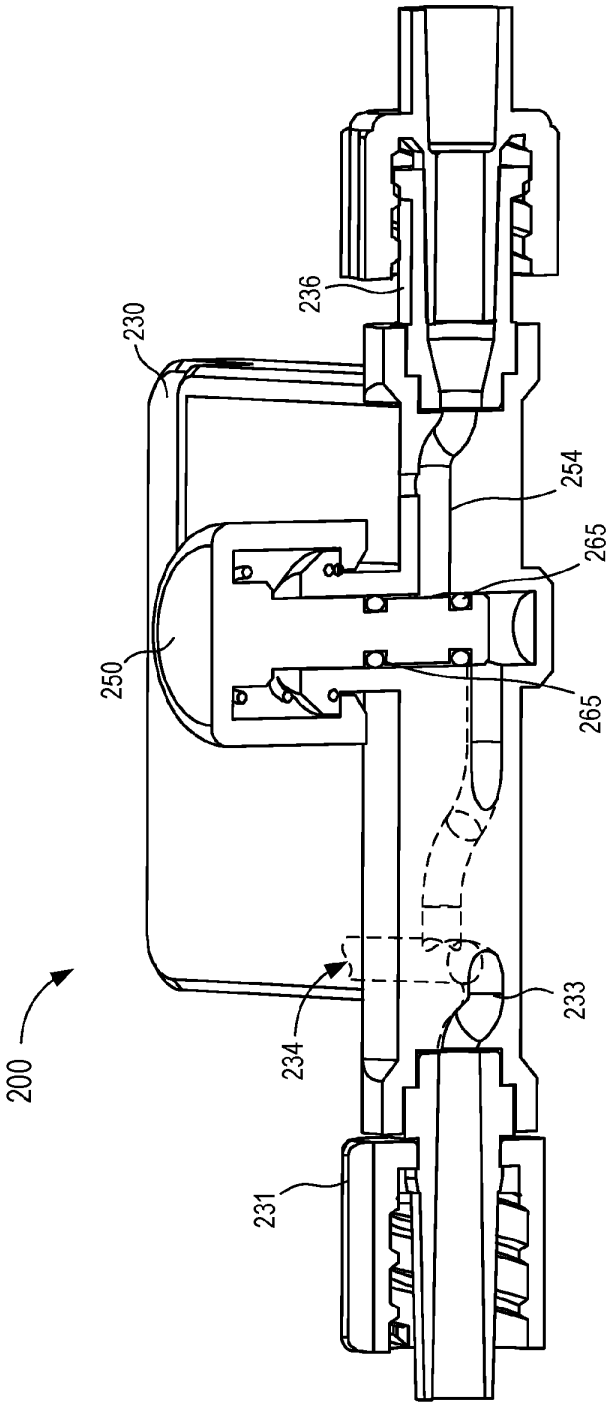


FIG. 5

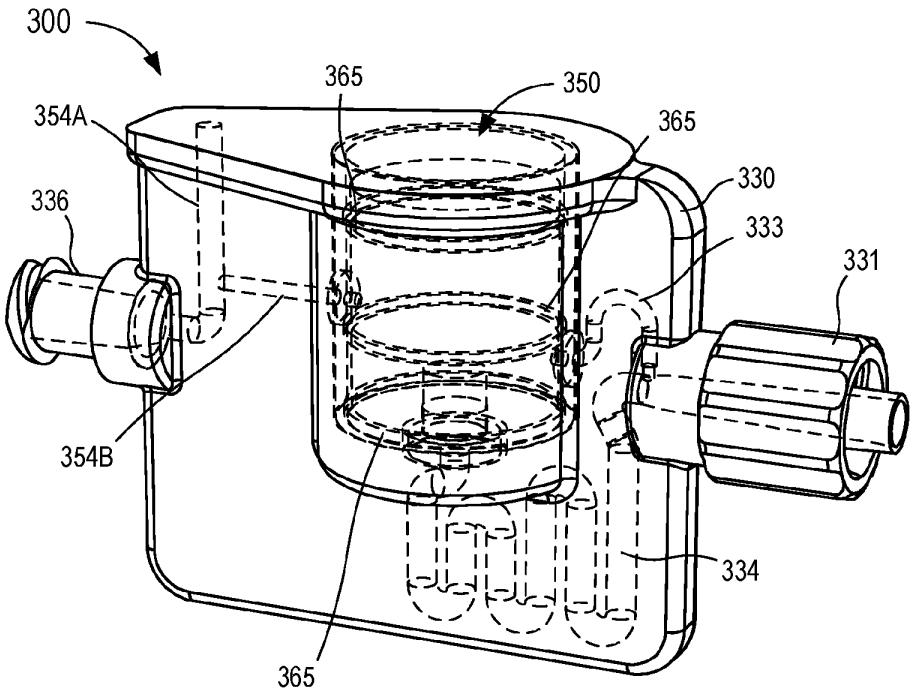

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FIG. 6

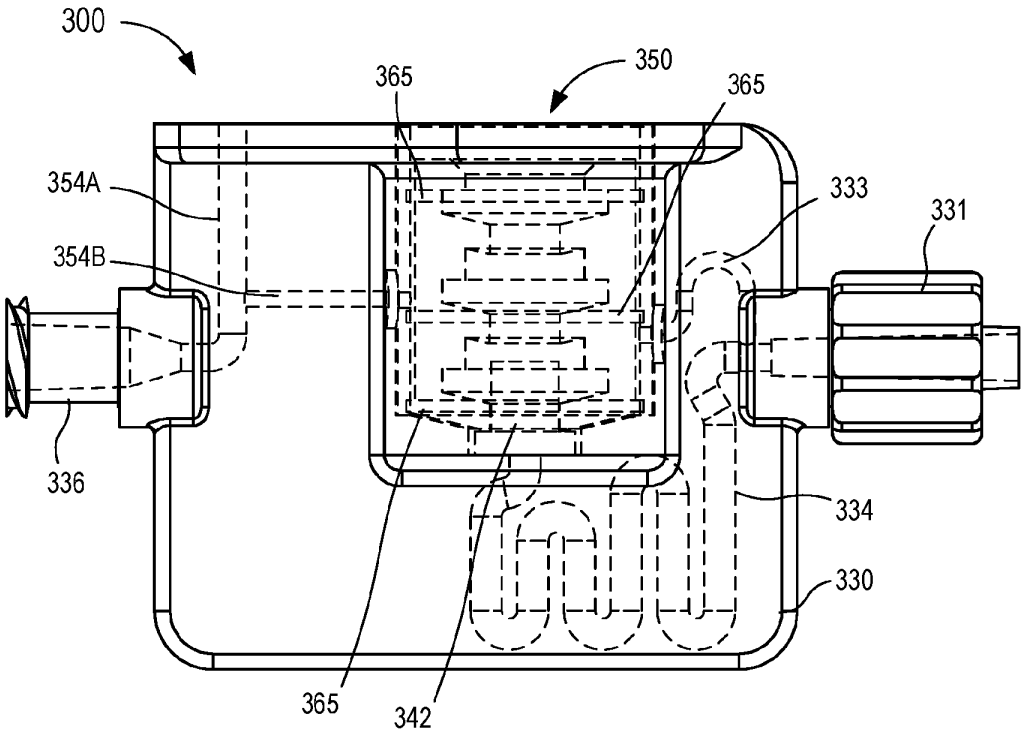

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FIG. 7

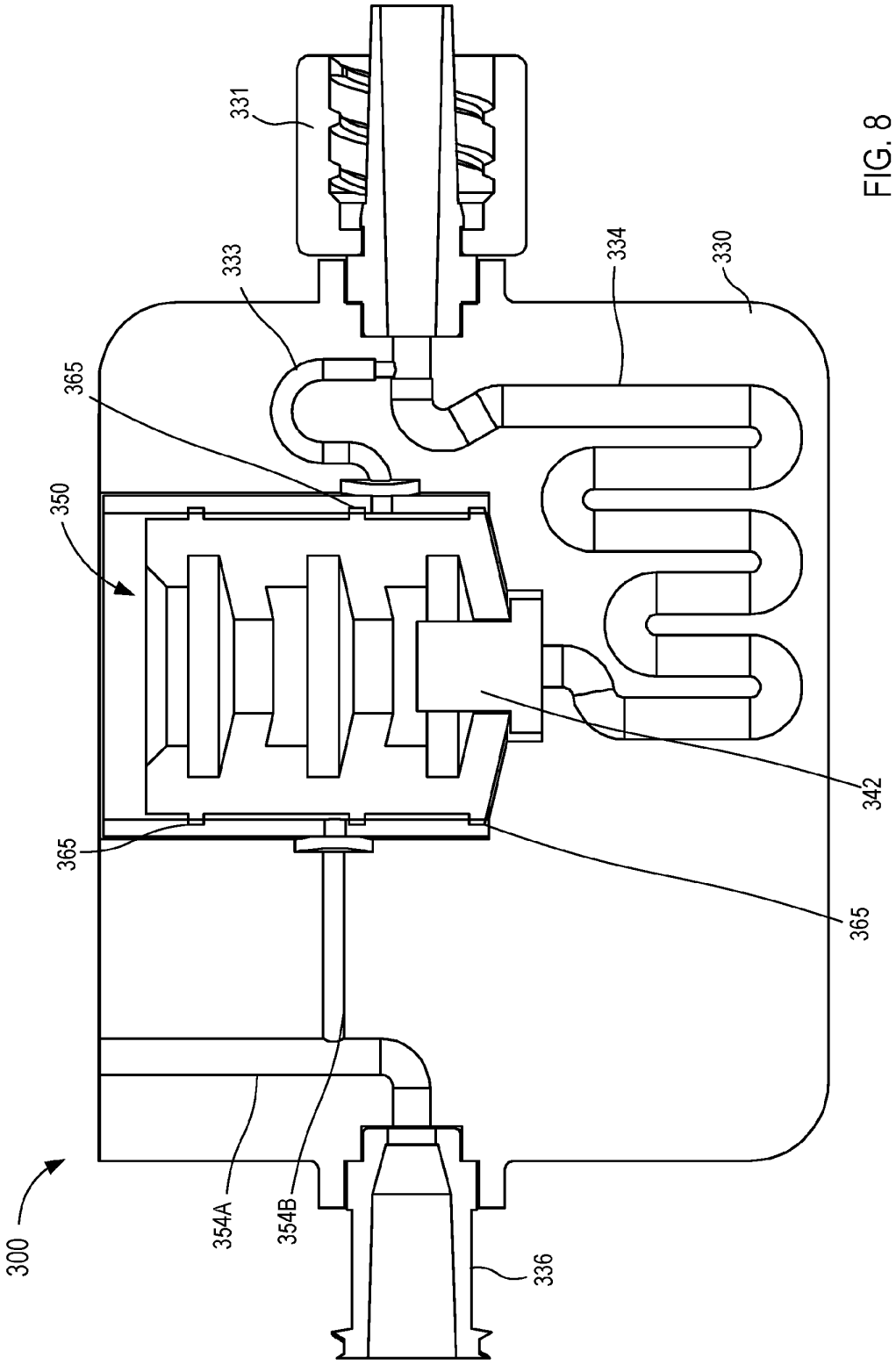


FIG. 8

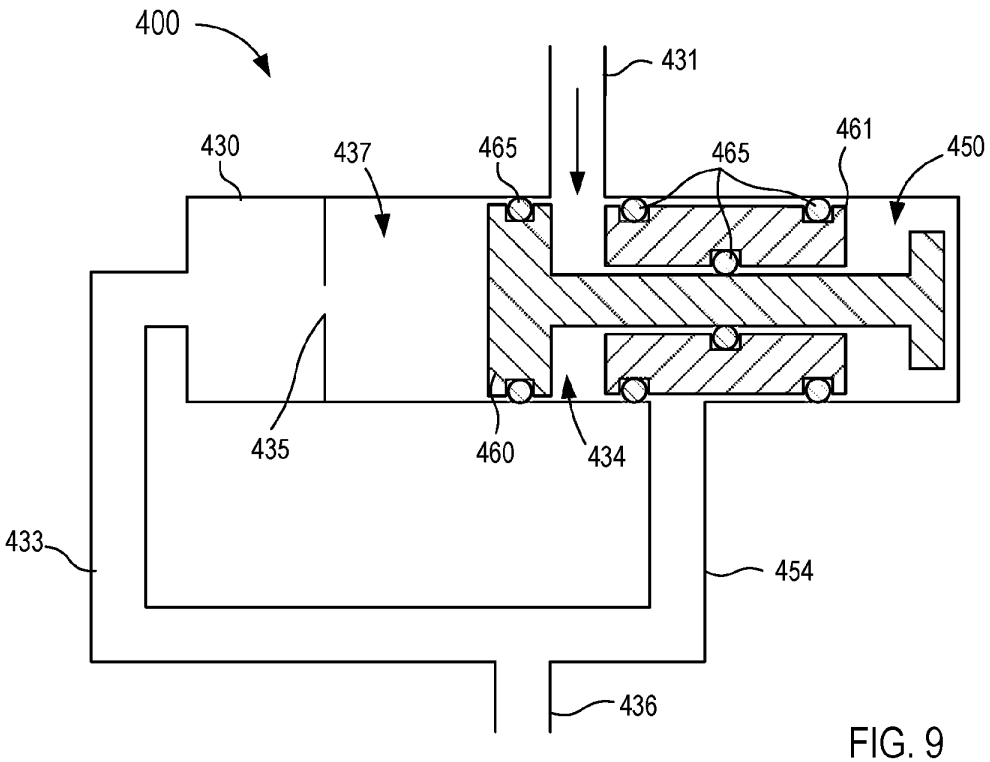

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FIG. 9

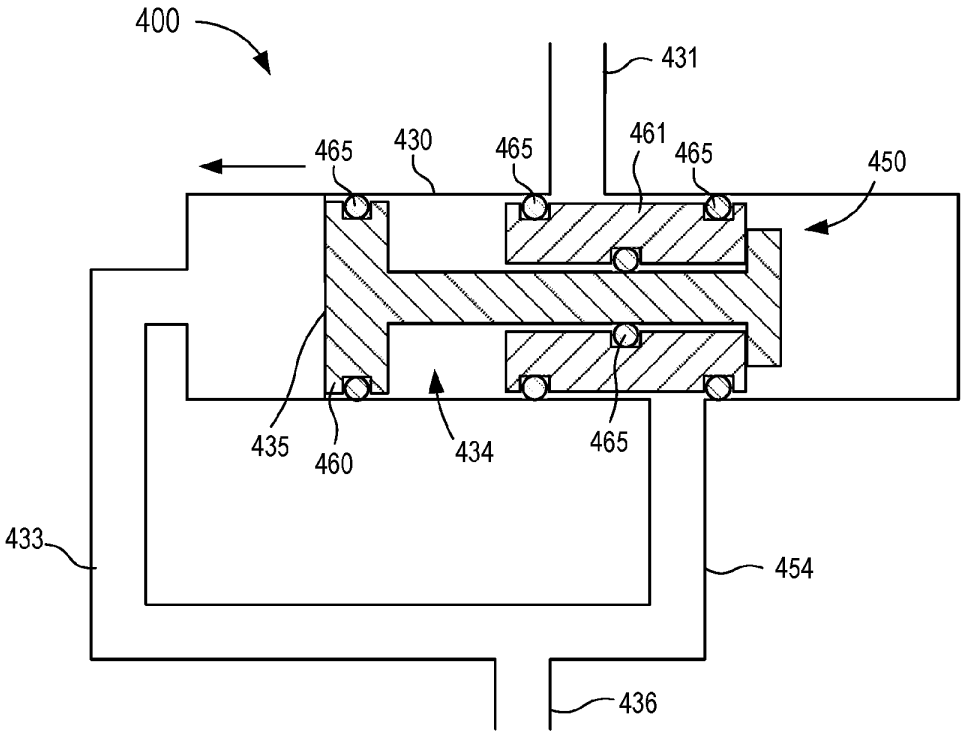

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FIG. 10

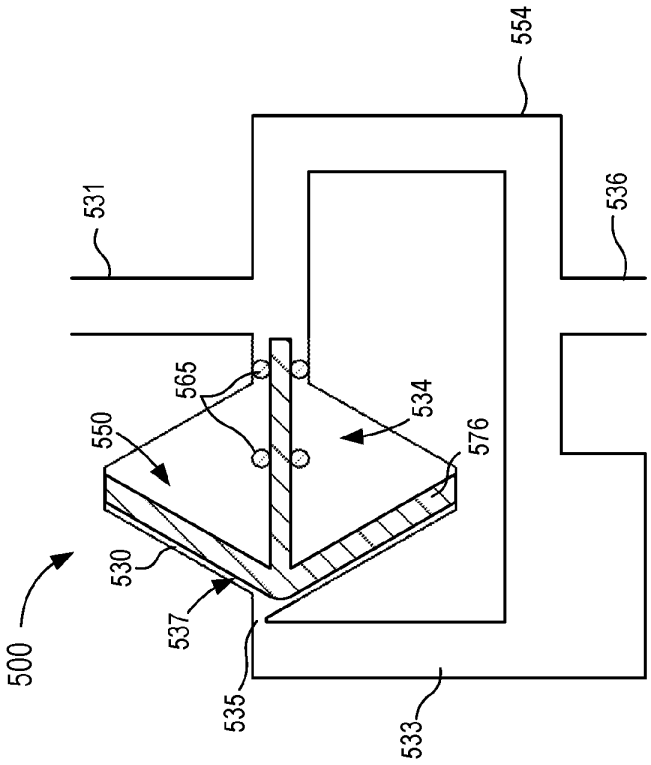

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FIG. 12

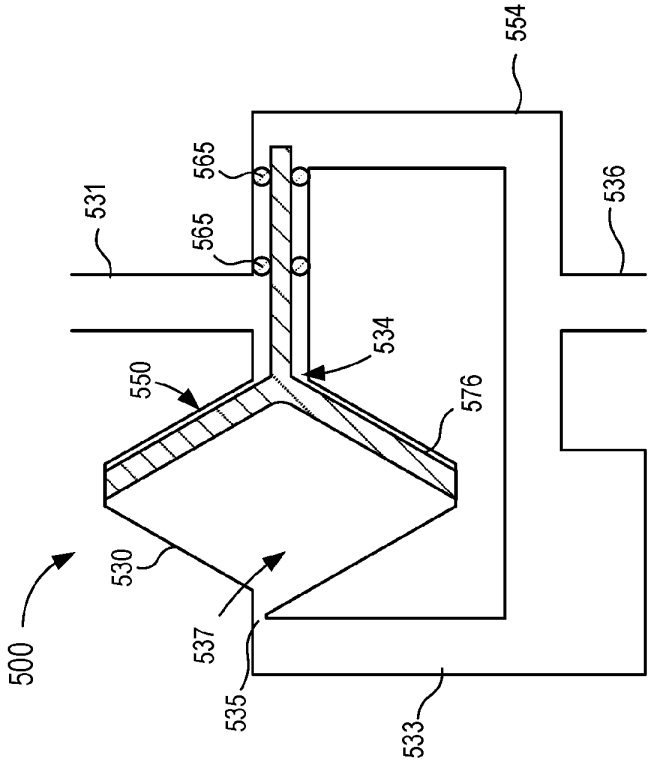

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FIG. 11

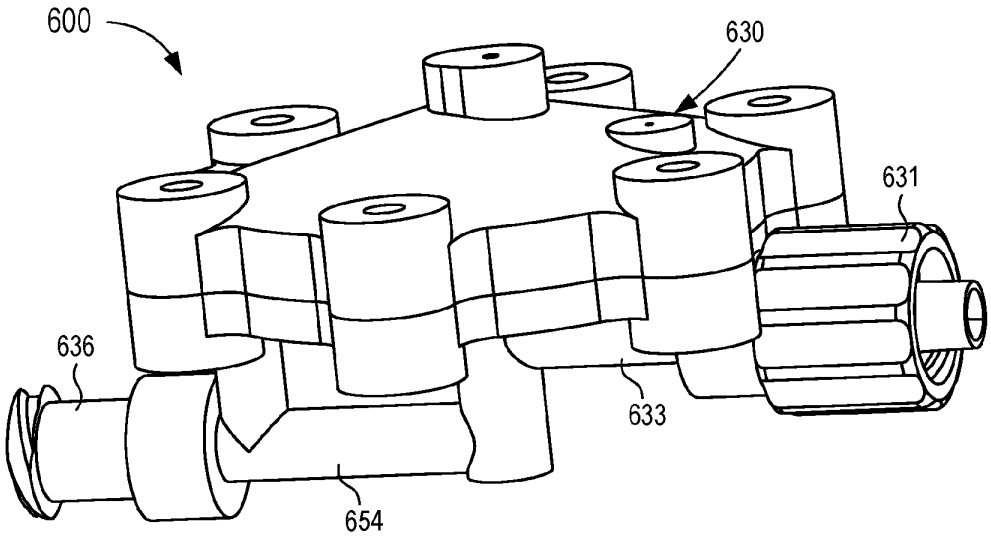

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FIG. 13

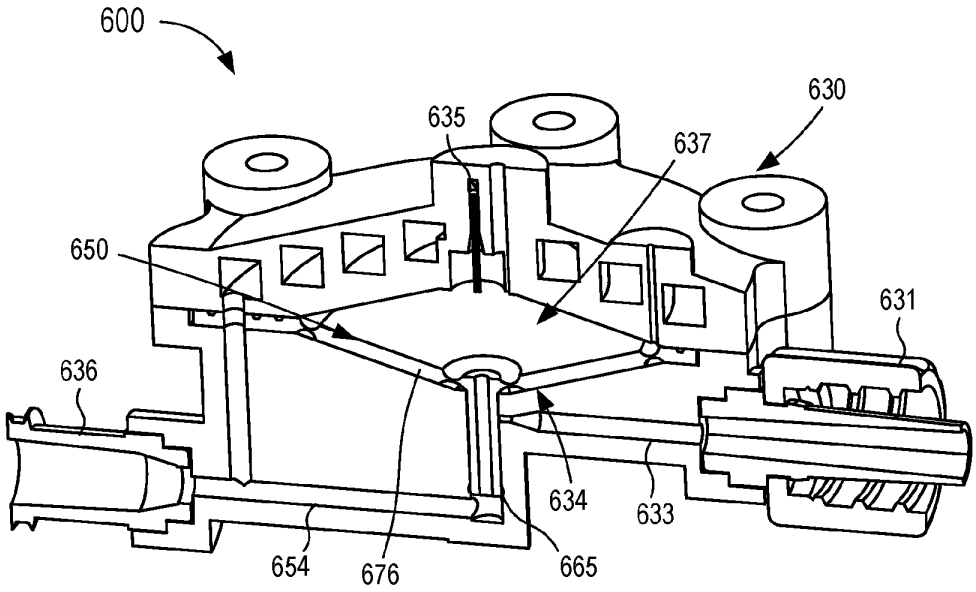

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FIG. 14

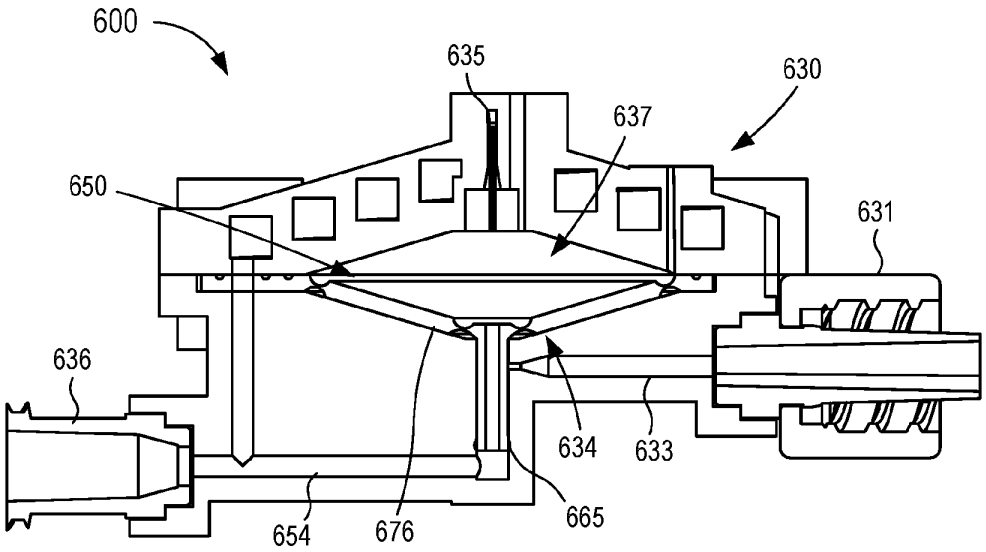


FIG. 15A

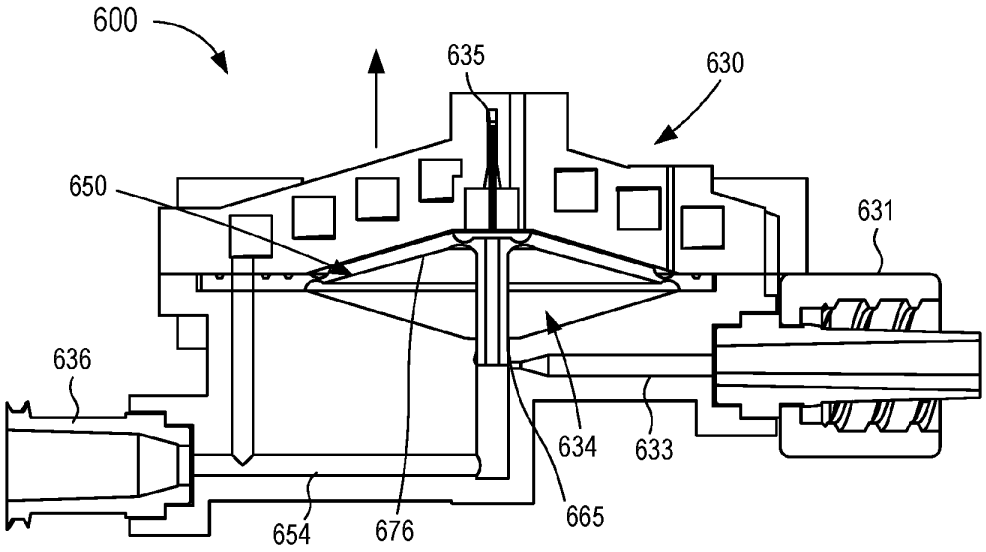


FIG. 15B

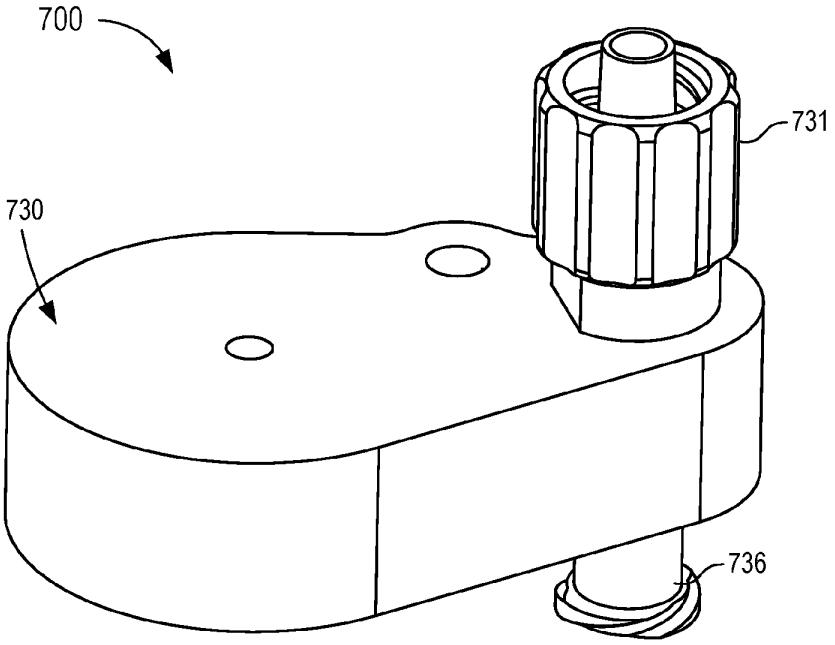


FIG. 16

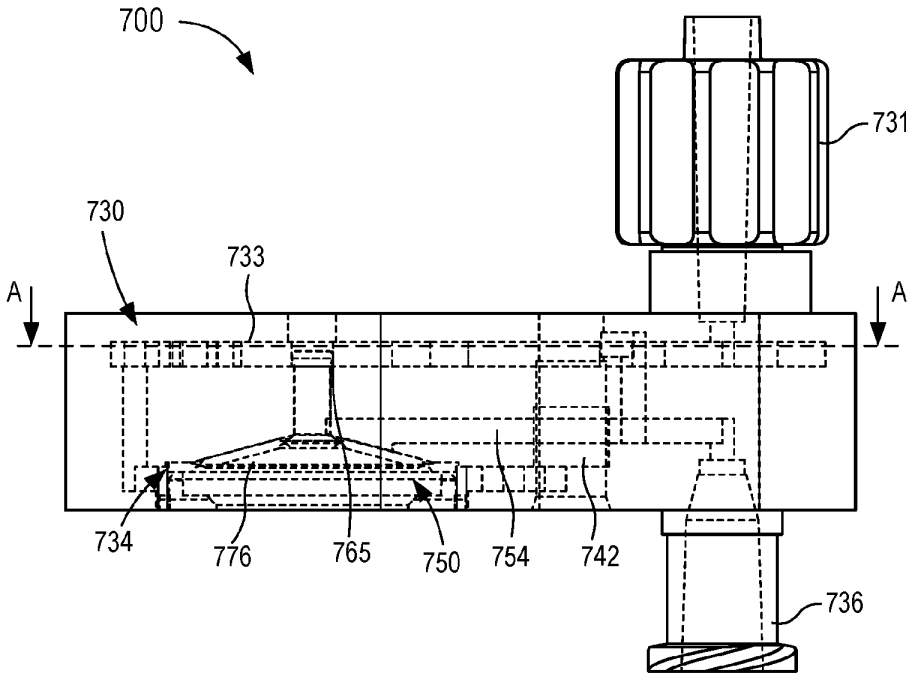


FIG. 17A

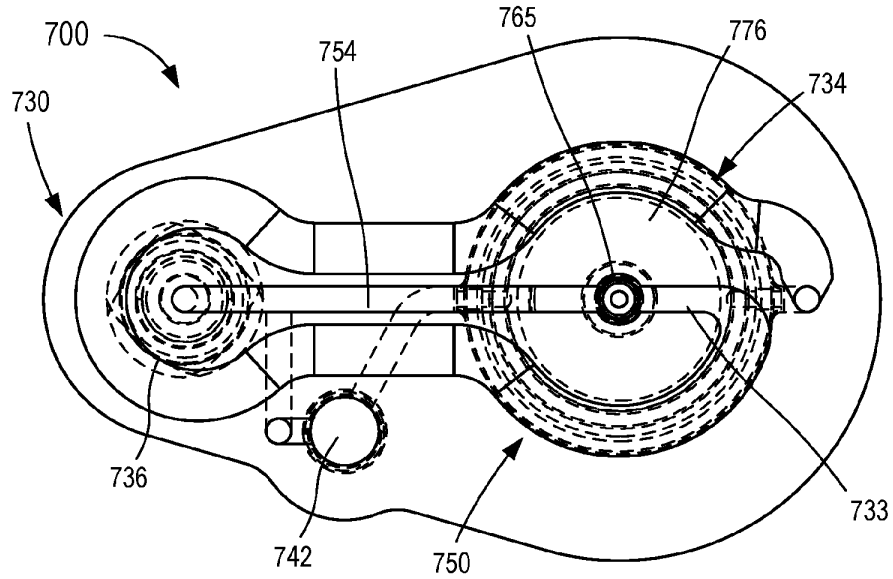


FIG. 17B

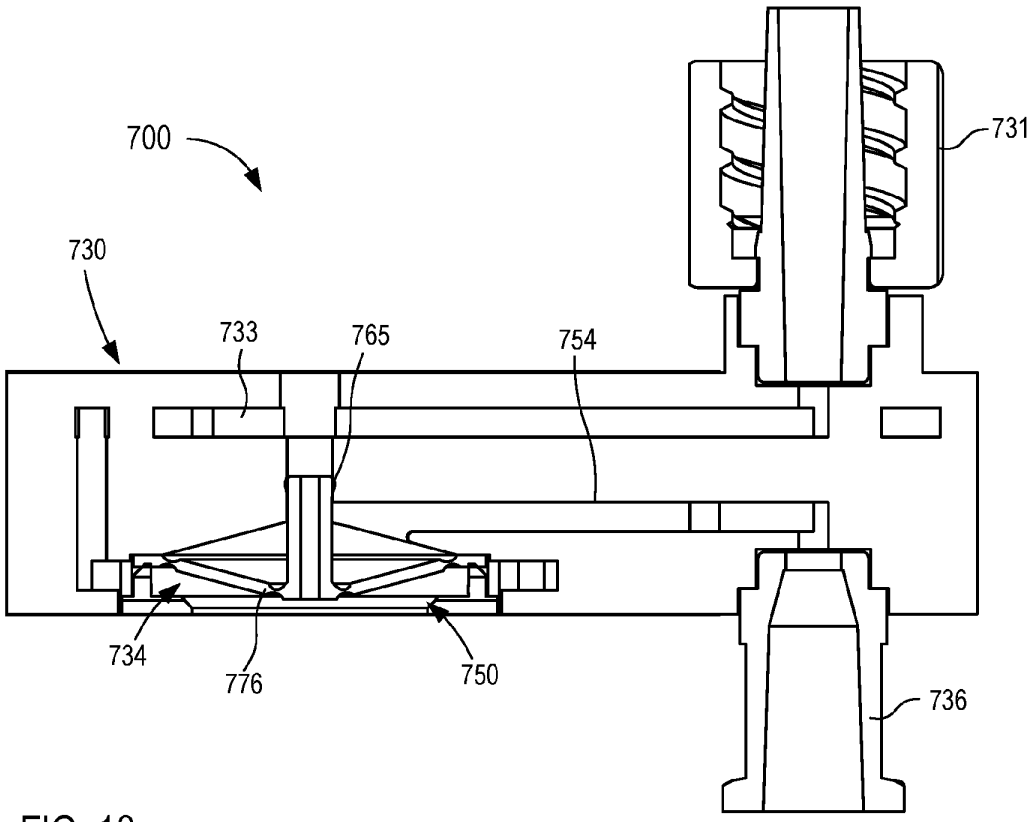


FIG. 18

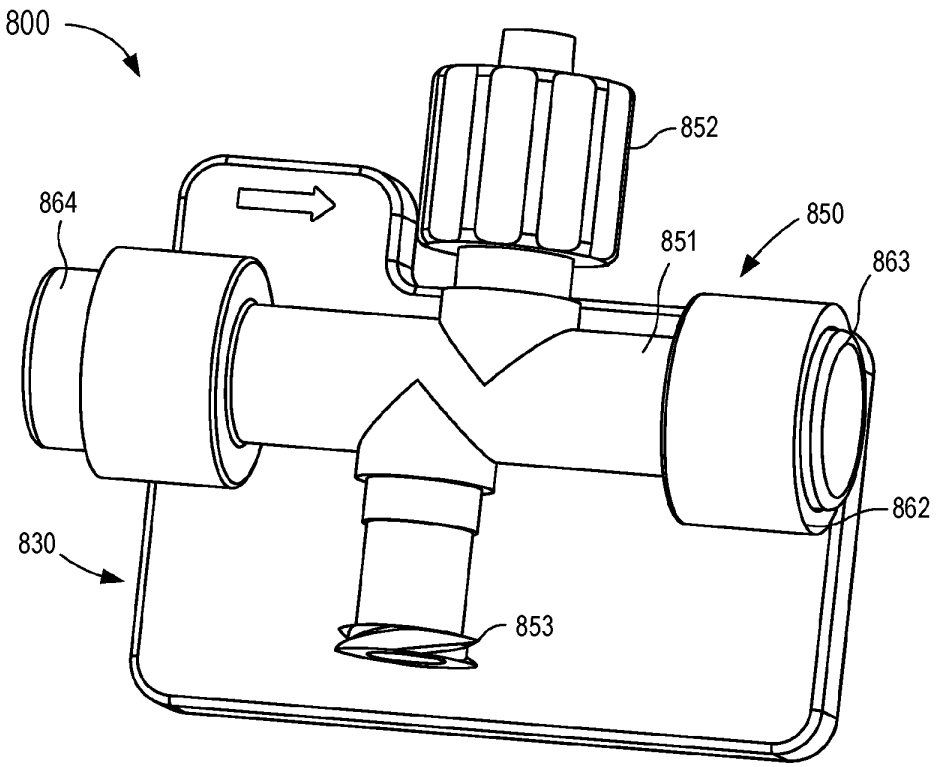


FIG. 19

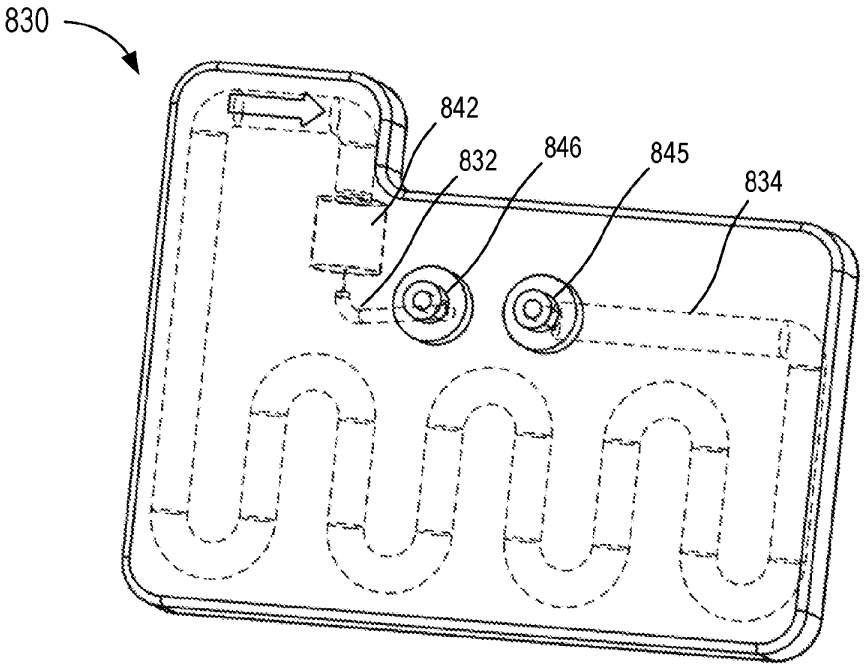


FIG. 20

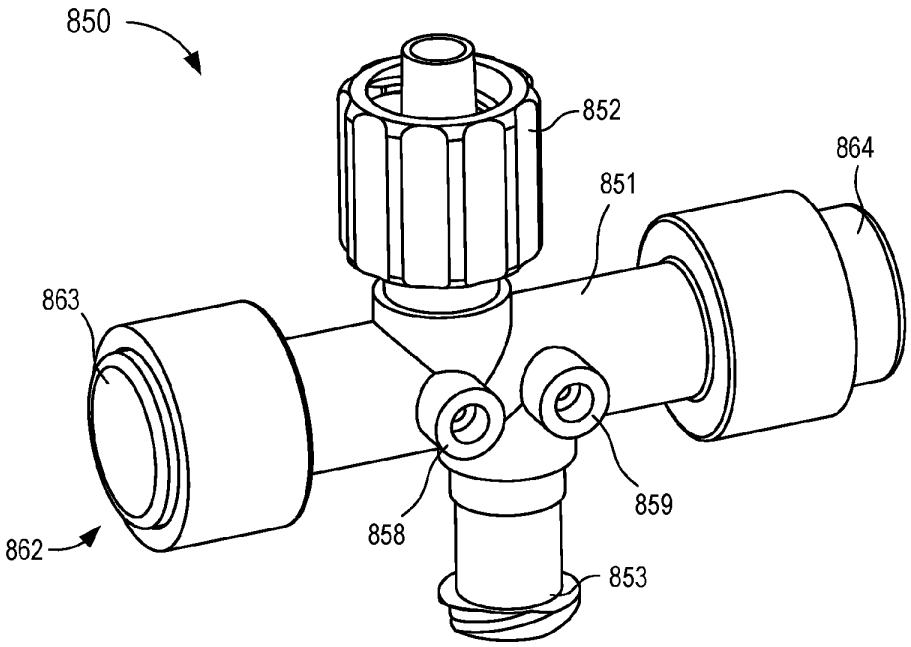


FIG. 21

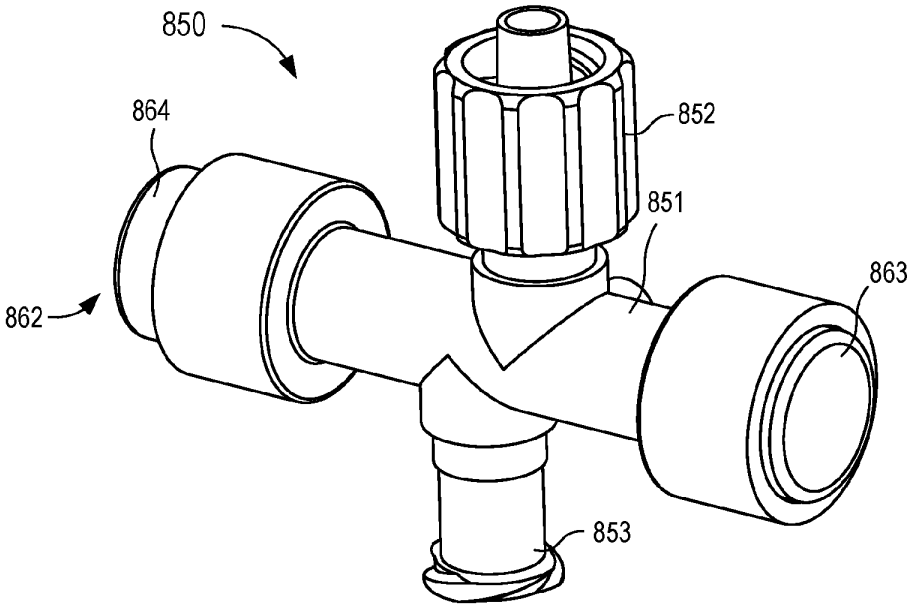


FIG. 22

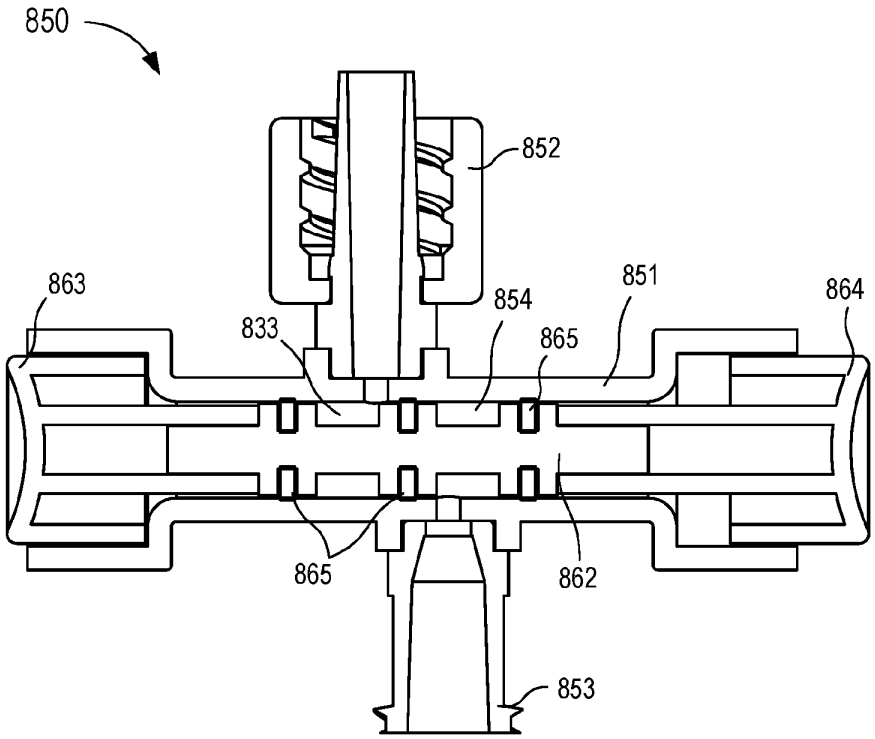

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FIG. 23

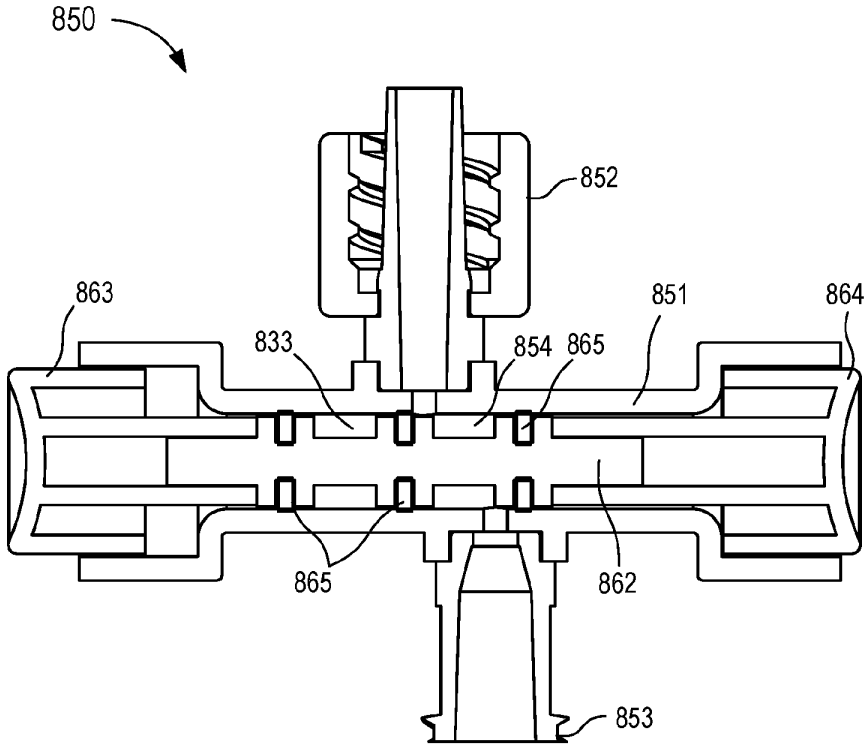

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FIG. 24

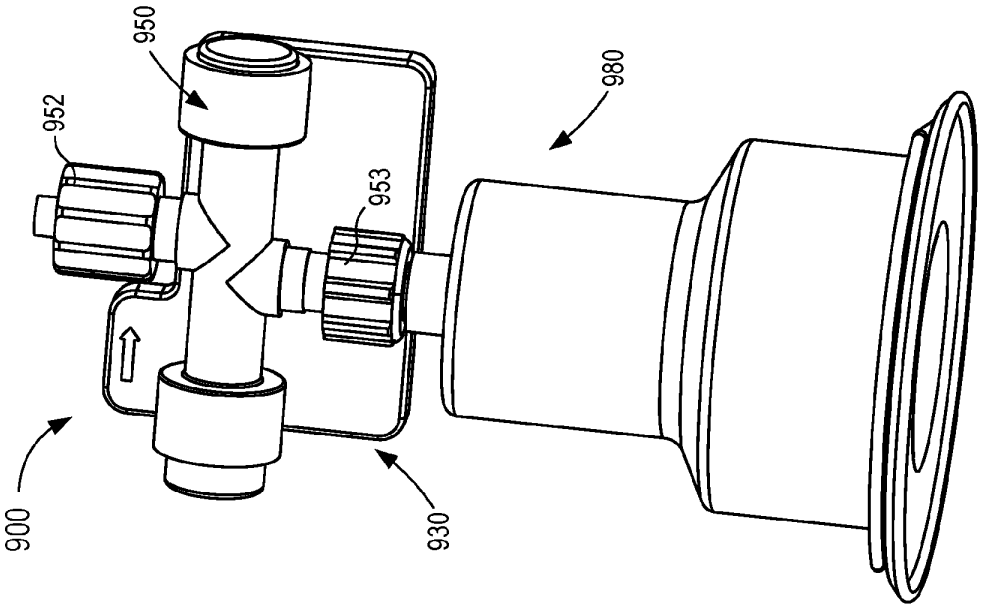


FIG. 26

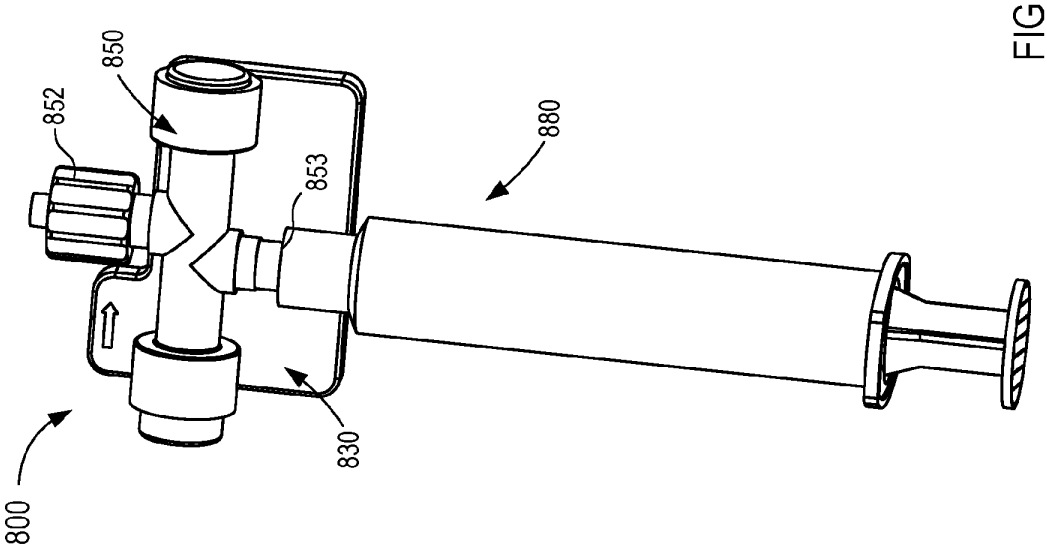


FIG. 25

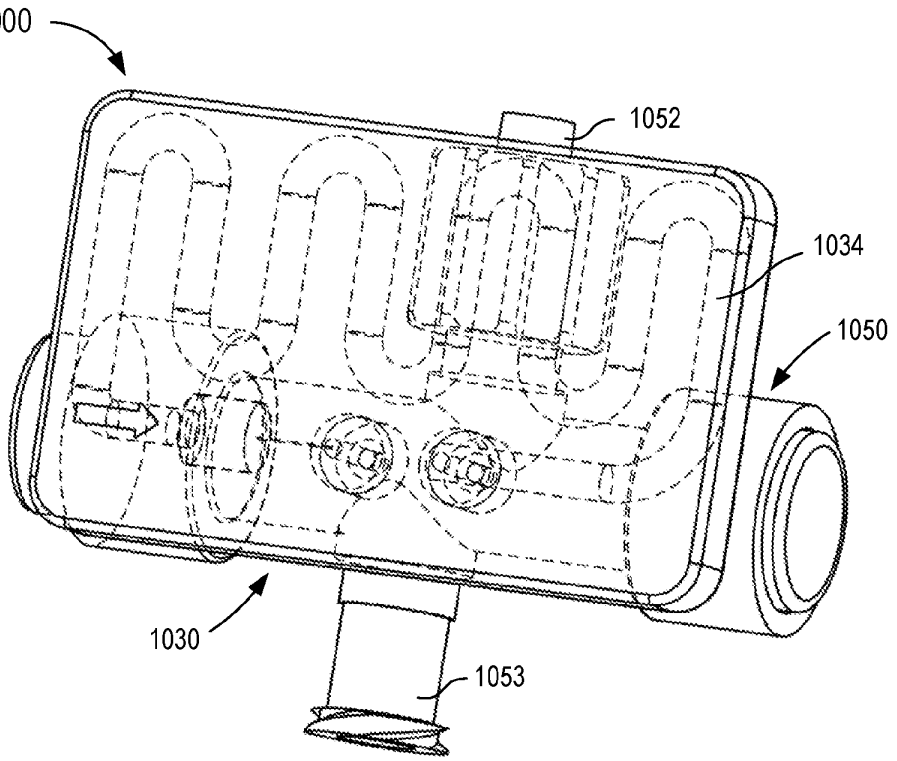


FIG. 27

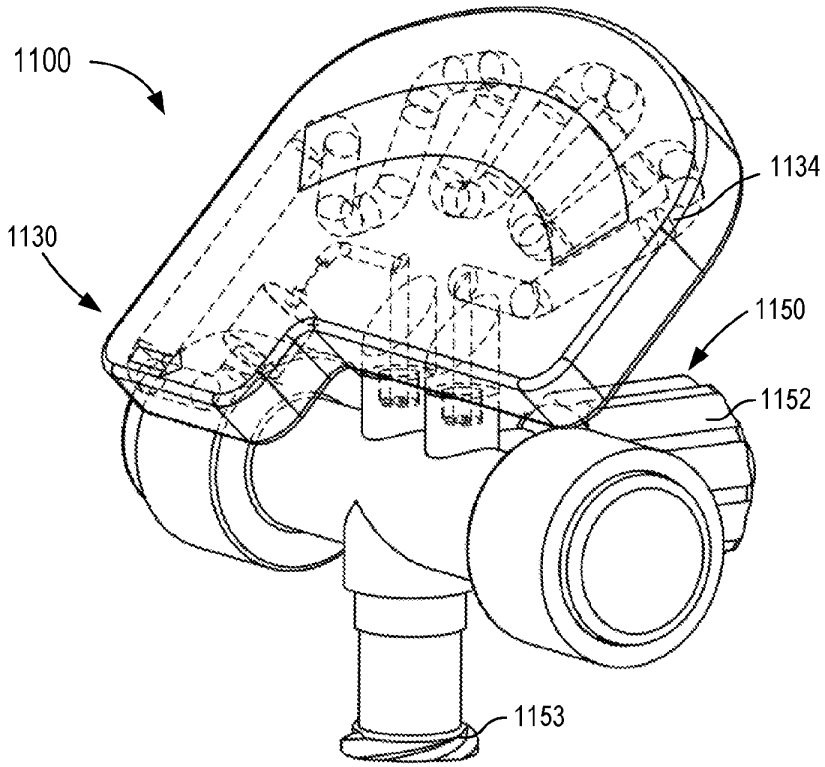


FIG. 28

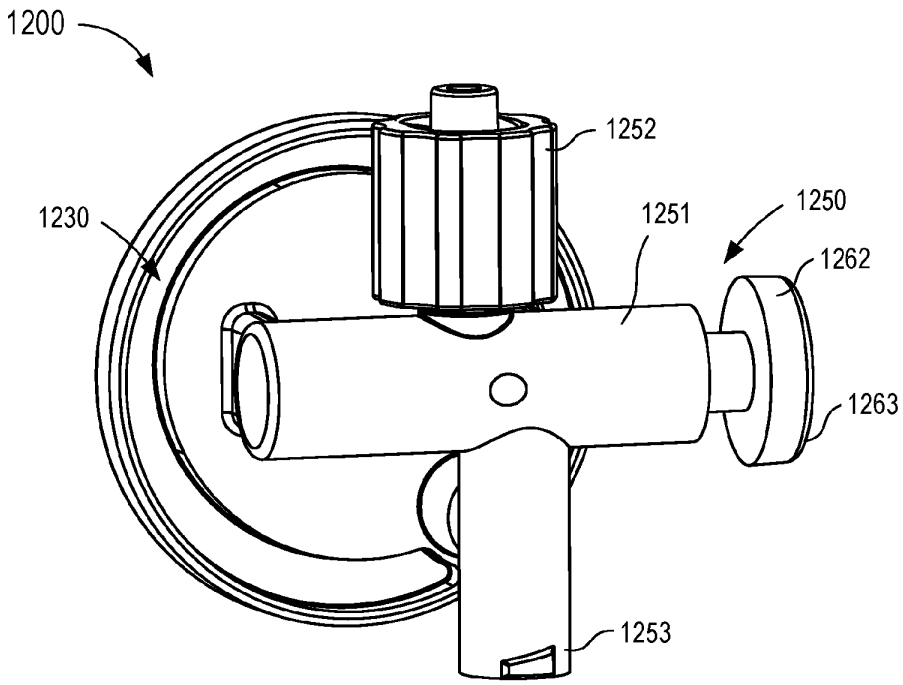

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FIG. 29

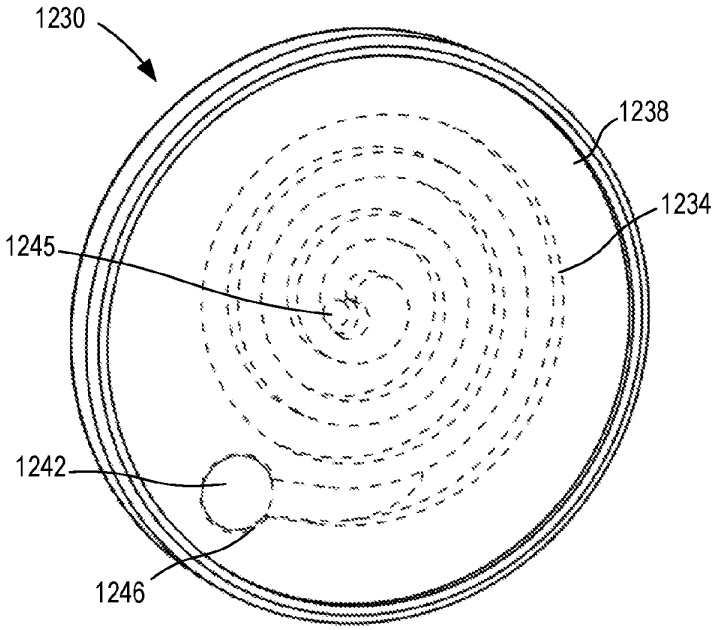

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FIG. 30

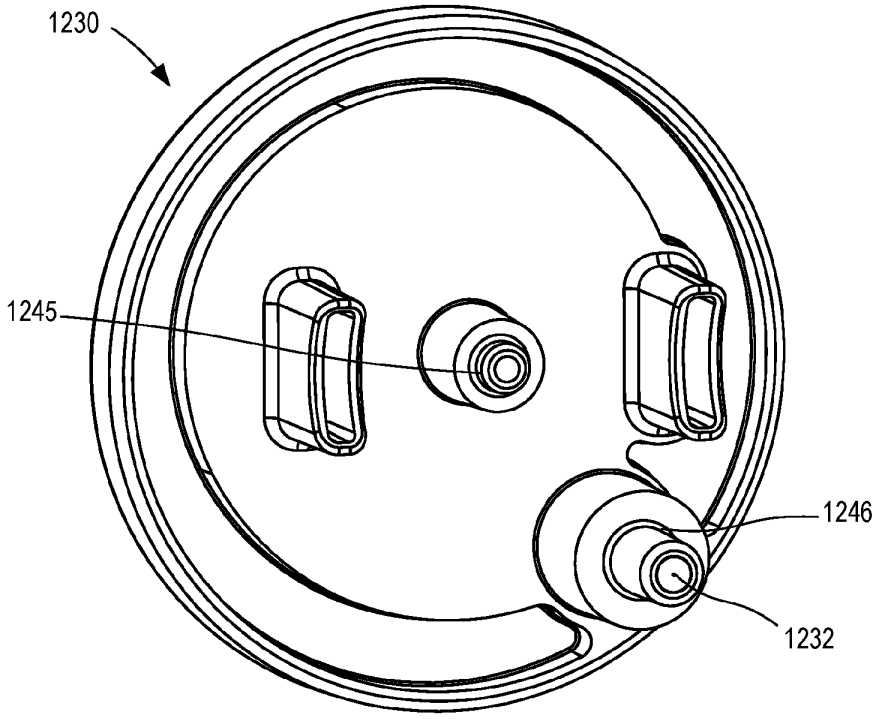

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FIG. 31

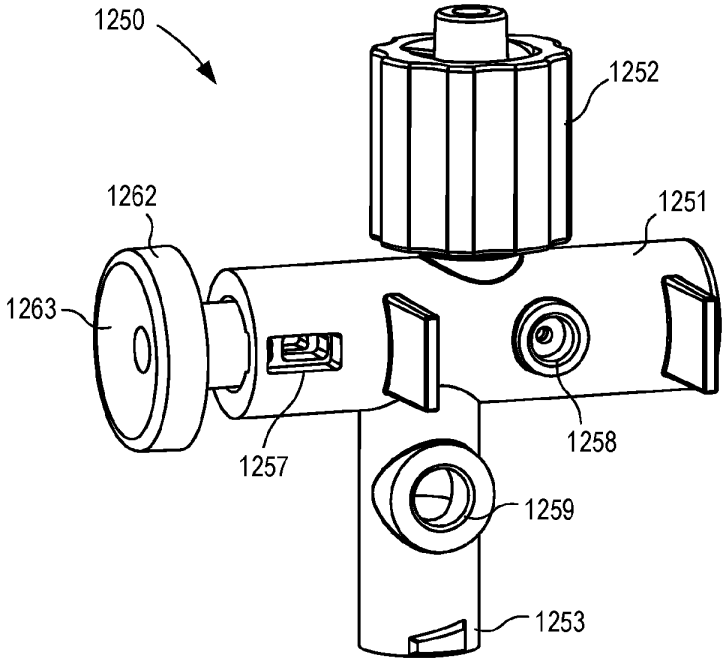

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FIG. 32

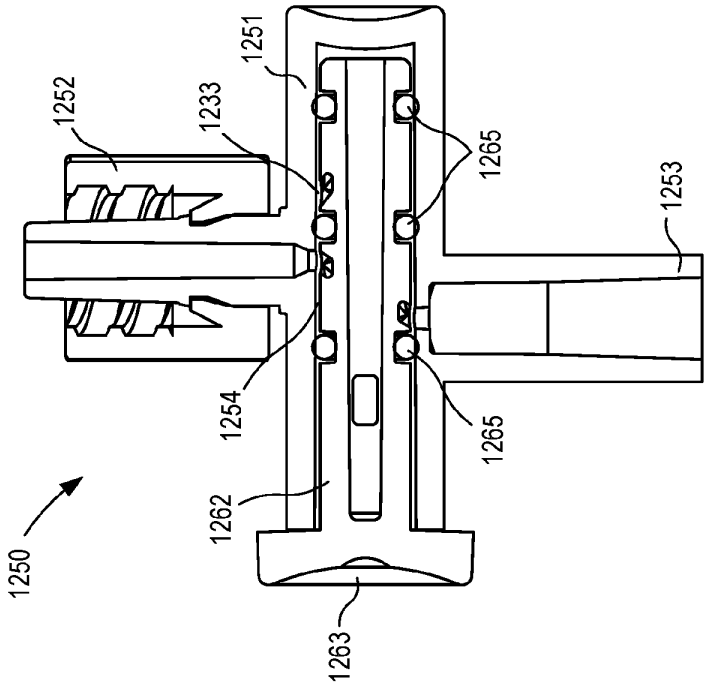

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FIG. 34

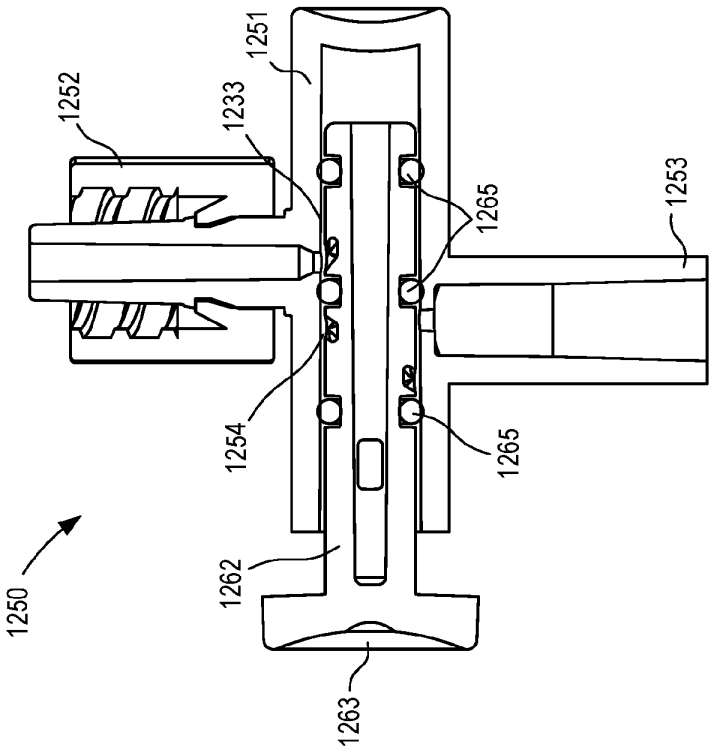

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FIG. 33

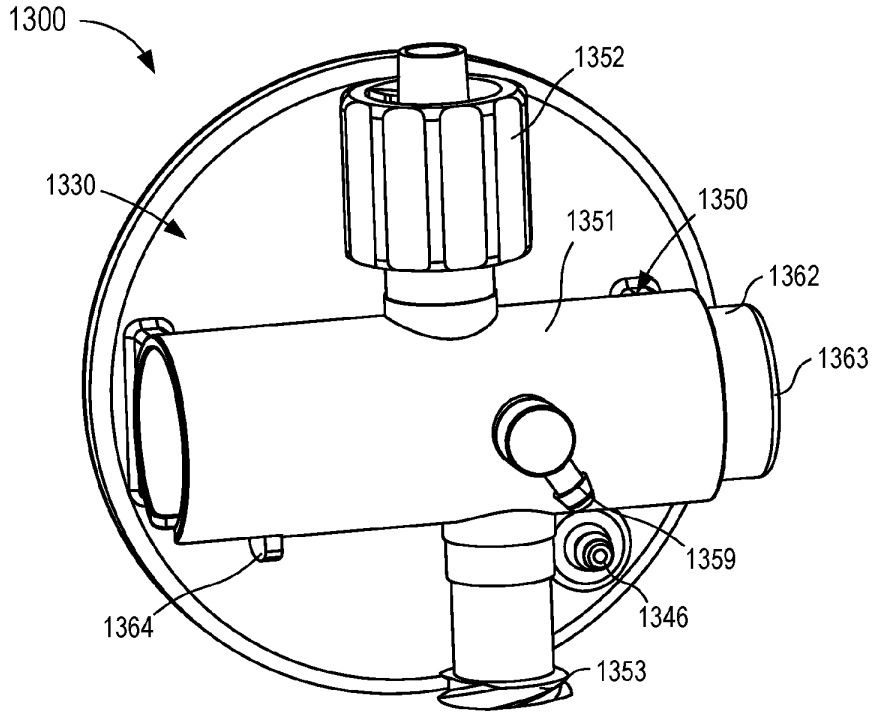

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FIG. 35

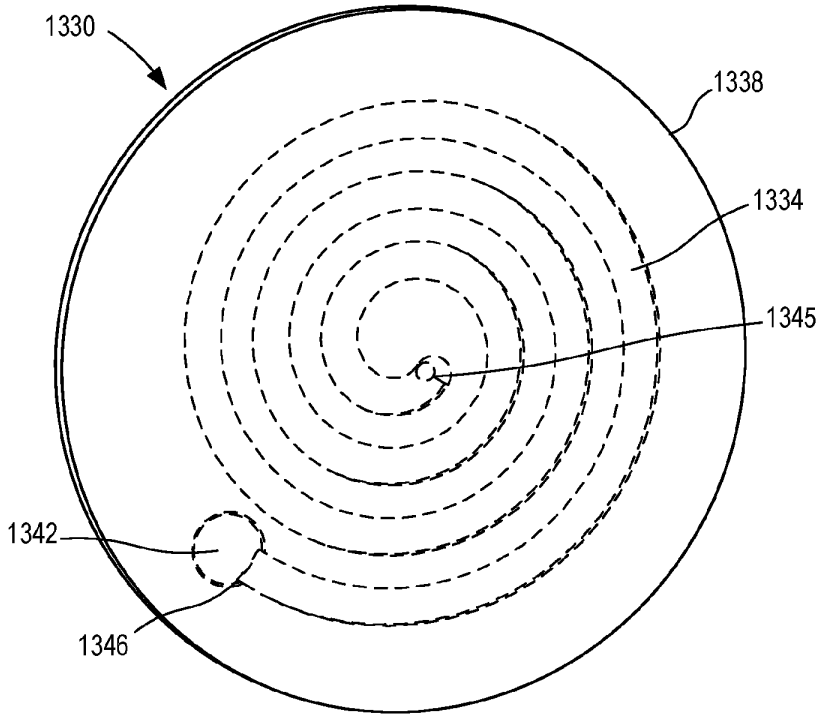

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FIG. 36

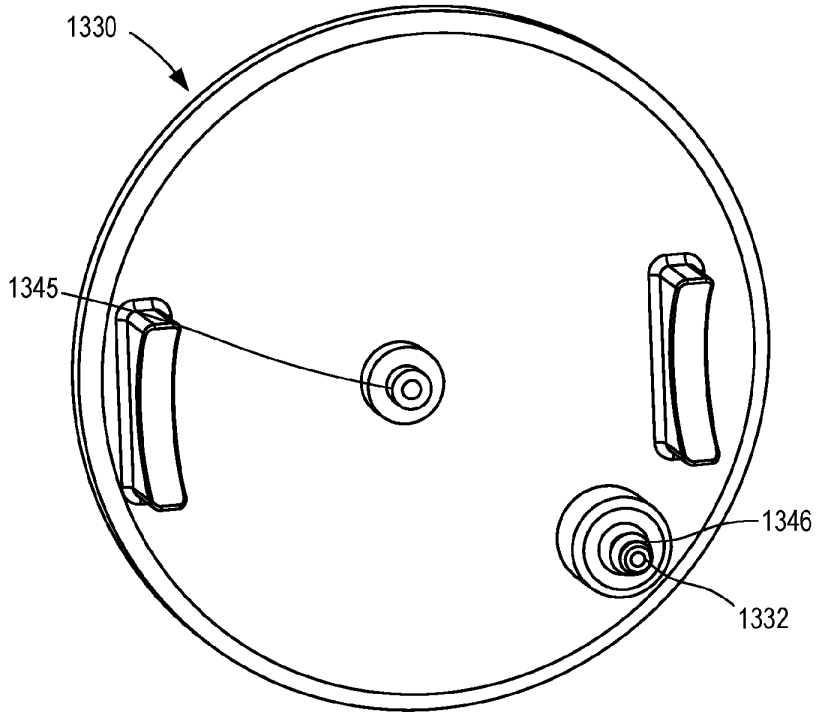


FIG. 37

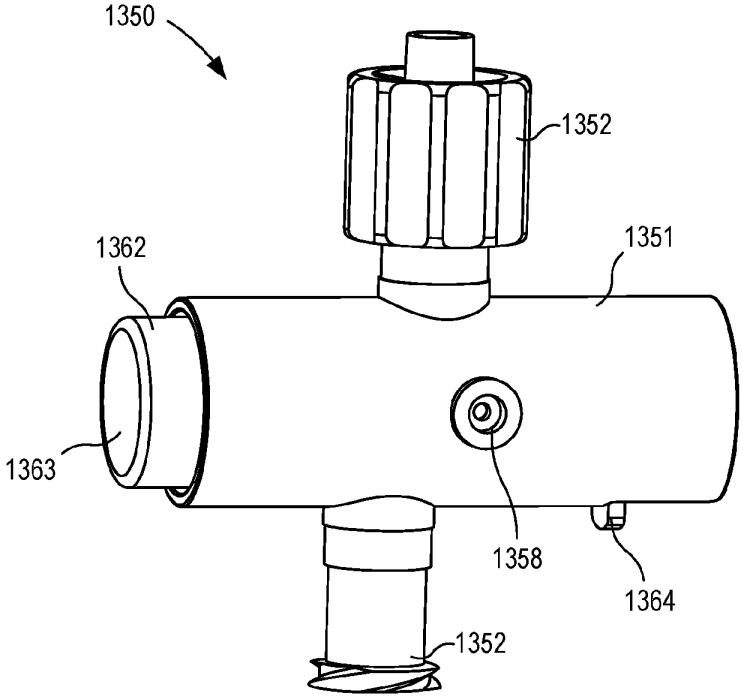


FIG. 38

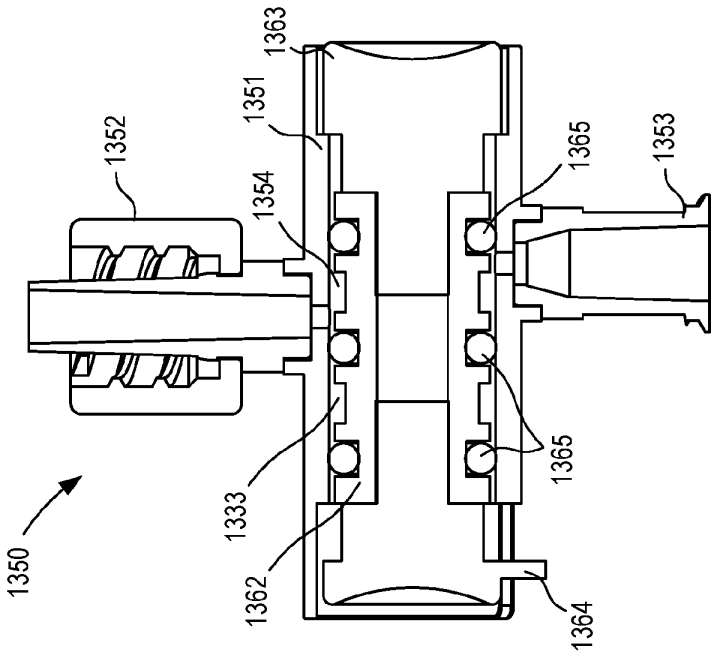

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FIG. 40

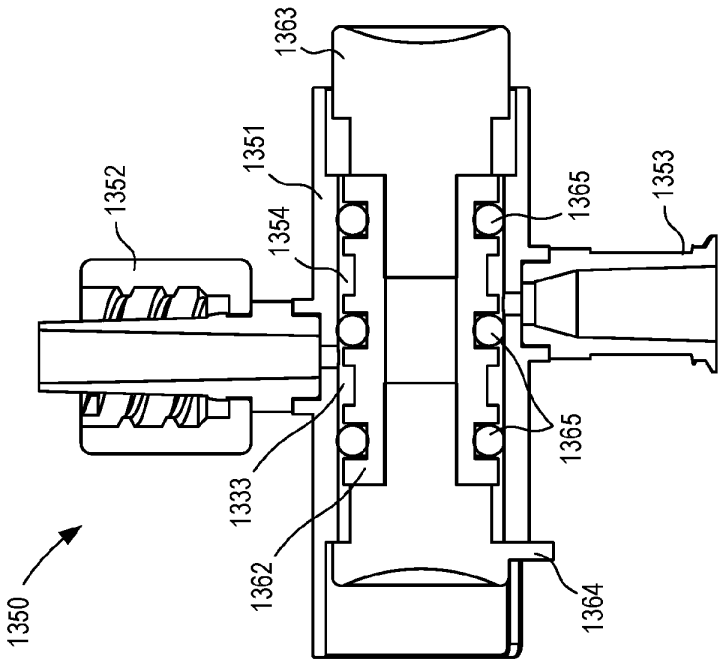

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FIG. 39

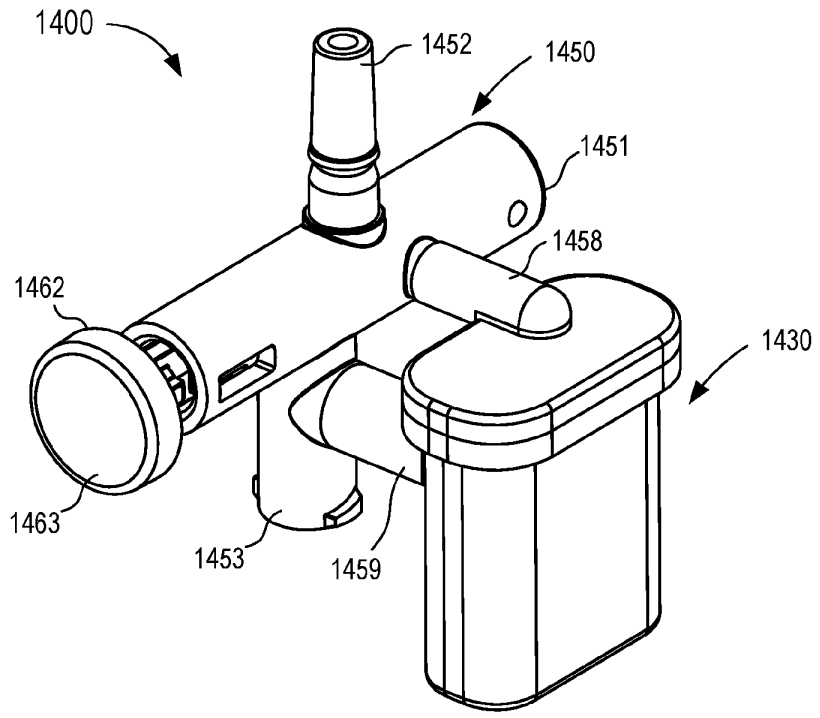

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FIG. 41

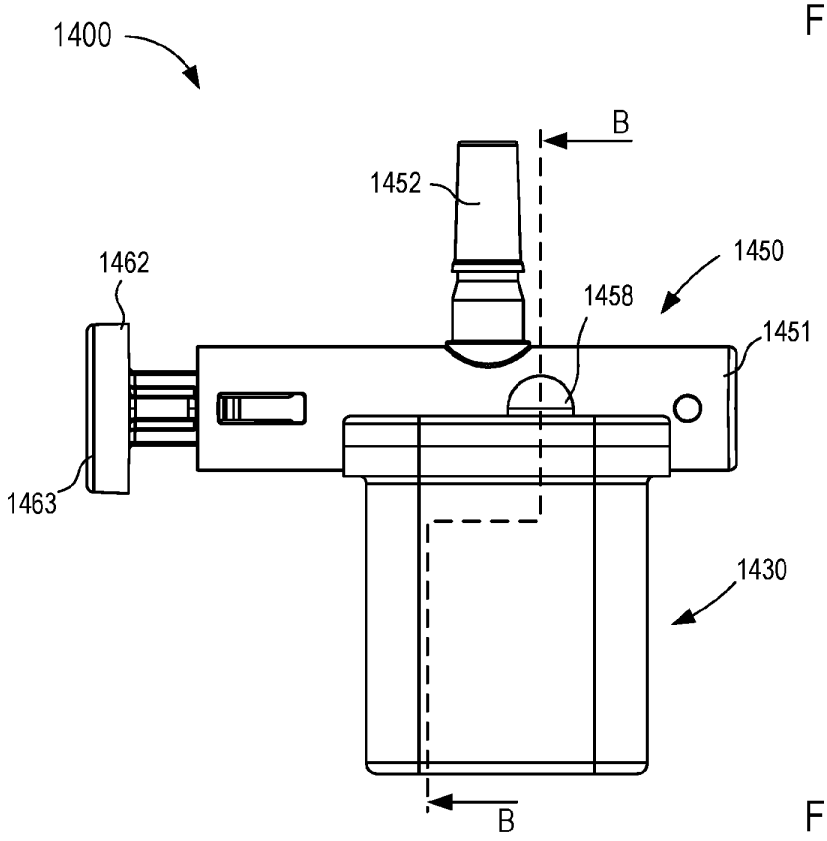

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FIG. 42

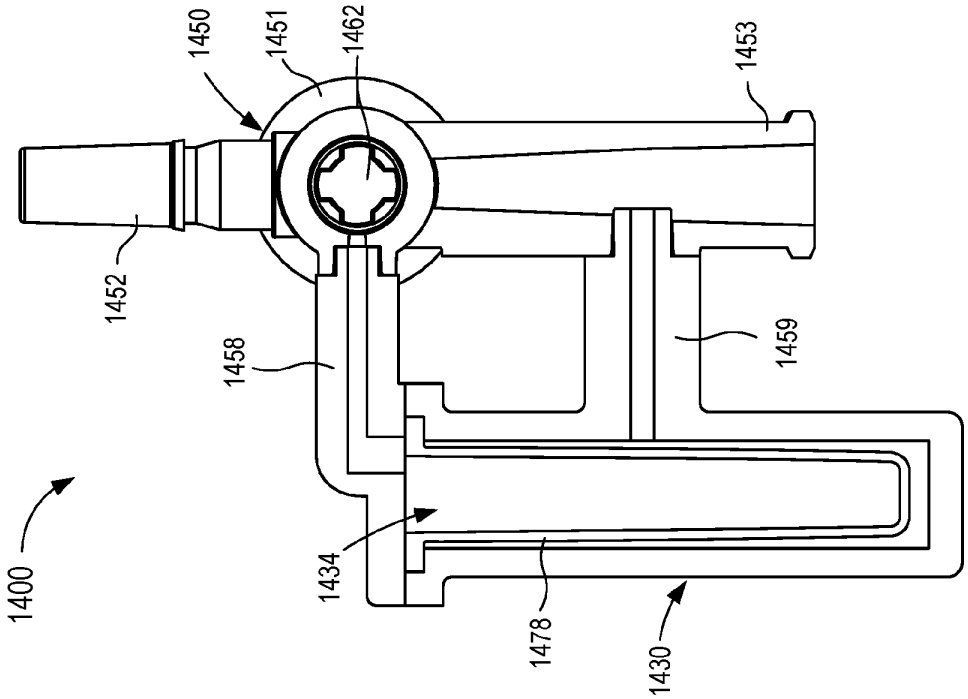

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SECTION B-B

FIG. 44

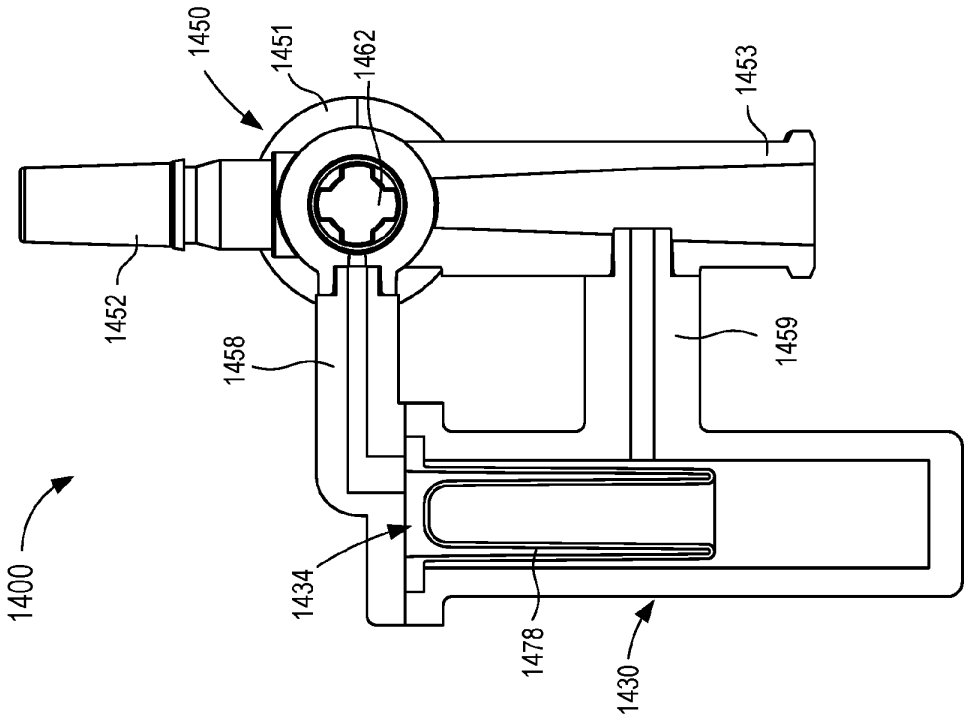

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SECTION B-B

FIG. 43

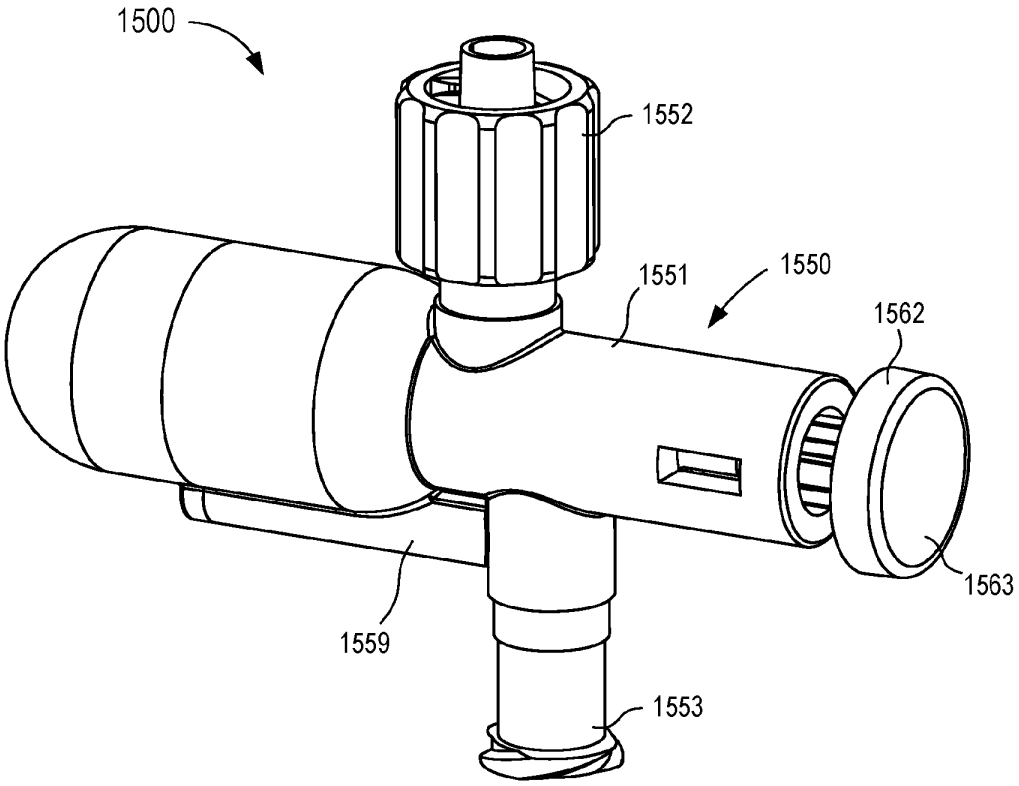

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FIG. 45

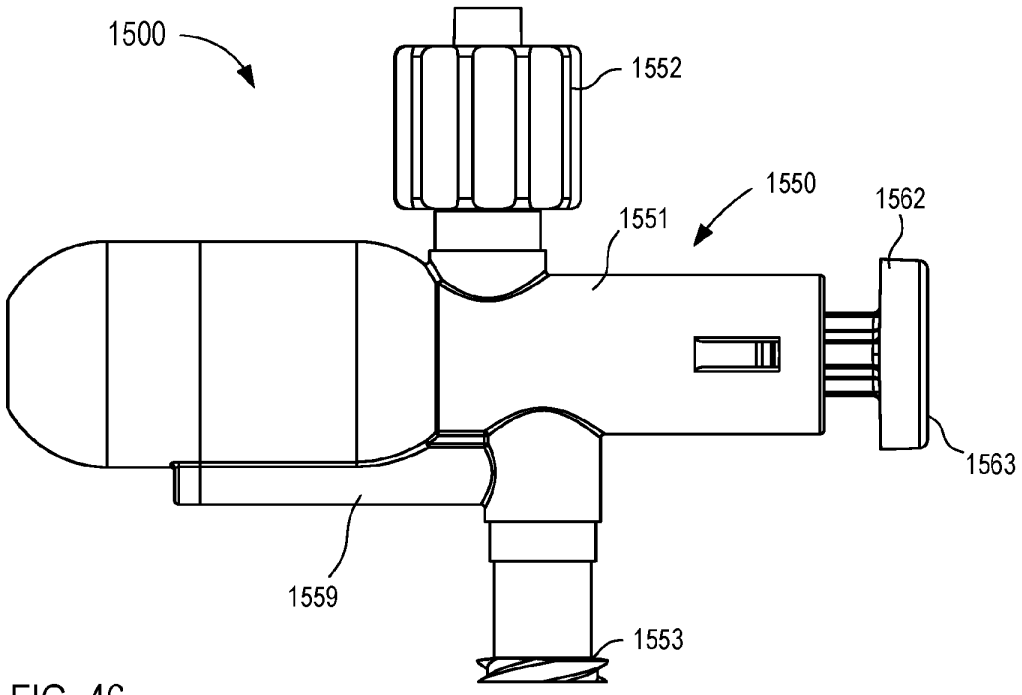

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FIG. 46

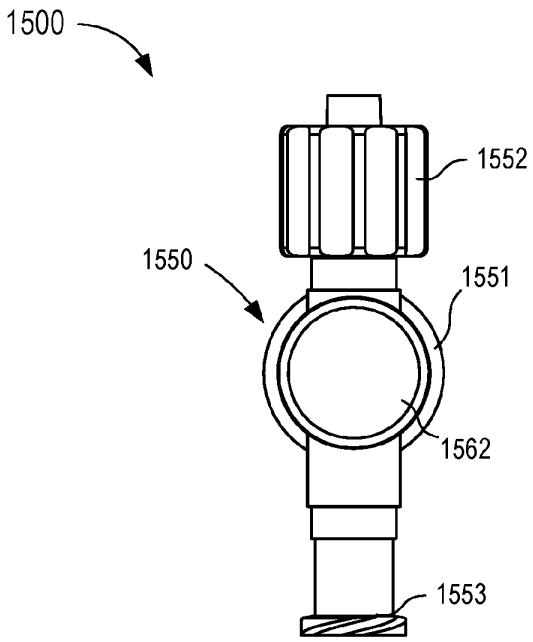

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FIG. 47

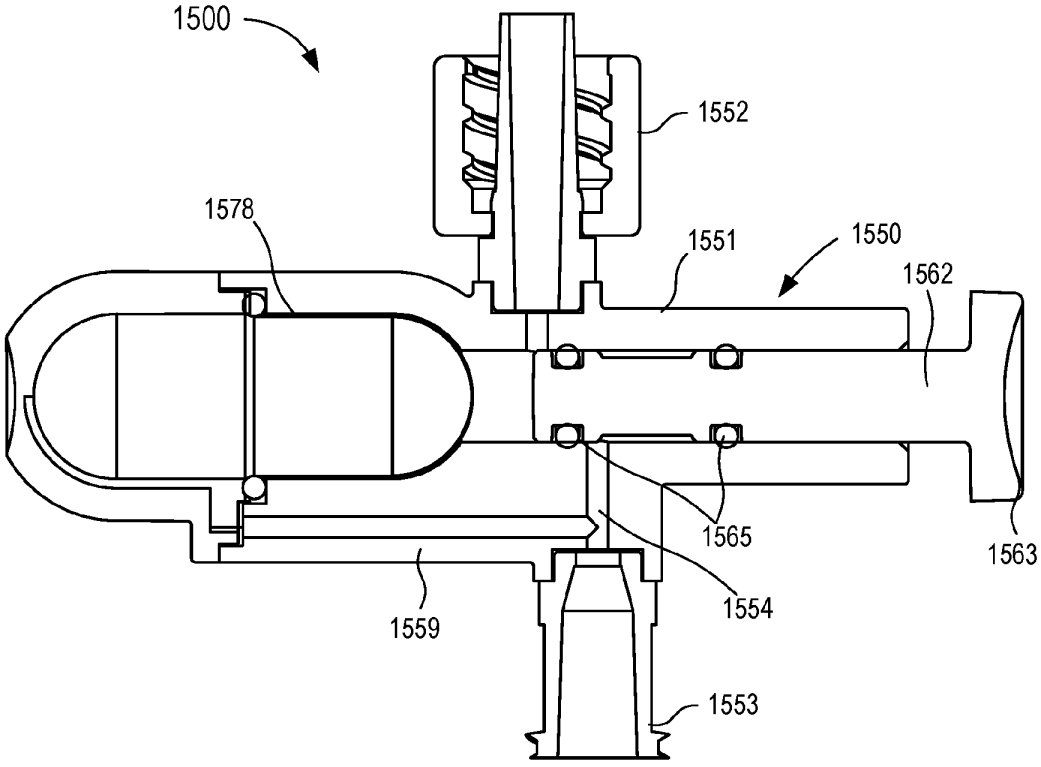

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FIG. 48

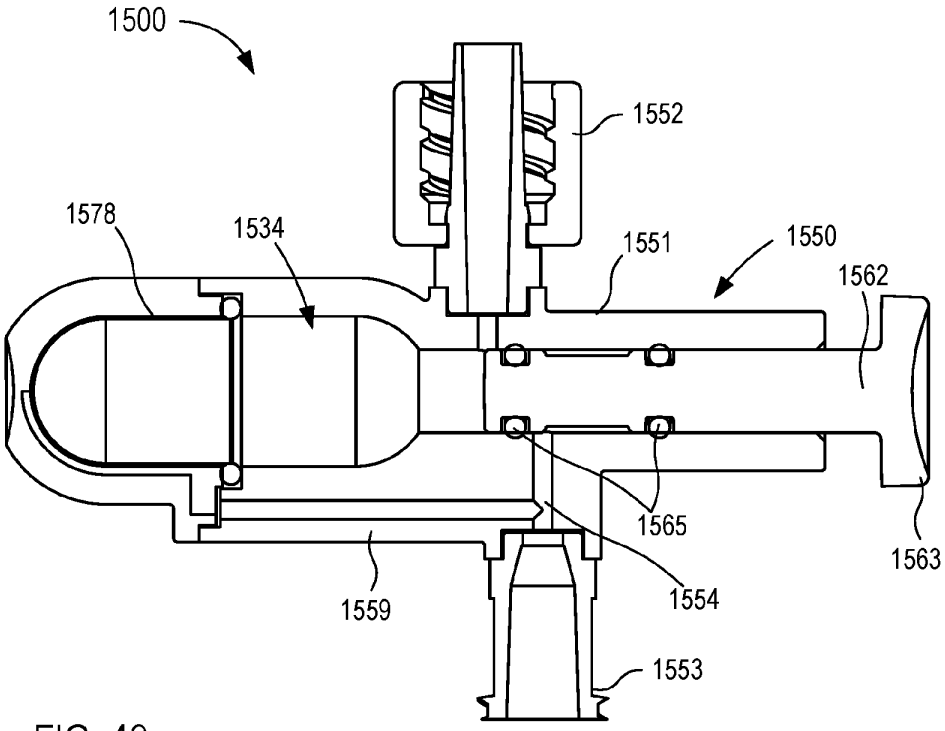

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FIG. 49

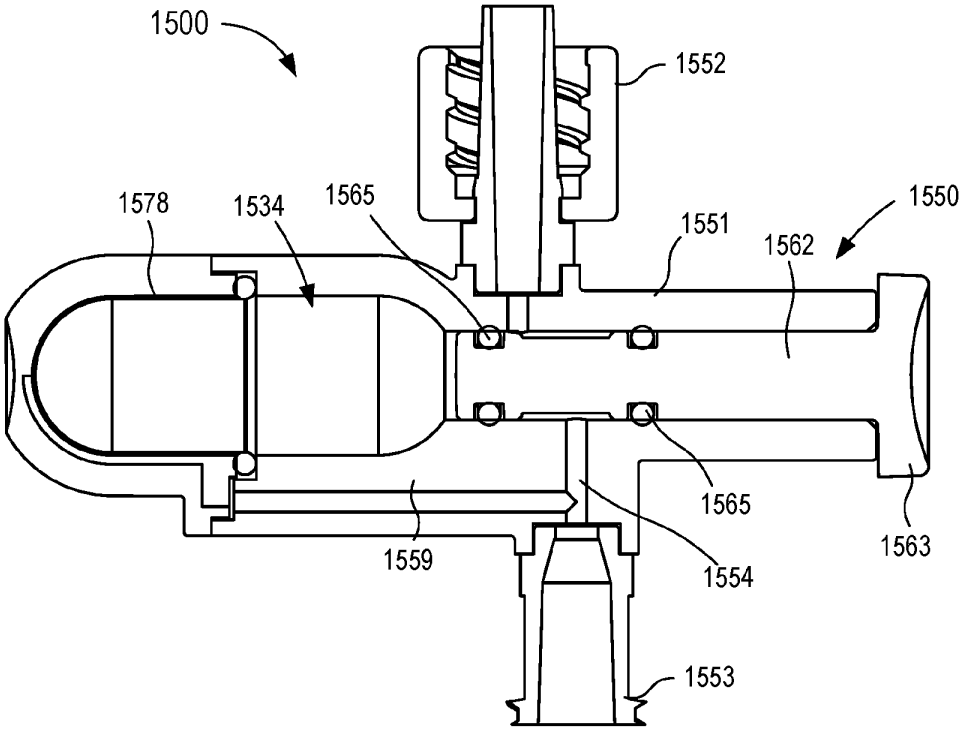

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FIG. 50

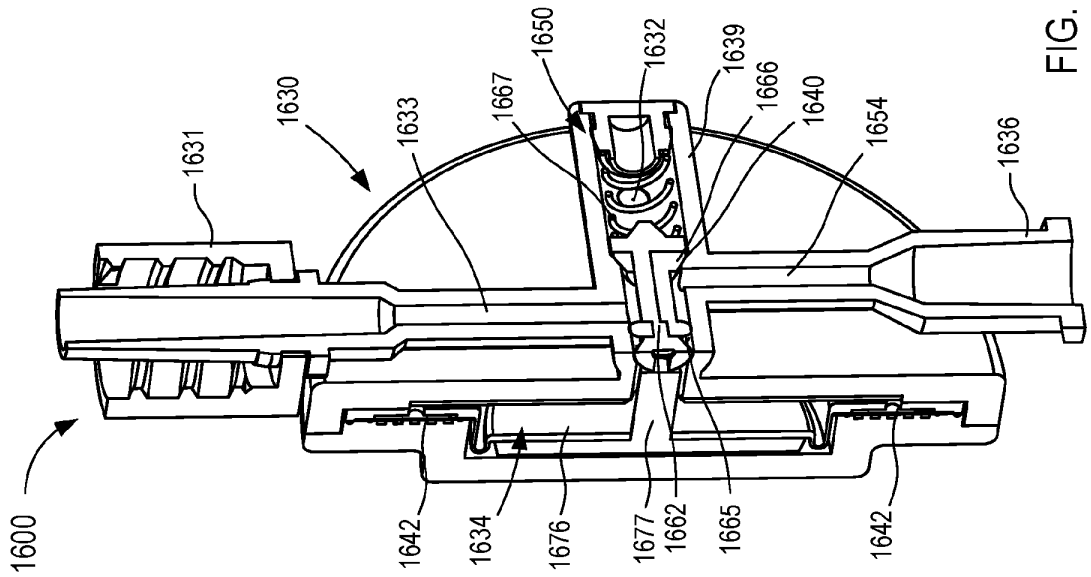

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FIG. 52

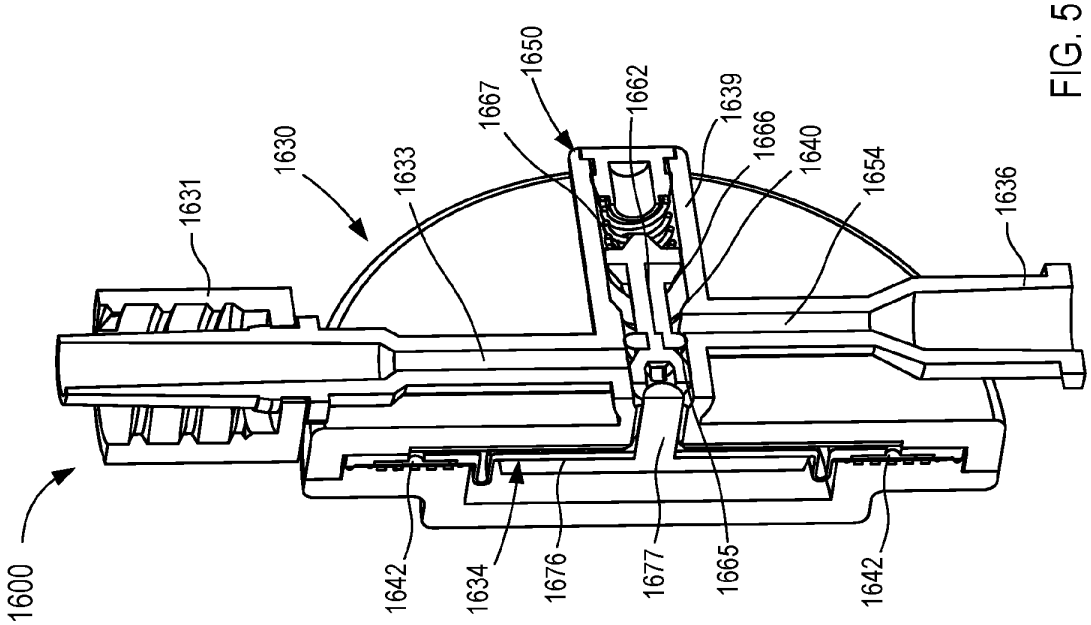

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FIG. 51

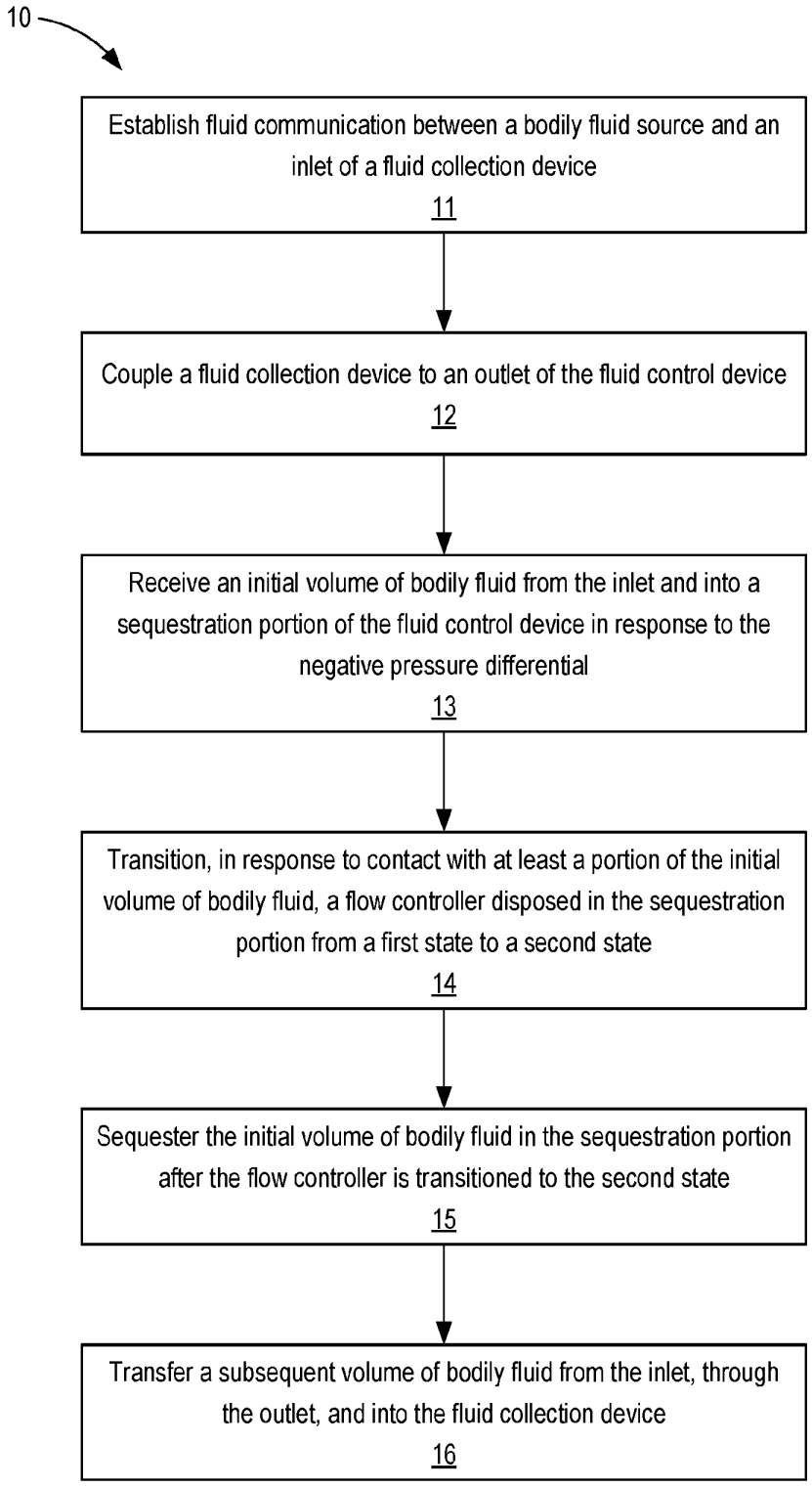

10
Establish fluid communication between a bodily fluid source and an inlet of a fluid collection device
11
Couple a fluid collection device to an outlet of the fluid control device
12
Receive an initial volume of bodily fluid from the inlet and into a sequestration portion of the fluid control device 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:

"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

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"O" document referring to an oral disclosure, use, exhibition or other means

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"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

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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)

Bibliographic data: EP3562397 (A1) — 2019-11-06

BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE AND METHOD

Inventor(s): ROGERS BOBBY E [US]; KANG GINO [US]; STROUP DAVID KARL [US]; COCHRAN JONAS DEAN [US]; DEPTALA ARTHUR [US]; DETLOFF JOHN [US]; POGUE LONNIE [US]; MACOWSKI BRIAN [US]; GARRETT CHAD [US] ± (ROGERS, Bobby E, ; KANG, Gino, ; STROUP, David Karl, ; COCHRAN, Jonas Dean, ; DEPTALA, Arthur, ; DETLOFF, John, ; POGUE, Lonnie, ; MACOWSKI, Brian, ; GARRETT, Chad)

Applicant(s): KURIN INC [US] ± (Kurin, Inc)

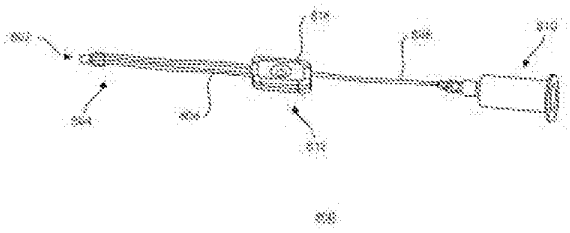
Classification: **- international:** ***A61B5/15; A61B5/153; A61B5/154; A61B5/157***
- cooperative: **A61B5/15003 (EP, US); A61B5/150213 (EP, US); A61B5/150221 (US); A61B5/150251 (EP, US); A61B5/150274 (EP, US); A61B5/150351 (US); A61B5/150755 (US); A61B5/150786 (US); A61B5/150946 (US); A61B5/150992 (EP, US); A61B5/1535 (EP, US); A61B5/1545 (EP, US);** A61B5/150389 (EP, US); A61B5/150488 (EP, US); A61B5/157 (EP, US)

Application number: EP20170840467 20171227 Global Dossier

Priority number(s): US201662439426P 20161227 ; WO2017US68569 20171227

Also published as: EP3562397 (B1) EP3777684 (A1) EP3777684 (B1) EP4091544 (A1) IL267684 (A) more

Abstract not available for EP3562397 (A1)
Abstract of corresponding document: US2018177445 (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.

(19) Europäisches Patentamt
European Patent Office
Office européen des brevets

(11) Veröffentlichungsnummer:
(11) Publication number: **EP 3 562 397 A0**
(11) Numéro de publication:

Internationale Anmeldung veröffentlicht durch die Weltorganisation für geistiges Eigentum unter der Nummer:

WO 2018/125929 (Art. 153(3) EPÜ).

International application published by the World Intellectual Property Organization under number:

WO 2018/125929 (Art. 153(3) EPC).

Demande internationale publiée par l'Organisation Mondiale de la Propriété Intellectuelle sous le numéro:

WO 2018/125929 (art. 153(3) CBE).

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
05 July 2018 (05.07.2018)

WIPO | PCT

(10) International Publication Number
WO 2018/125929 A1

(51) International Patent Classification:
A61B 5/15 (2006.01) *A61B 5/154* (2006.01)
A61B 5/153 (2006.01) *A61B 5/157* (2006.01)

(21) International Application Number:
PCT/US2017/068569

(22) International Filing Date:
27 December 2017 (27.12.2017)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
62/439,426 27 December 2016 (27.12.2016) US

(71) Applicant: **KURIN, INC.** [US/US]; 10755 Scripps Poway Parkway, No. 257, San Diego, California 92131 (US).

(72) Inventors: **ROGERS, Bobby E.**; c/o Kurin, Inc., 10755 Scripps Poway Parkway, No. 257, San Diego, California 92131 (US). **KANG, Gino**; c/o Kurin, Inc., 10755 Scripps Poway Parkway, No. 257, San Diego, California 92131 (US). **STROUP, David Karl**; c/o Kurin, Inc., 10755 Scripps Poway Parkway, No. 257, San Diego, California 92131 (US). **COCHRAN, Jonas Dean**; c/o Kurin, Inc., 10755 Scripps Poway Parkway, No. 257, San Diego, California 92131 (US). **DEPTALA, Arthur**; c/o Kurin, Inc., 10755 Scripps Poway Parkway, No. 257, San Diego, California 92131 (US). **DETLOFF, John**; c/o Kurin, Inc., 10755 Scripps Poway Parkway, No. 257, San Diego, California 92131 (US). **POGUE, Lonnie**; c/o Kurin, Inc., 10755 Scripps Poway Parkway, No. 257, San Diego, California 92131 (US). **MACOWSKI, Brian**; c/o Kurin, Inc., 10755 Scripps Poway Parkway, No. 257, San Diego, California 92131 (US). **GARRETT, Chad**; c/o Kurin, Inc., 10755 Scripps Poway Parkway, No. 257, San Diego, California 92131 (US).

(74) Agent: **DEVERNOE, David** et al.; TROUTMAN SANDERS, LLP, 600 Peachtree Street NE, Suite 5200, Atlanta, Georgia 30308 (US).

(54) Title: BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE AND METHOD

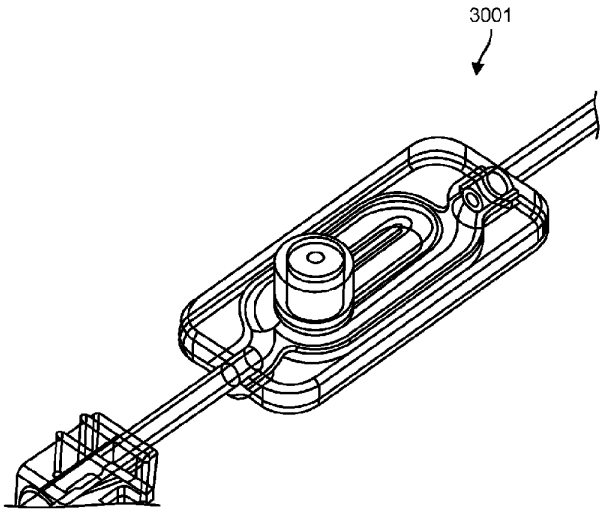


FIG. 30B

(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.

WO 2018/125929 A1

[Continued on next page]

(81) **Designated States** *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JO, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) **Designated States** *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Published:

— *with international search report (Art. 21(3))*

— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))*

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.

[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 0.045 inches, but can have a diameter of between 0.01 inches or less to 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.

CLAIMS

1. A blood sequestration device comprising;

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 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;

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 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 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 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 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 attached on the blood sampling pathway between the proximal end and distal end of the blood sampling pathway, the blood sequestration device comprising:

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, 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 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;

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.

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.

15. A blood sequestration device comprising;

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 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;

the sequestration chamber, the sampling channel and the junction being 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.

16. The blood sequestration device in accordance with claim 15, further comprising a housing that houses and defines the inlet port, the outlet port, the sequestration chamber, and the sampling channel.

17. The blood sequestration device in accordance with claim 15, wherein the vent further includes an inner wall within the outer wall and that contains the air permeable blood barrier.

18. The blood sequestration device in accordance with claim 15, wherein the one-way seal is positioned over the inner wall and within the outer wall of the vent.

19. The blood sequestration device in accordance with claim 18, 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.

20. The blood sequestration device in accordance with claim 15, wherein the air permeable blood barrier includes a sealing material that seals the vent upon contact with blood.

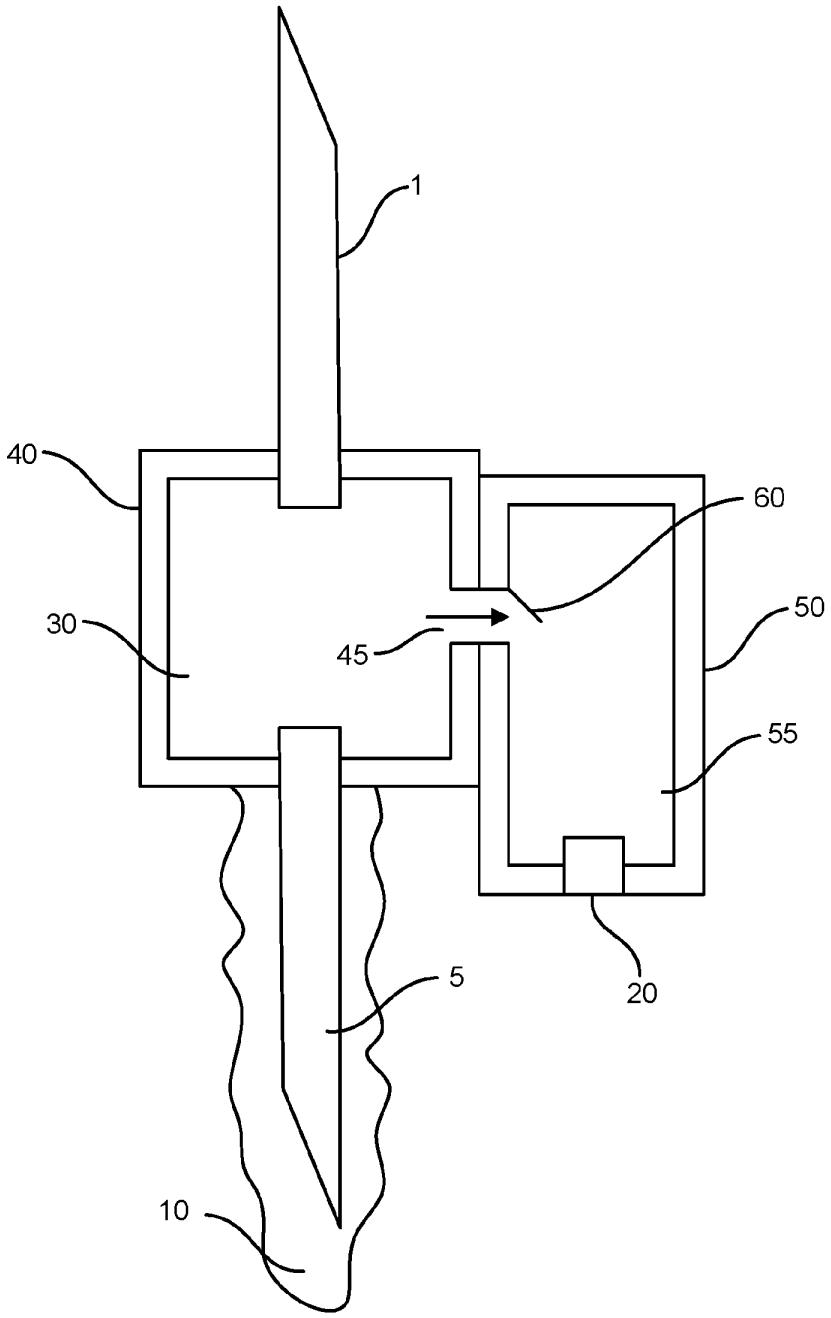


FIG. 1

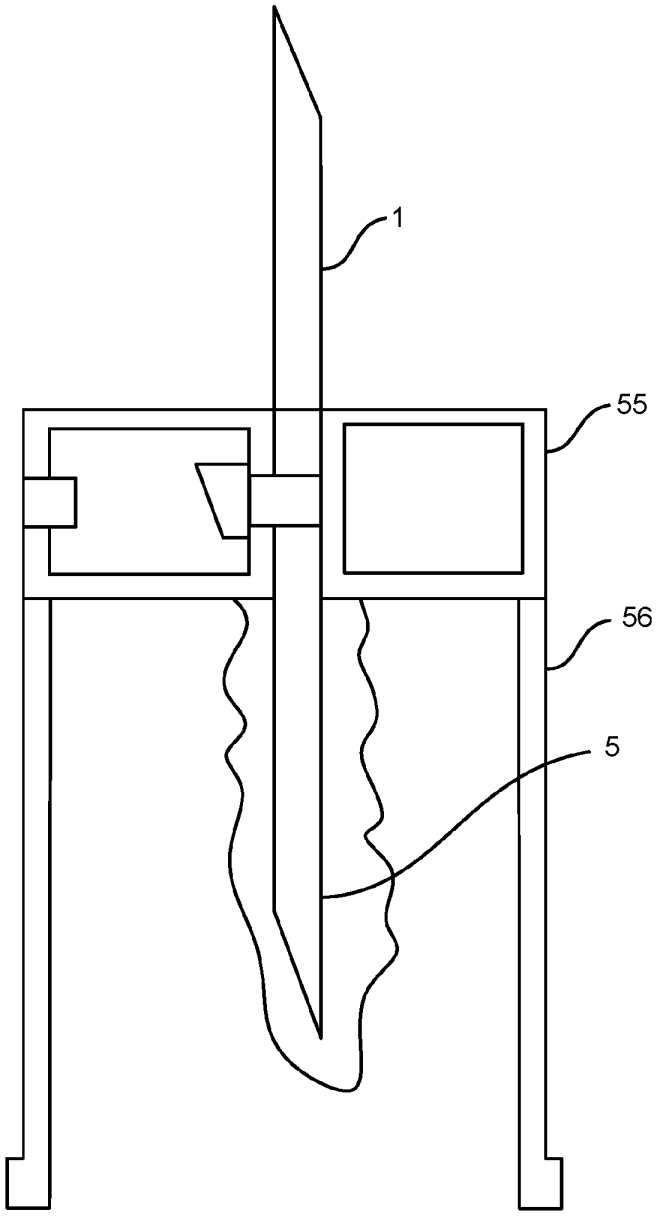


FIG. 2

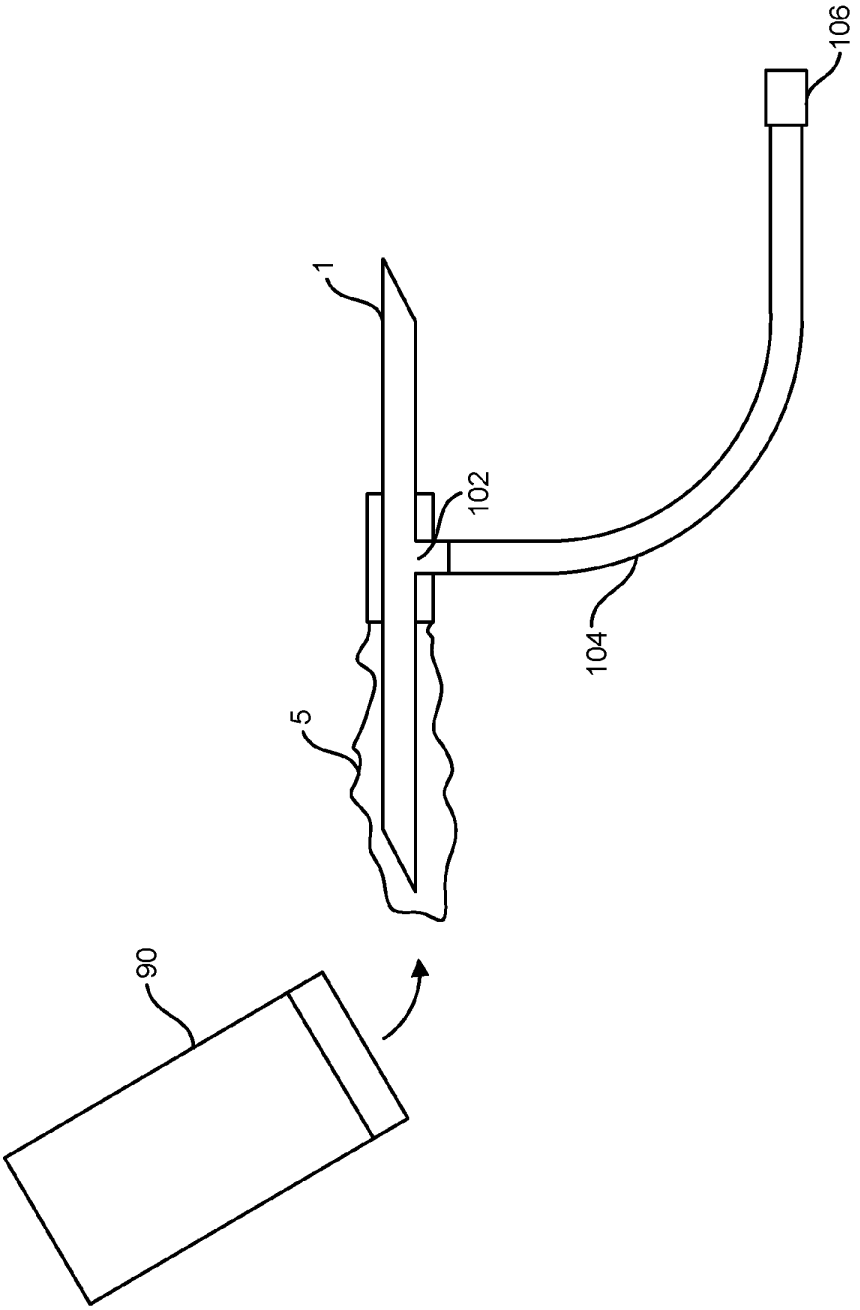


FIG. 3

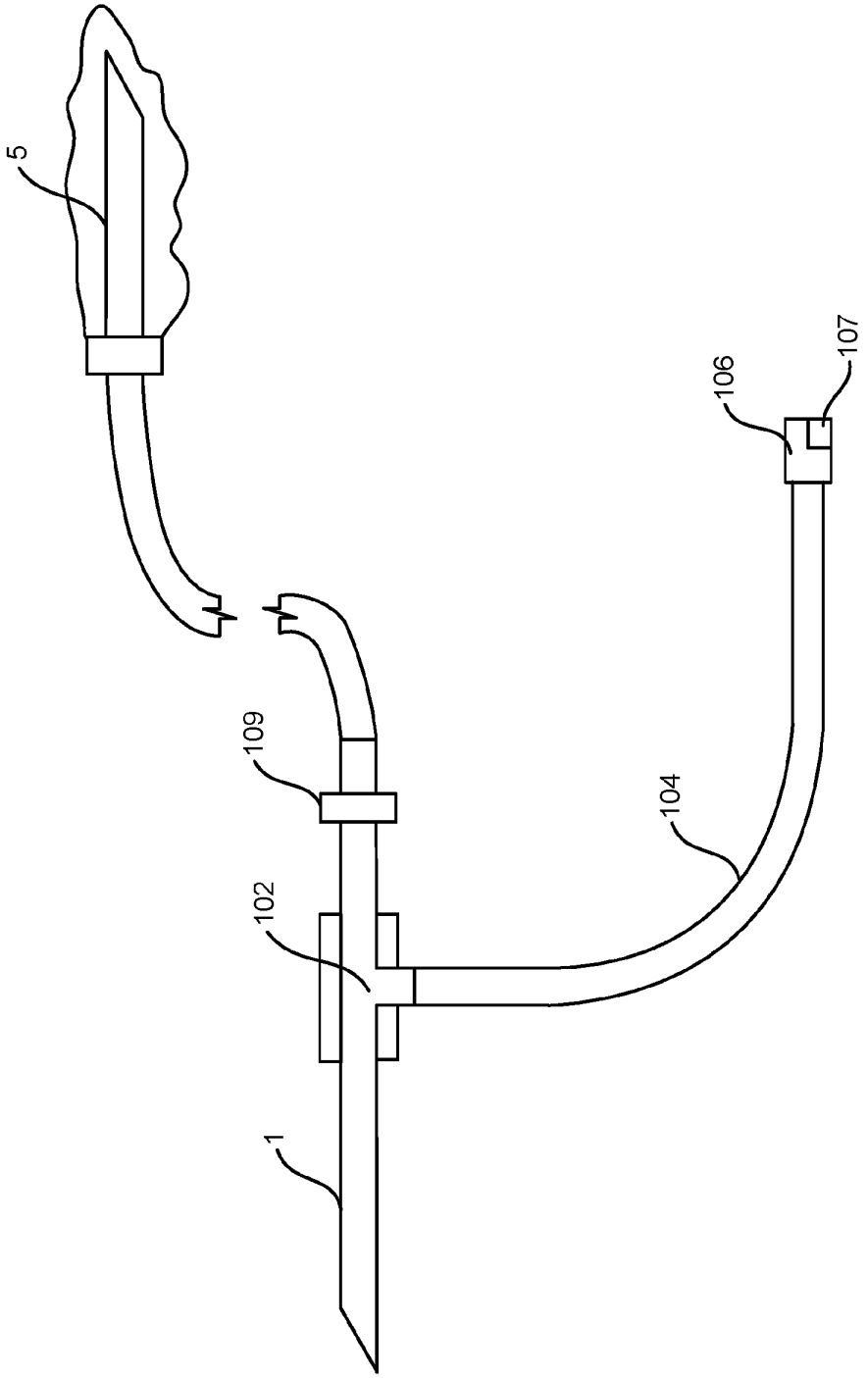


FIG. 4

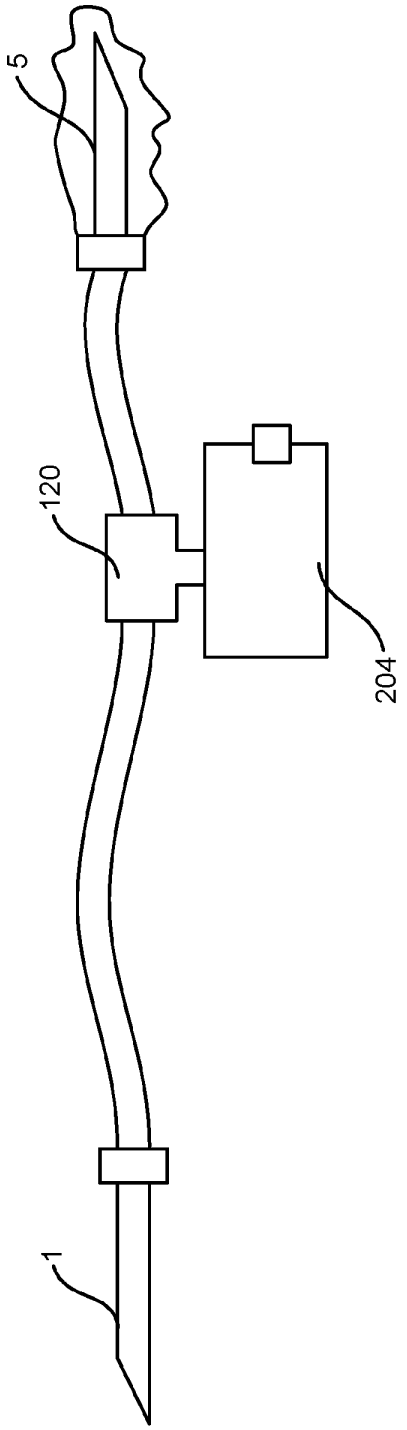


FIG. 5

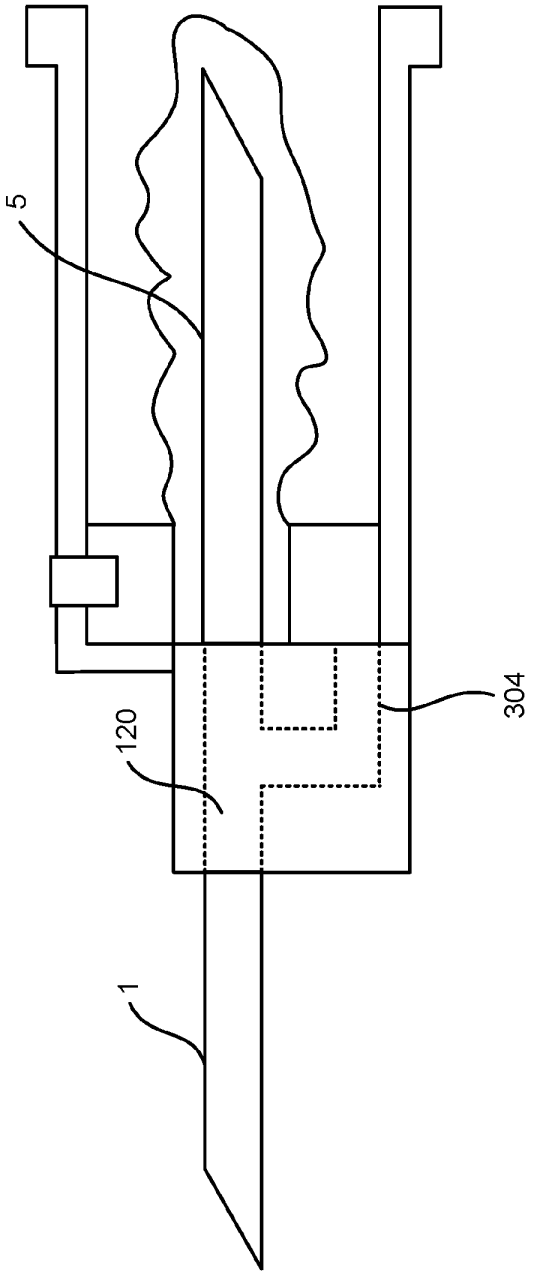


FIG. 6

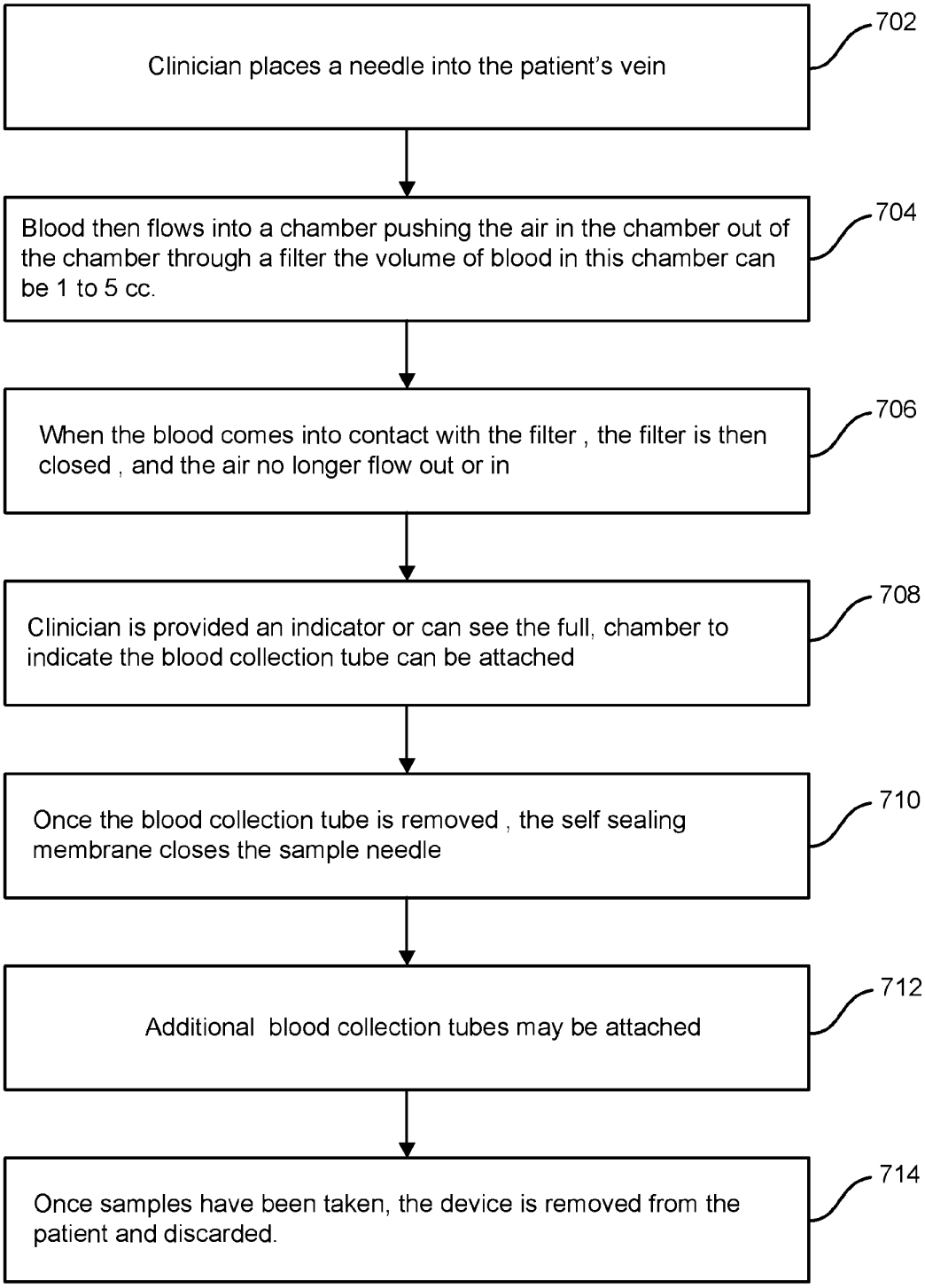

Clinician places a needle into the patient's vein
702
Blood then flows into a chamber pushing the air in the chamber out of the chamber through a filter the volume of blood in this chamber can be 1 to 5 cc.
704
When the blood comes into contact with the filter , the filter is then closed , and the air 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

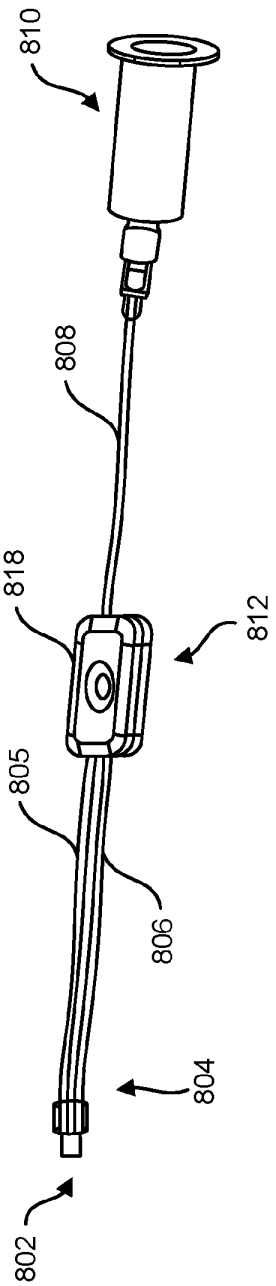


FIG. 8A

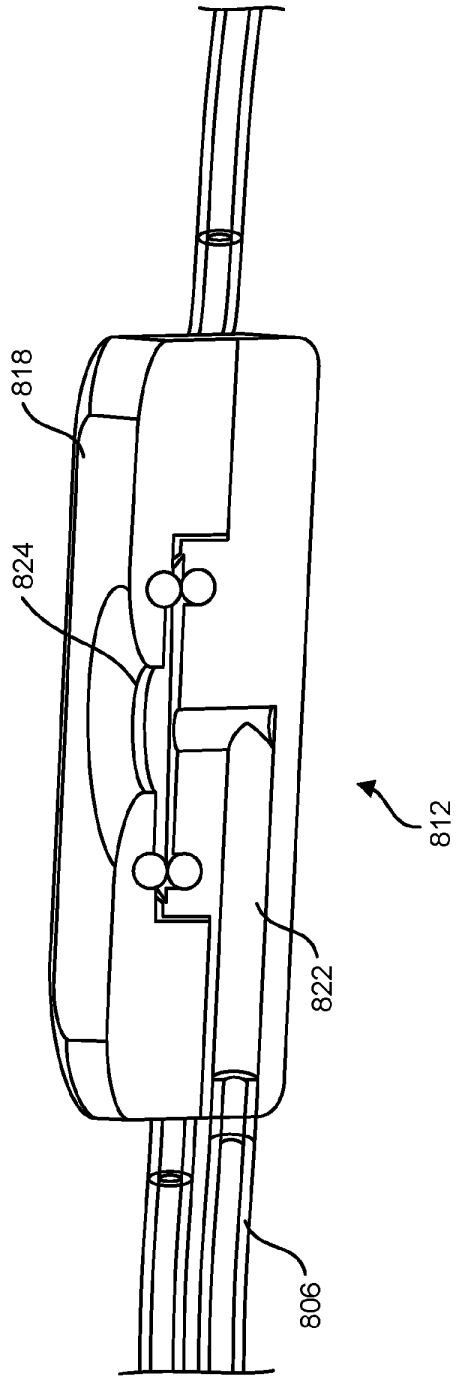


FIG. 8B

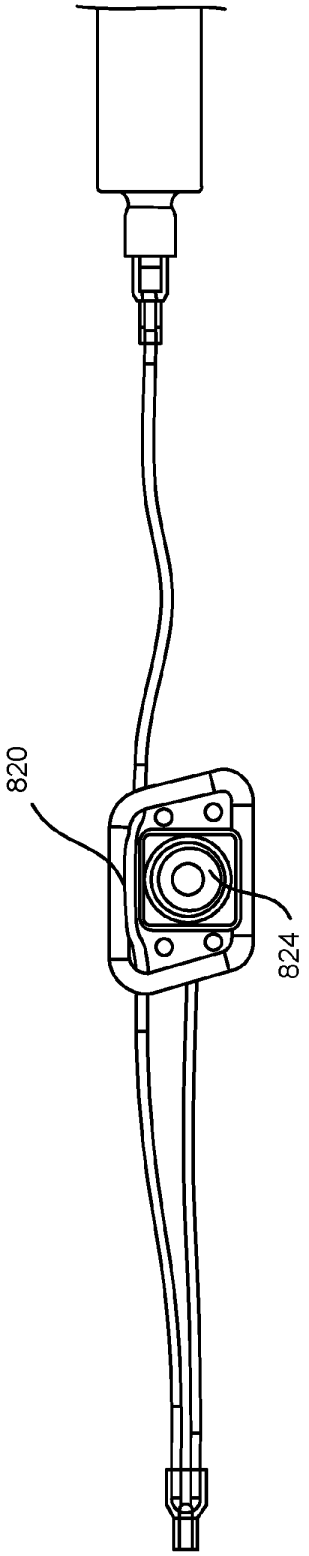


FIG. 8C

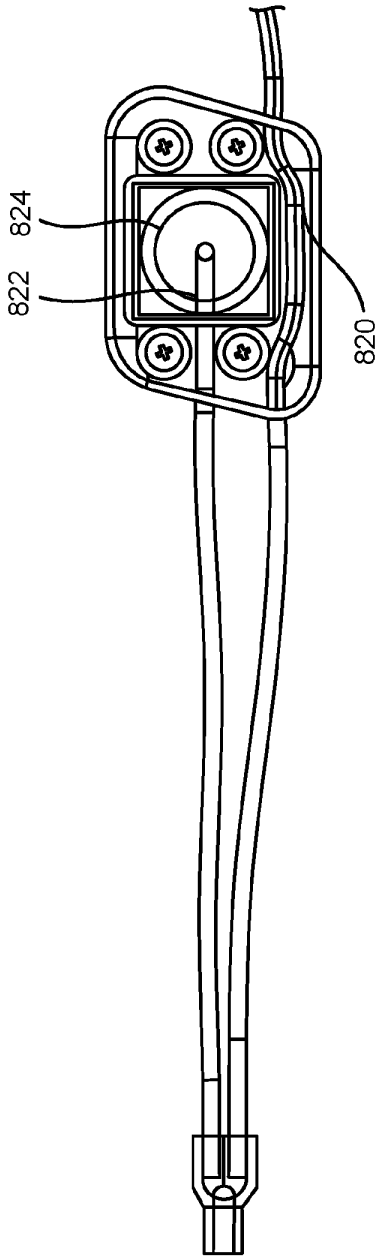


FIG. 8D

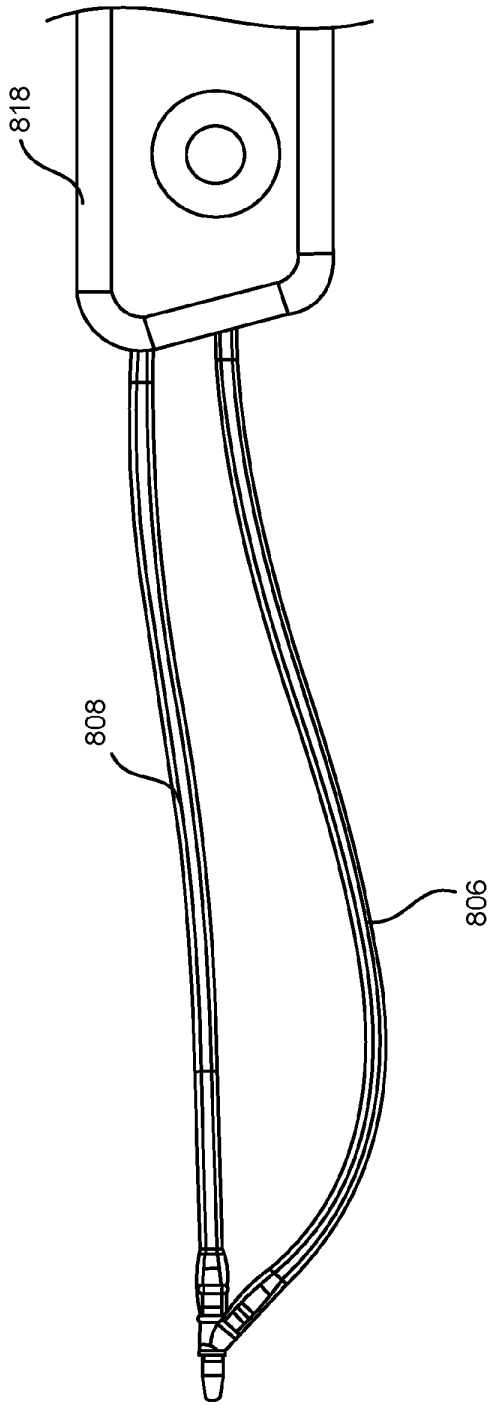


FIG. 8E

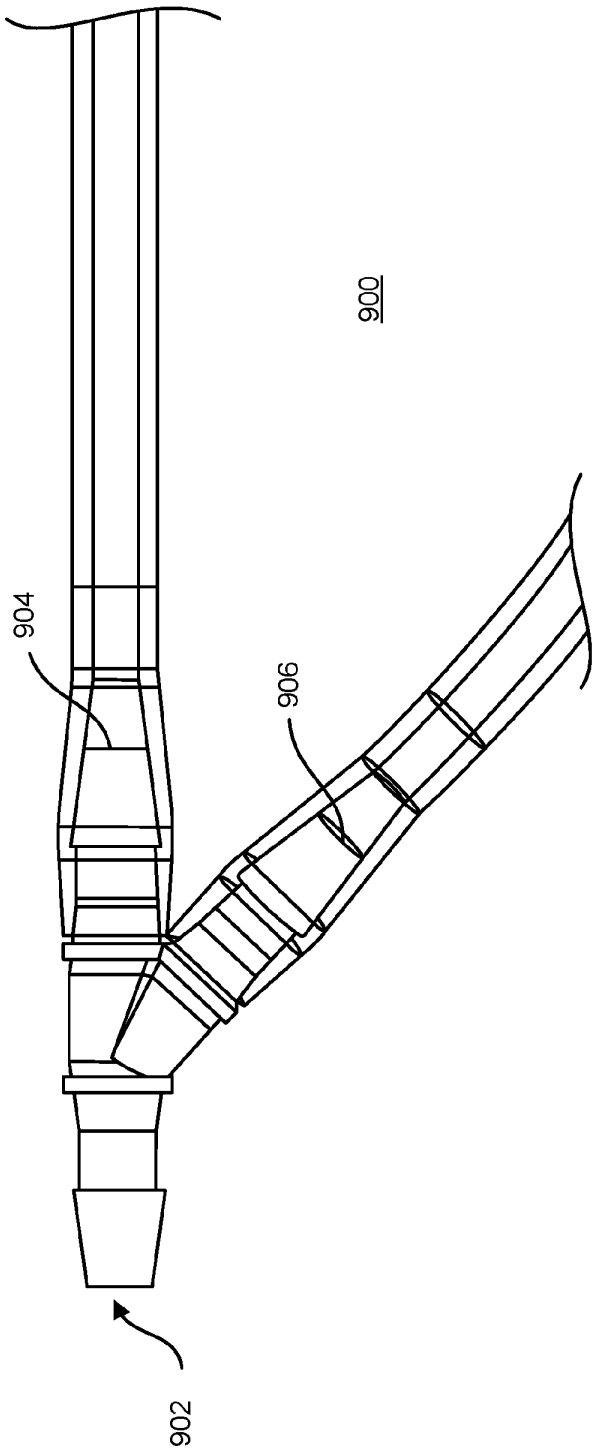


FIG. 9

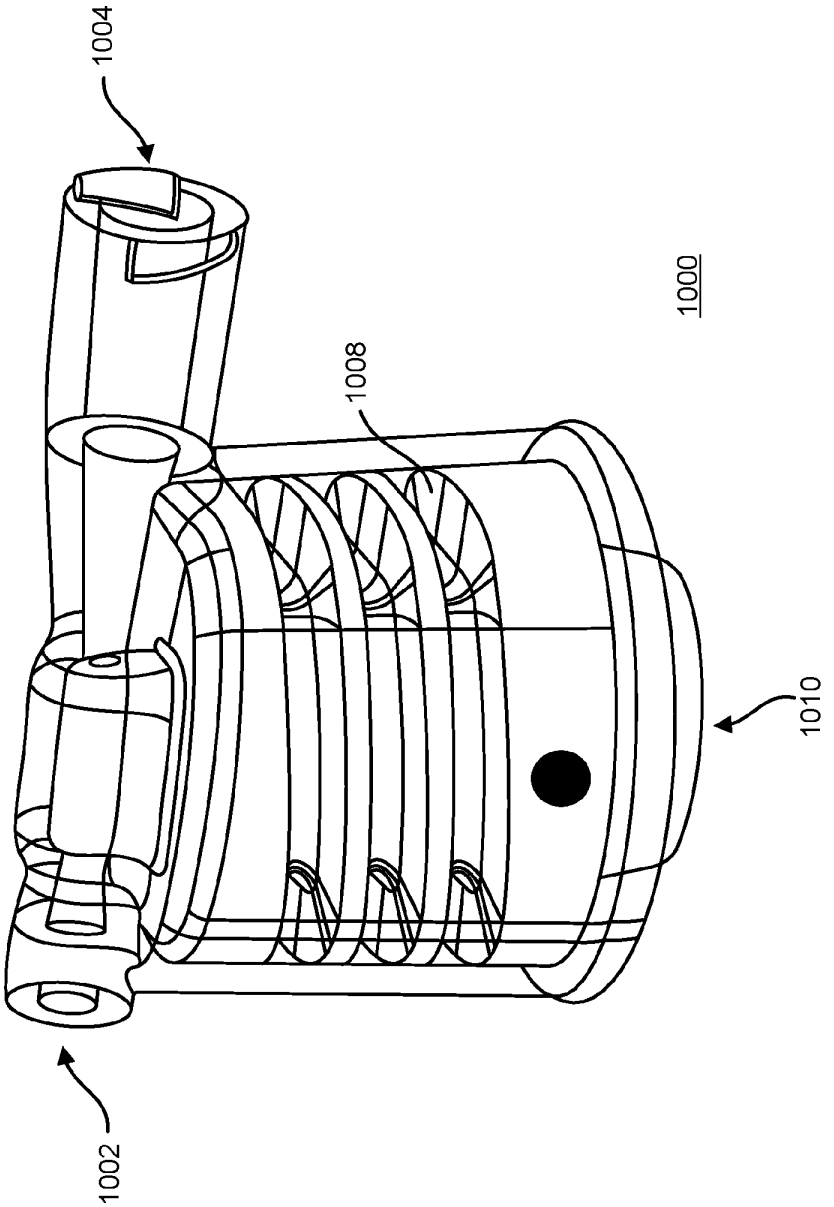


FIG. 10A

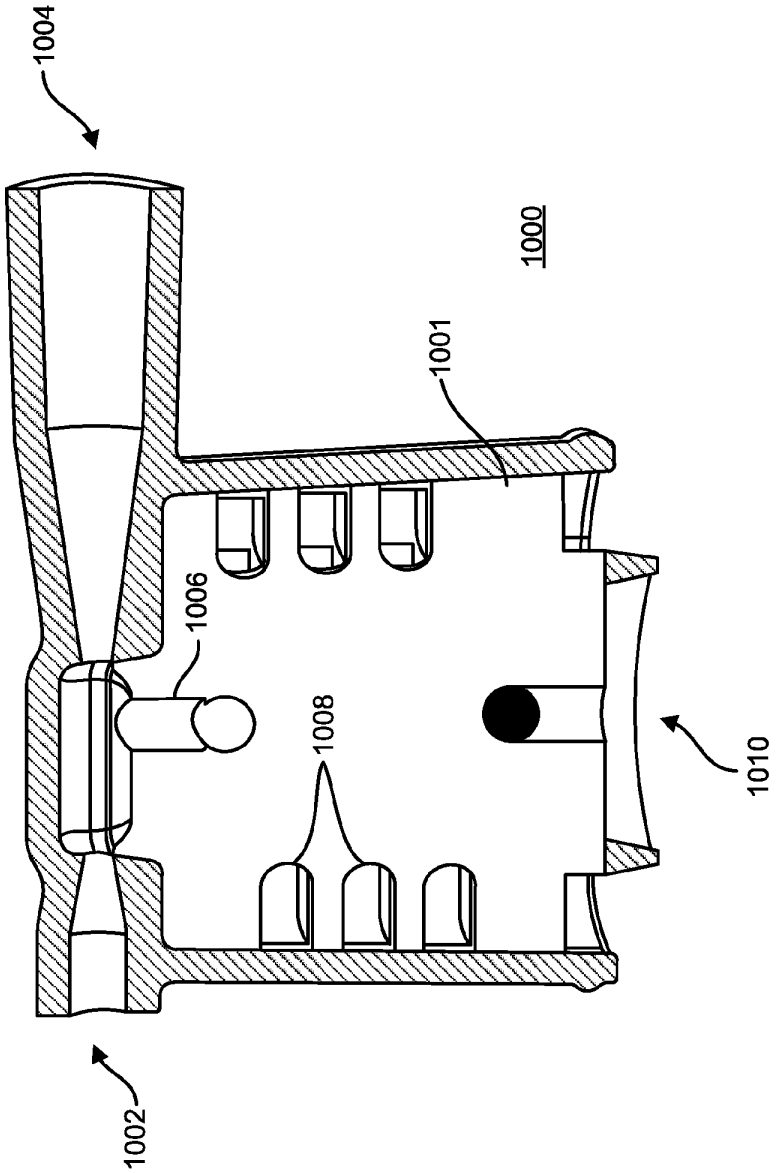


FIG. 10B

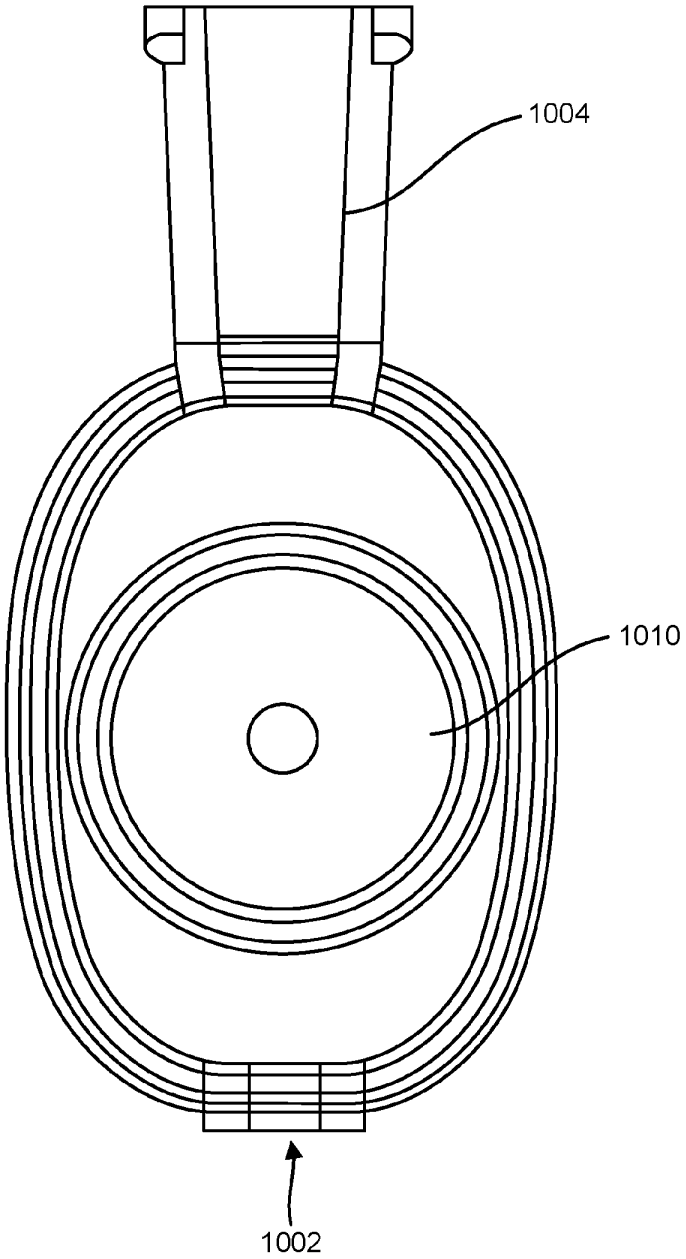


FIG. 10C

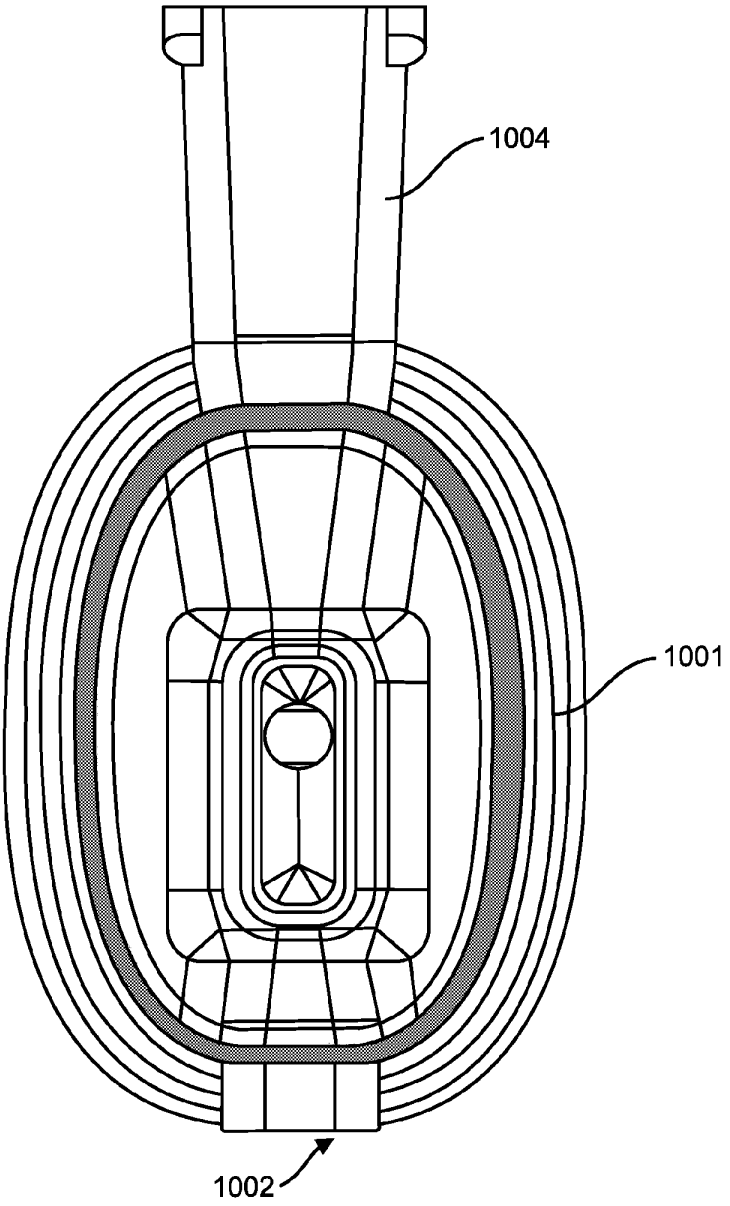


FIG. 10D

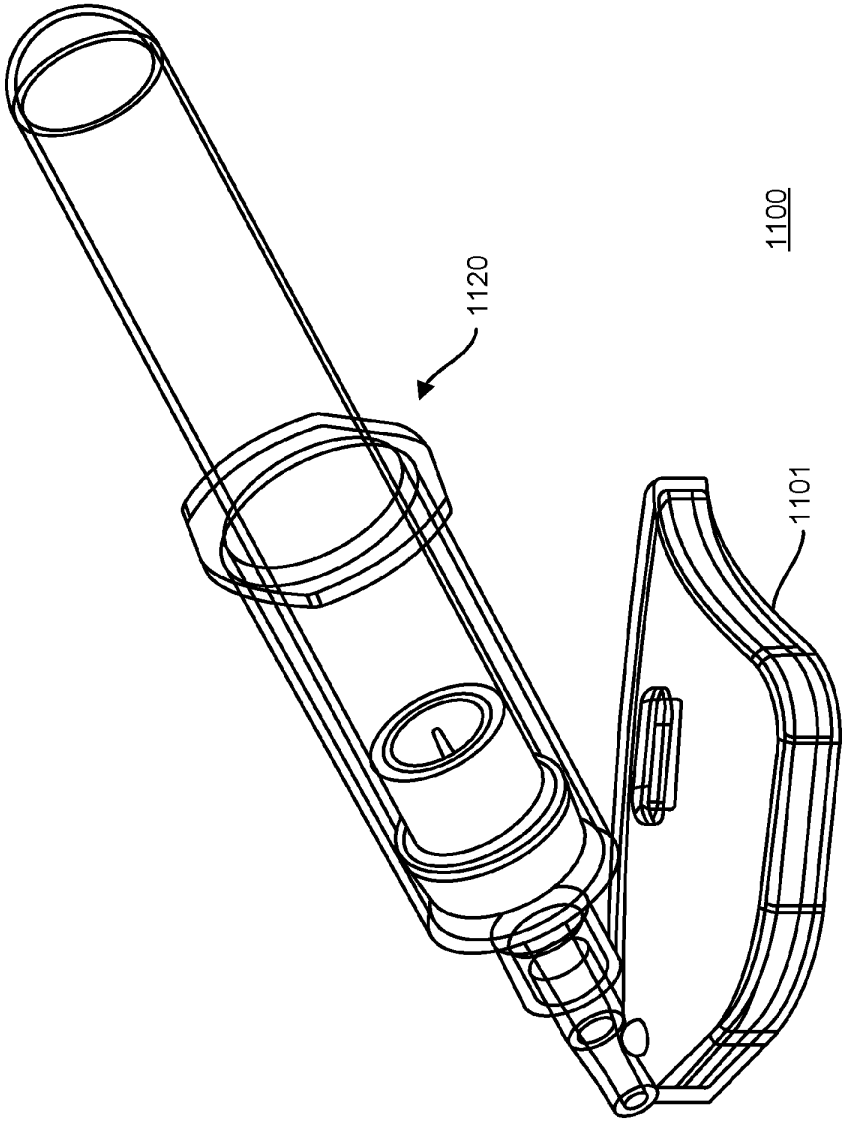


FIG. 11A

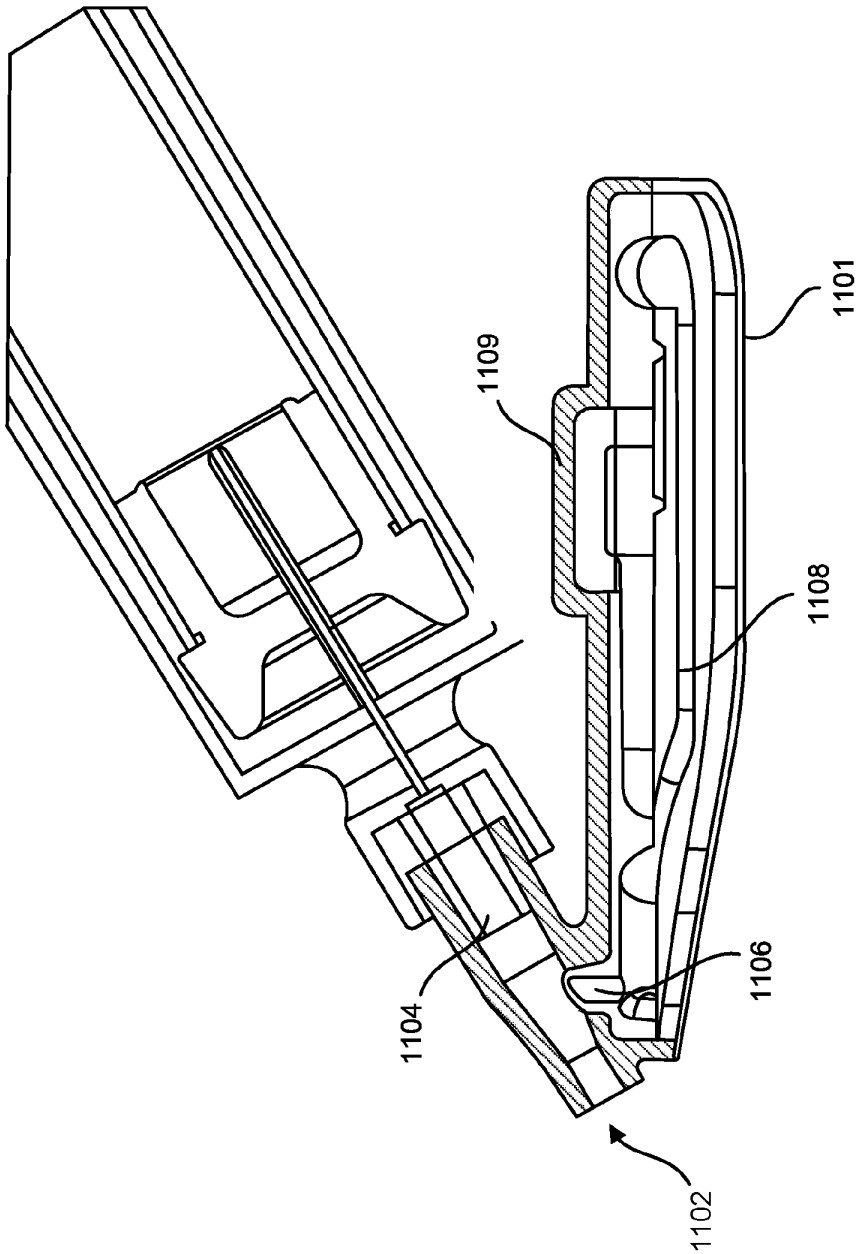


FIG. 11B

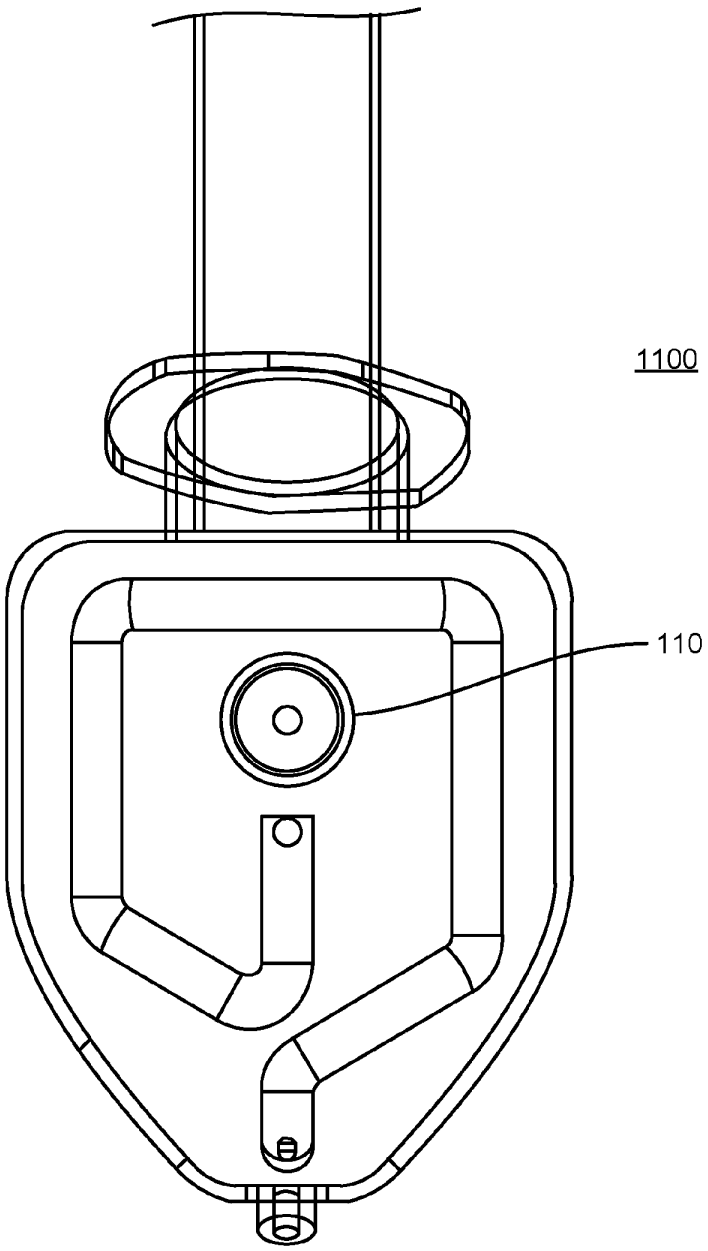


FIG. 11C

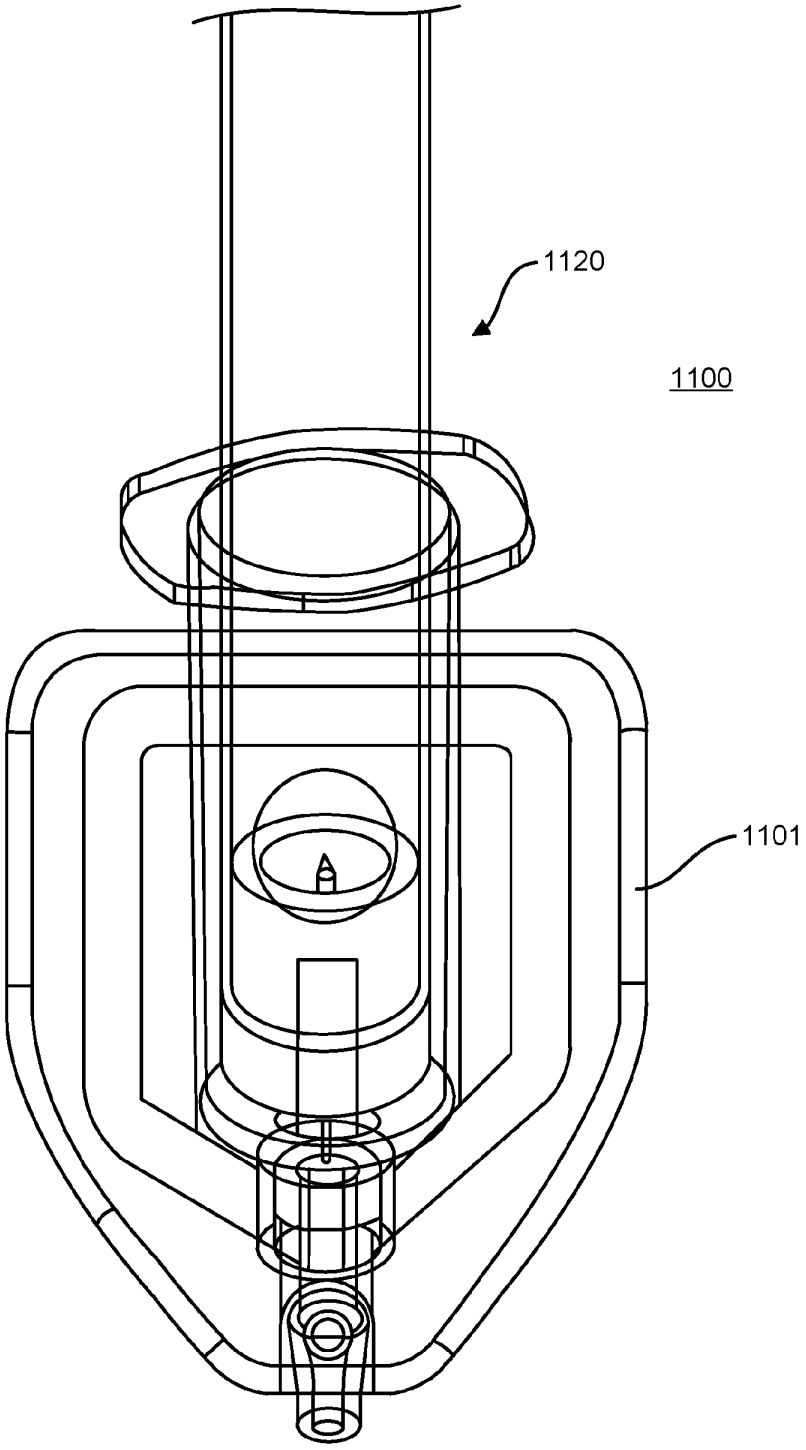


FIG. 11D

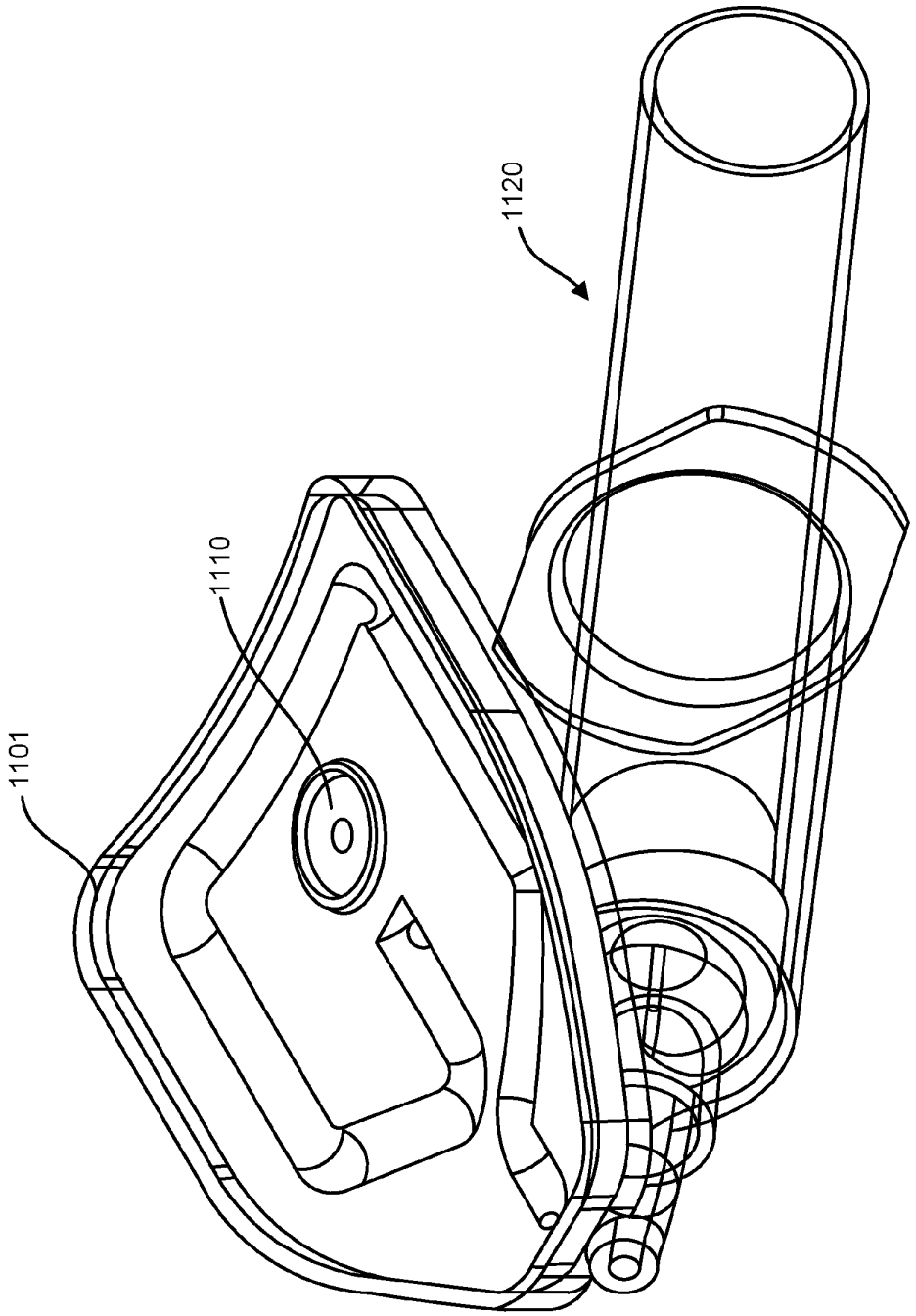


FIG. 11E

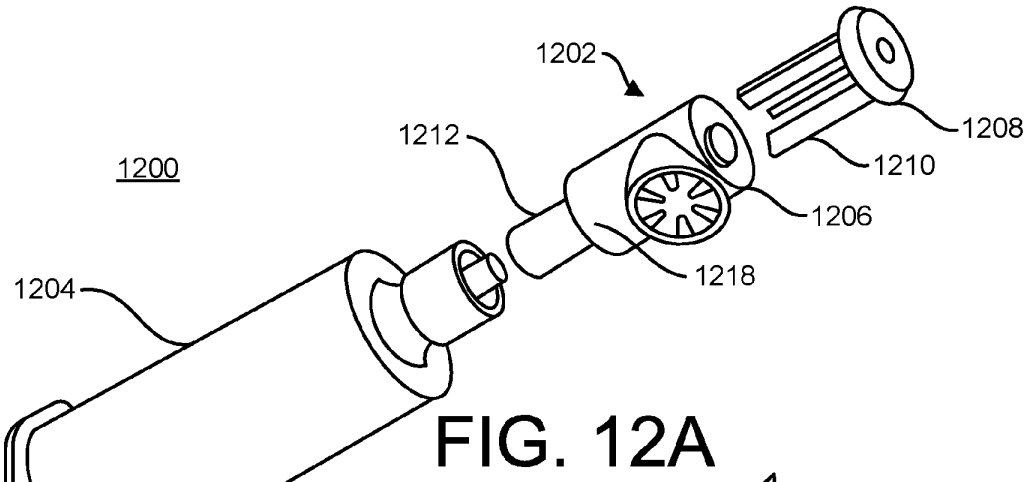


FIG. 12A

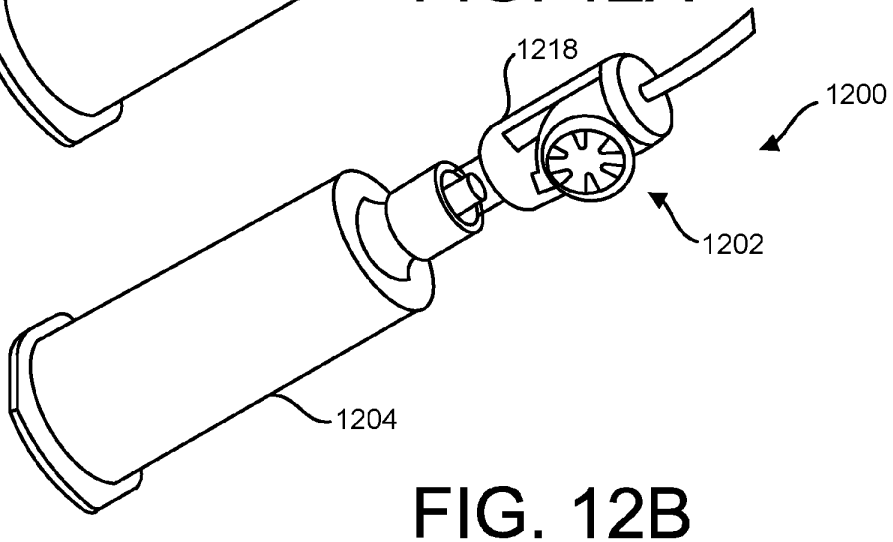


FIG. 12B

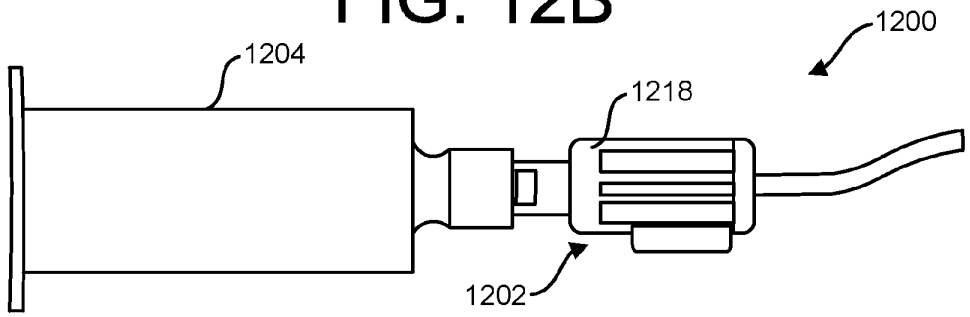


FIG. 12C

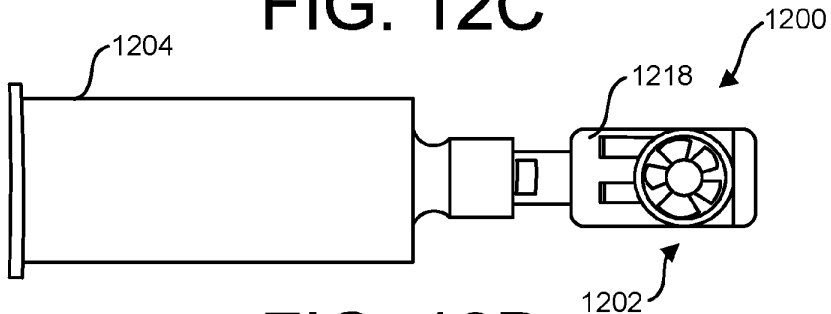


FIG. 12D

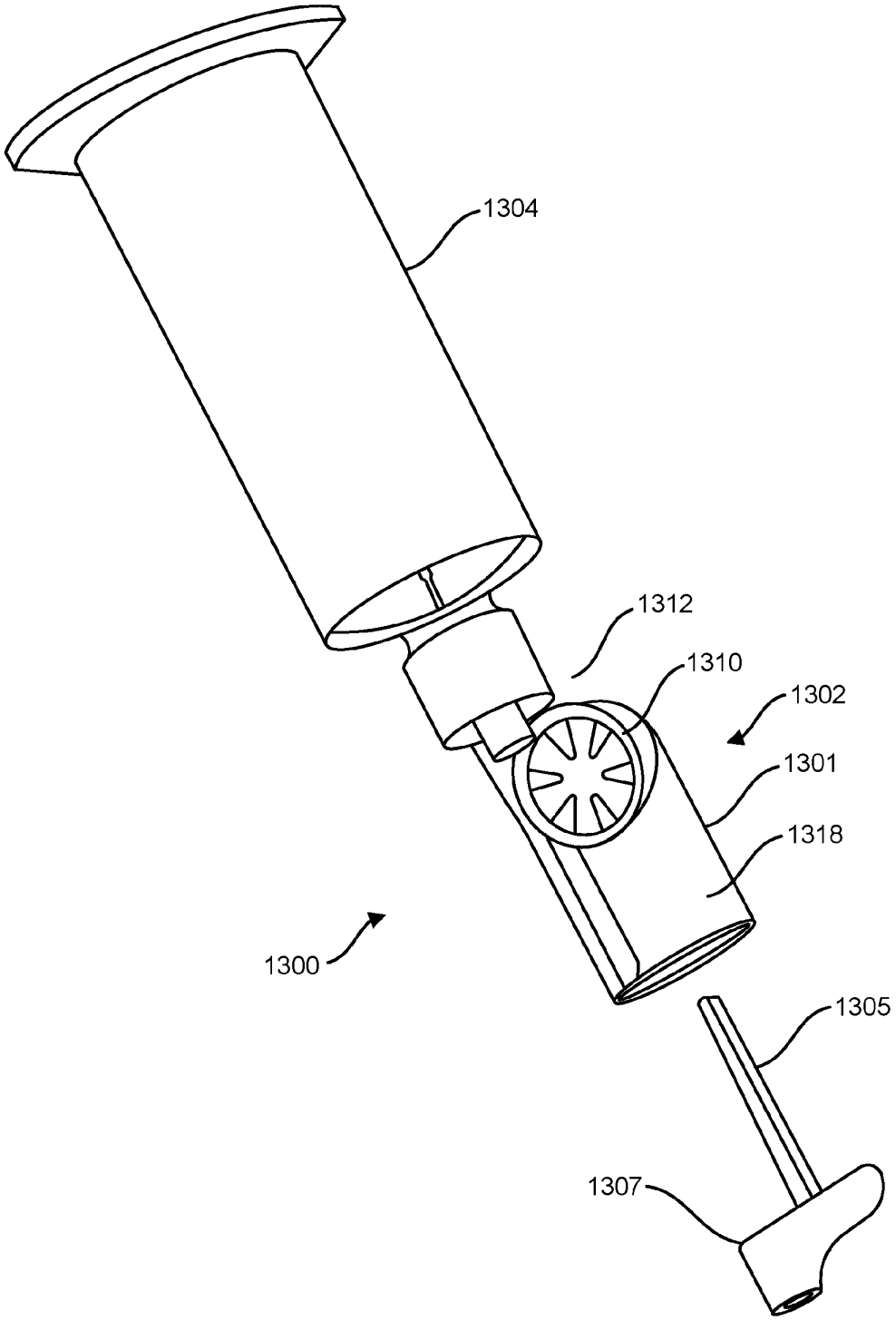


FIG. 13A

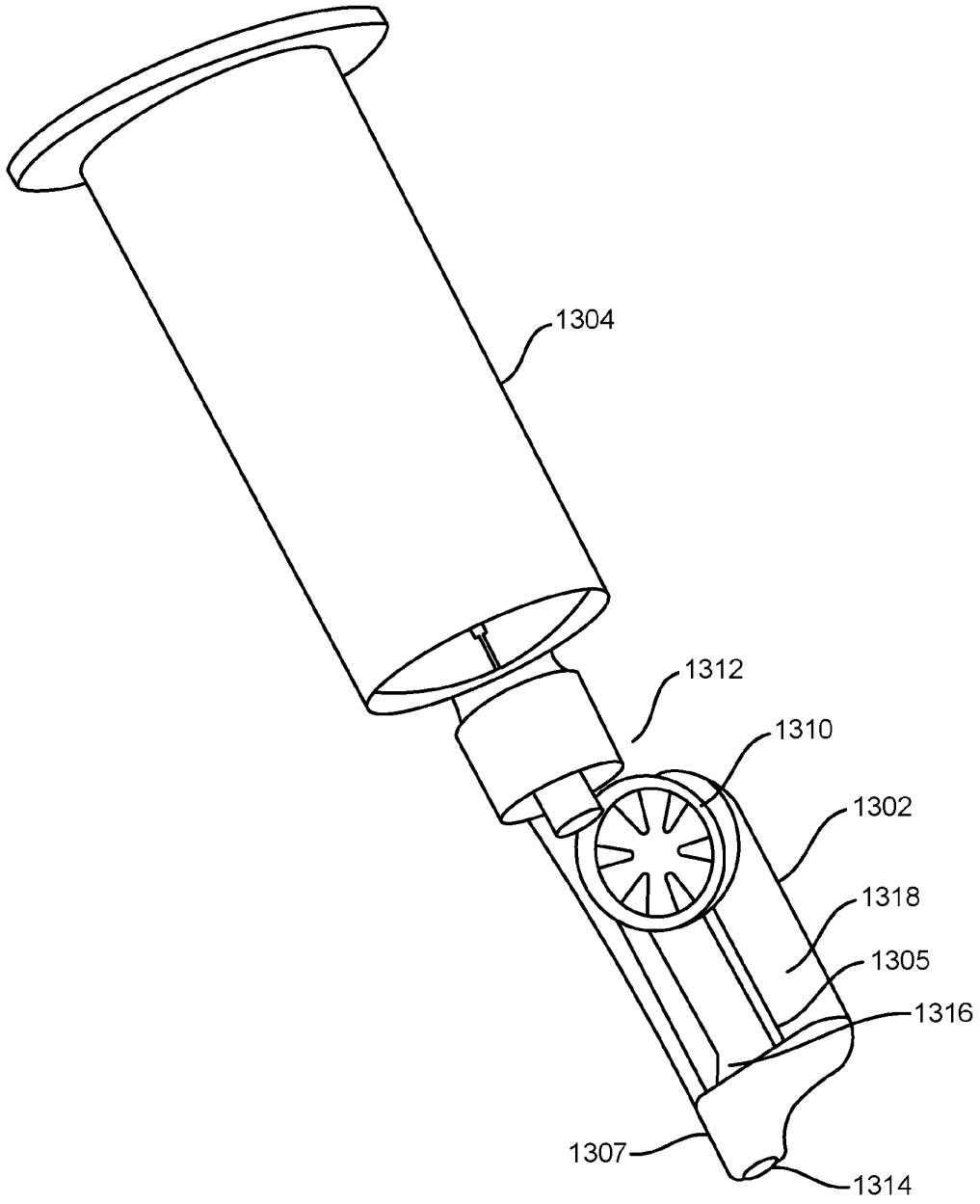


FIG. 13B

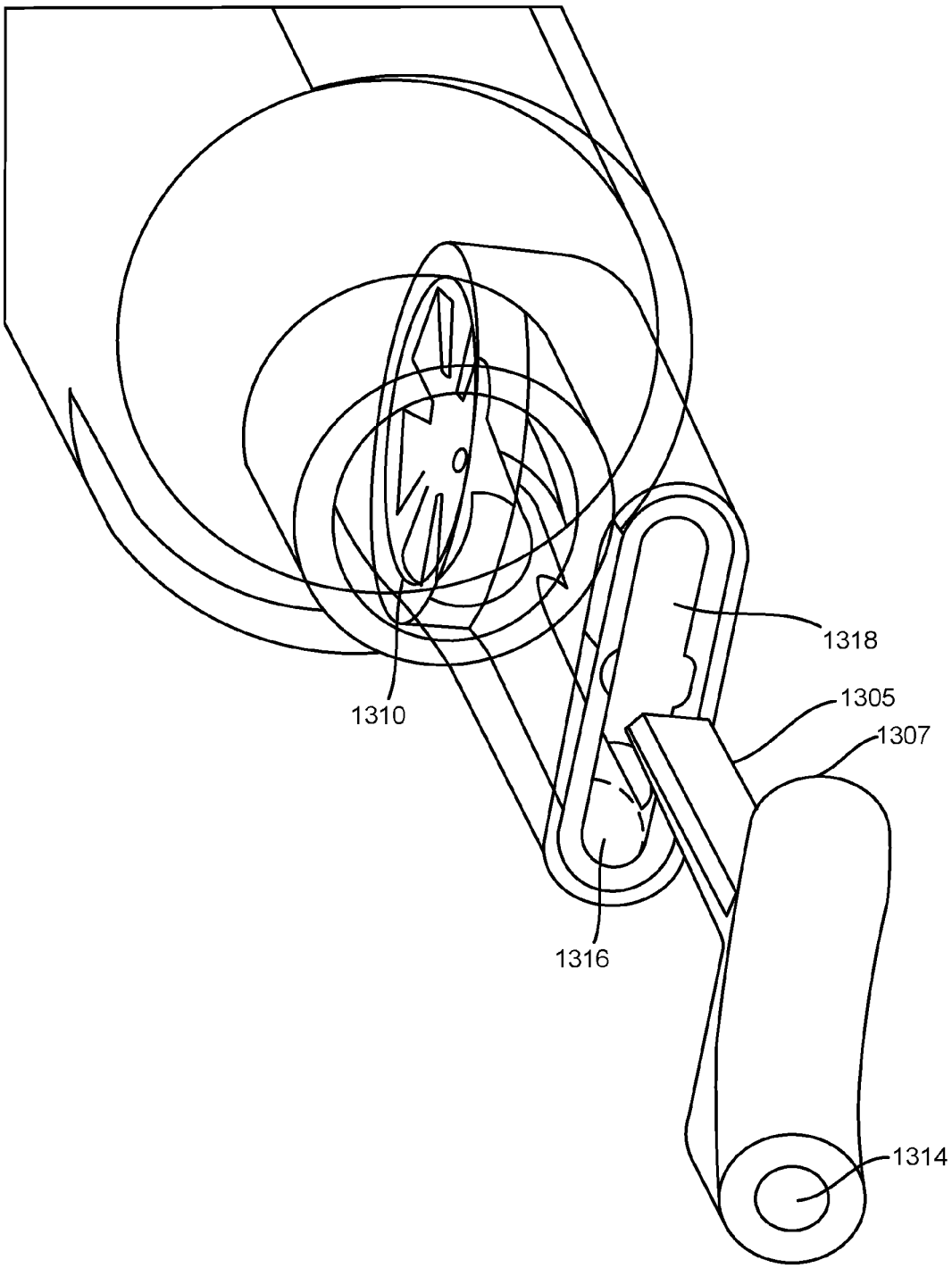


FIG. 13C

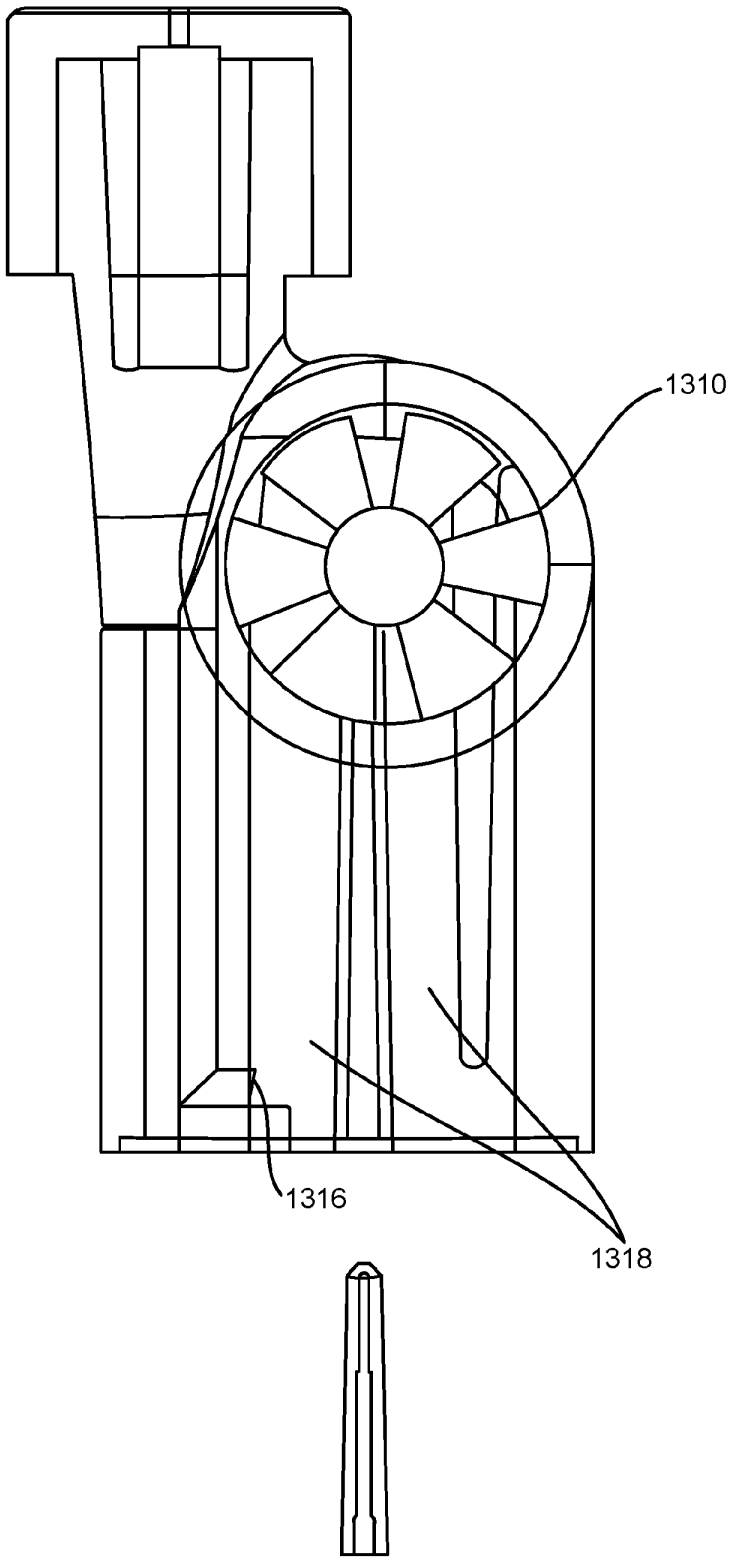


FIG. 13D

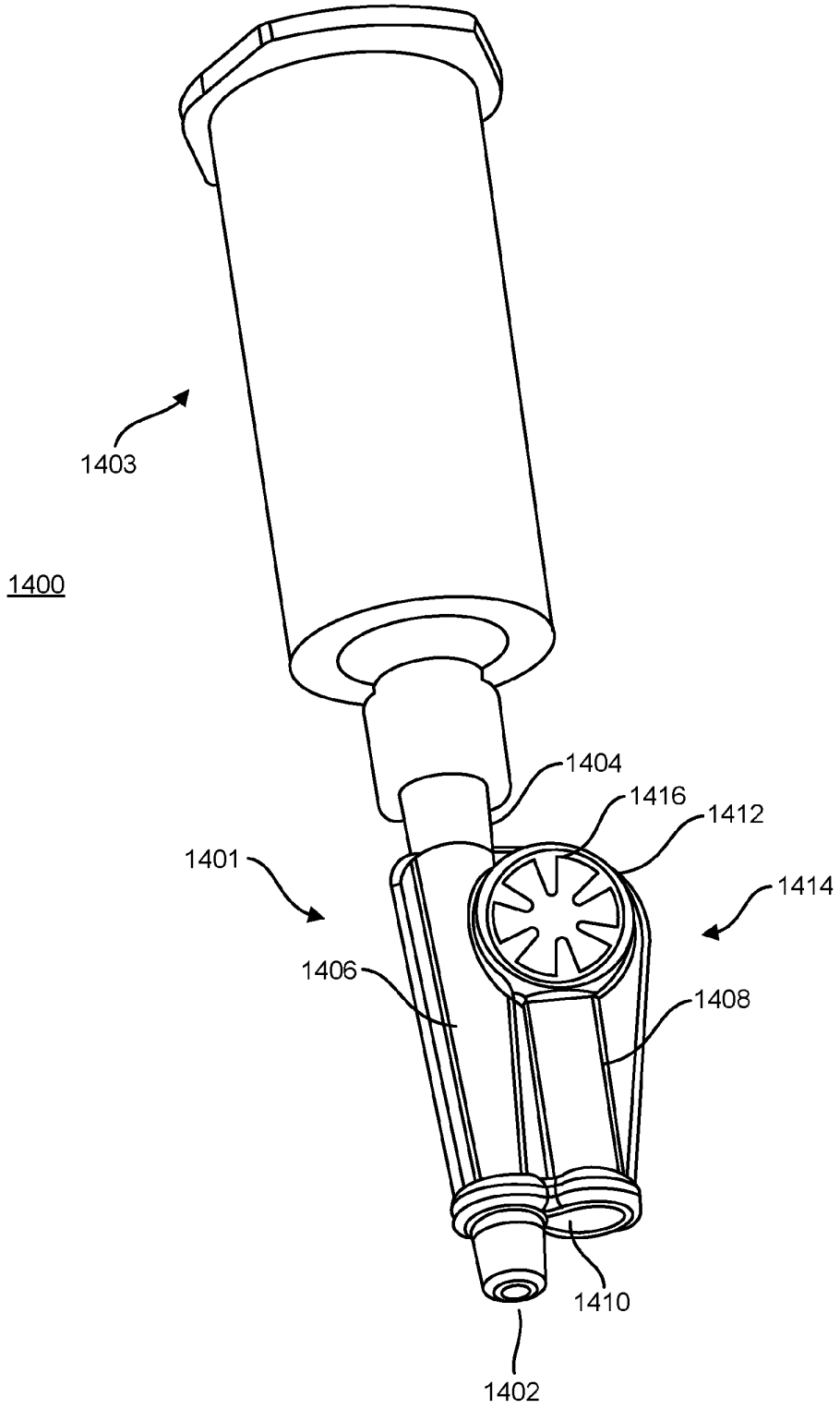


FIG. 14A

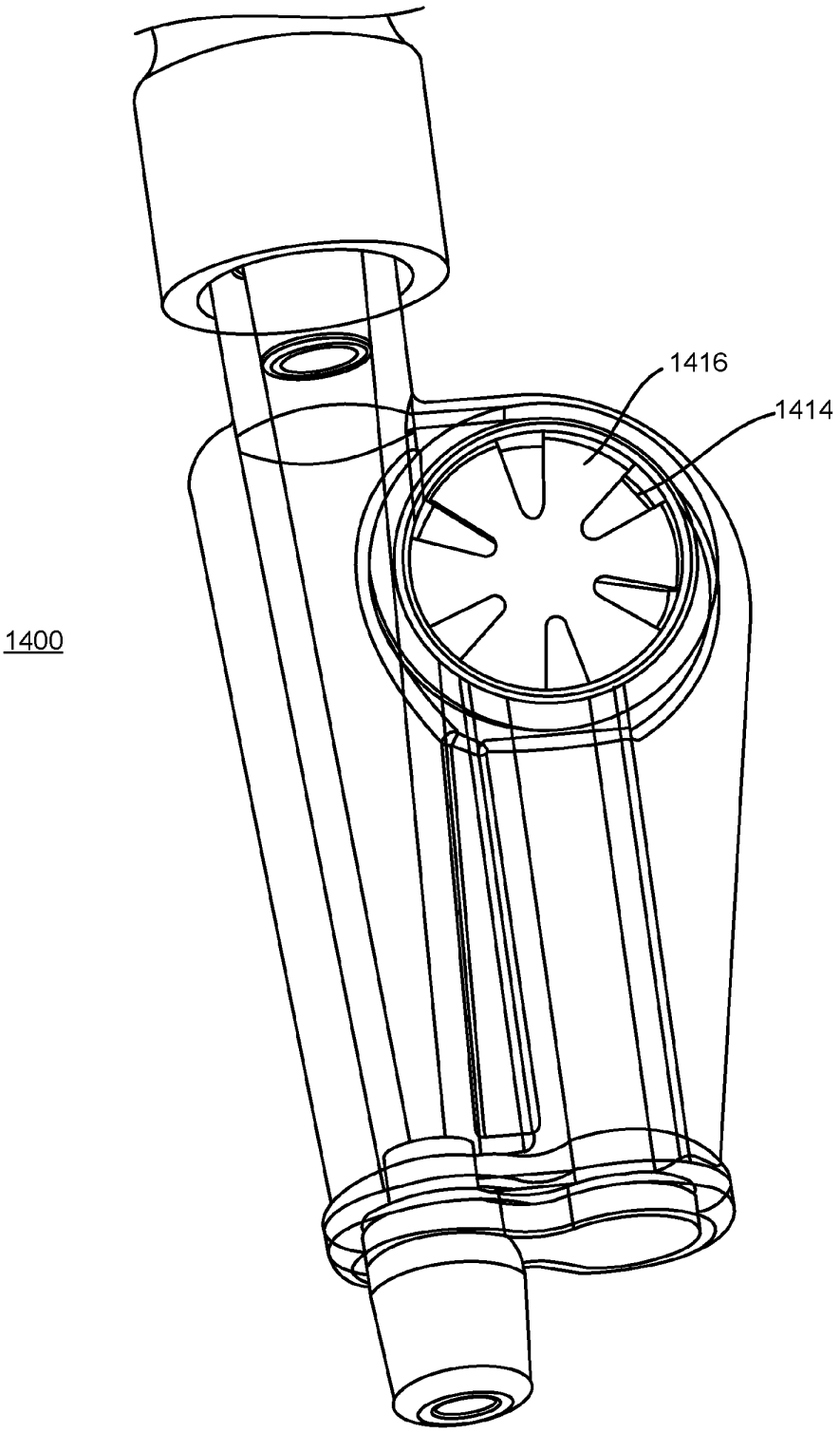


FIG. 14B

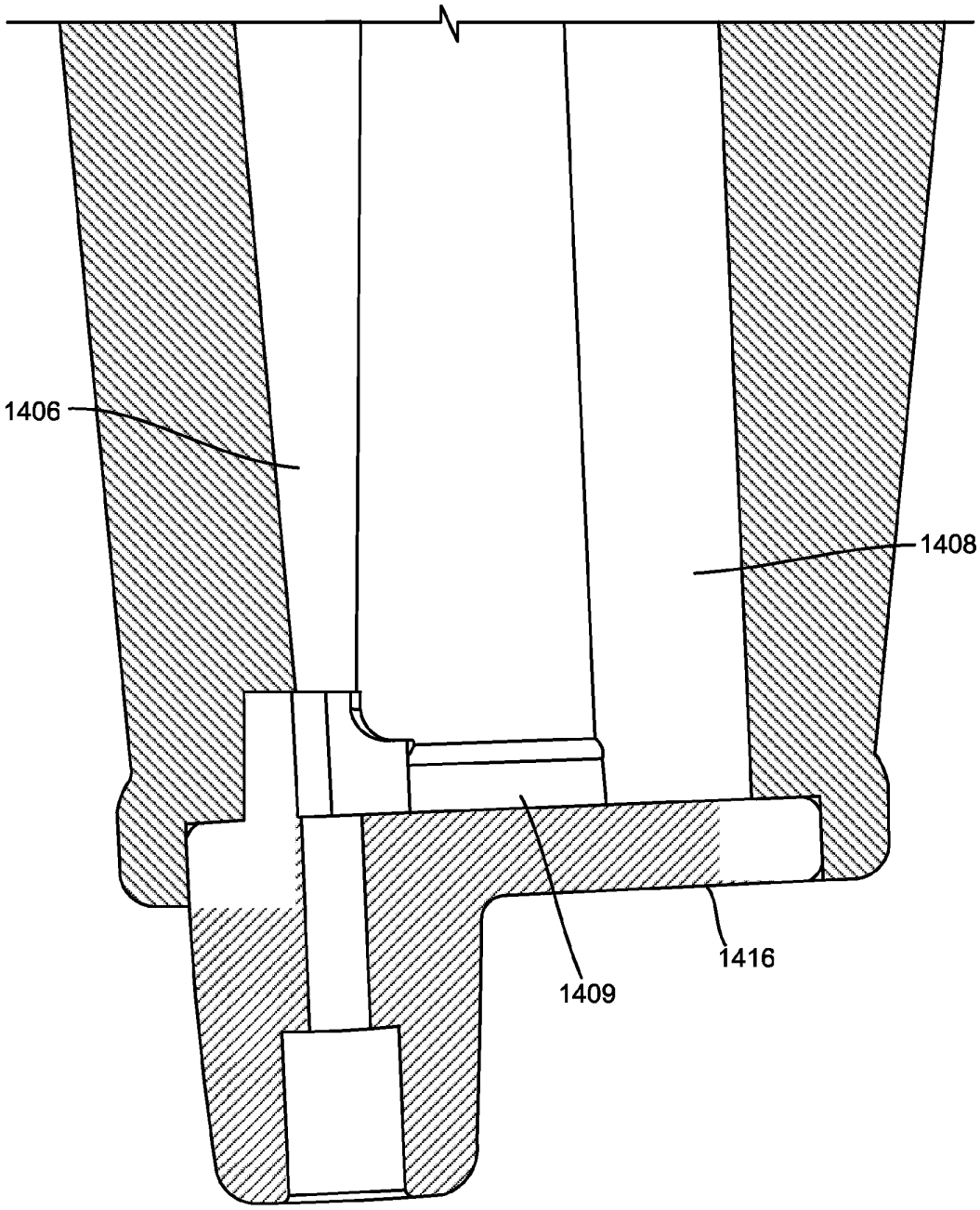


FIG. 14C

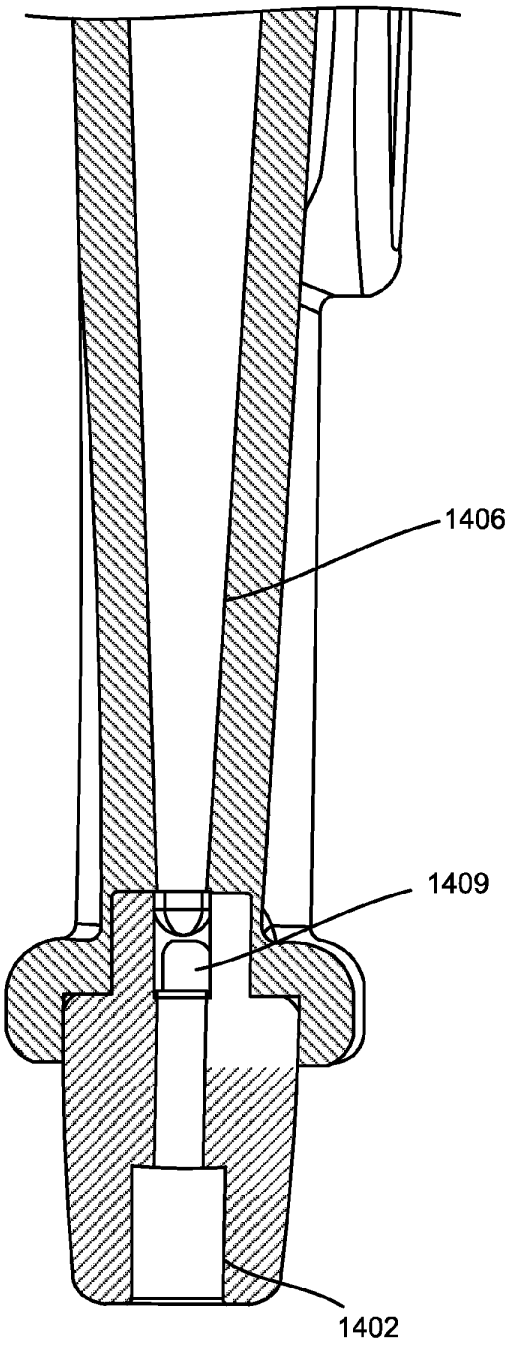


FIG. 14D

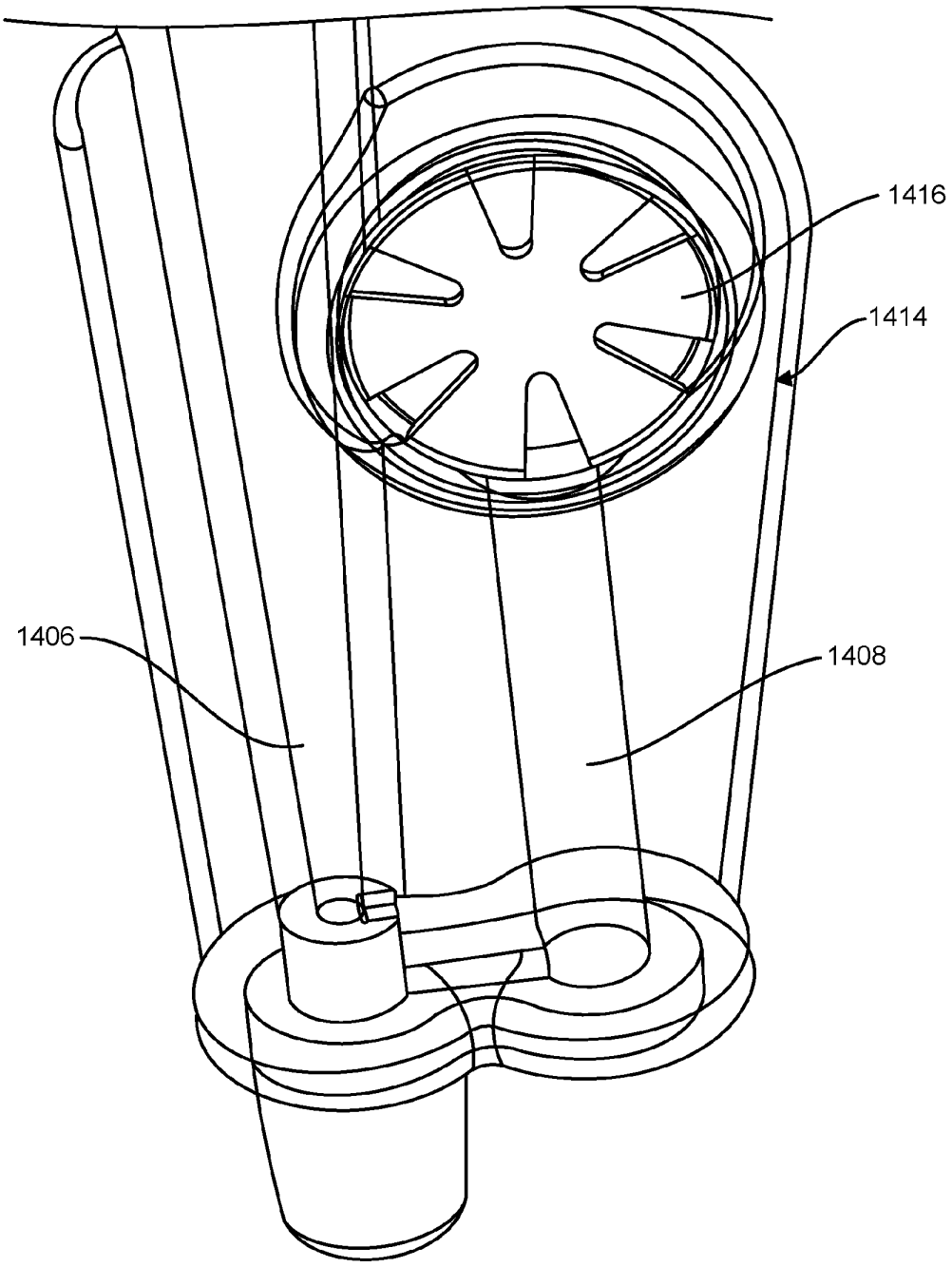


FIG. 14E

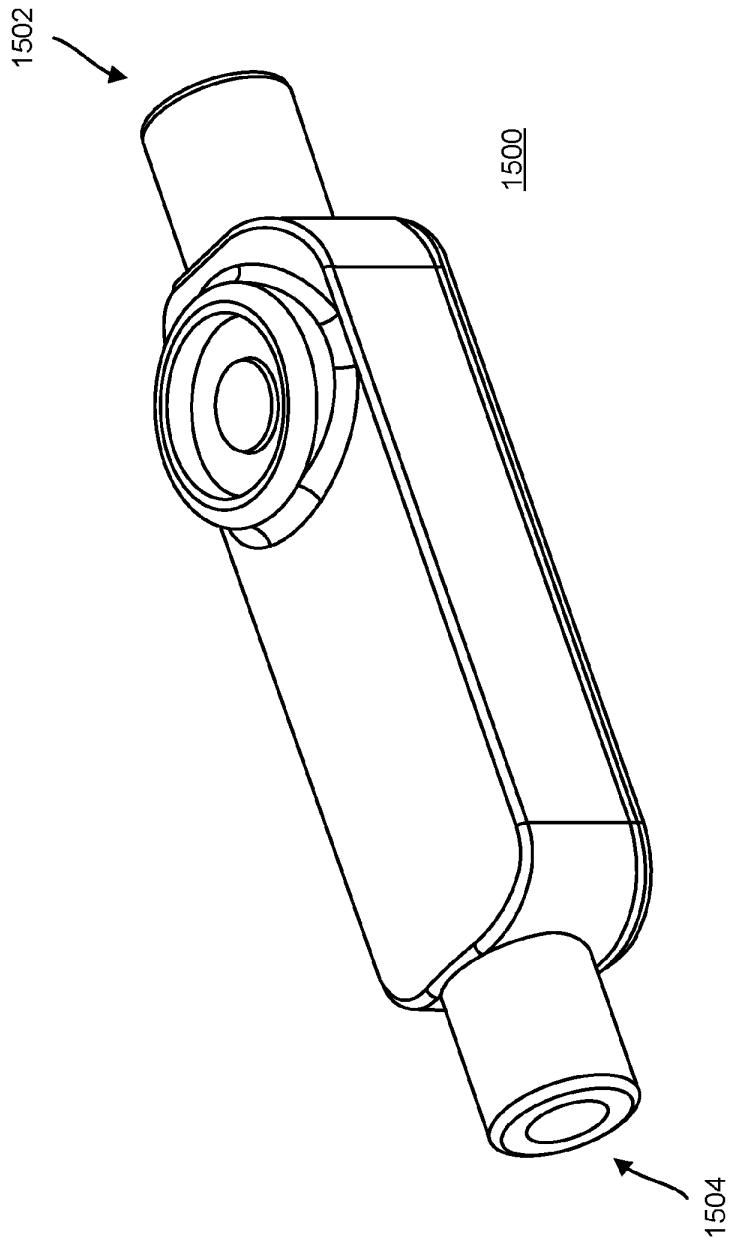


FIG. 15A

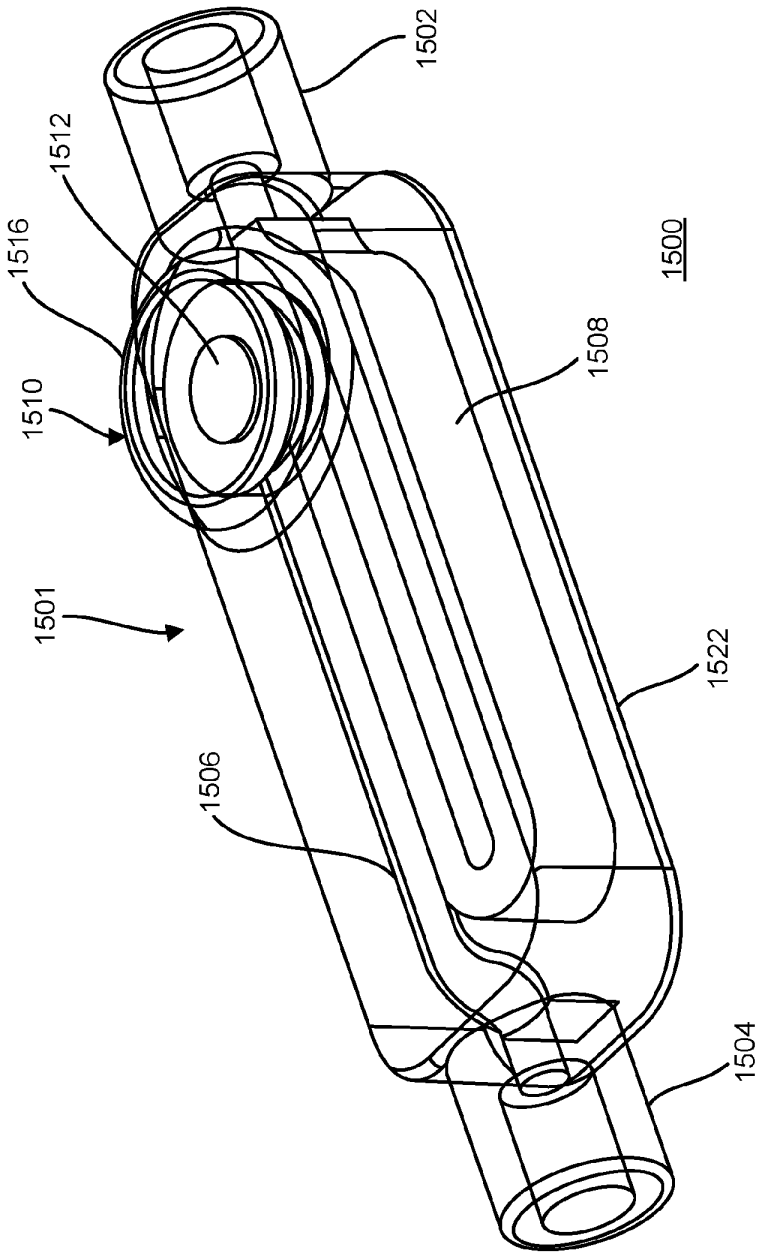


FIG. 15B

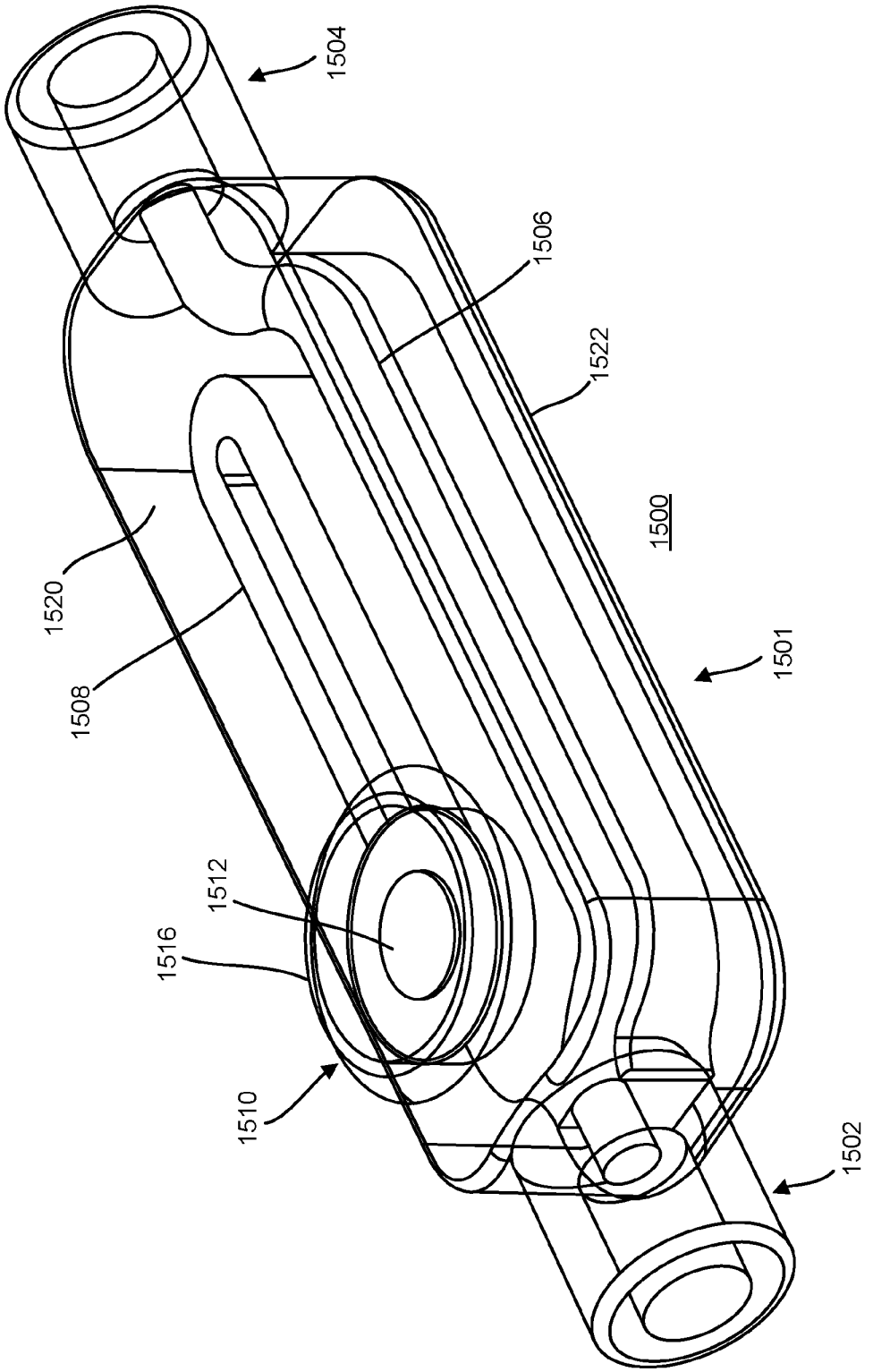


FIG. 15C

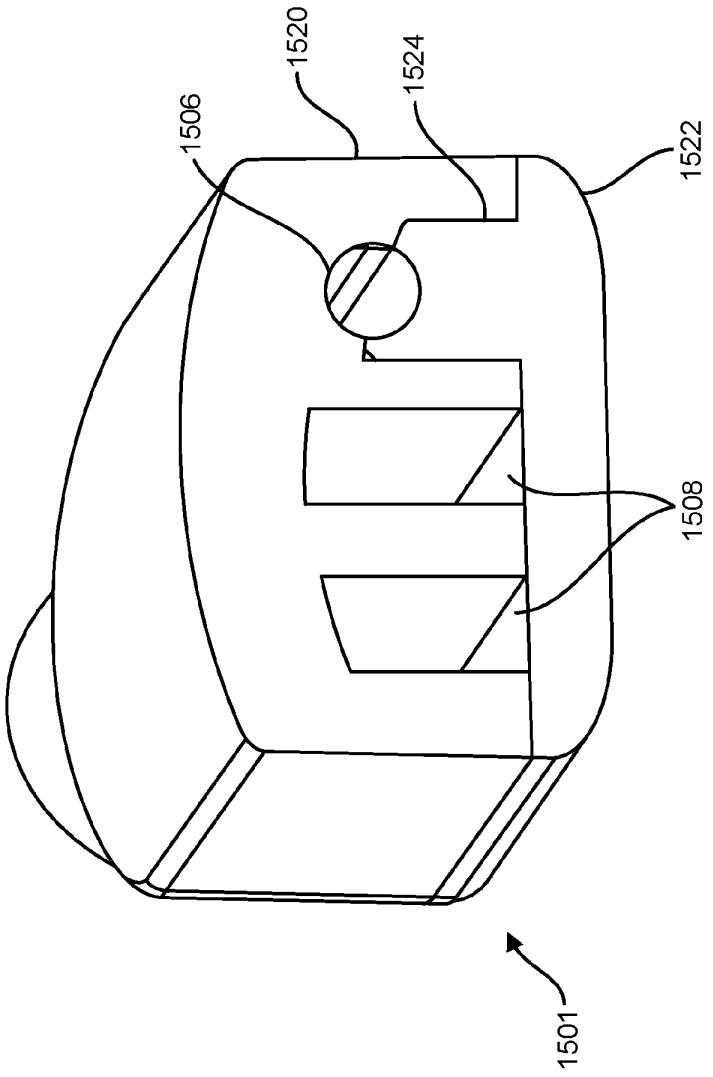


FIG. 15D

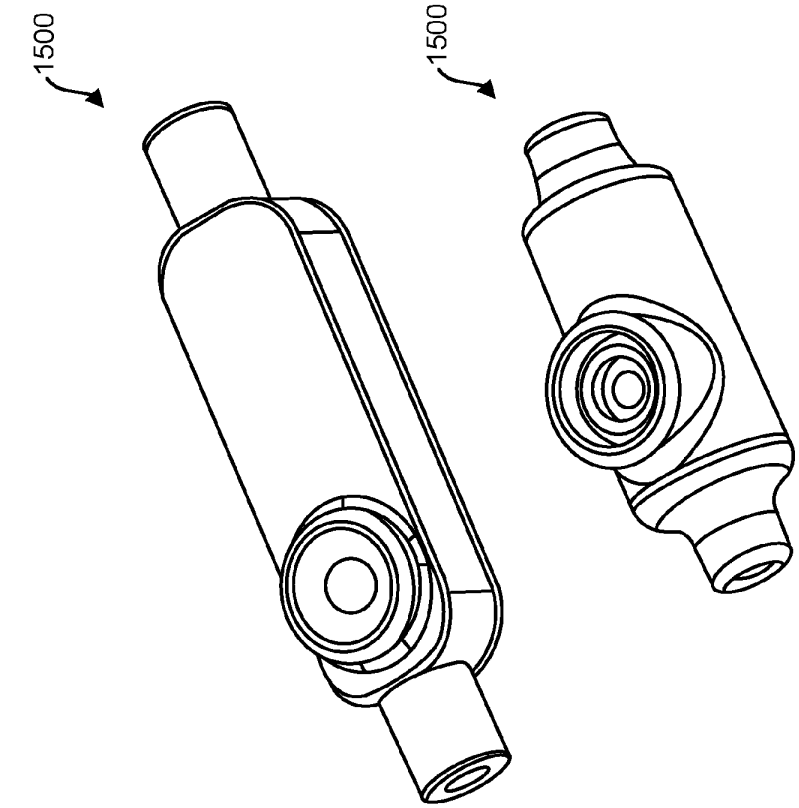


FIG. 15F

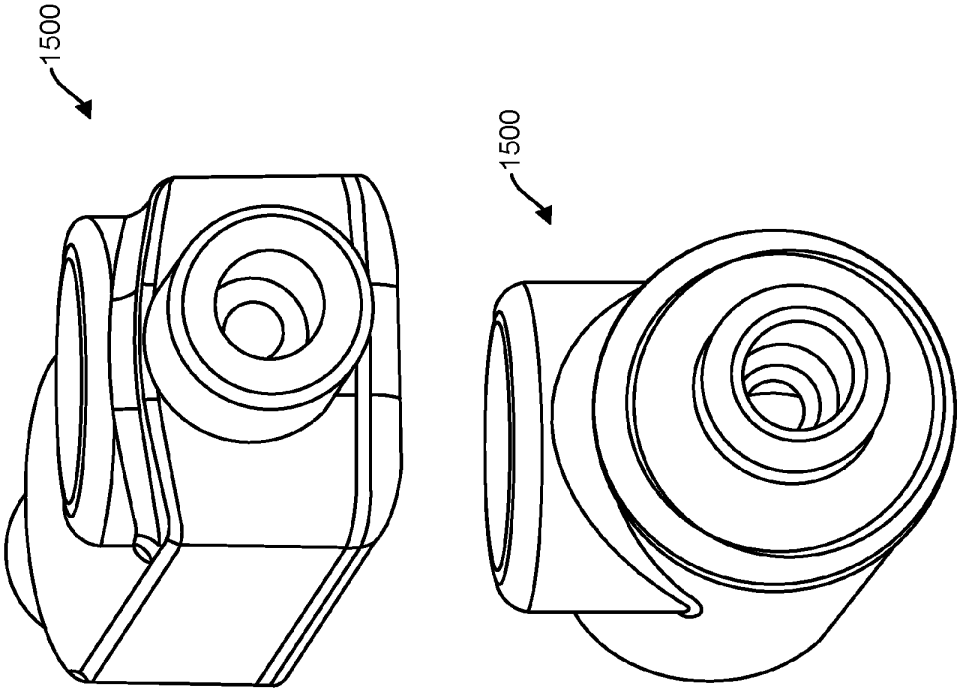


FIG. 15E

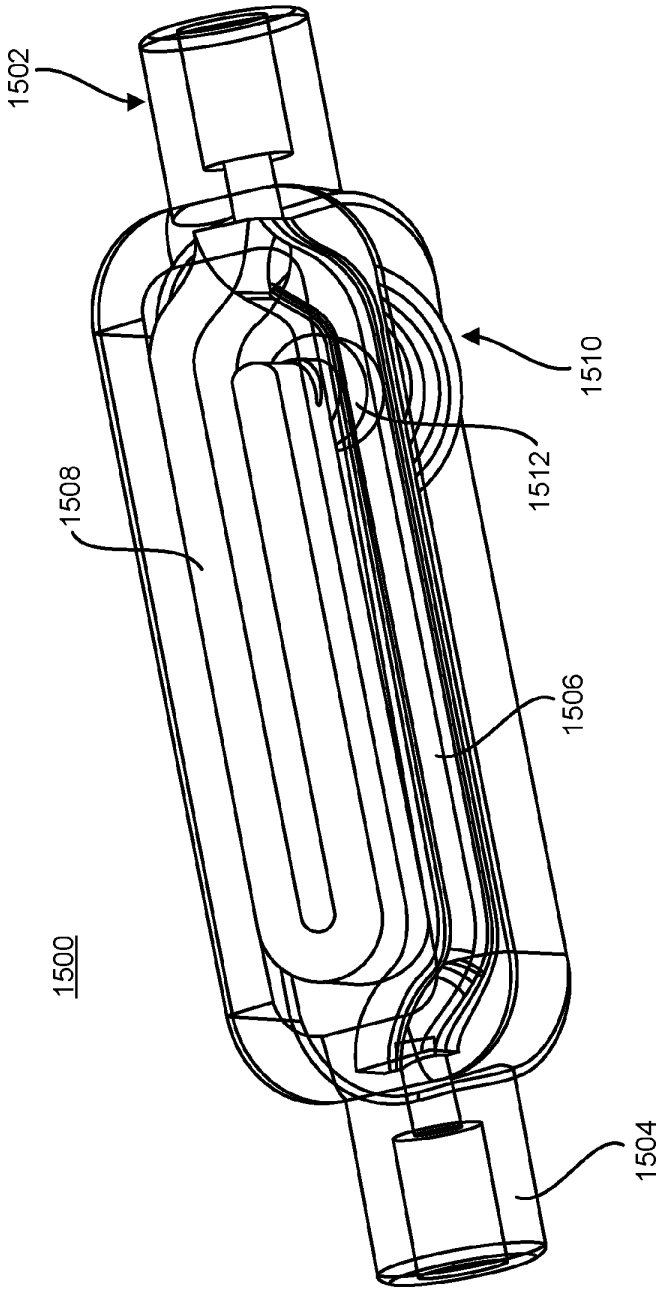


FIG. 15G

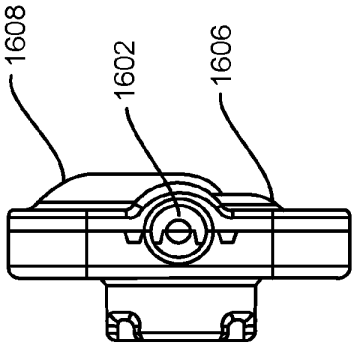


FIG. 16C

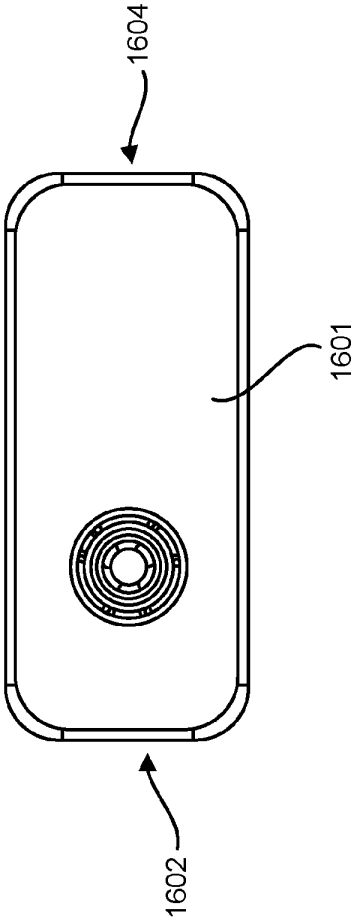


FIG. 16A

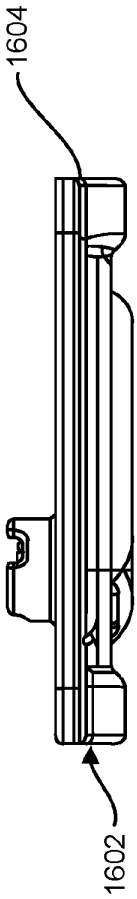


FIG. 16B

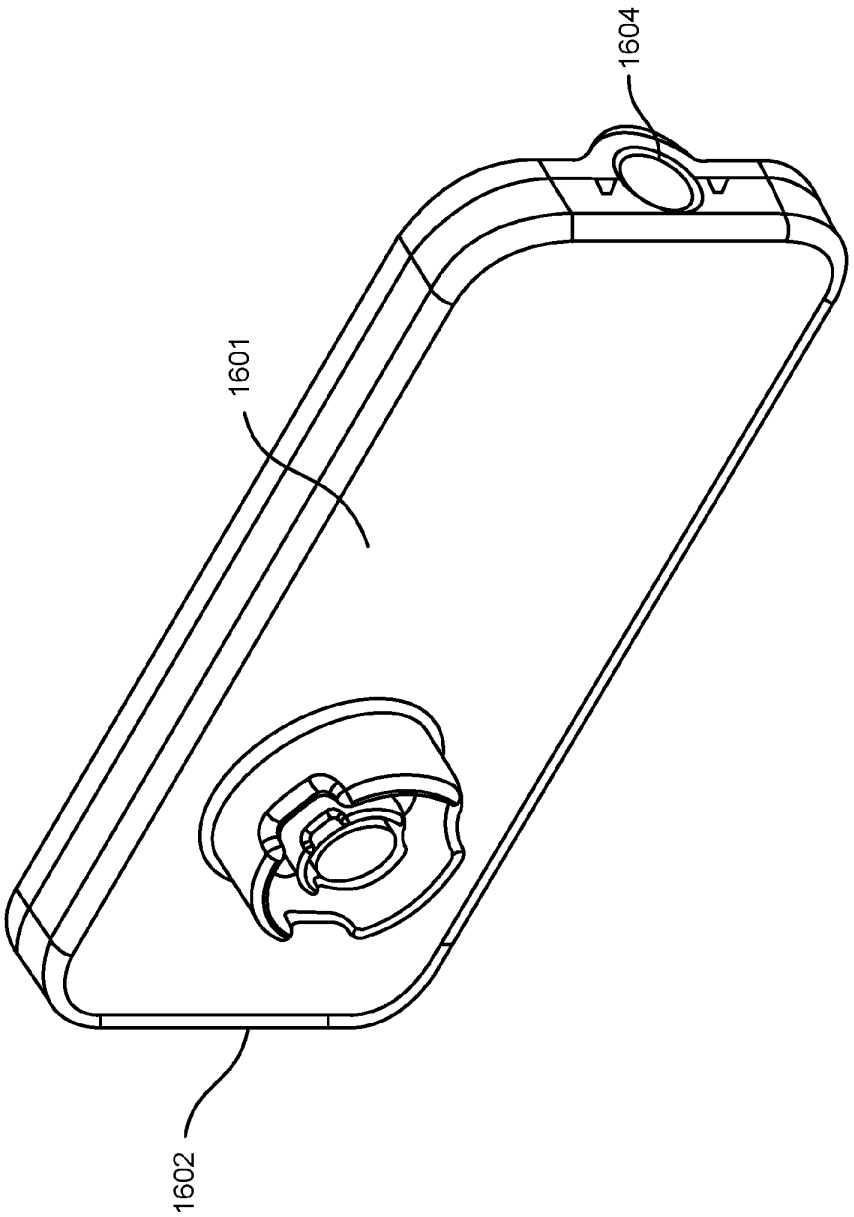


FIG. 16D

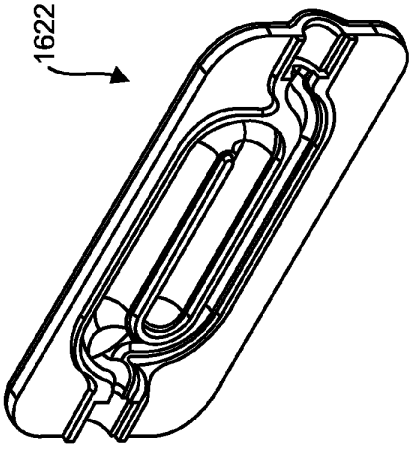


FIG. 17B



FIG. 17E

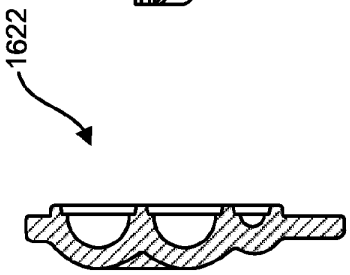


FIG. 17D

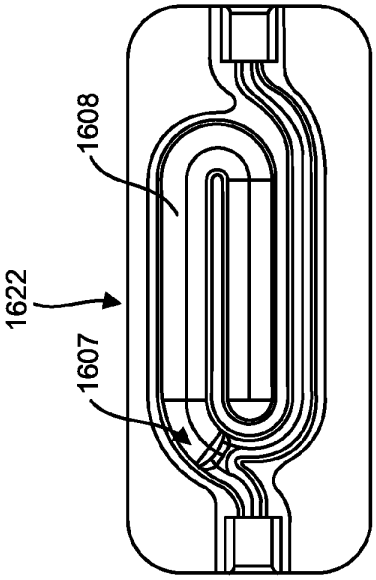


FIG. 17A

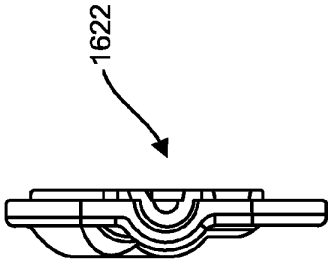


FIG. 17C

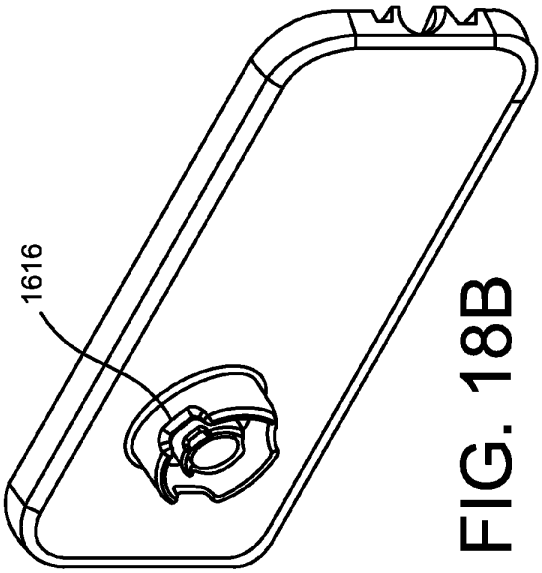


FIG. 18B

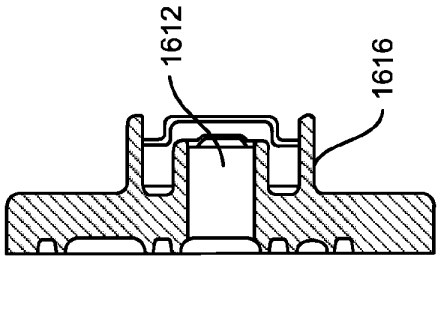


FIG. 18F

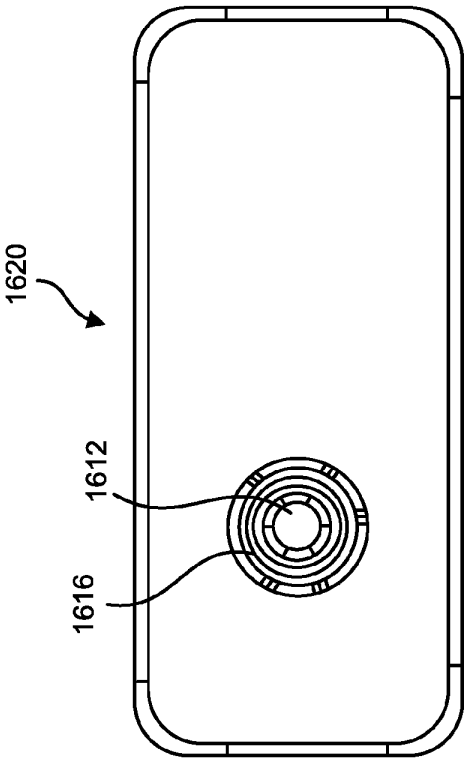


FIG. 18A

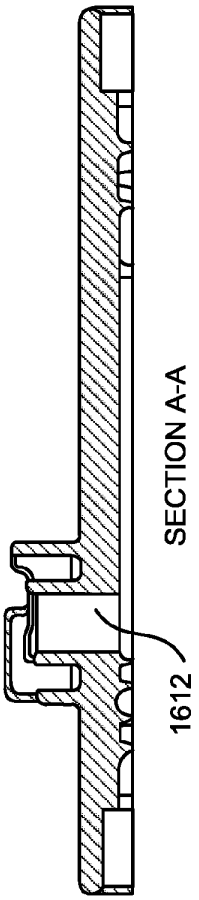


FIG. 18D

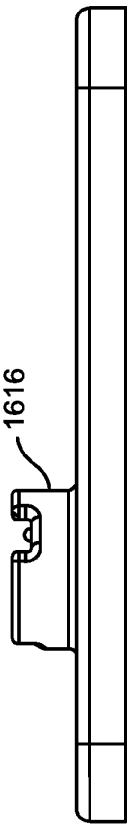


FIG. 18E

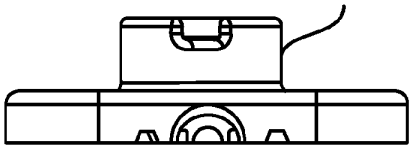


FIG. 18C

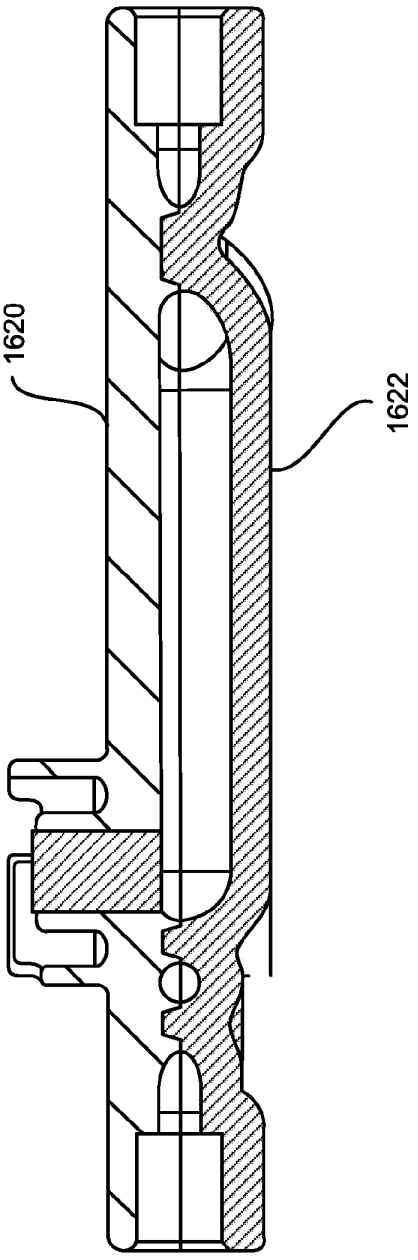


FIG. 19A

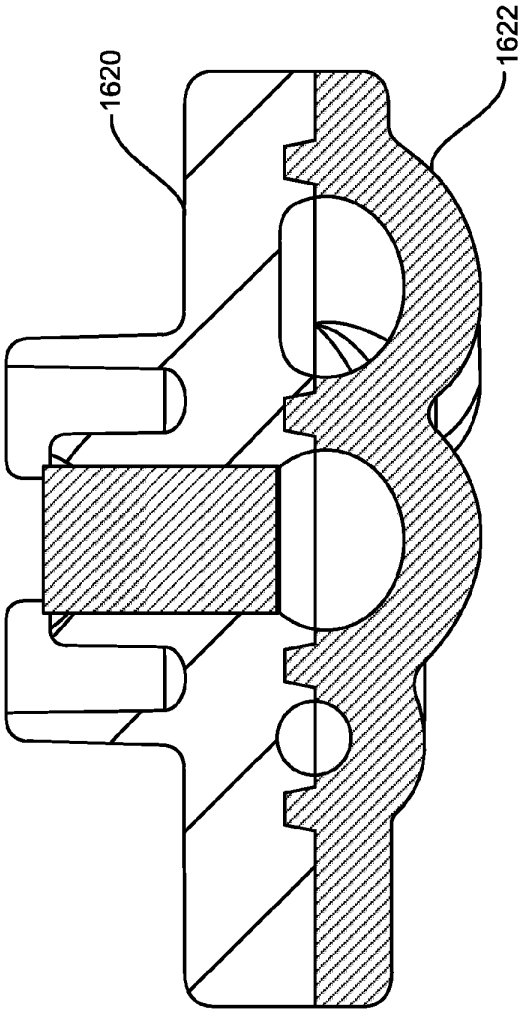


FIG. 19B

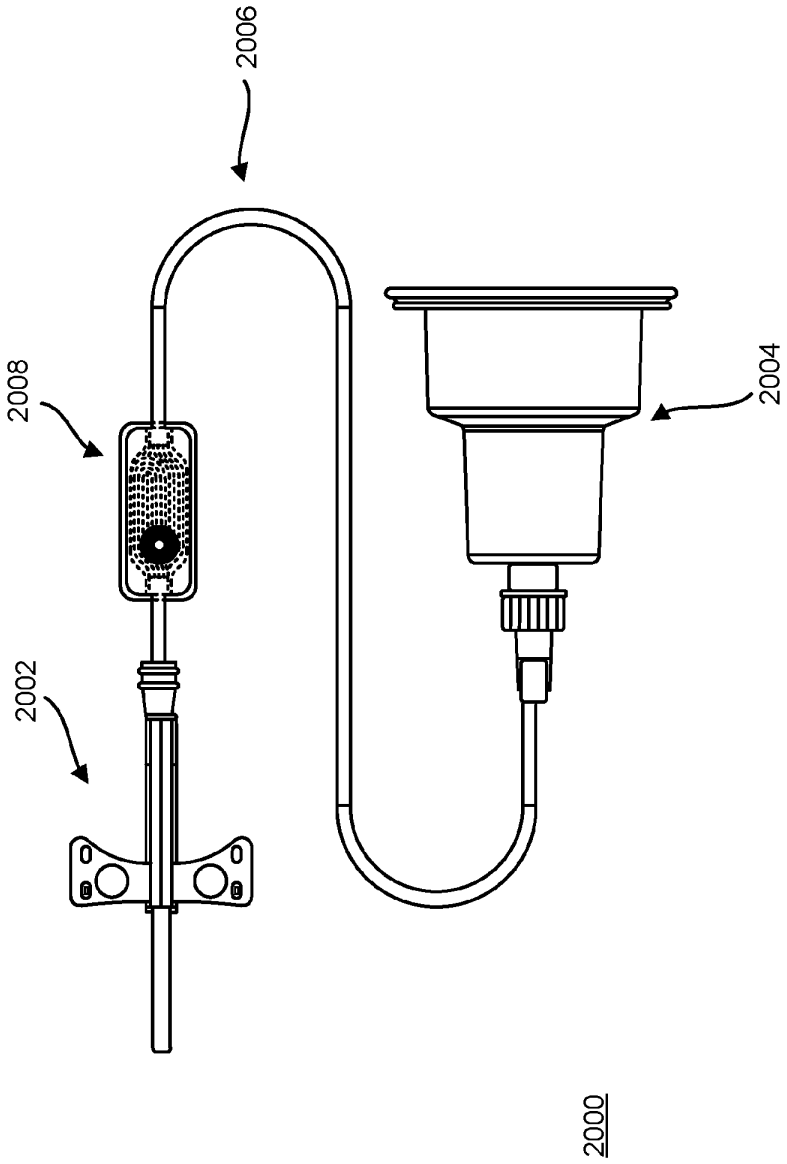


FIG. 20

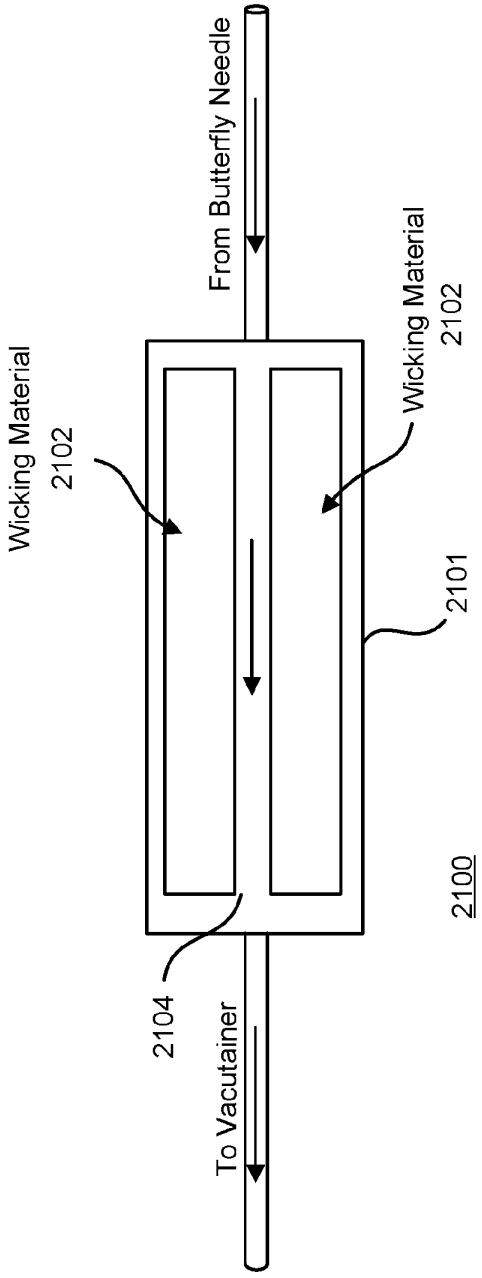

From Butterfly Needle
Wicking Material
2102
Wicking Material
2102
2101
2100
2104
To Vacutainer

FIG. 21

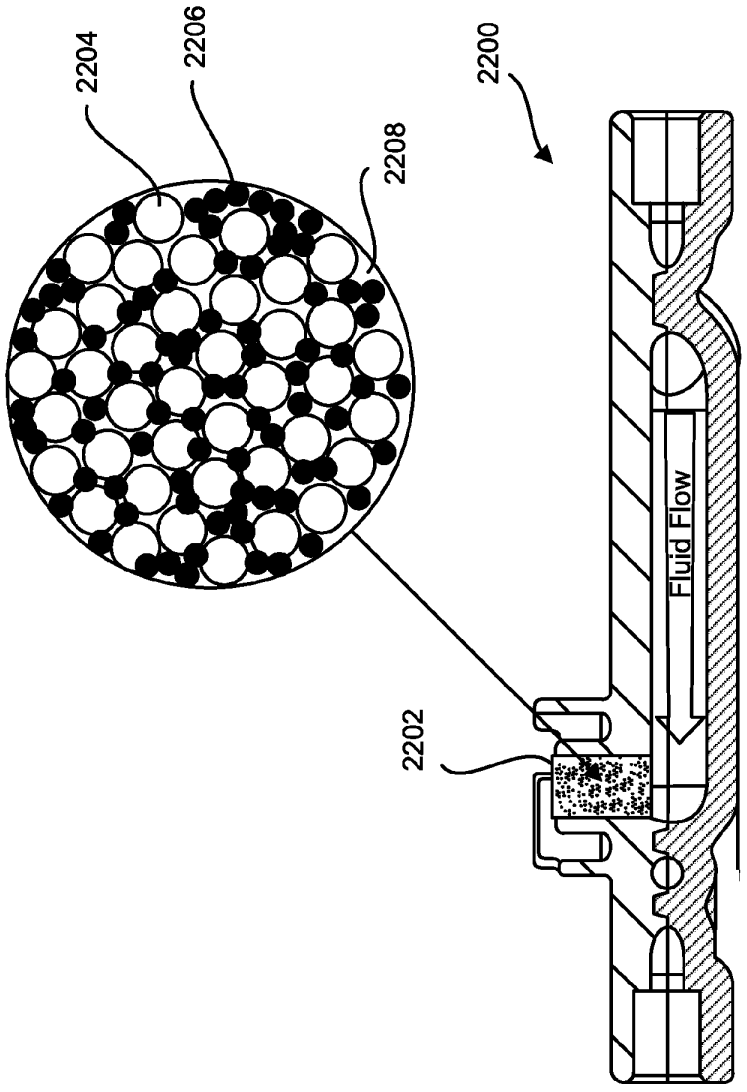


FIG. 22A

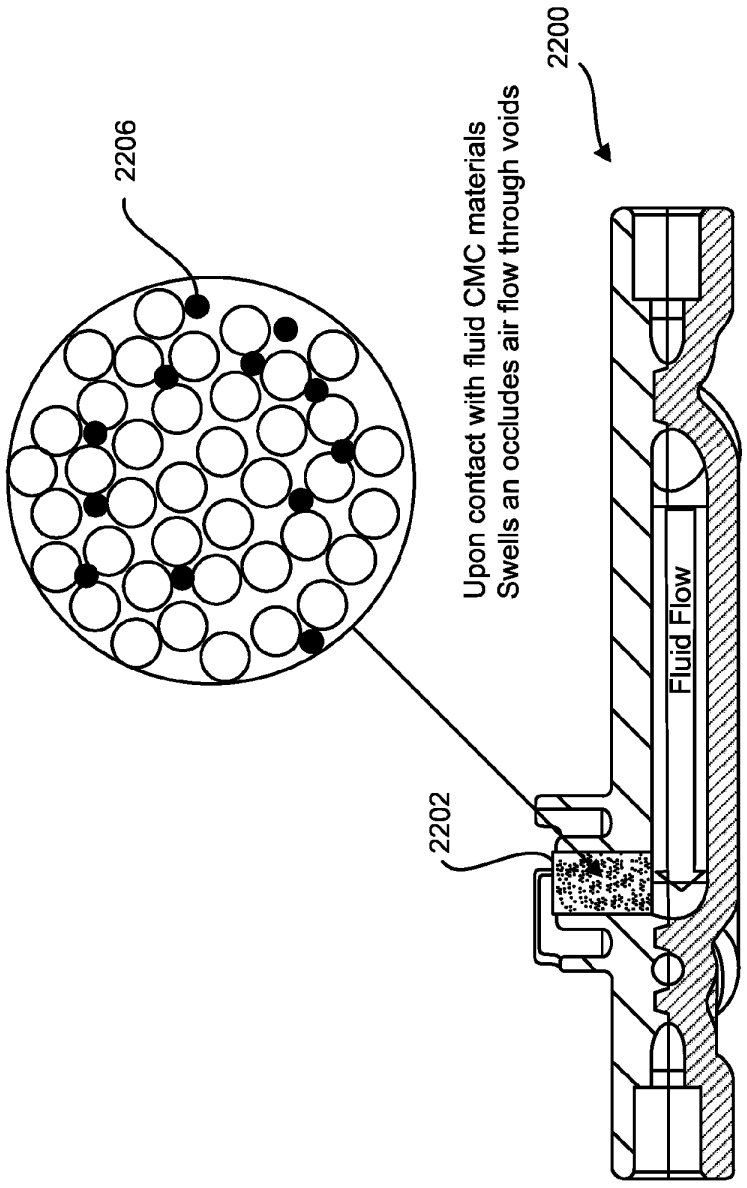

2200
2206
Upon contact with fluid CMC materials
Swells an occludes air flow through voids
Fluid Flow
2202

FIG. 22B

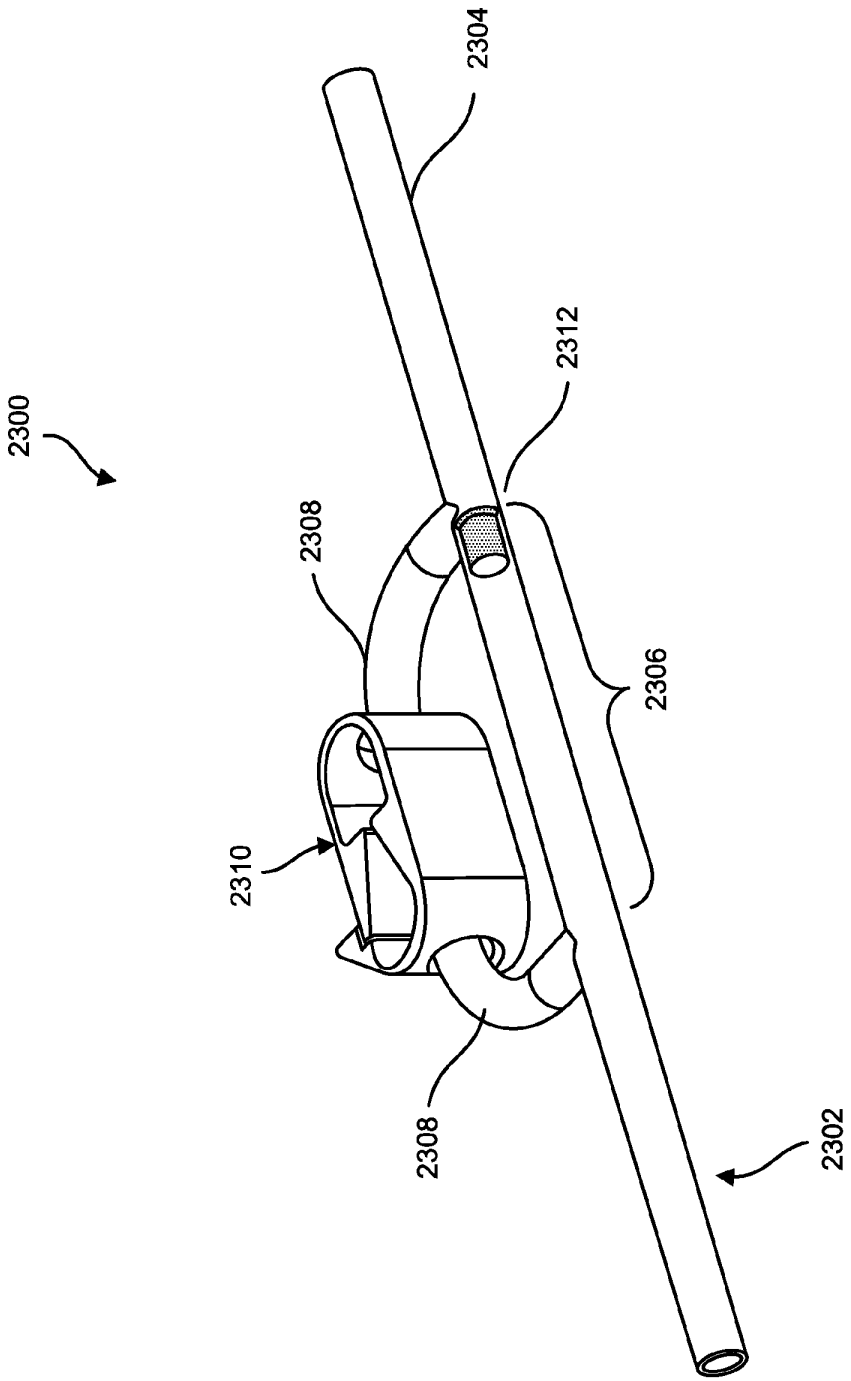


FIG. 23A

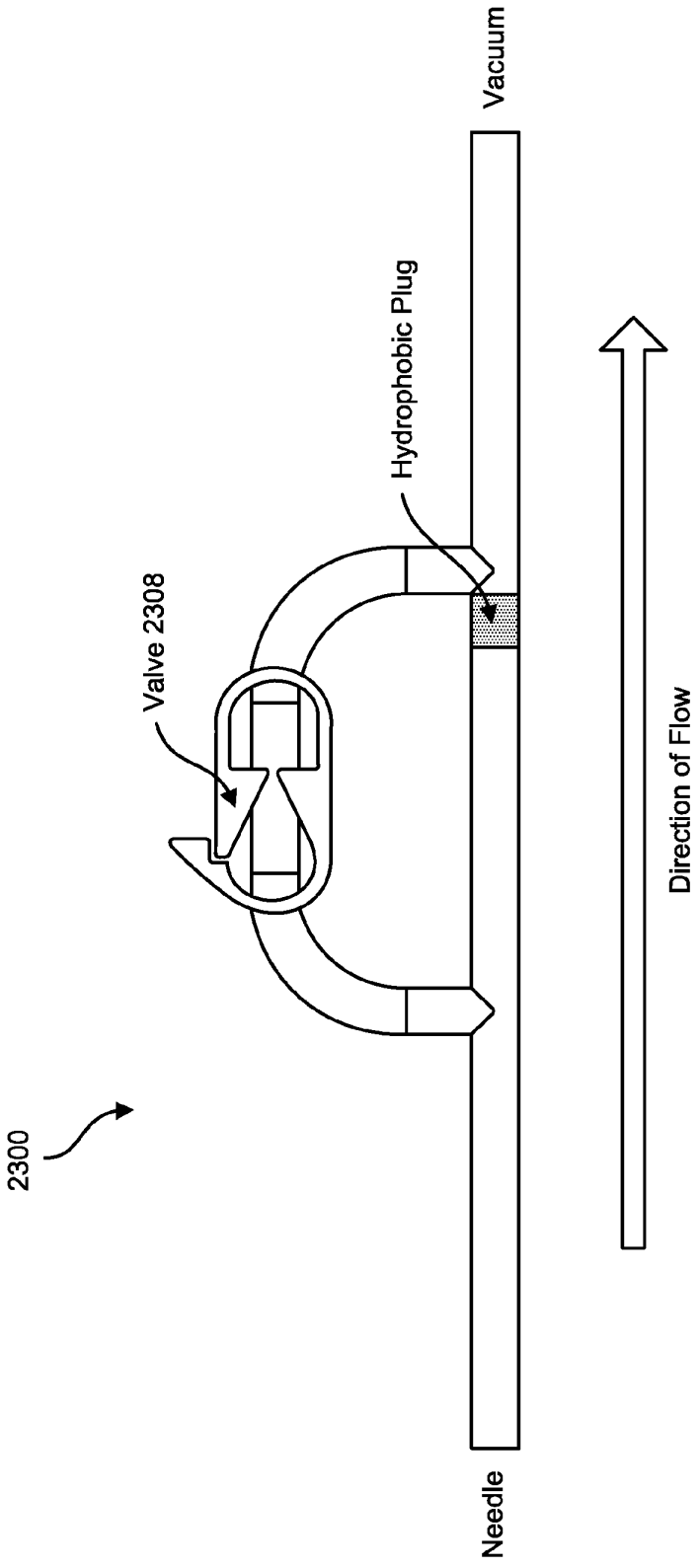

Vacuum
Hydrophobic Plug
Valve 2308
Direction of Flow
2300
Needle

FIG. 23B

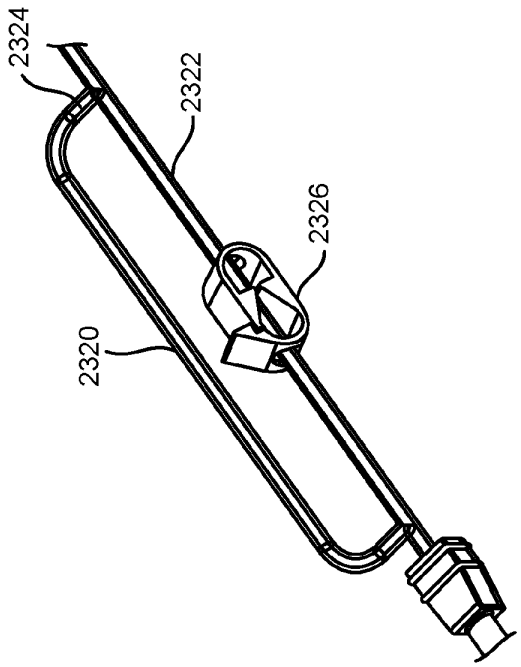


FIG. 23D

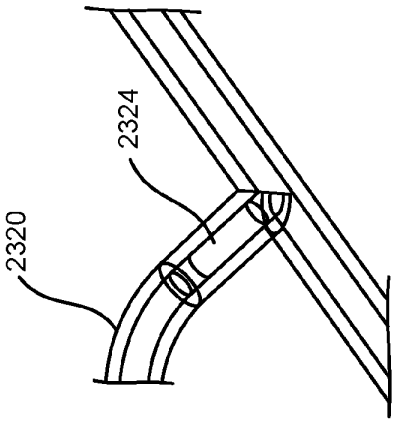


FIG. 23E

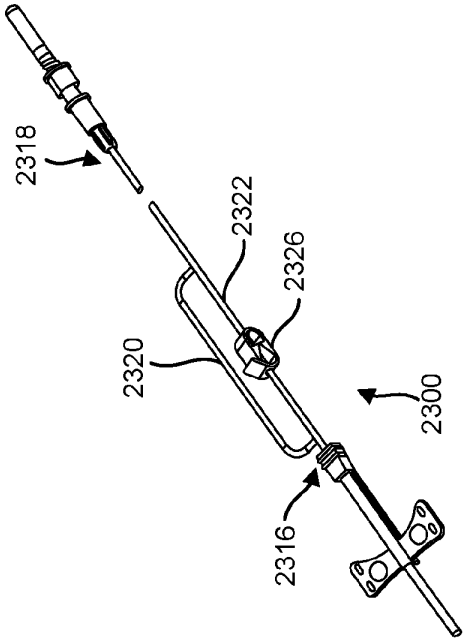


FIG. 23C

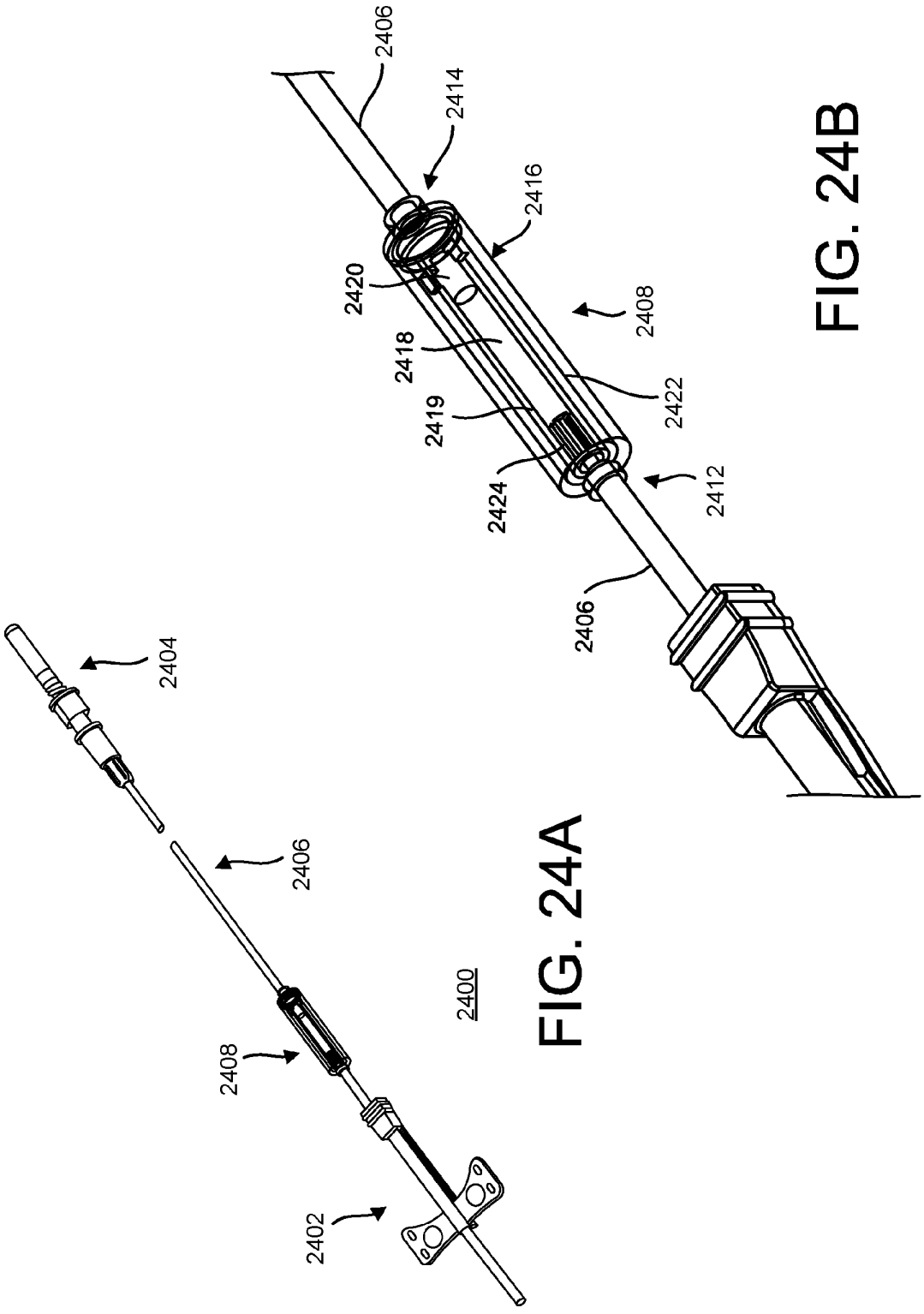


FIG. 24B

FIG. 24A

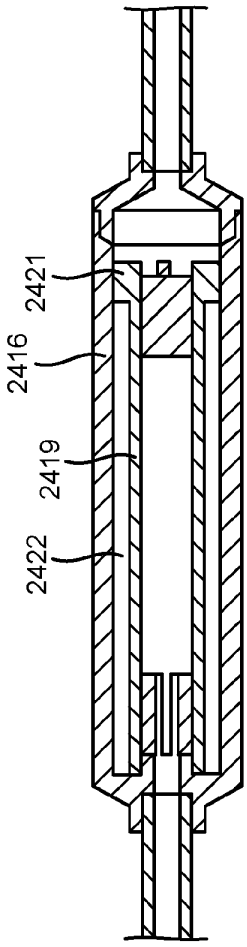


FIG. 24C

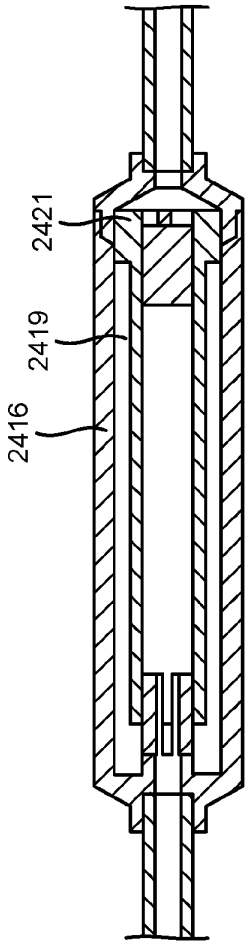


FIG. 24D

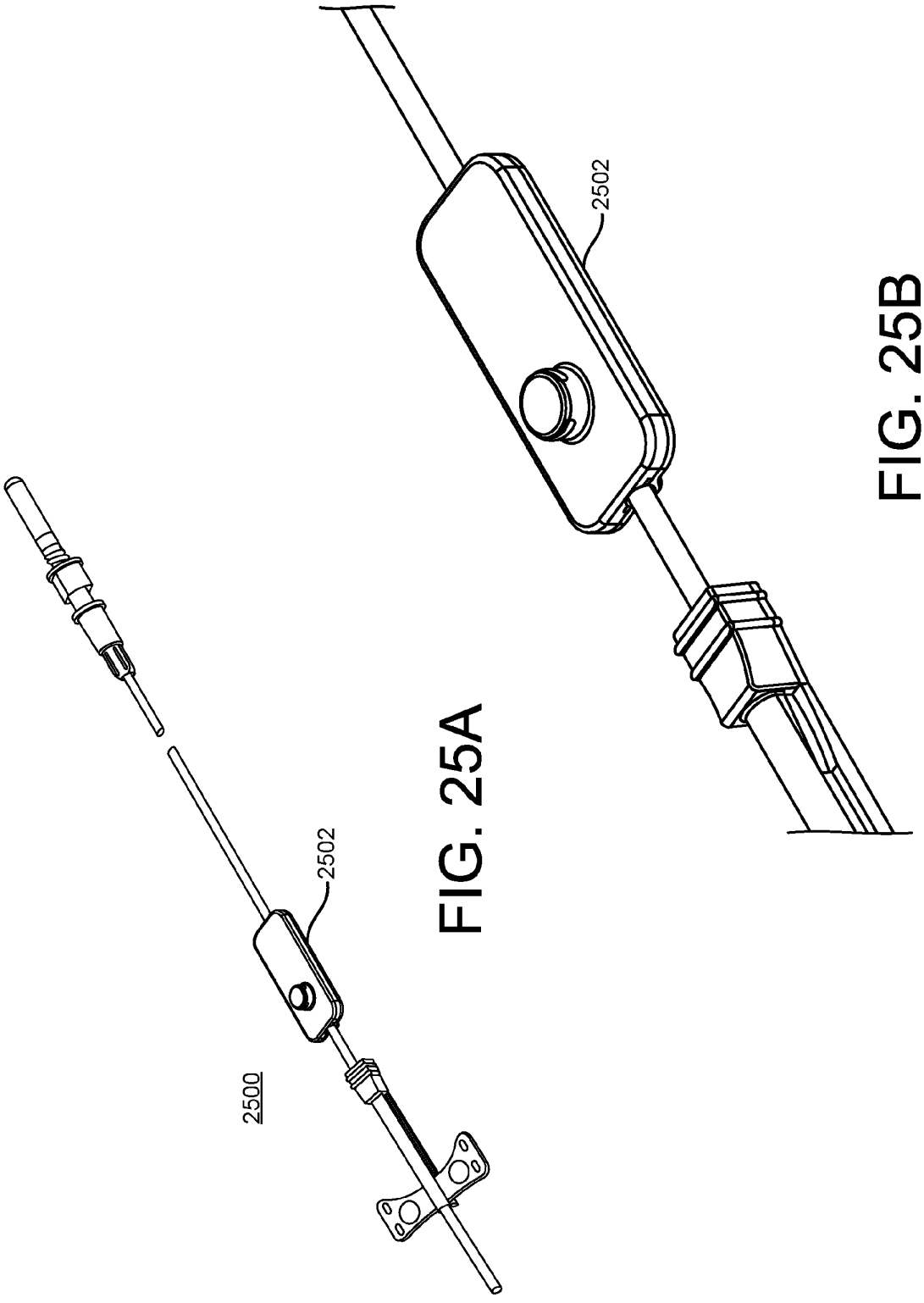


FIG. 25A

FIG. 25B

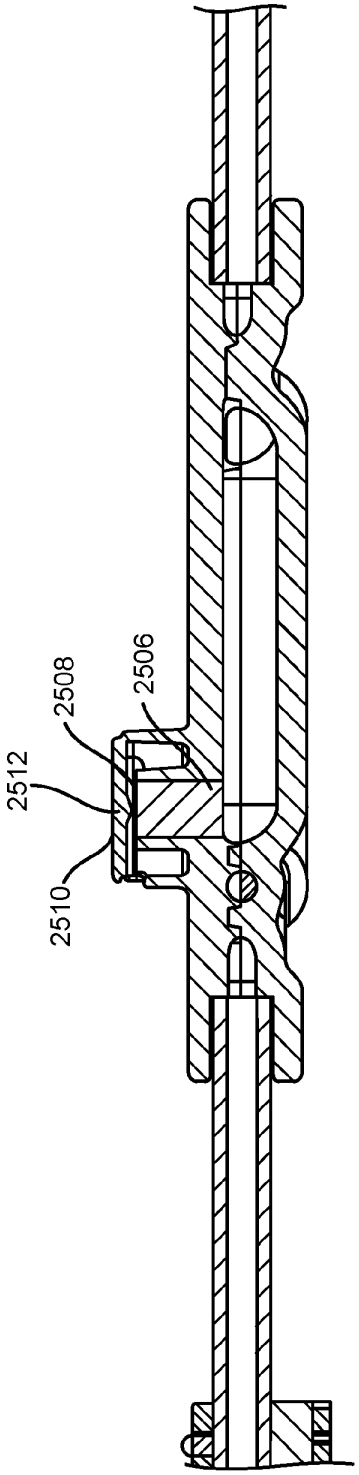


FIG. 25C

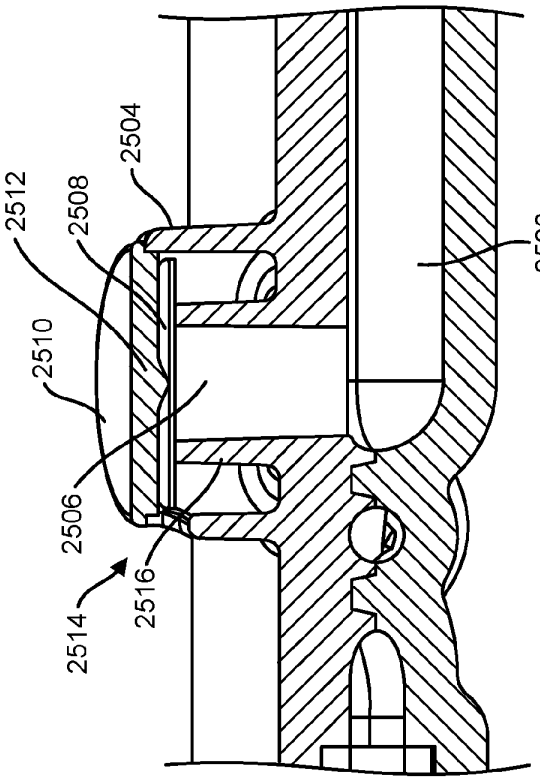


FIG. 25D

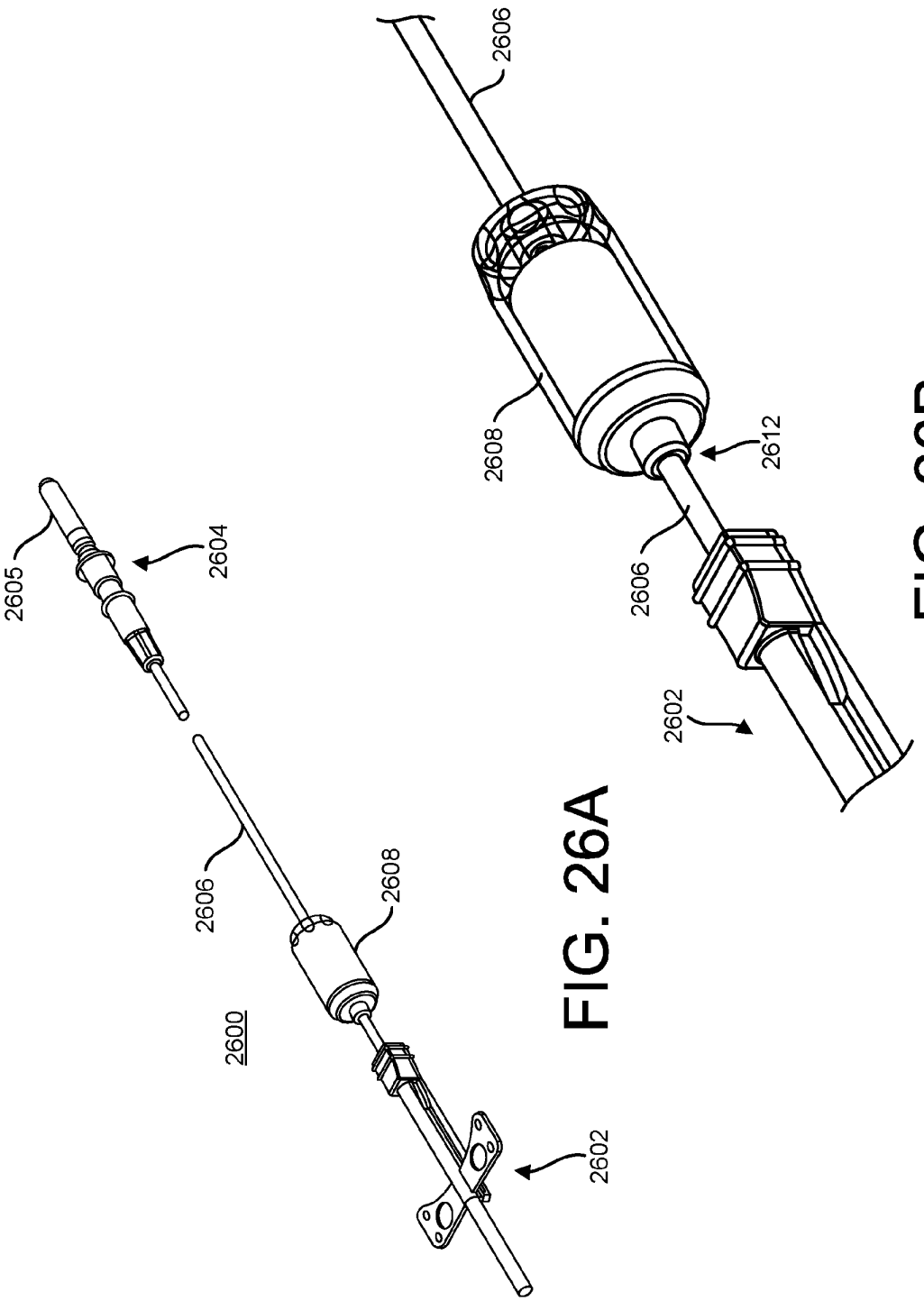


FIG. 26A

FIG. 26B

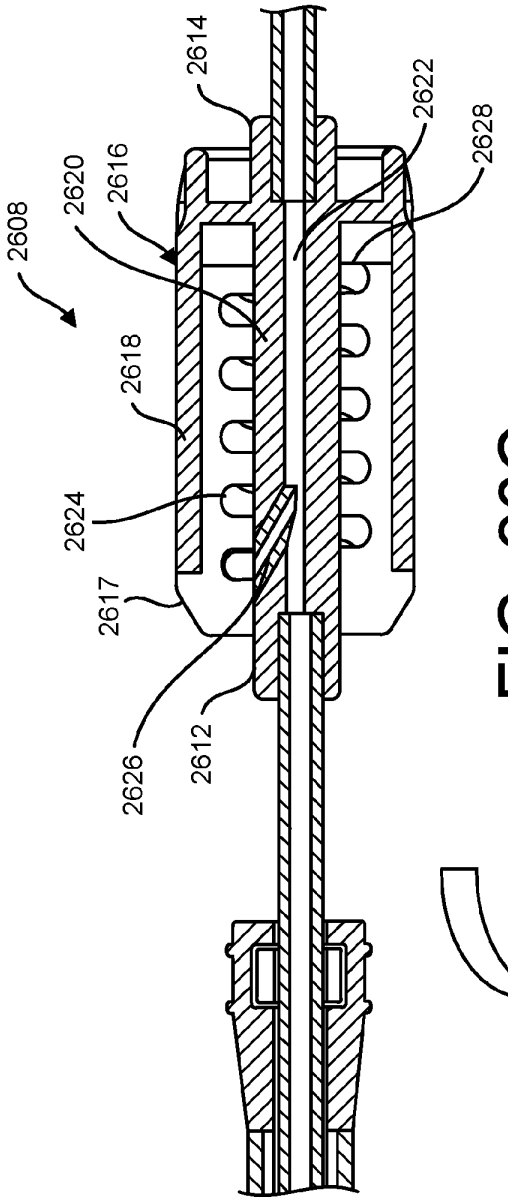


FIG. 26C

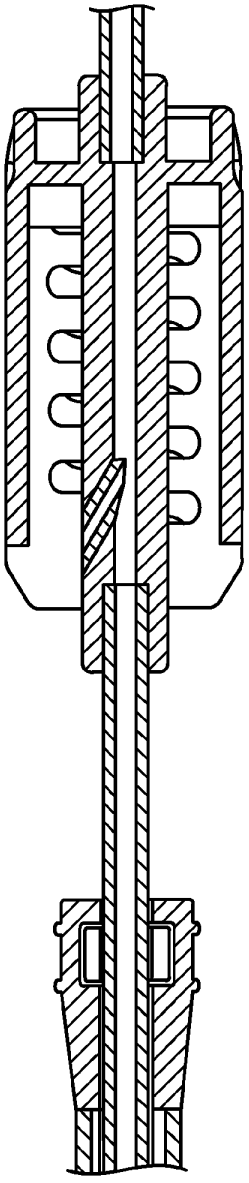


FIG. 26D

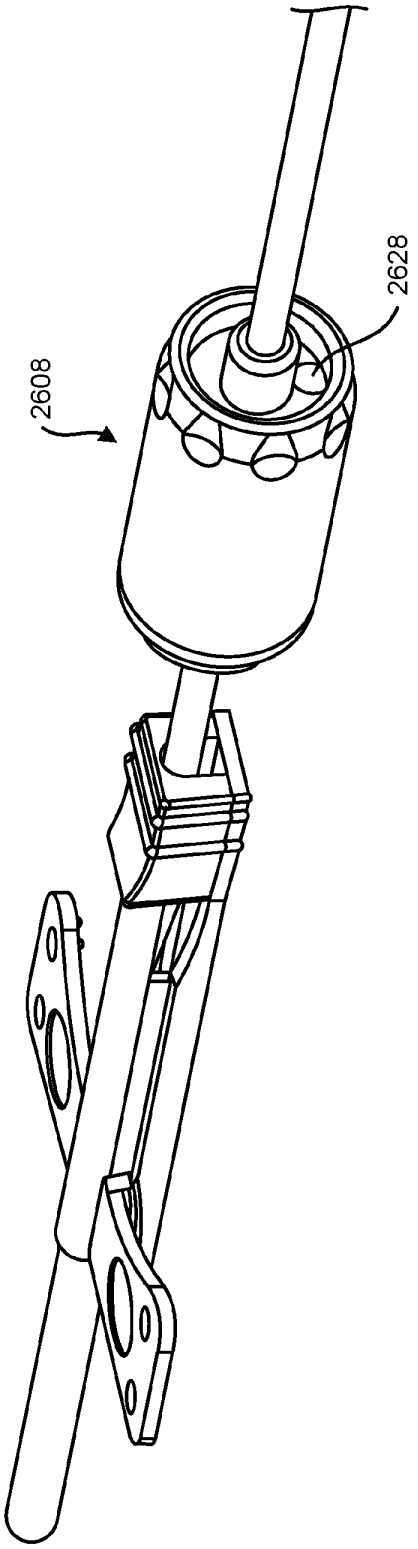


FIG. 26E

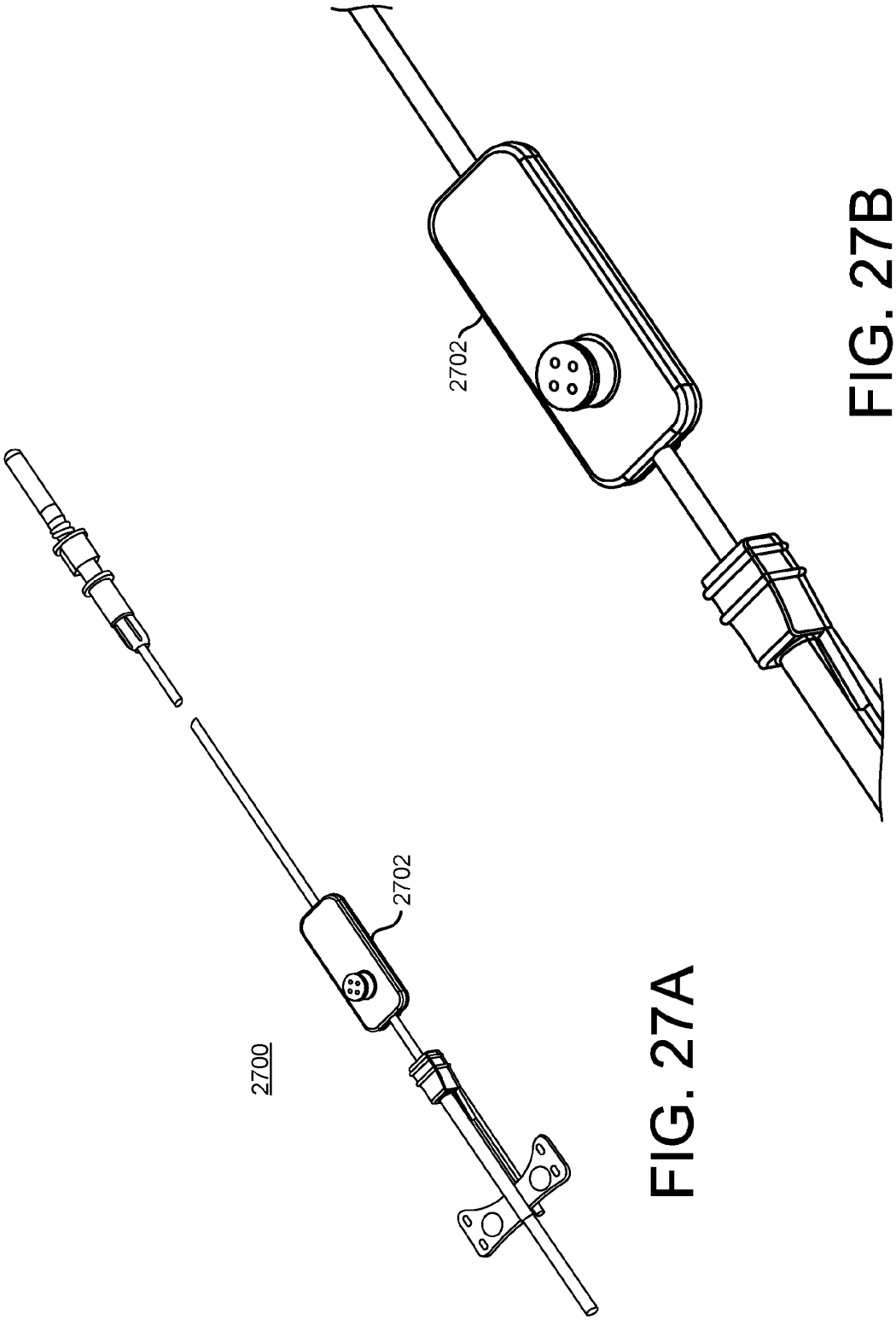


FIG. 27A

FIG. 27B

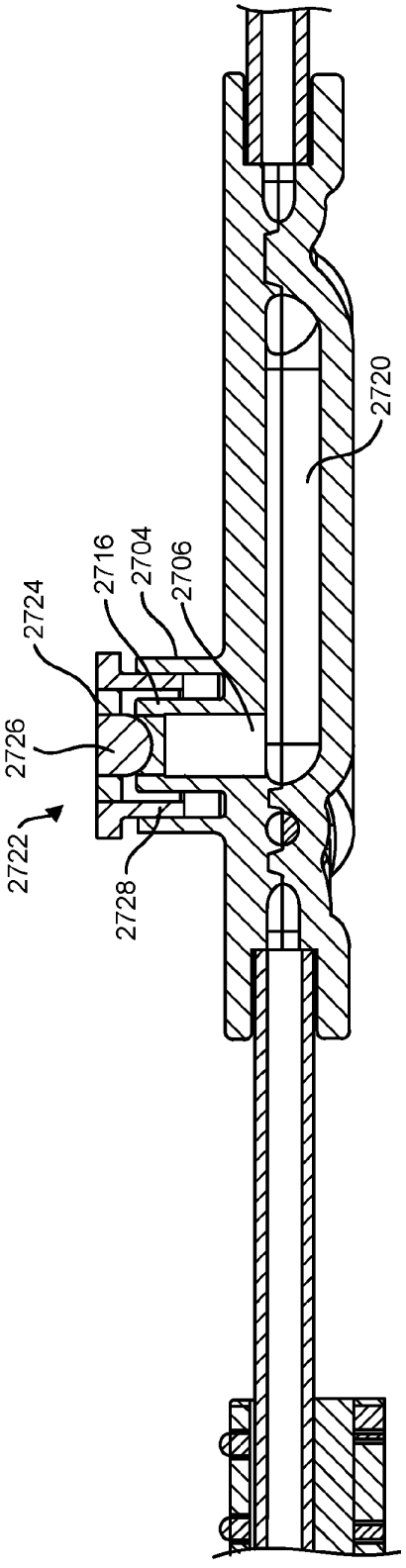


FIG. 27C

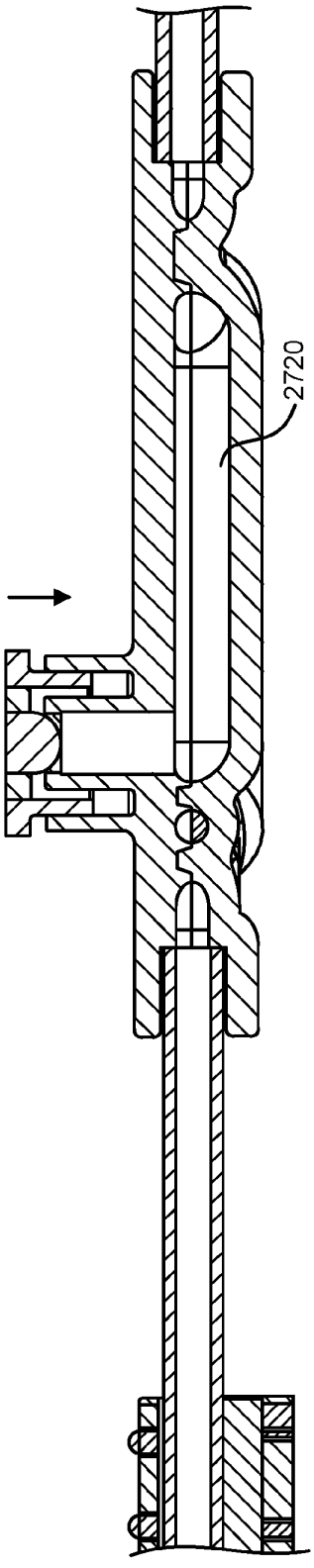


FIG. 27D

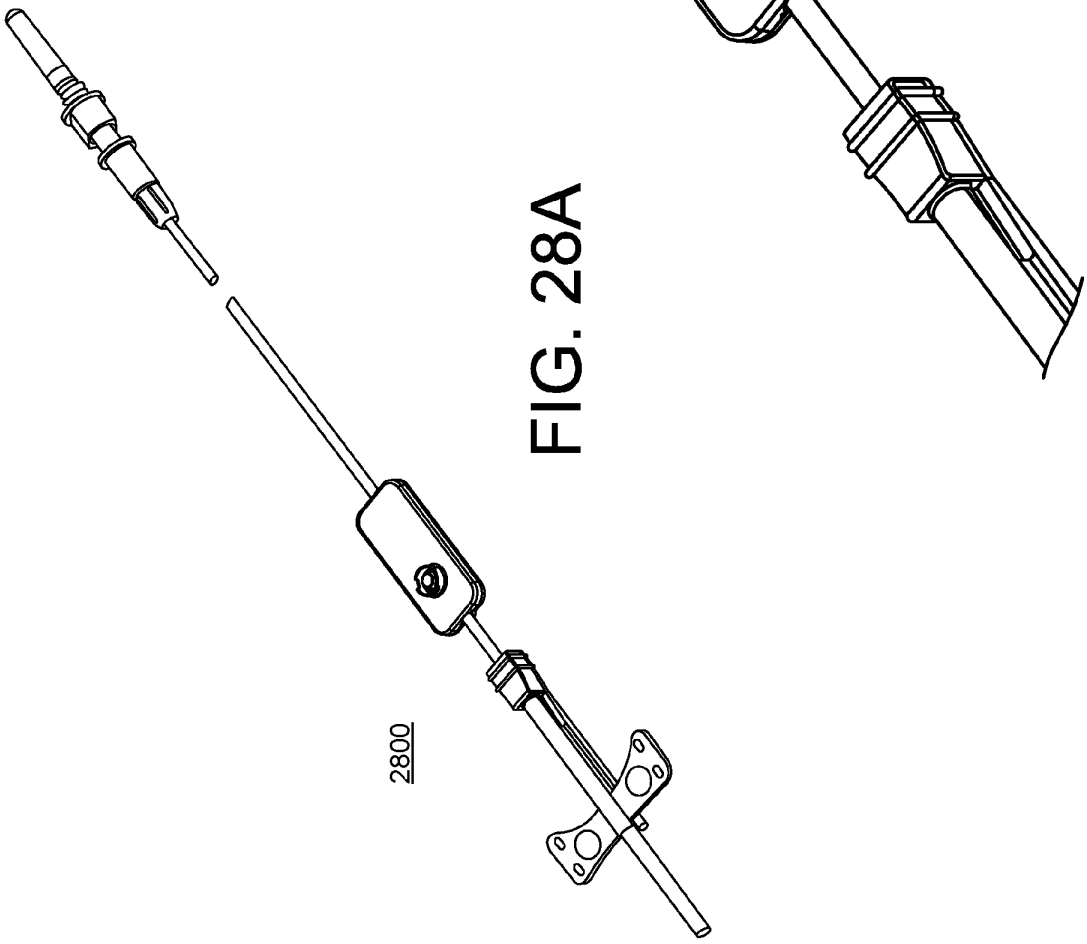


FIG. 28A

FIG. 28B

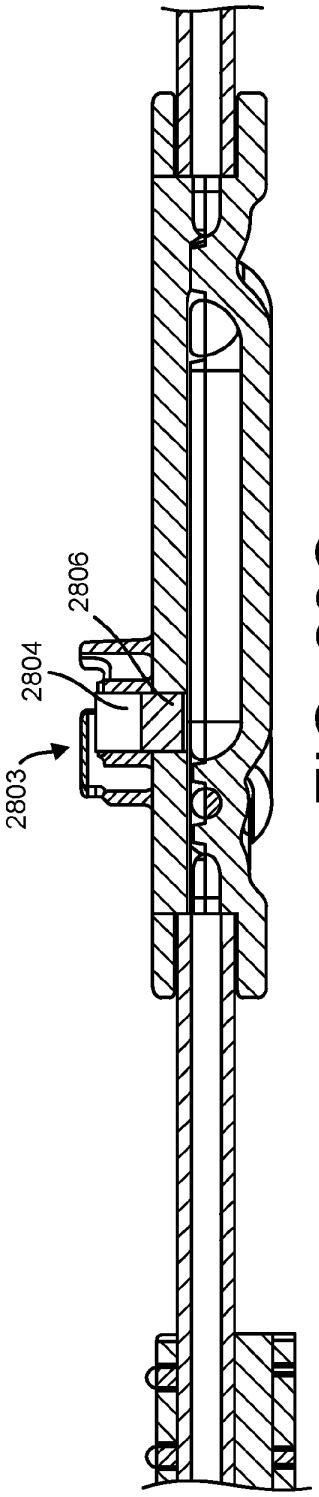


FIG. 28C

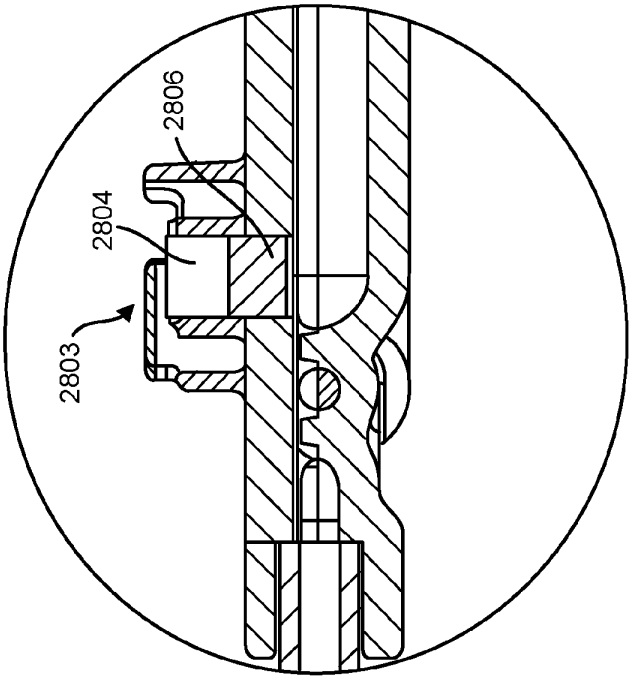


FIG. 28D

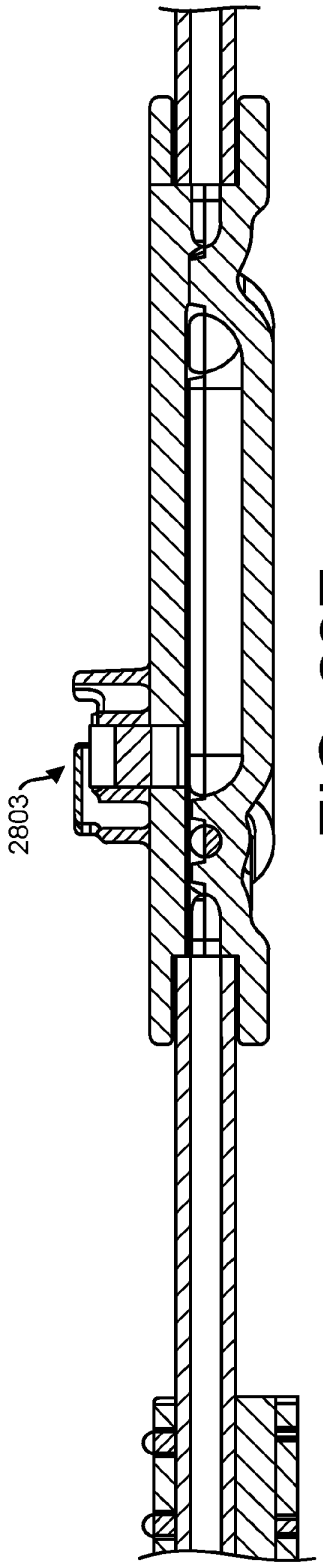


FIG. 28E

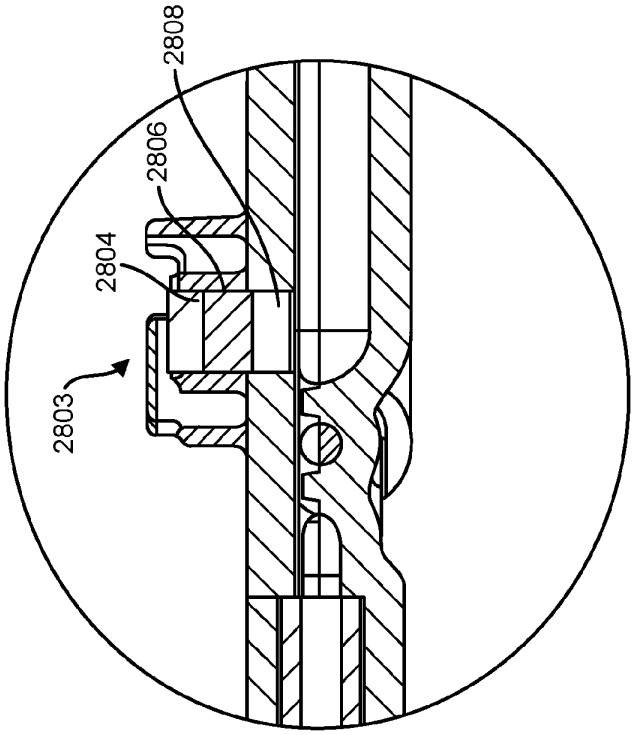


FIG. 28F

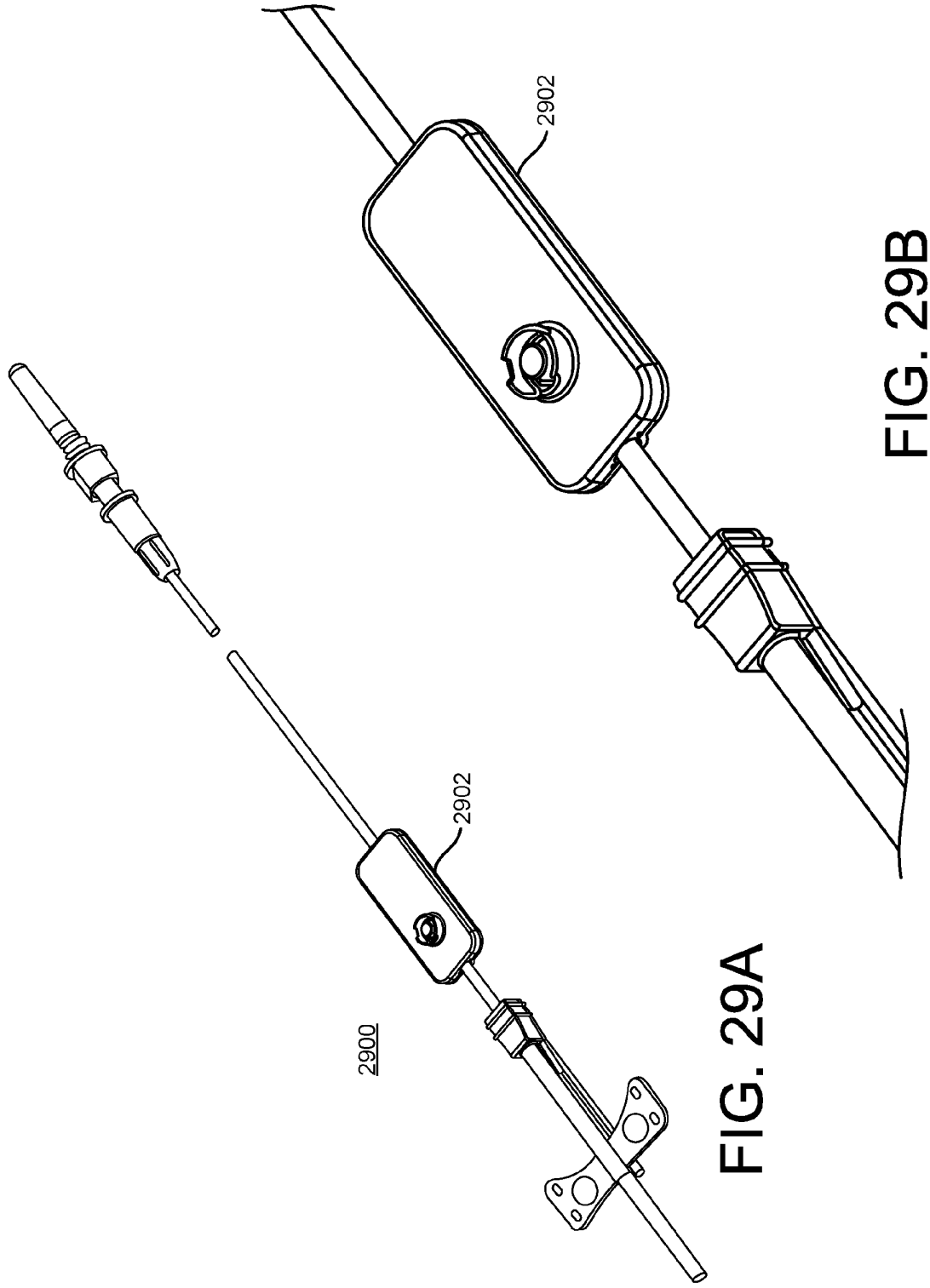


FIG. 29B

FIG. 29A

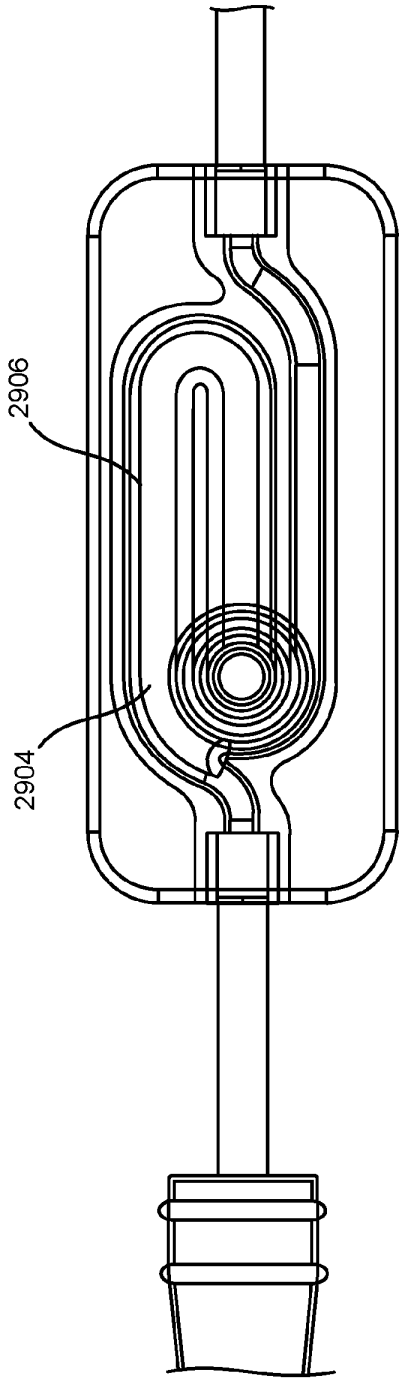


FIG. 29C

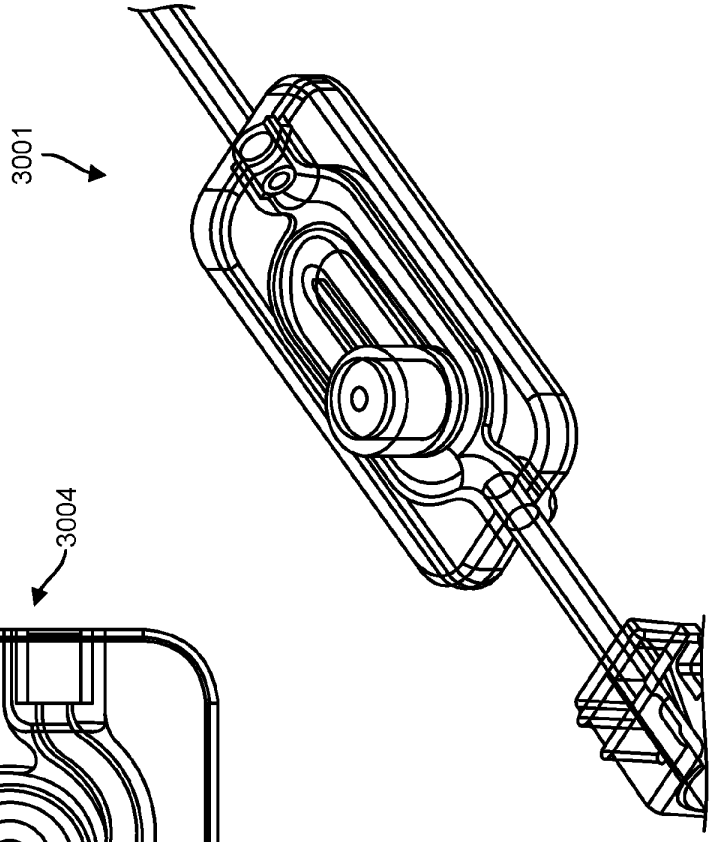


FIG. 30B

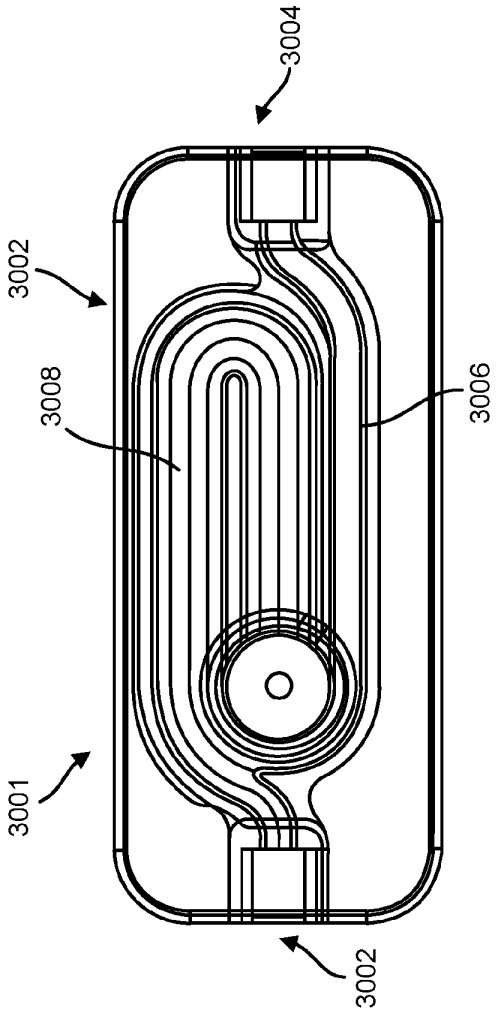


FIG. 30A

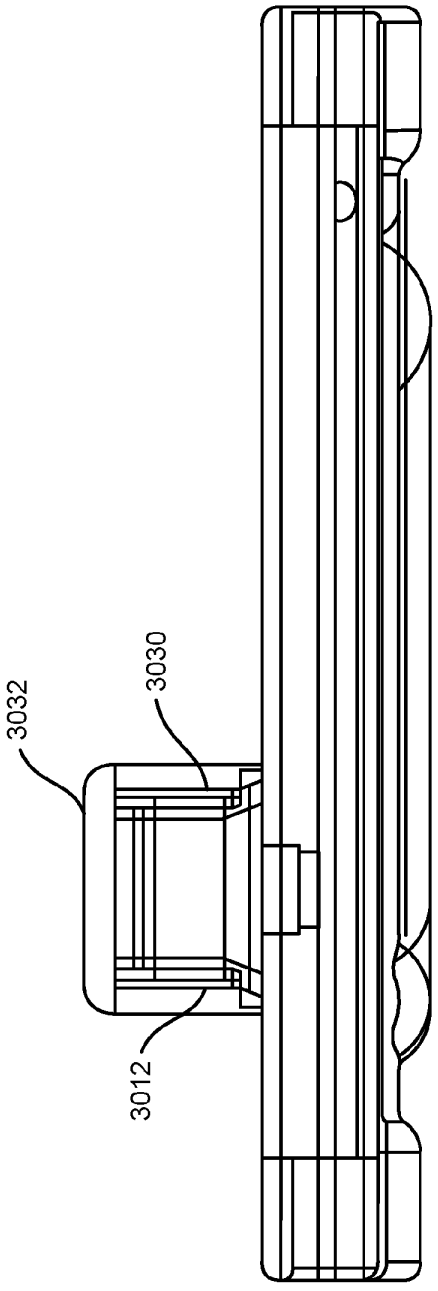


FIG. 30C

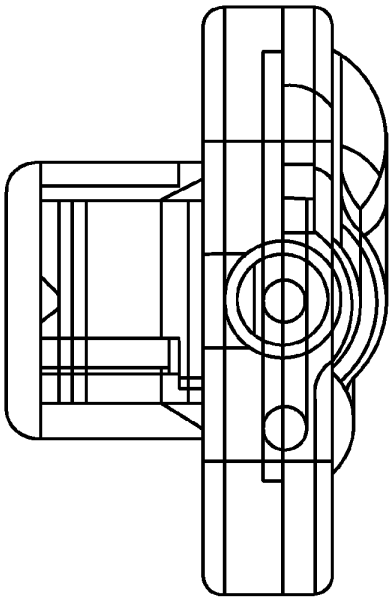


FIG. 30D

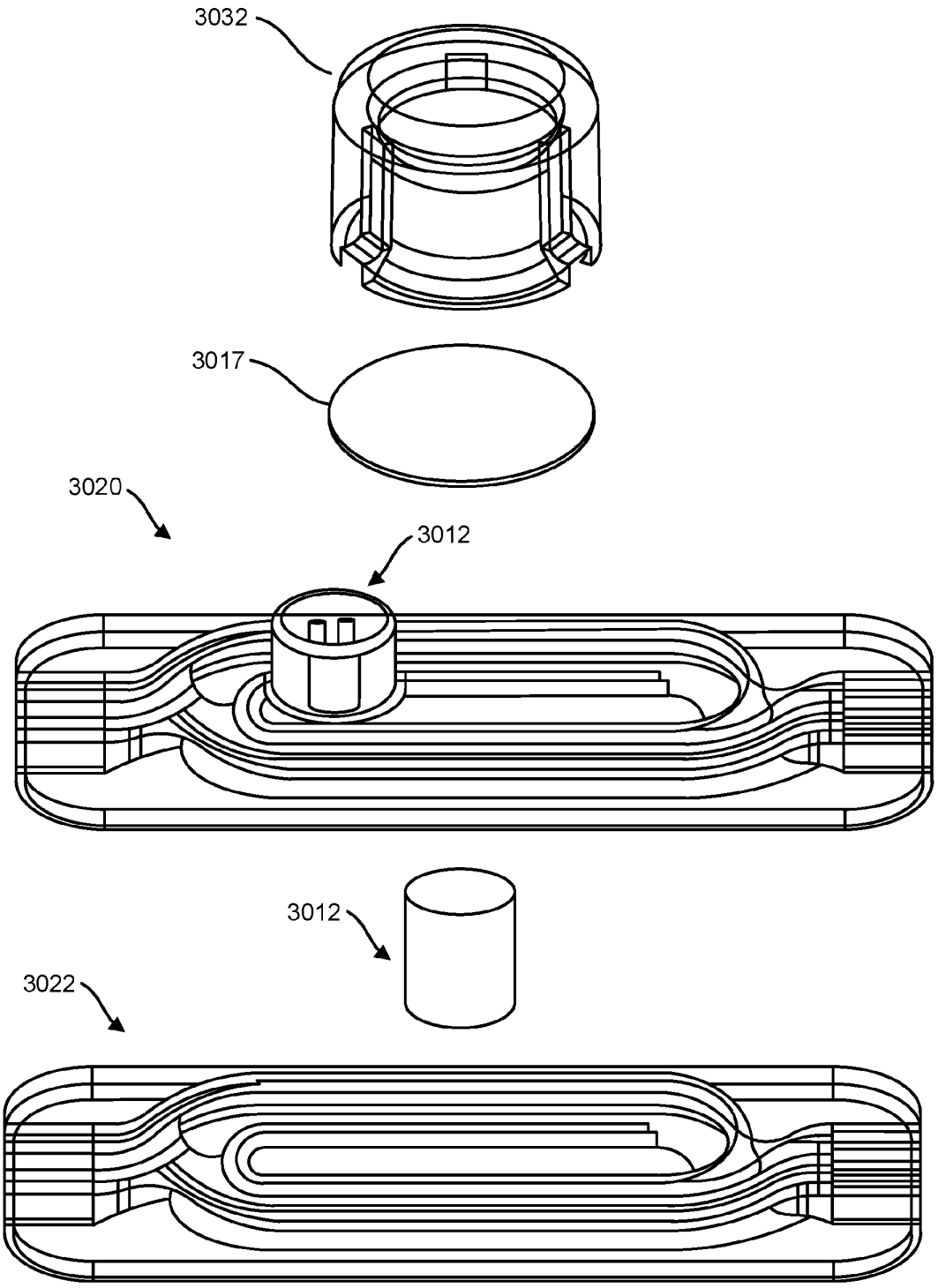


FIG. 30E

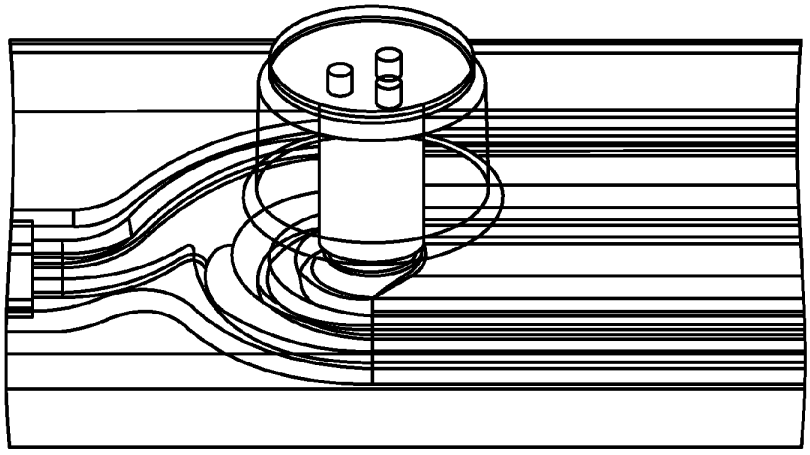


FIG. 30F

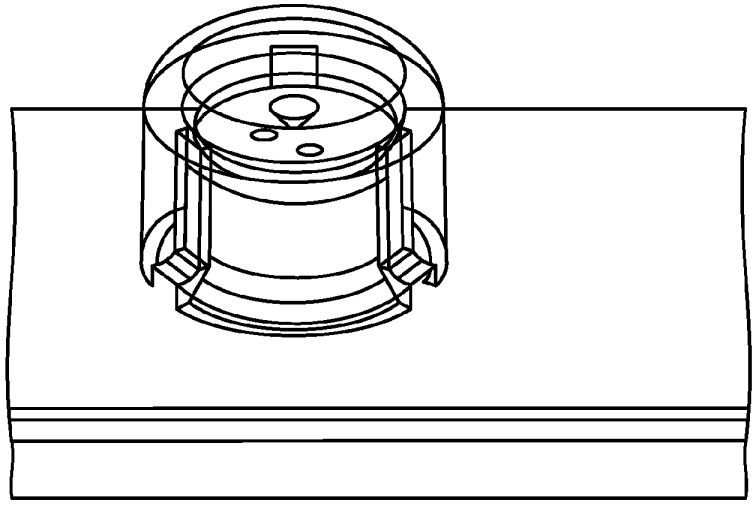


FIG. 30G

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2017/068569

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61B5/15 A61B5/153 A61B5/154 A61B5/157
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 2014/039348 A1 (BULLINGTON GREGORY J [US] ET AL) 6 February 2014 (2014-02-06) the whole document	1-20
A	US 2014/107564 A1 (BULLINGTON GREGORY J [US] ET AL) 17 April 2014 (2014-04-17) the whole document	1-20
A	US 4 813 433 A (DOWNEY JOHN M [US]) 21 March 1989 (1989-03-21) the whole document	1-20
A	US 2013/317391 A1 (BULLINGTON GREGORY J [US] ET AL) 28 November 2013 (2013-11-28) abstract paragraph [0048] - paragraph [0075]; figures 2-12	1-20

-/--

[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

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Date of the actual completion of the international search	Date of mailing of the international search report
29 March 2018	25/04/2018

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	Nielsen, Michael

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INTERNATIONAL SEARCH REPORT

International application No
PCT/US2017/068569

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 2013/181352 A1 (MAGNOLIA MEDICAL TECHNOLOGIES INC [US]; BULLINGTON GREGORY J [US]; PAT) 5 December 2013 (2013-12-05) abstract paragraph [1090]; figures 11,12	1-20

1

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2017/068569

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		US 2016113560 A1	28-04-2016
		WO 2014022275 A1	06-02-2014
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		WO 2013181352 A1	05-12-2013

Bibliographic data: EP3562397 (A1) — 2019-11-06

BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE AND METHOD

Inventor(s): ROGERS BOBBY E [US]; KANG GINO [US]; STROUP DAVID KARL [US]; COCHRAN JONAS DEAN [US]; DEPTALA ARTHUR [US]; DETLOFF JOHN [US]; POGUE LONNIE [US]; MACOWSKI BRIAN [US]; GARRETT CHAD [US] ± (ROGERS, Bobby E, ; KANG, Gino, ; STROUP, David Karl, ; COCHRAN, Jonas Dean, ; DEPTALA, Arthur, ; DETLOFF, John, ; POGUE, Lonnie, ; MACOWSKI, Brian, ; GARRETT, Chad)

Applicant(s): KURIN INC [US] ± (Kurin, Inc)

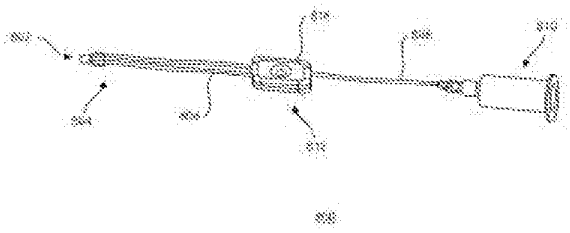
Classification: **- international:** ***A61B5/15; A61B5/153; A61B5/154; A61B5/157***
- cooperative: **A61B5/15003 (EP, US); A61B5/150213 (EP, US); A61B5/150221 (US); A61B5/150251 (EP, US); A61B5/150274 (EP, US); A61B5/150351 (US); A61B5/150755 (US); A61B5/150786 (US); A61B5/150946 (US); A61B5/150992 (EP, US); A61B5/1535 (EP, US); A61B5/1545 (EP, US);** A61B5/150389 (EP, US); A61B5/150488 (EP, US); A61B5/157 (EP, US)

Application number: EP20170840467 20171227 Global Dossier

Priority number(s): US201662439426P 20161227 ; WO2017US68569 20171227

Also published as: EP3562397 (B1) EP3777684 (A1) EP3777684 (B1) EP4091544 (A1) IL267684 (A) more

Abstract not available for EP3562397 (A1)
Abstract of corresponding document: US2018177445 (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.

(19) Europäisches Patentamt
European Patent Office
Office européen des brevets

(11) Veröffentlichungsnummer:
(11) Publication number: **EP 3 562 397 A0**
(11) Numéro de publication:

Internationale Anmeldung veröffentlicht durch die Weltorganisation für geistiges Eigentum unter der Nummer:

WO 2018/125929 (Art. 153(3) EPÜ).

International application published by the World Intellectual Property Organization under number:

WO 2018/125929 (Art. 153(3) EPC).

Demande internationale publiée par l'Organisation Mondiale de la Propriété Intellectuelle sous le numéro:

WO 2018/125929 (art. 153(3) CBE).

PCT WORLD INTELLECTUAL PROPE
International Bu

INTERNATIONAL APPLICATION PUBLISHED UNDER WO 9605875A1

(51) International Patent Classification 6 :		(11) International Publication Number: WO 96/05875
A61M 5/00	A1	(43) International Publication Date: 29 February 1996 (29.02.96)

(21) International Application Number: PCT/US95/10702

(22) International Filing Date: 22 August 1995 (22.08.95)

(30) Priority Data:
08/296,207 25 August 1994 (25.08.94) US

(71) Applicant: BAXTER INTERNATIONAL INC. [US/US]; One Baxter Parkway, Deerfield, IL 60015 (US).

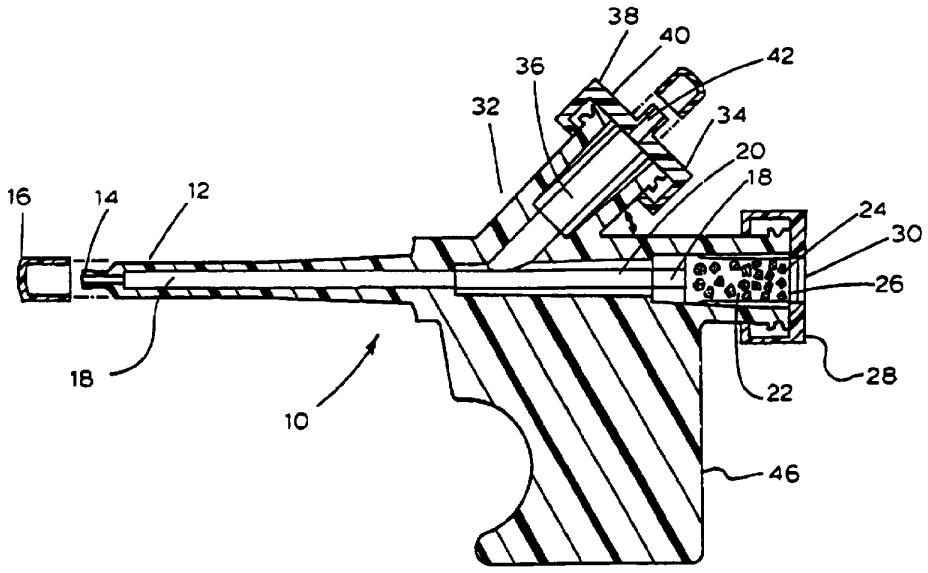
(72) Inventors: DESECKI, Vincent, C.; 28420 West Big Hollow Road, Ingleside, IL 60041 (US). BROWNE, Glennie; 944 Hidden Lake Drive, Buffalo Grove, IL 60089 (US).

(74) Agents: NICHOLS, Jeffrey, C. et al.; One Baxter Parkway, Deerfield, IL 60015 (US).

(81) Designated States: AU, CA, JP, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).

Published
With international search report.
Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.

(54) Title: CLOSED SYSTEM BLOOD SAMPLING DEVICE



(57) Abstract

The invention comprises a closed system blood sampling device comprising a bifurcated capillary tube (10) which has a first branch (12) having a cannula shaped end (14) for withdrawing and conveying blood to a communicating blood collection zone. The second branch of the bifurcated capillary tube (32) is connected to and is in fluid communication with the blood collection zone. It terminates in an opening adapted to receive a blood withdrawal device.

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CLOSED SYSTEM BLOOD SAMPLING DEVICE

FIELD OF THE INVENTION

The invention relates to closed system blood sampling devices.

BACKGROUND OF THE INVENTION

Arterial blood gas sampling is a standard procedure often used to help assess respiratory function in the critically ill. In some cases, samples can be drawn as many as 20 times a day. For the typical neonatal patient weighing 1000 grams and having approximately 85 cc of total body fluid capacity, the volume of blood samples becomes a critical factor.

A technique called the 3 drop method is gaining substantial clinical acceptance in neonatal units across the country. This method calls for inserting a blunt hypodermic needle as far as possible into a standard sleeve stoppered T-Connector. Three drops of blood estimated to be approximately .06 cc are allowed to drip onto a gauge pad, thereby clearing the cannula of heparinized or non-circulating blood while providing a fresh arterial sample to the surface. 3 more drops are then collected in a micro container followed by cannula withdrawal. Blood cannula contents within the cannula lumen and the previously collected micro container sample are then aspirated into a tuberculin type syringe for transport to the blood lab for testing. A flush of the T-Connector to eliminate residual blood then ensues. This procedure provides the ability to withdraw a controlled blood volume; .06 cc as necessary

discard and .12 cc to perhaps .20 cc for actual blood gas testing.

Several opportunities for procedural improvement exist. One challenge is the open environment method of collection which could foster blood contamination and/or the spread of infectious diseases. Secondarily, the collection process in regard to volume accuracy is difficult to control and highly sensitive to variations in clinician technique, catheter positioning and arterial pressure. If a device can be designed for closed system collection which could also insure consistency of sample volume time after time, treatment of neonatal patients where blood volume levels are critical, accuracy improvements could be a major clinical benefit.

THE DRAWINGS

Fig. 1 is a horizontal cut away side view showing the closed system blood sampling device of the invention.

Fig. 2 is a vertical, partial schematic view showing the closed system blood sampling device connected to an injection site which, in turn, is fitted into a venipuncture device used to withdraw arterial blood.

In the drawings, like parts have like numbers.

THE INVENTION

The invention is a closed system blood sampling device comprising a bifurcated capillary tube which has a first branch having a cannula shaped end for withdrawing and conveying blood to a communicating blood collection zone. The blood

collection zone is for storing a quantity of withdrawn blood. It also feeds an initial fraction of withdrawn blood to a communicating blood disposal chamber which has an air permeable liquid sealed end.

The second branch of the bifurcated capillary tube is connected to and is in fluid communication with the blood collection zone. It terminates in an opening adapted to receive a blood withdrawal device.

In preferred embodiments the closed system blood sampling device the cannula shaped end is blunt, the blood disposal chamber has its end fitted with a cap containing an air permeable hydrophobic membrane, and the blood disposal chamber contains a porous blood adsorbent. The second branch has an interior angle not greater than 90 degrees and preferably the interior angle is 60 degrees. It is also desirable that the cannula shaped end be tapered so that it snugly fits into the preferred injection sites more fully described hereafter.

Preferably, the closed system blood sampling device is removed from the injection site before the blood sample is withdrawn therefrom by means such as a tuberculum syringe or aspirated directly into a blood gas analyzer.

While the closed blood sampling device is particularly suited for obtaining neonatal blood samples it is readily adapted to obtain samples from a variety of patient types.

DETAILED DESCRIPTION OF THE INVENTION

In Fig. 1 the closed system blood sampling device is designated generally by the numeral 10. It is preferably constructed of a clear chemically inert non-toxic plastic such as polycarbonate. It comprises a blood withdrawal cannula shaped end 12. The cannula tip 14 is blunt and necked down to prevent injection site from blood flash back during arterial sampling. To maintain sterility the cannula tip is fitted with a removable cap 16 which is removed just before the blood sampling device is to be used.

Fig. 1 shows the cannula shaped end 12 to be tapered. This particular configuration was selected so that the cannula may engage and generally mate with a particular injection site, the details of which will be more fully described hereafter. The interior bore 18 of the cannula shaped end is dimensioned to allow withdrawn blood to move along the bore by means of capillary action driven by normally positive arterial blood pressure.

The interior capillary bore 18 connects with and continues into a larger outer diameter lumen 20. The continuous bore 18 of the cannula 12 and the lumen 20 comprise a blood collection zone. Bore 18 as it exits the lumen 20 empties into blood disposal chamber 22. In a preferred embodiment of the invention, blood disposal chamber 22 contains a blood retaining means such as adsorbing material 24 which may be rayon or cellulosic wadding. The open end 26 of the blood disposal

chamber 22 is closed with a cap 28 that has its top fitted with a liquid tight, air permeable hydrophobic membrane 30 which allows air to be evacuated from the blood sampling device 10 of the invention. A suitable membrane material is sheet polytetrafloroethylene having a thickness of about 0.8 microns.

Fitted to the lumen 20, and in fluid communication therewith, is the second branch or port 32. It is positioned so as to have an interior angle 34 not exceeding 90 degrees. The interior angle is preferably about 60 degrees. The bore 36 connects with and corresponds in dimension with bore 18. Port 32 terminates and is sealed by adapter cap 38 whose top 40 is fitted with a capillary luer 42. The capillary luer is protected from contamination by means of protective cap 44 which is removed just prior to blood being withdrawn from the closed blood sampling device. The port 32 and its bore 36 form a part of the blood collection zone previously described. For convenience of use, the closed blood sampling device is fitted with pistol grip handle 46.

The blood collection zone has a larger liquid capacity than the liquid capacity of the blood disposal chamber. If the closed blood sampling device described were to be used in neonatal blood sampling, the liquid capacity of the blood collection zone might be 0.12 cc and the liquid capacity of the blood disposal chamber 22 would be about 0.06 cc.

The use of the closed blood sampling device of the invention to withdraw and sample blood is illustrated in Fig. 2 which shows artery 48 in communication with a venipuncture

device 50 which was inserted through subcutaneous tissue 52. The neck 54 of the venipuncture device 50 is adapted to receive an injection site 56. While conventional injection sites may be used as such or adapted to be used in the practice of the invention, it is preferred that the injection site be of the type having a resilient resealable septum which is preferably pre-slit. An injection site of this type is available from Baxter Healthcare Corporation and is a Neonatal T-Connector Luer sold under the brand name, InterLink, a registered trademark of Baxter Healthcare Corporation.

Such pre-slit, resilient, resealable injection sites and their method of fabrication are described in U.S. 5,188,620 the disclosure of which is incorporated herein by reference. The pre-slit resilient resealable injection sites described in this patent are designed to receive blunt cannulas. Another injection site related to the injection sites detailed in U.S. 5,188,620 is described in U.S. 5,300,034. This patent also details numerous publications and references which describe the preferred injection sites used in the practice of this invention. This patent and the publications listed therein also are incorporated herein by reference.

The injection site 56 is fitted with T-connector 58 which, in turn, is fitted with microbore tubing which, through female luer 62, is connected to IV line 64. The distal end 64 of the injection site 56 is connected to the neck 54 of the venipuncture device 50. The proximal end 66 of the injection site 56 is fitted with a pre-slit resilient resealing septum 68 adapted to receive

the blood withdrawal cannula 12 which is dimensioned to fit snugly into the injection site. Inserted into the second branch or port 32 is a conventional syringe 70, such as a tuberculum blood draw syringe, or an arterial blood gas loss of resistance syringe.

The device's cannula 12 would be inserted through the septum 68 of the injection site 56 and positioned so that the tip 14 of the cannula 12 was fully inserted into the injection site adjacent to the venipuncture device. In doing so, the residual volume of the actual T-Housing would be eliminated as a measurable factor in blood draw volume. Arterial pressure would cause blood flow to enter and flow up the device via capillary action. As blood moved up the hydrophobic membrane 30 of the device, air would escape via the upstream hydrophobic membrane 30. Original blood first present in the catheter would be pushed beyond the luer bifurcation for retention in the device and eventual disposal. The device would be withdrawn from the T-Connector as soon as visual confirmation of the blood filled lumen was made. The vented removal cap 44 would be removed from the bifurcated luer 42 and replaced by the syringe 70 which would be aspirated to remove the arterial blood sample. Residual blood volume upstream of the bifurcation would remain in the device for subsequent disposal.

WE CLAIM:

1. A closed system blood sampling device comprising a bifurcated capillary tube comprising:

a. a first branch having a cannula shaped end for withdrawing and conveying blood to a communicating;

b. blood collection zone for storing a quantity of withdrawn blood and feeding an initial fraction of withdrawn blood to a communicating;

c. blood disposal chamber having an air permeable liquid sealed end; and,

d. a second branch connected to and in fluid communication with the blood collection zone which terminates in an opening adapted to receive a blood withdrawal device.

2. The closed system blood sampling device of Claim 1 where the cannula shaped end is blunt, the blood disposal chamber has its end fitted with a cap containing an air permeable hydrophobic membrane, and the blood disposal chamber contains a porous blood adsorbent.

3. The closed system blood sampling device of Claim 1 where the second branch has an interior angle not greater than 90 degrees.

4. The closed system blood sampling device of Claim 3 where the second branch has an angle of about 60 degrees.

5. The closed system blood sampling device of Claim 2 where the cannula shaped end is tapered.

6. The closed system blood sampling device of Claim 2 where the blunt cannula shaped end is adapted to be received by a injection site which contains a resilient resealing means.

7. The closed system blood sampling device of Claim 6 where the injection site is a pre-slit injection site.

8. The closed system blood sampling device of Claim 2 where the blood collection zone has a volume greater than the volume of the blood disposal chamber.

9. A method of sampling blood from a patient having an artery fitted with a venipuncture device which is attached to an injection site containing the closed blood sampling device of Claim 1 which comprises the steps of:

a. withdrawing blood through the cannula shaped end of the closed blood sampling device thereby sequentially filling the blood disposal chamber and then the blood collection zone;

b. withdrawing through the opening in the second branch the blood contained in the blood collection zone for subsequent processing; and, then,

c. discarding the closed system blood sampling device

10. The method of Claim 9 where the cannula is blunt, the blood disposal chamber has its end fitted with a cap containing an air permeable hydrophobic membrane, and contains a porous blood adsorbent.

11. The method of Claim 9 where the second branch has an interior angle not greater than 90 degrees.

12. The method Claim 11 where the second branch has an angle of about 60 degrees.

13. The method of Claim 10 where the cannula shaped end is tapered.

14. The method of Claim 10 where the blunt cannula shaped end is adapted to be received by a injection site which contains a resilient resealing means.

15. The method of Claim 14 where the injection site is a pre-slit injection site.

16. The method of Claim 10 where the blood collection zone has a volume greater than the volume of the blood disposal chamber.

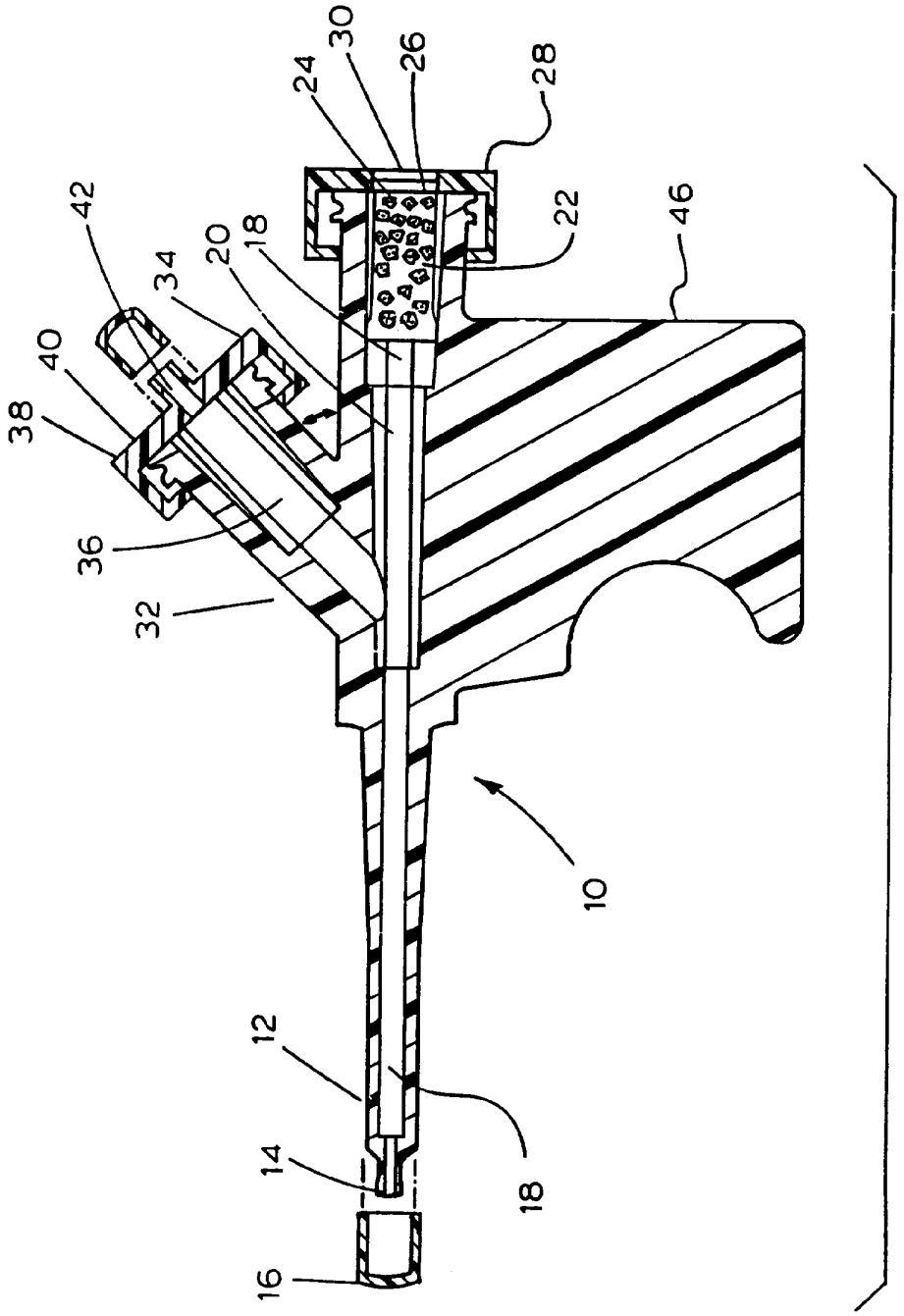


FIG. 1

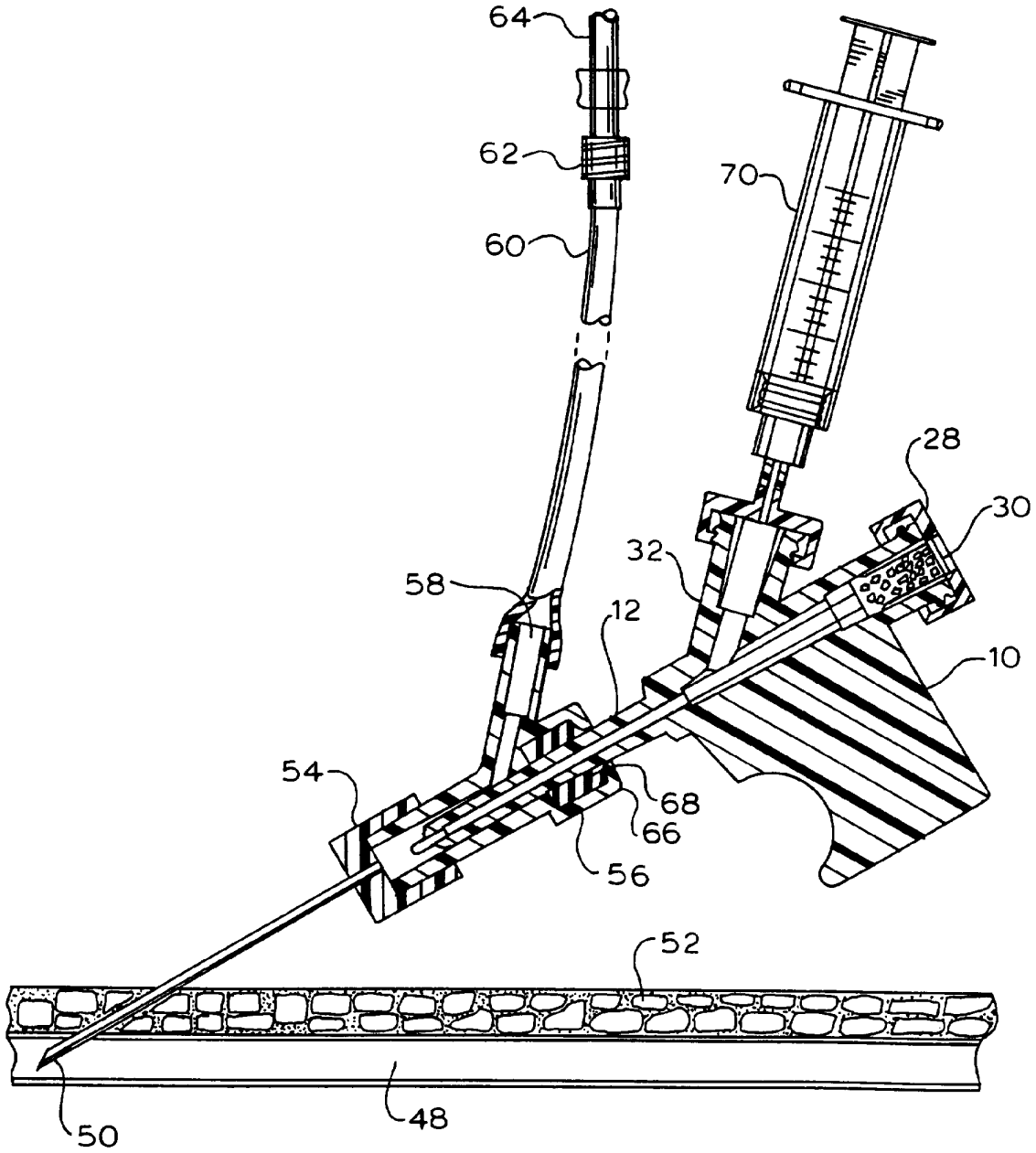


FIG. 2

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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)*

Bibliographic data: WO2017019552 (A1) — 2017-02-02

BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE AND METHOD

Inventor(s): ROGERS BOBBY [US]; KANG GINO [US]; DETLOFF JOHN [US] ± (ROGERS, Bobby, ; KANG, Gino, ; DETLOFF, John)

Applicant(s): KURIN INC [US] ± (KURIN, INC)

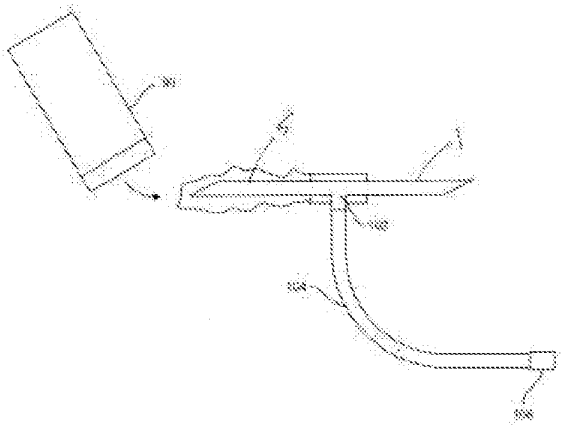
Classification: - **international:** ***A61B5/15; A61B5/153; A61B5/154***
- **cooperative:** **A61B5/15003 (EP, IL, US); A61B5/150213 (EP, IL, US); A61B5/150221 (IL, US); A61B5/150389 (EP, IL, US); A61B5/150473 (EP, IL, US); A61B5/150572 (EP, IL, US); A61B5/150992 (IL, US); A61B5/153 (EP, IL, US); A61B5/154 (EP, IL, US); A61M39/04 (IL, US); A61M39/0693 (IL, US);** A61M2039/0202 (IL, US); A61M2039/0633 (IL, US); A61M2039/068 (IL, US)

Application number: WO2016US43709 20160722 Global Dossier

Priority number(s): US201562196797P 20150724 ; US201562238636P 20151007 ; US201662318194P 20160404 ; US201615140448 20160427 ; US201615140443 20160427

Also published as: AU2016297849 (A1) AU2021202622 (A1) CA2993646 (A1) EP3324845 (A1) EP3324845 (B1) more

Abstract of WO2017019552 (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 (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.

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
2 February 2017 (02.02.2017)

WIPO | PCT

(10) International Publication Number
WO 2017/019552 A1

(51) International Patent Classification:
A61B 5/15 (2006.01) *A61B 5/154* (2006.01)
A61B 5/153 (2006.01)

(21) International Application Number:
PCT/US2016/043709

(22) International Filing Date:
22 July 2016 (22.07.2016)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

62/196,797	24 July 2015 (24.07.2015)	US
62/238,636	7 October 2015 (07.10.2015)	US
62/318,194	4 April 2016 (04.04.2016)	US
15/140,448	27 April 2016 (27.04.2016)	US
15/140,443	27 April 2016 (27.04.2016)	US

(71) Applicant: **KURIN, INC.** [US/US]; 10755 Scripps Poway Parkway No. 257, San Diego, CA 92131 (US).

(72) Inventors: **ROGERS, Bobby**; 10755 Scripps Poway Parkway No. 257, San Diego, CA 92131 (US). **KANG, Gino**; 10755 Scripps Poway Parkway No. 257, San Diego, CA 92131 (US). **DETLOFF, John**; 10755 Scripps Poway Parkway No. 257, San Diego, CA 92131 (US).

(74) Agents: **CLEARY, James, P.** et al.; Mintz Levin Cohn Ferris Glovsky And Popeo, P.C., 3580 Carmel Mountain Road, Suite 300, San Diego, CA 92130-6768 (US).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Published:

— *with international search report (Art. 21(3))*

(54) Title: BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE AND METHOD

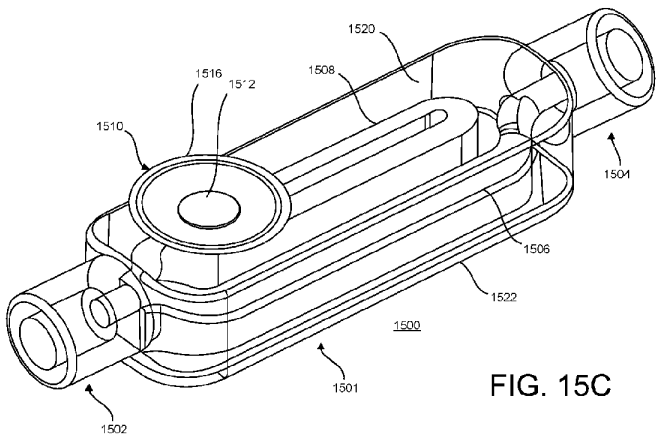


FIG. 15C

(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 (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.

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BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE AND METHOD

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 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 – 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.

[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 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 claim 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 claim 1, wherein the sequestration chamber includes a sequestration channel defined in the housing.

4. The blood sequestration device in accordance with claim 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 claim 3, 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 claim 1, 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 claim 3, 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 claim 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 claim 8, 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 claim 8, 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 claim 8, wherein the sequestration chamber includes a sequestration channel defined in the housing.

13. The blood sequestration device in accordance with claim 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 claim 8, 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 claim 8, 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 claim 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 claim 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 claim 17, 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 claim 17, wherein the air permeable blood barrier includes an air permeable material that seals upon contact with blood.

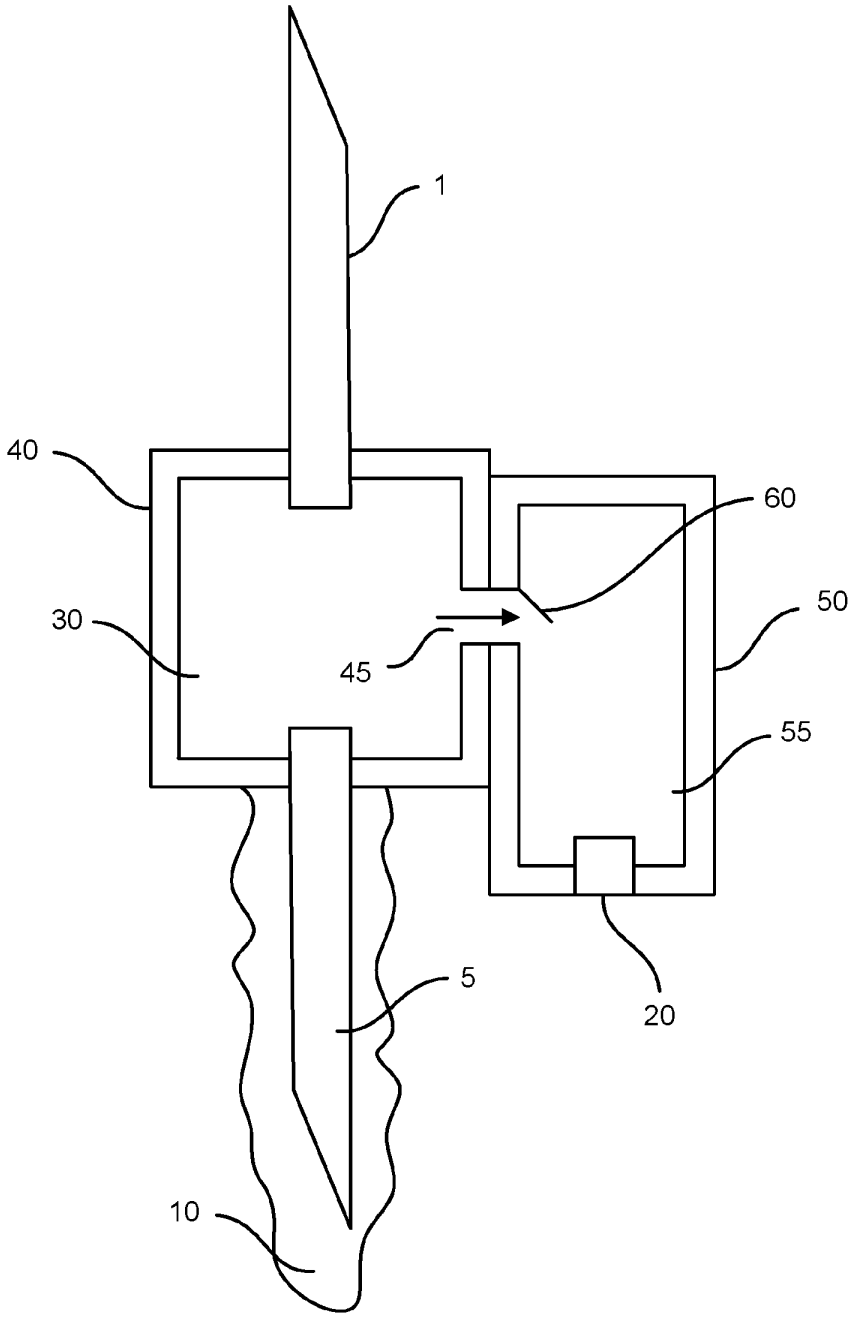


FIG. 1

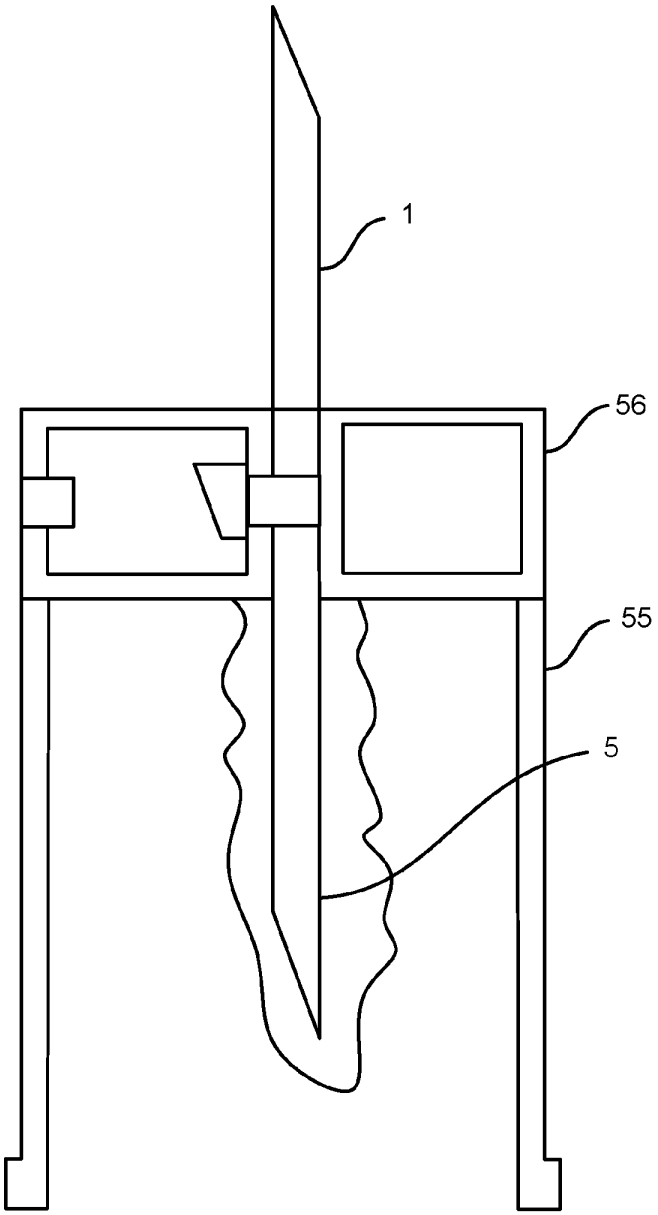


FIG. 2

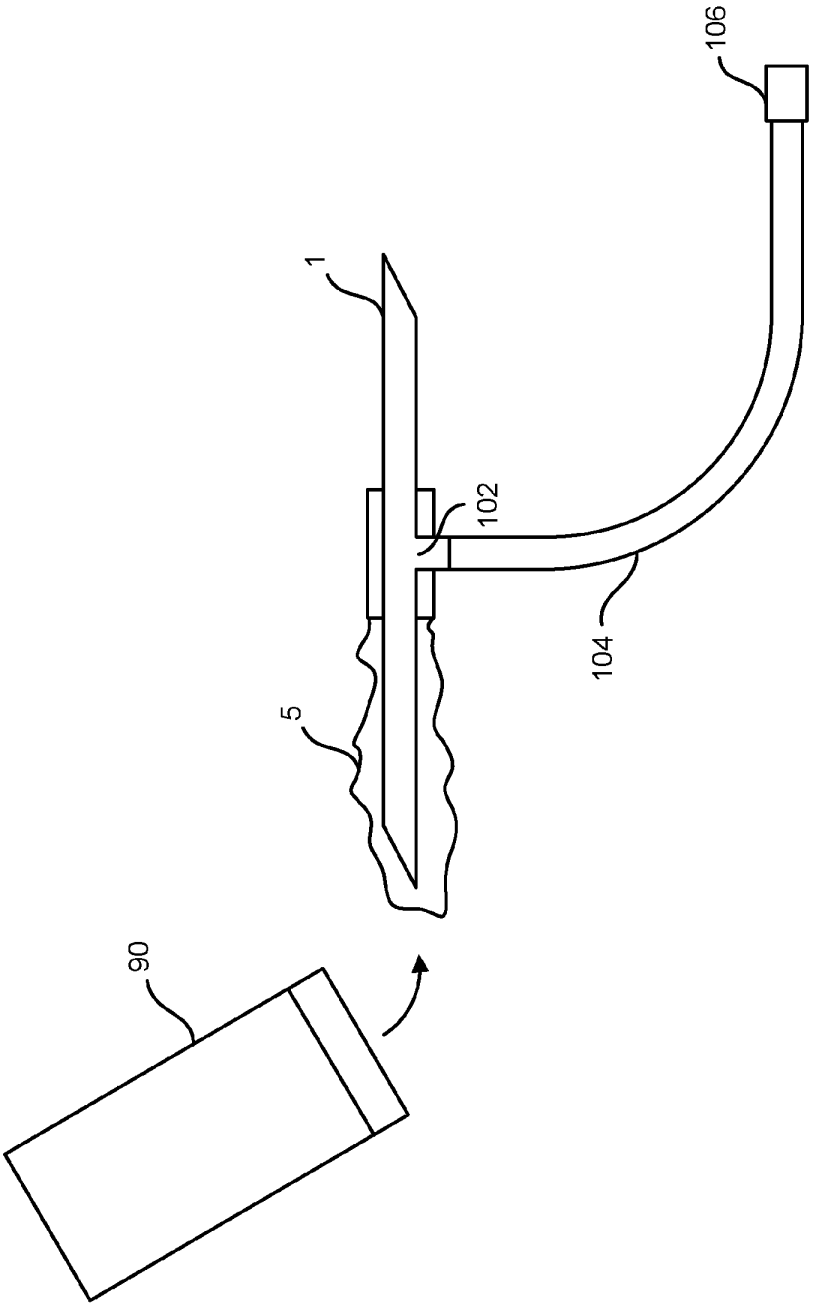


FIG. 3

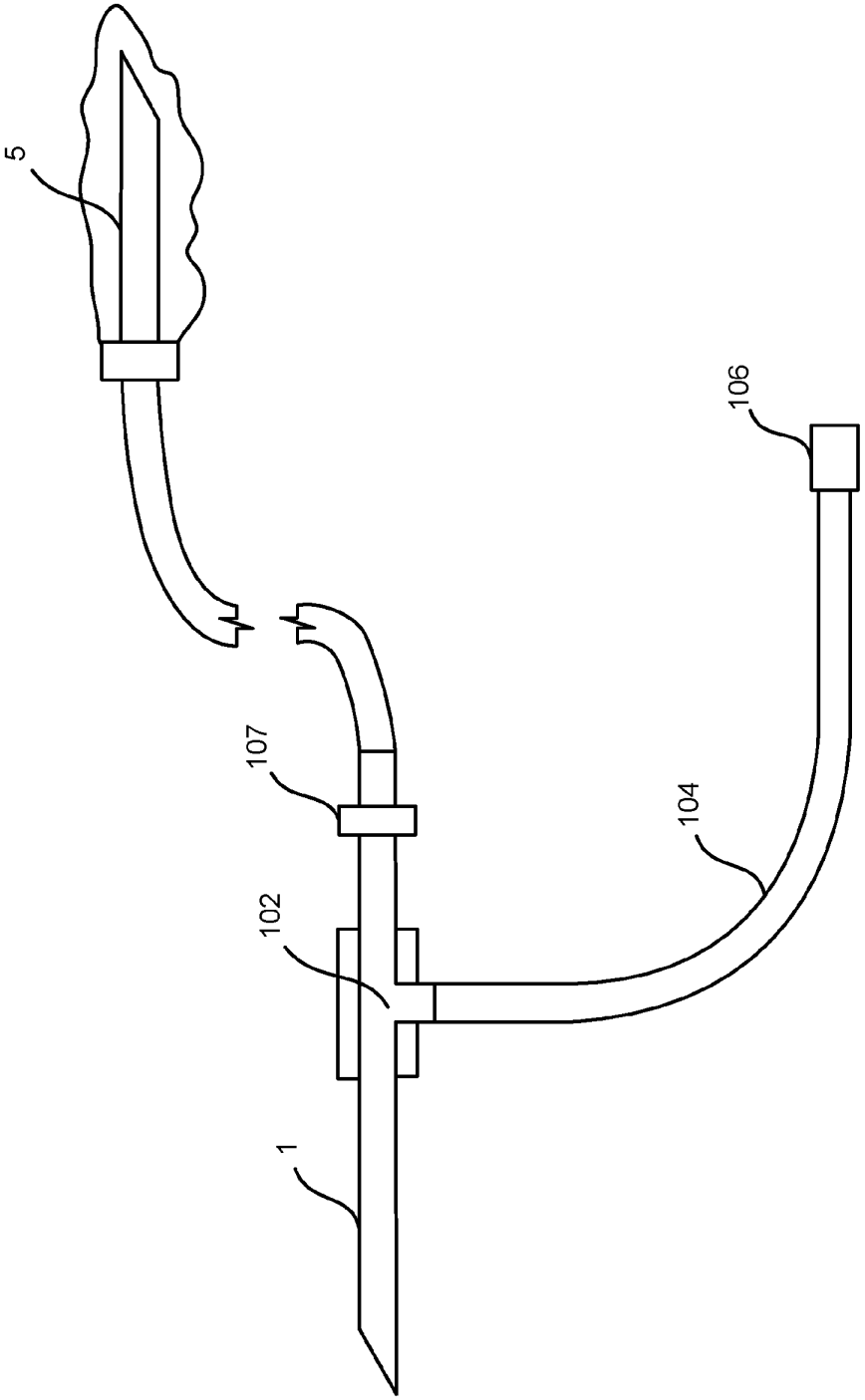


FIG. 4

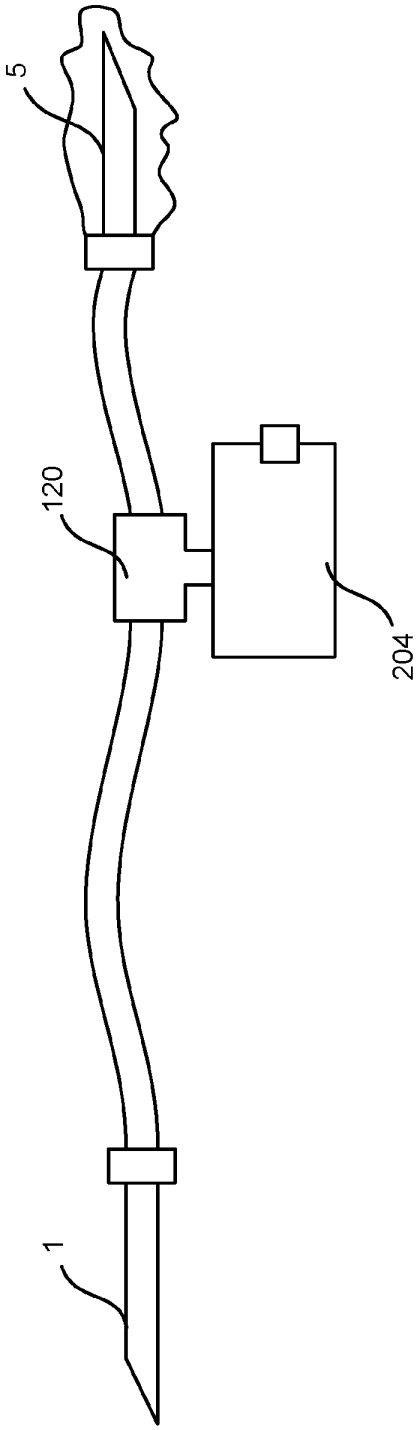


FIG. 5

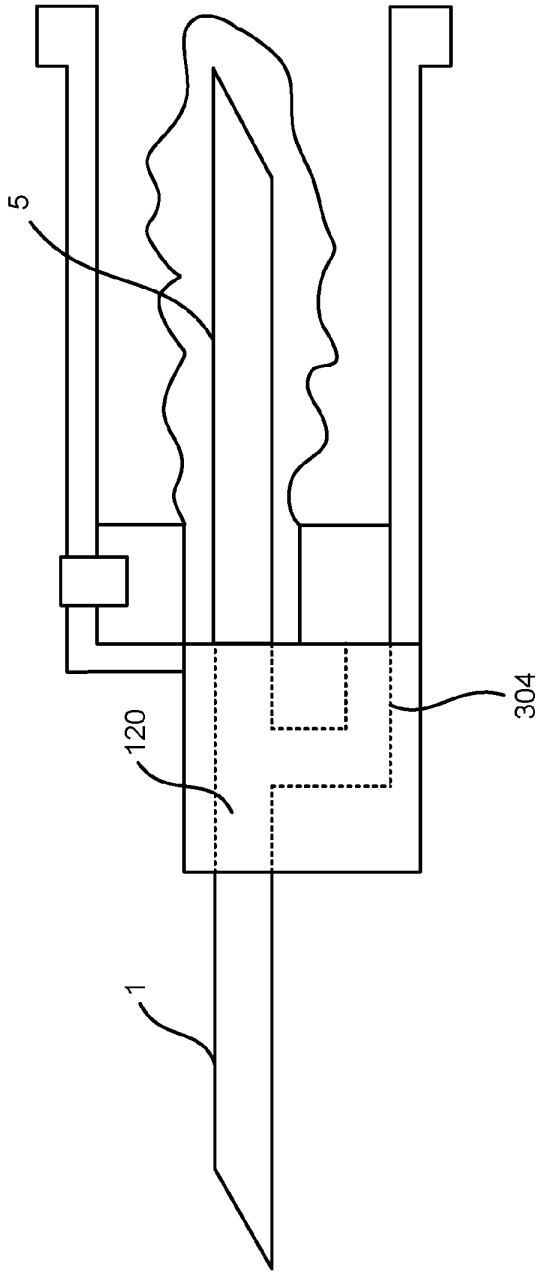


FIG. 6

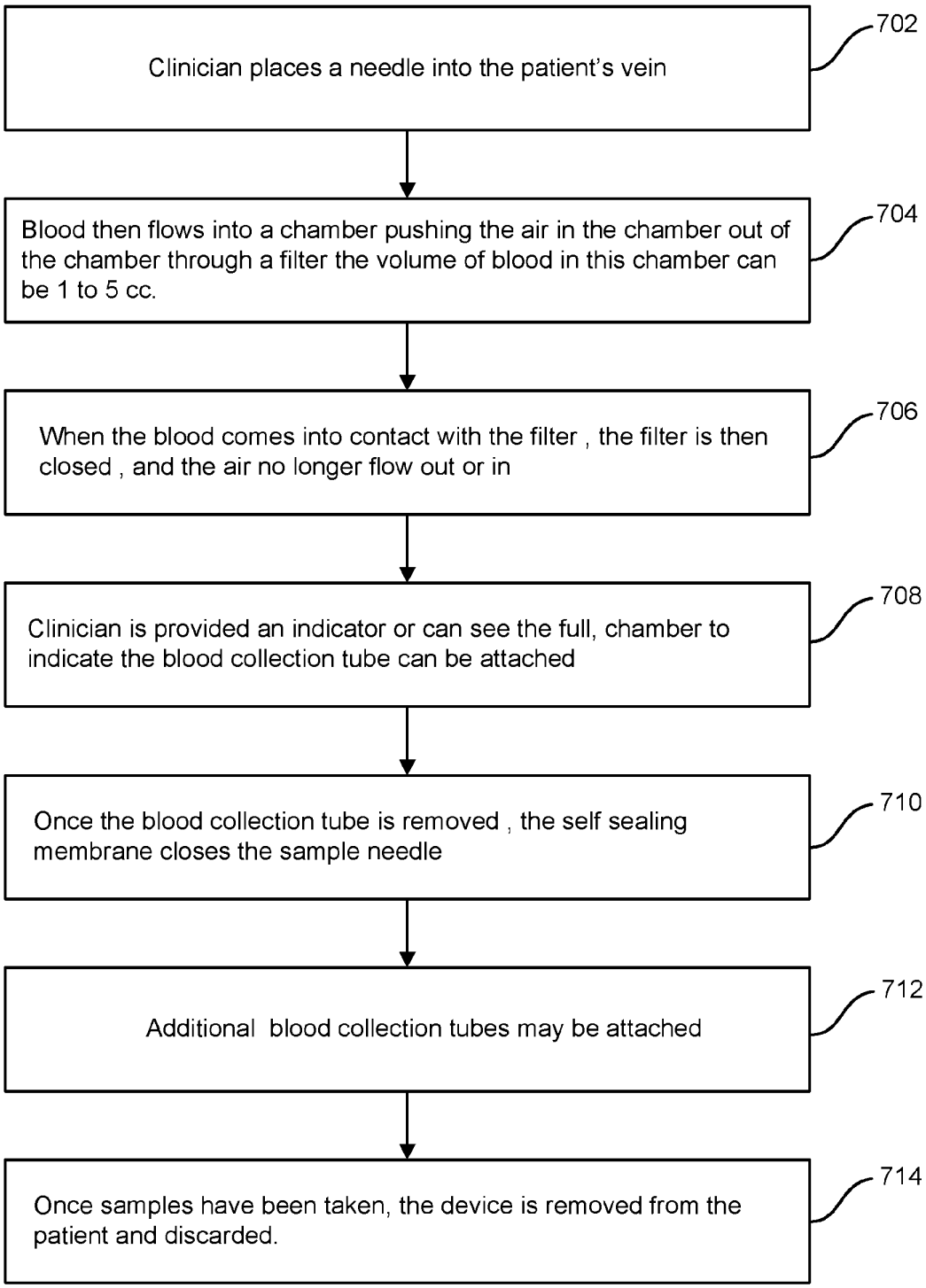
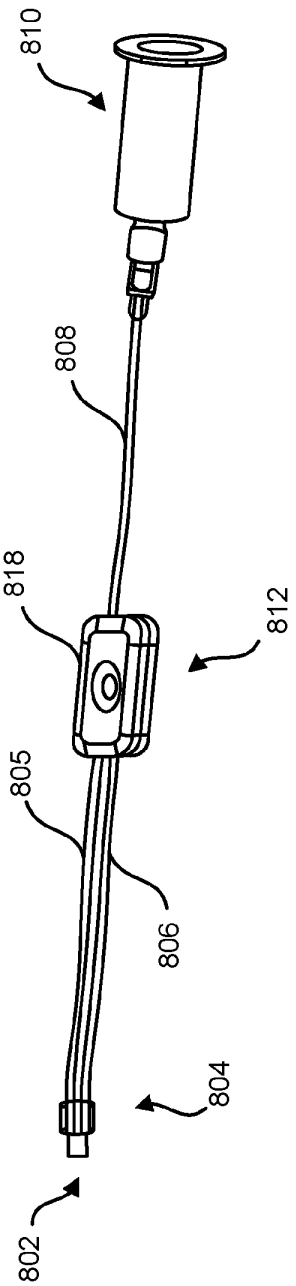

Clinician places a needle into the patient's vein
702
Blood then flows into a chamber pushing the air in the chamber out of the chamber through a filter the volume of blood in this chamber can be 1 to 5 cc.
704
When the blood comes into contact with the filter , the filter is then closed , and the air 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

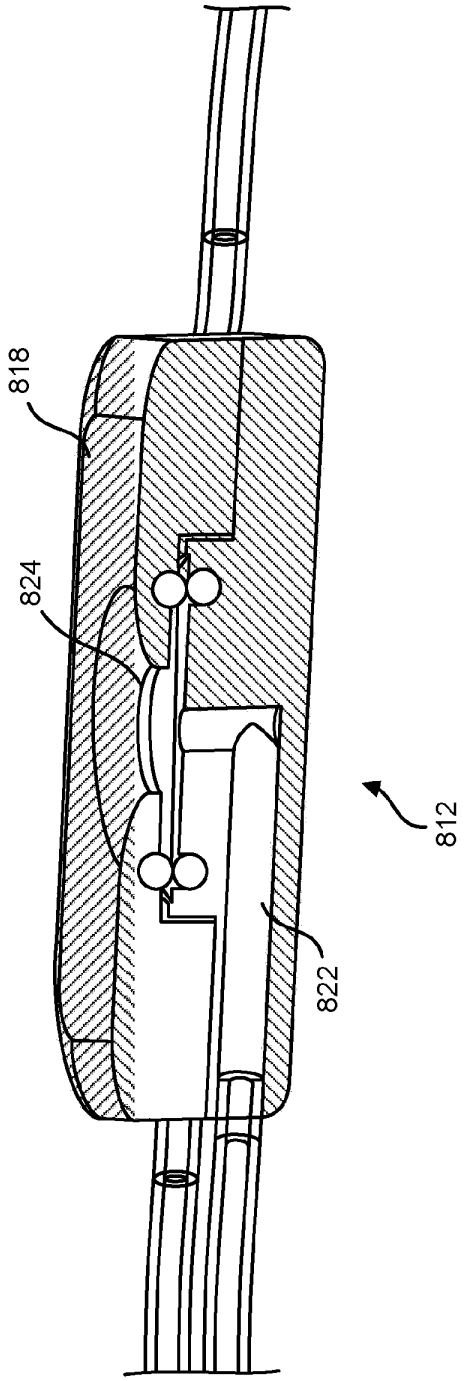


FIG. 8B

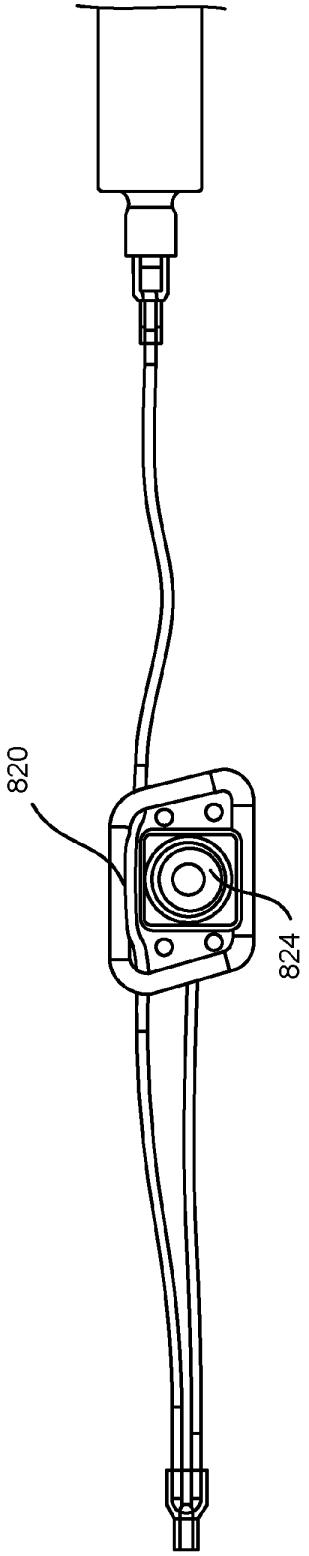


FIG. 8C

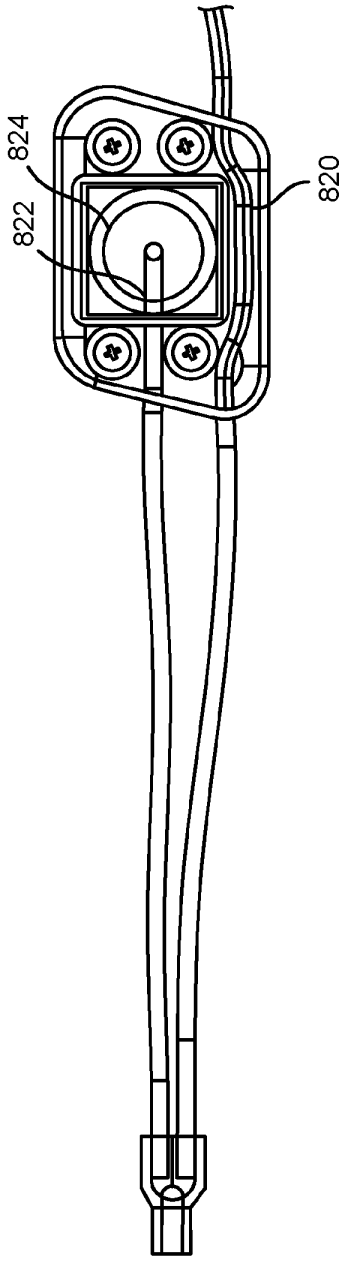


FIG. 8D

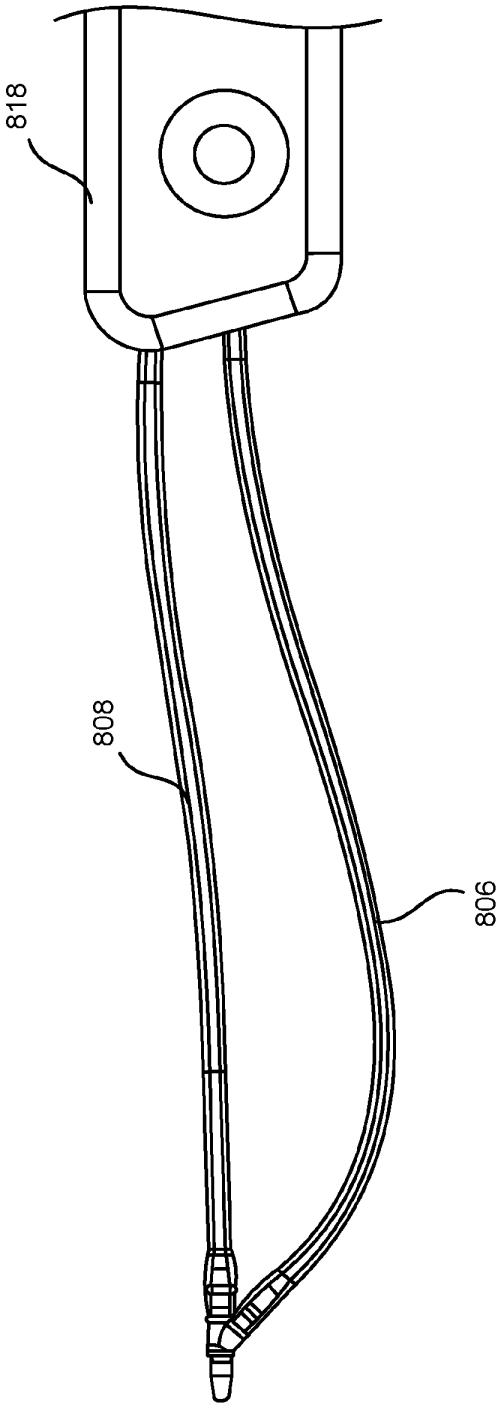


FIG. 8E

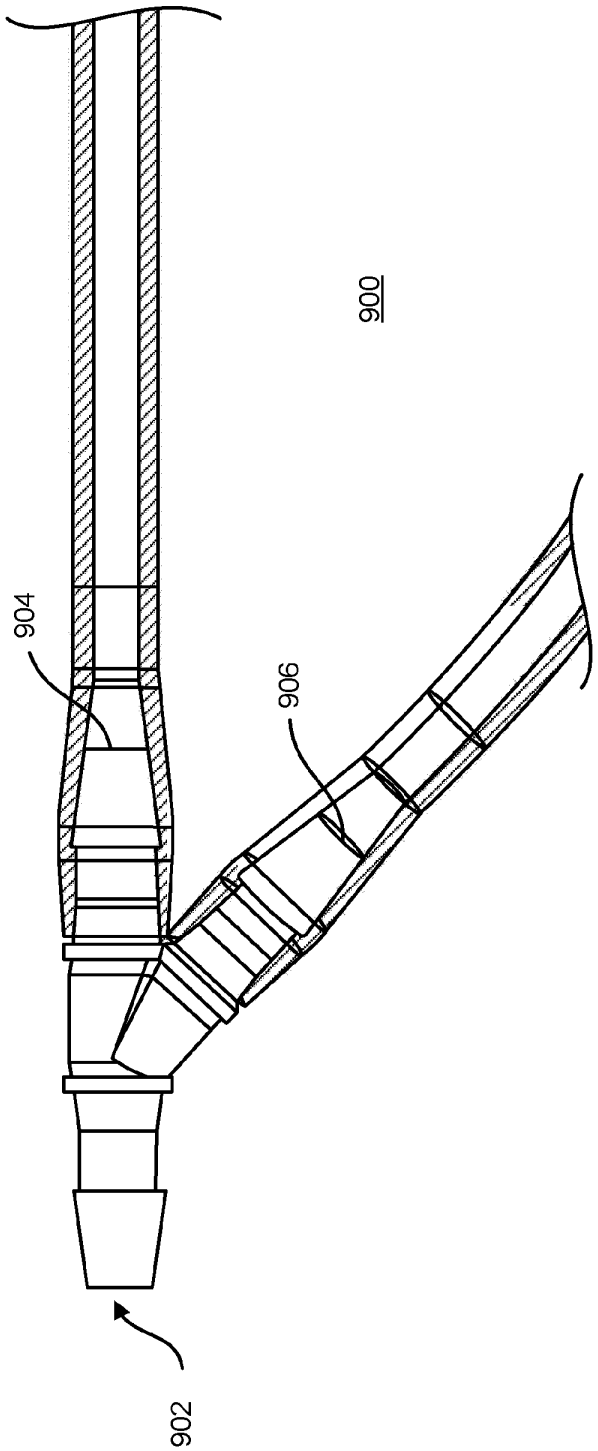


FIG. 9

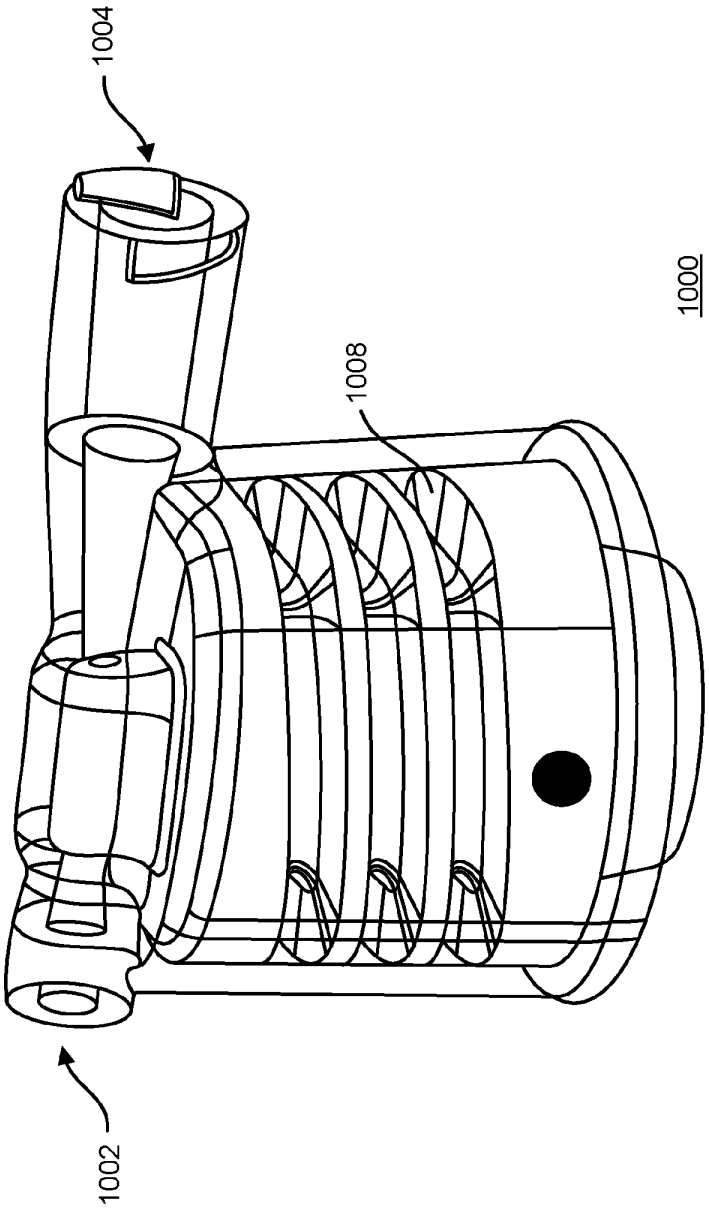


FIG. 10A

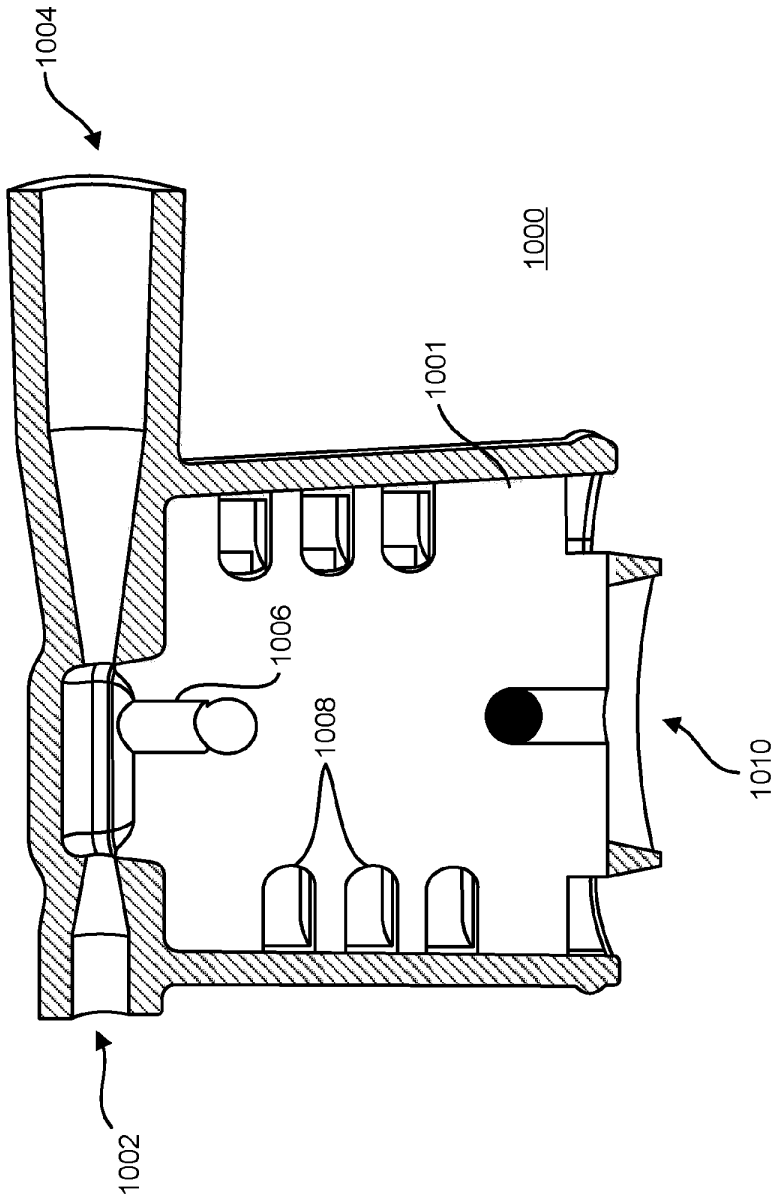


FIG. 10B

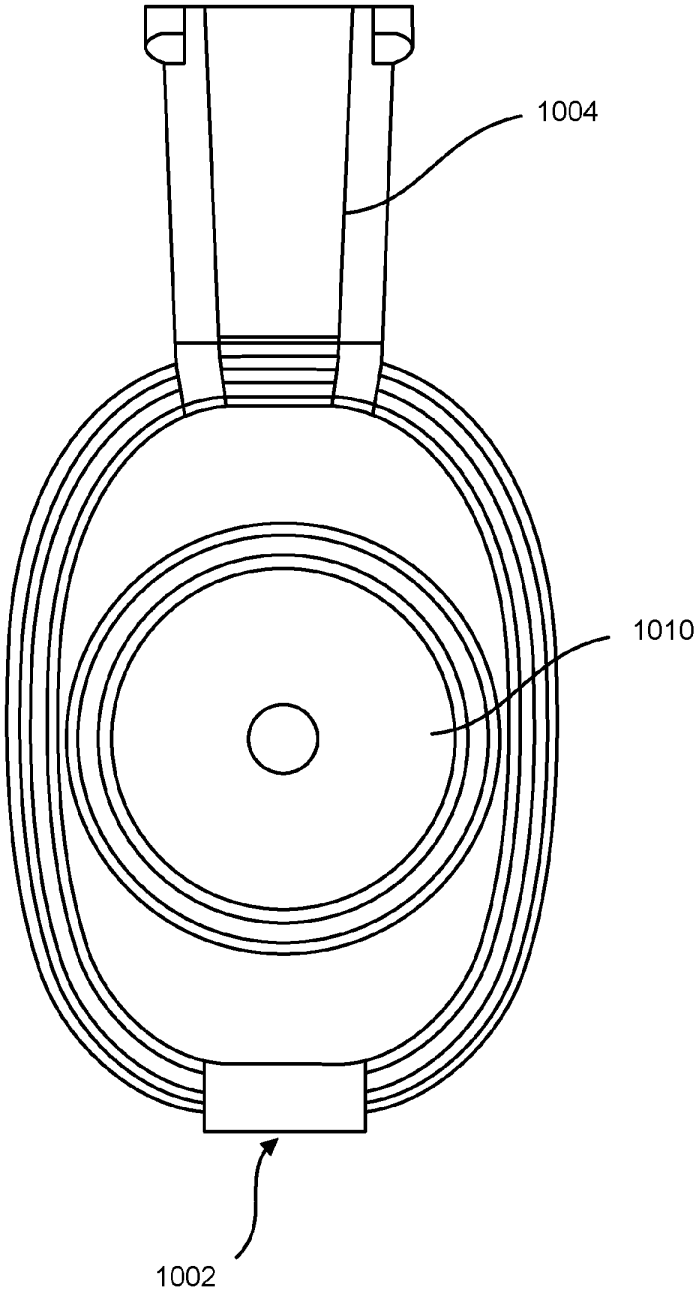


FIG. 10C

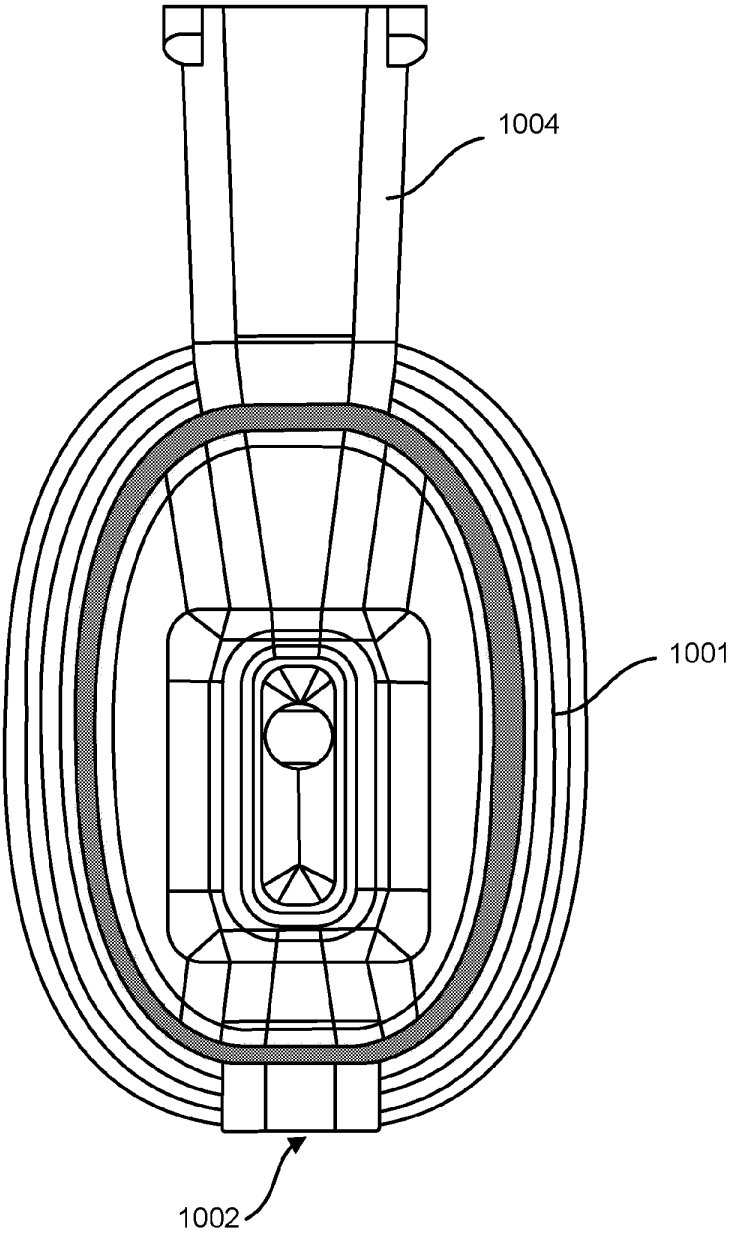


FIG. 10D

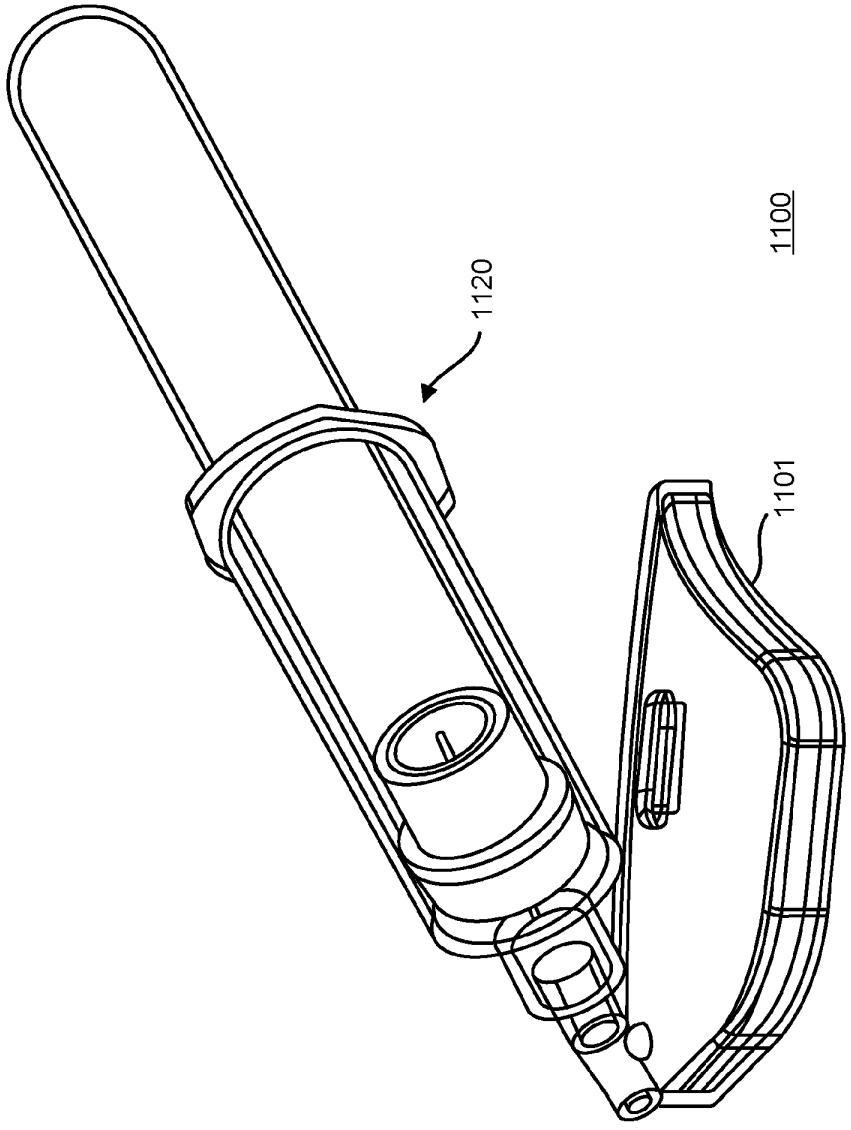


FIG. 11A

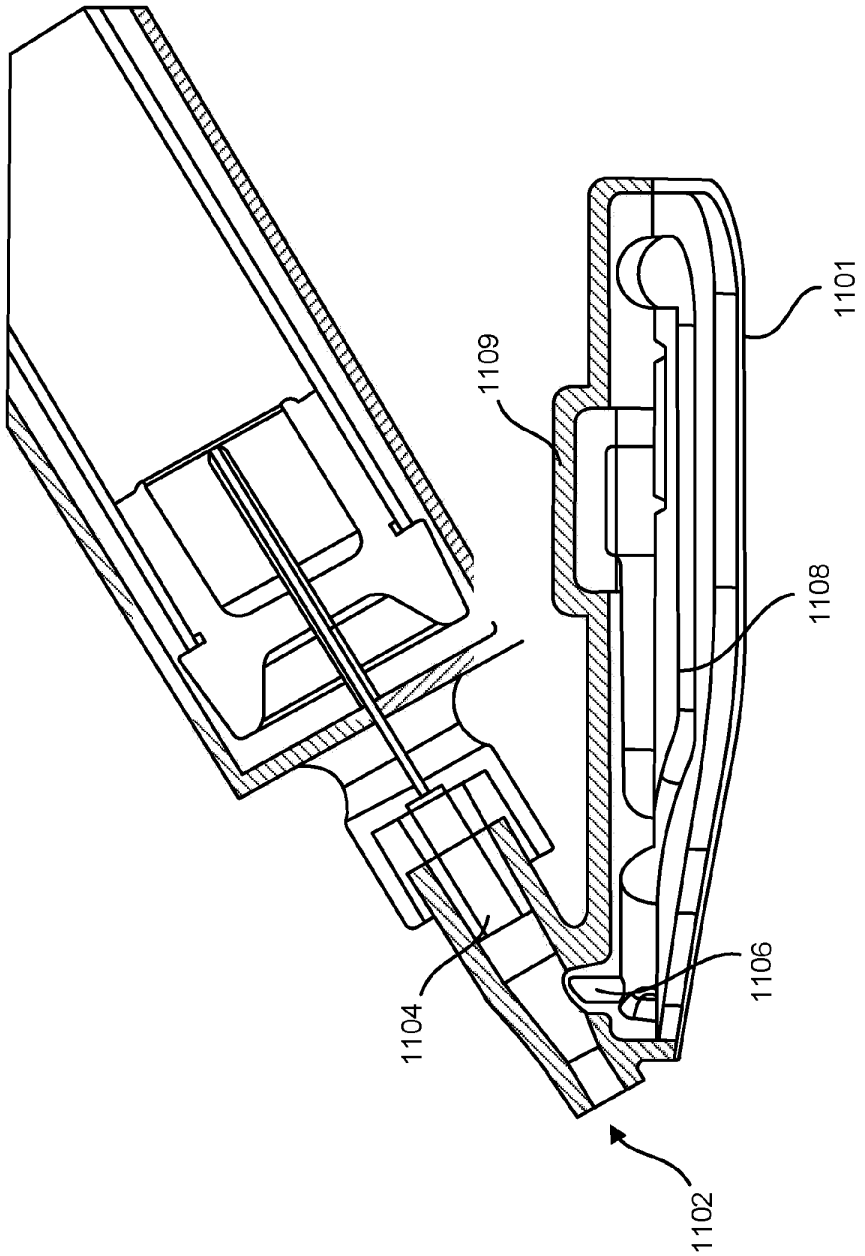


FIG. 11B

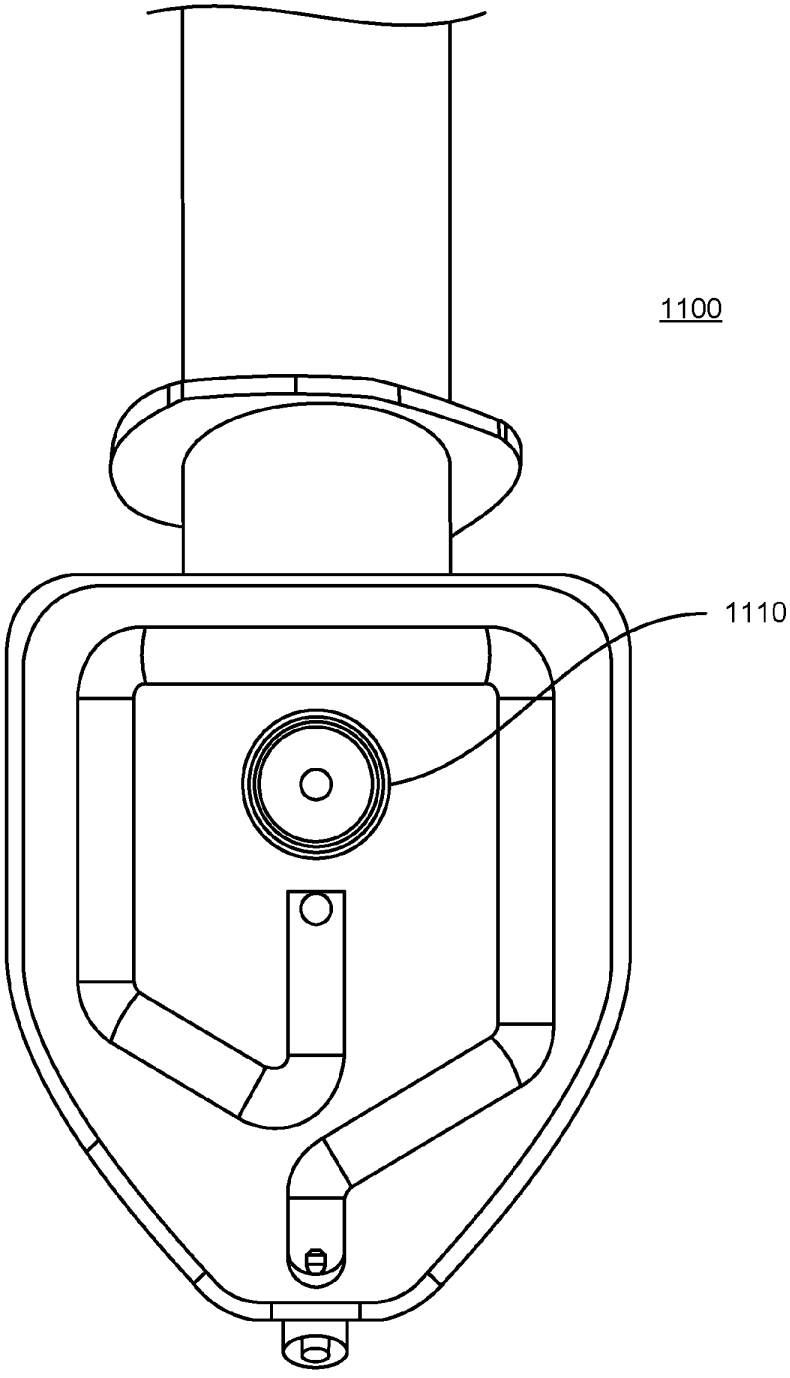


FIG. 11C

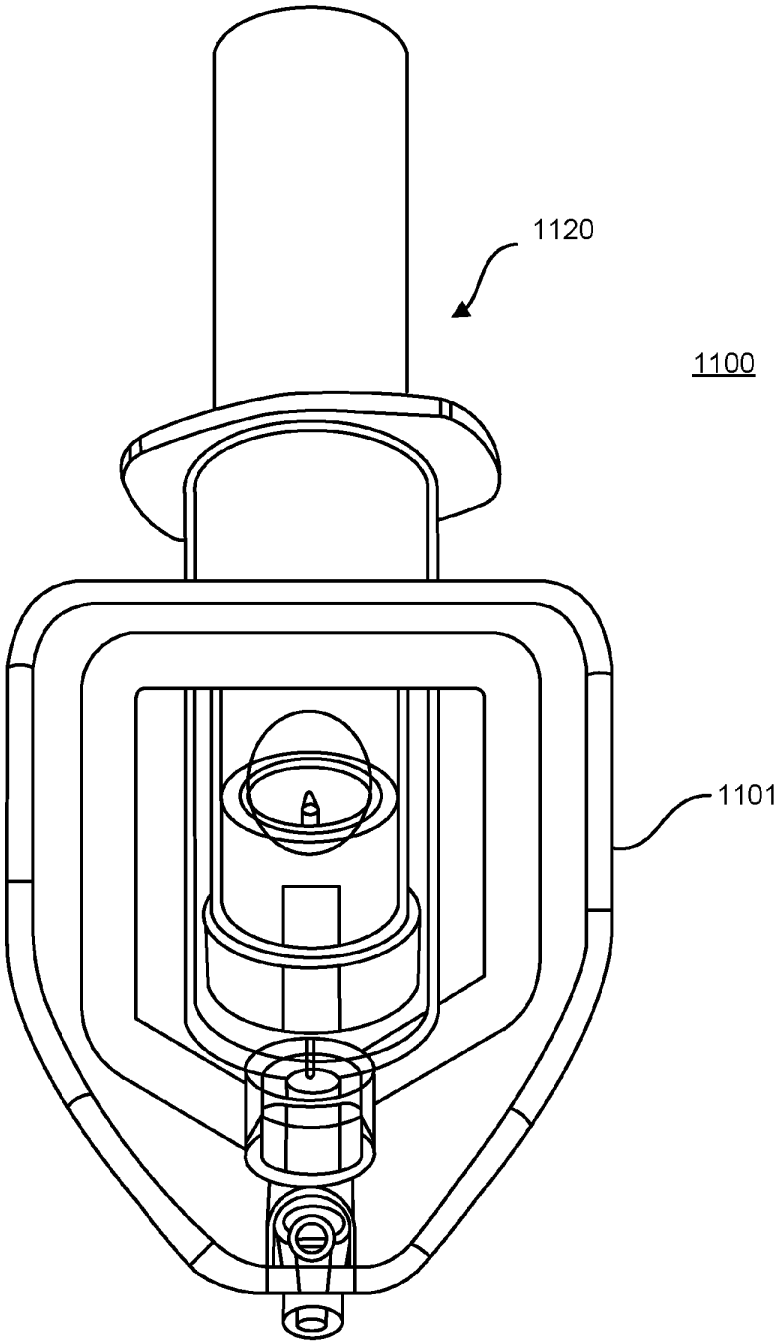


FIG. 11D

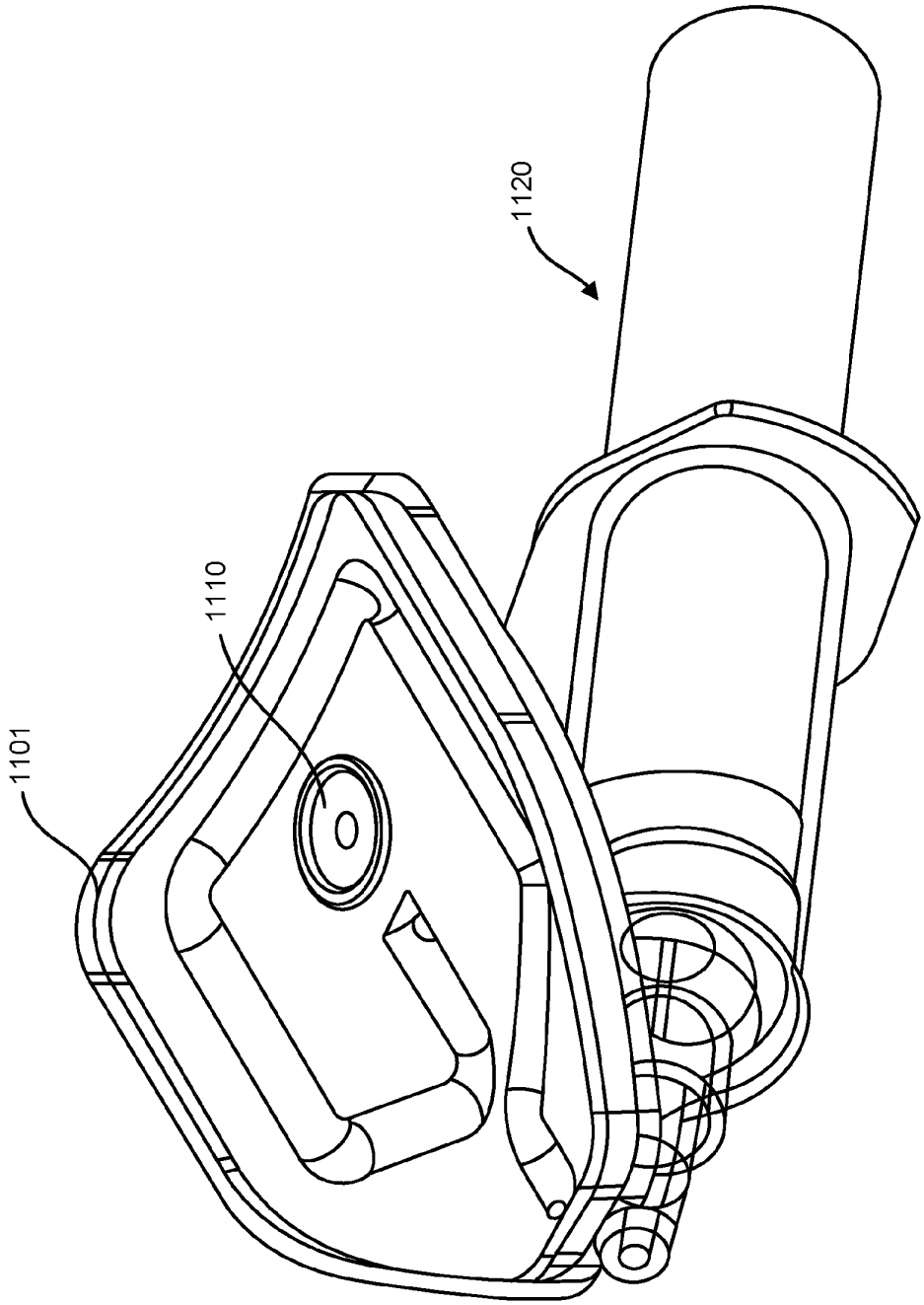


FIG. 11E

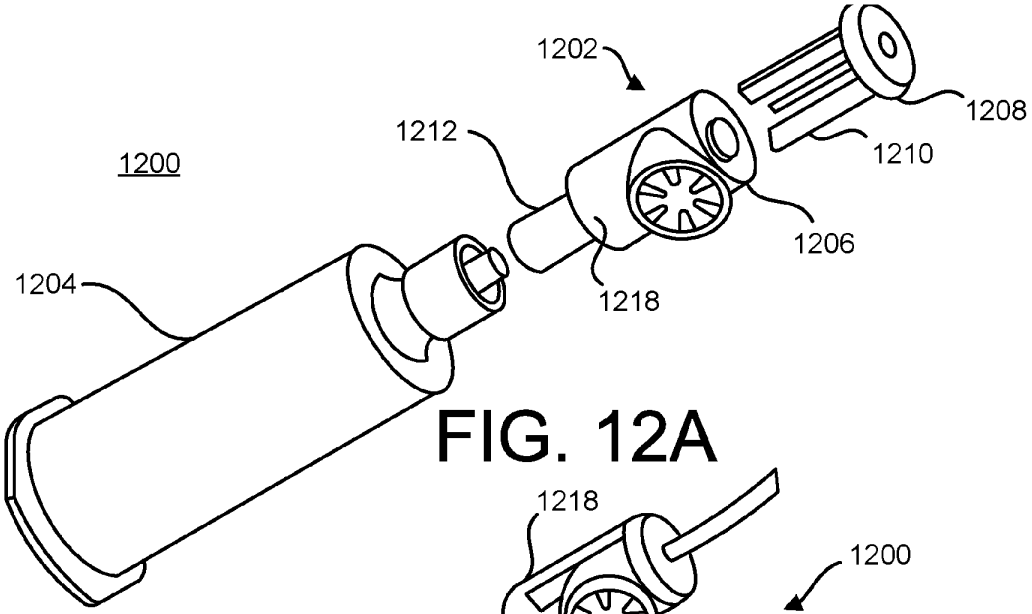


FIG. 12A

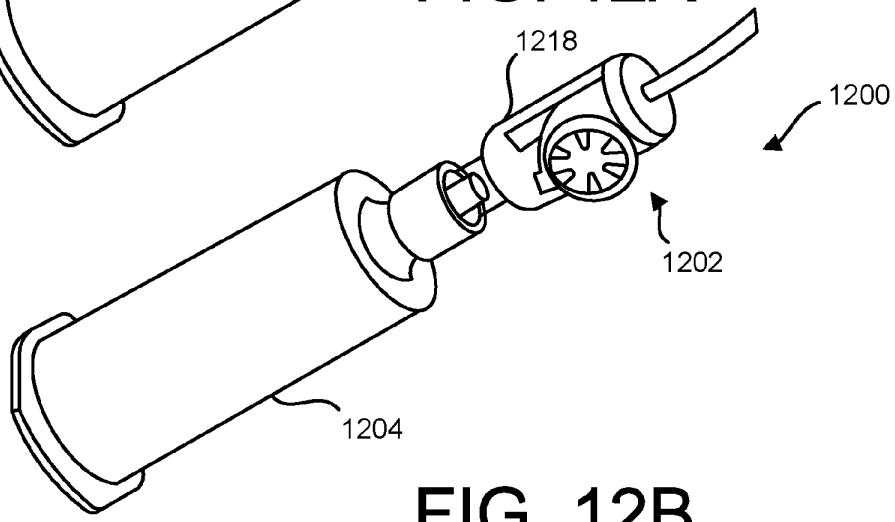


FIG. 12B

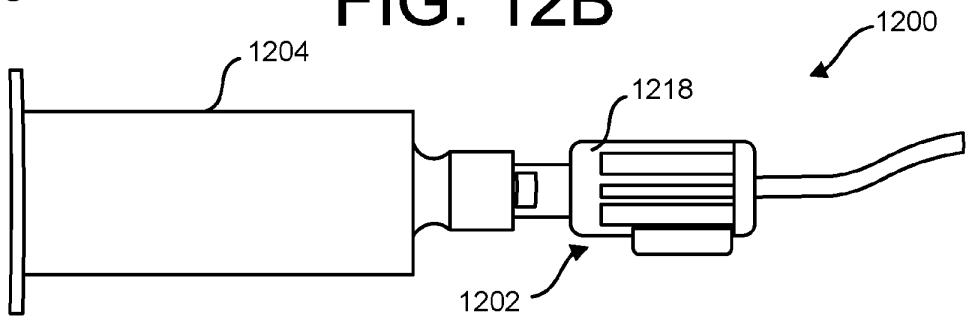


FIG. 12C

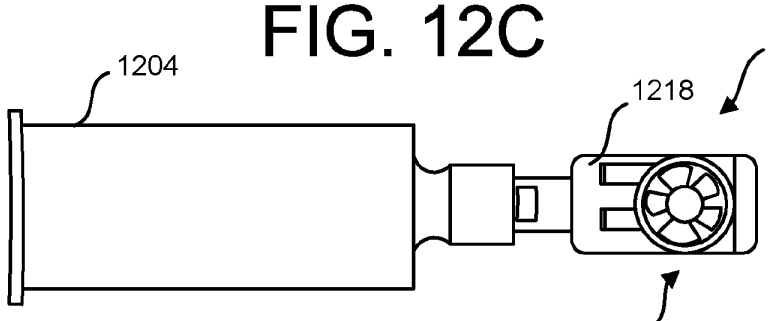


FIG. 12D

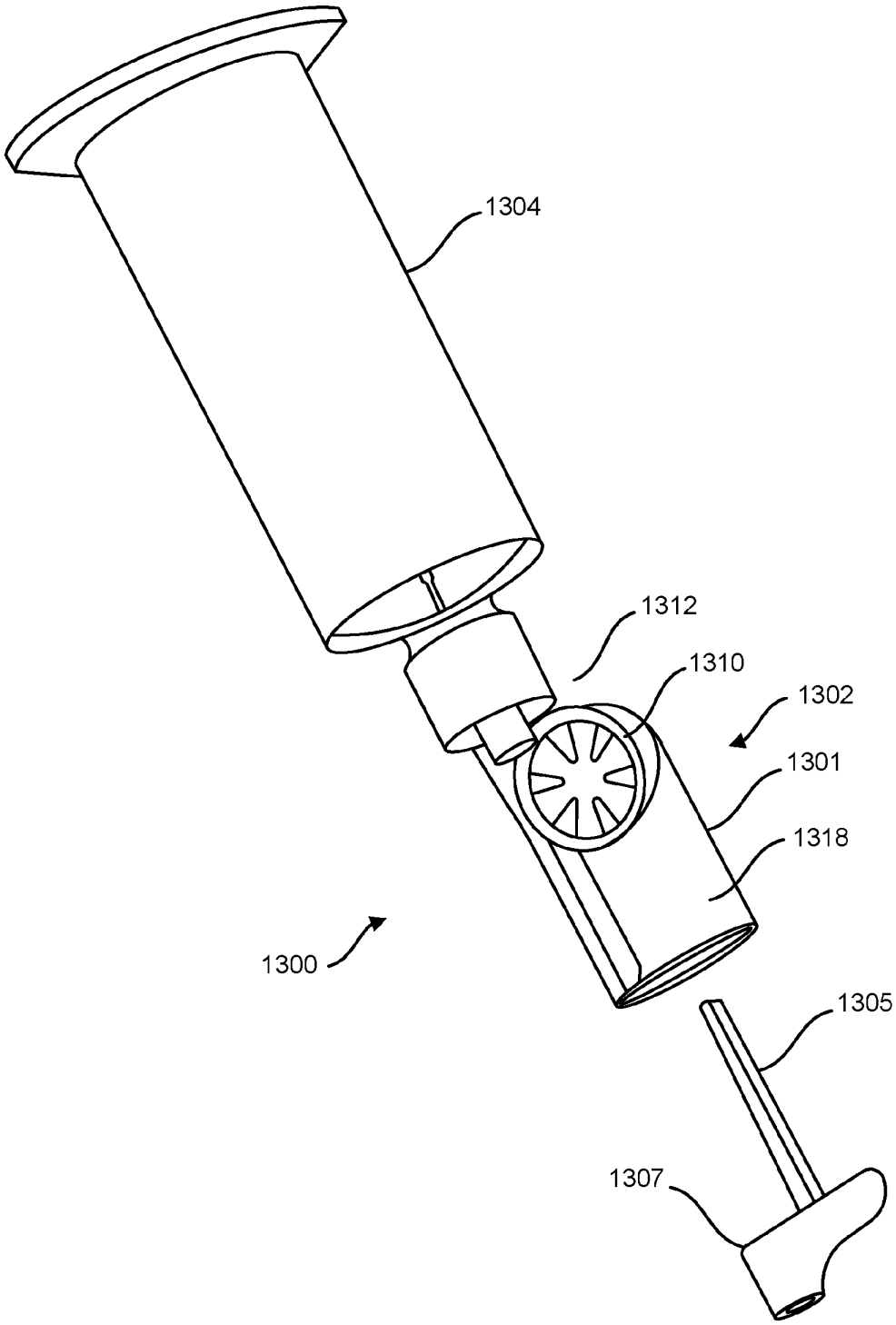


FIG. 13A

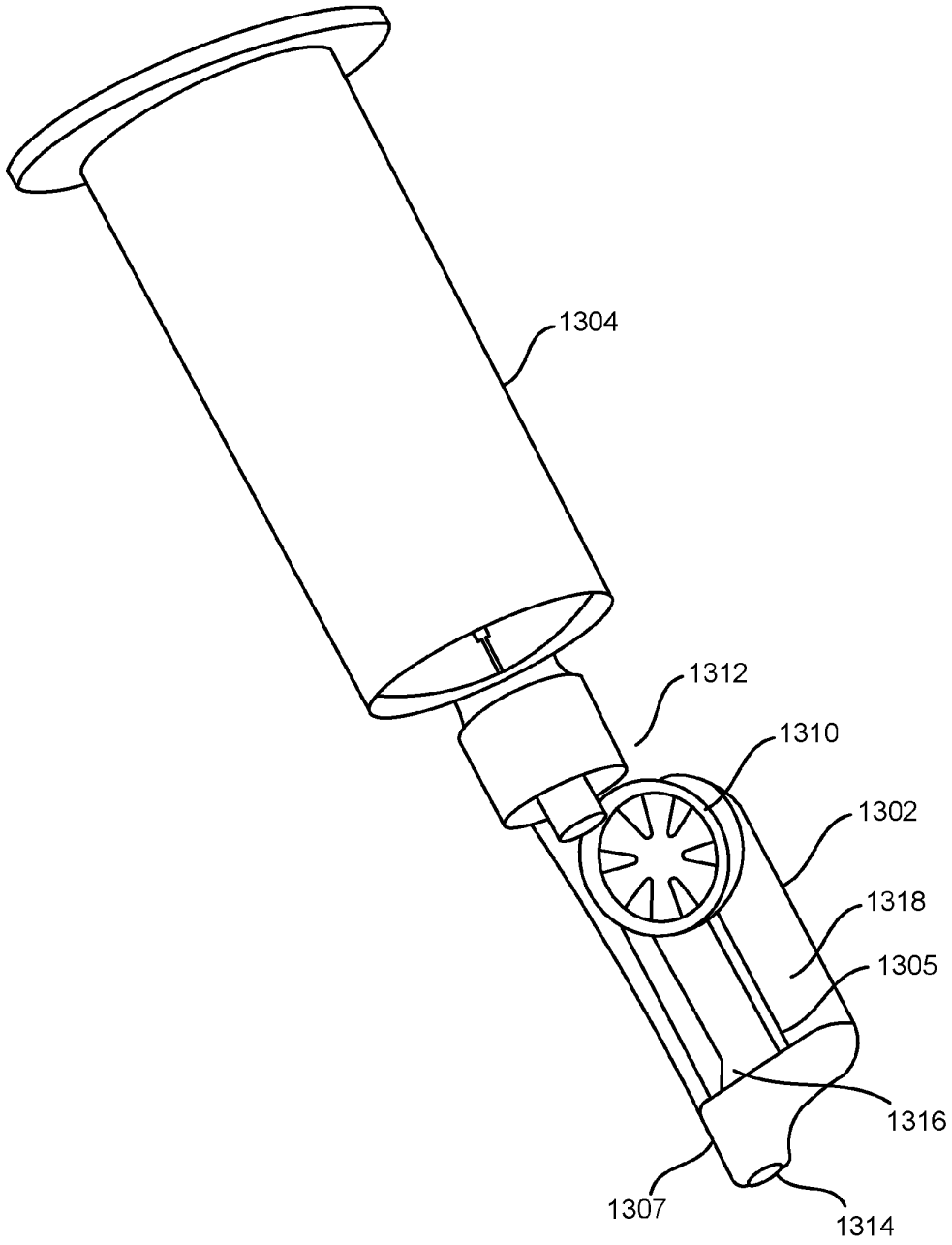


FIG. 13B

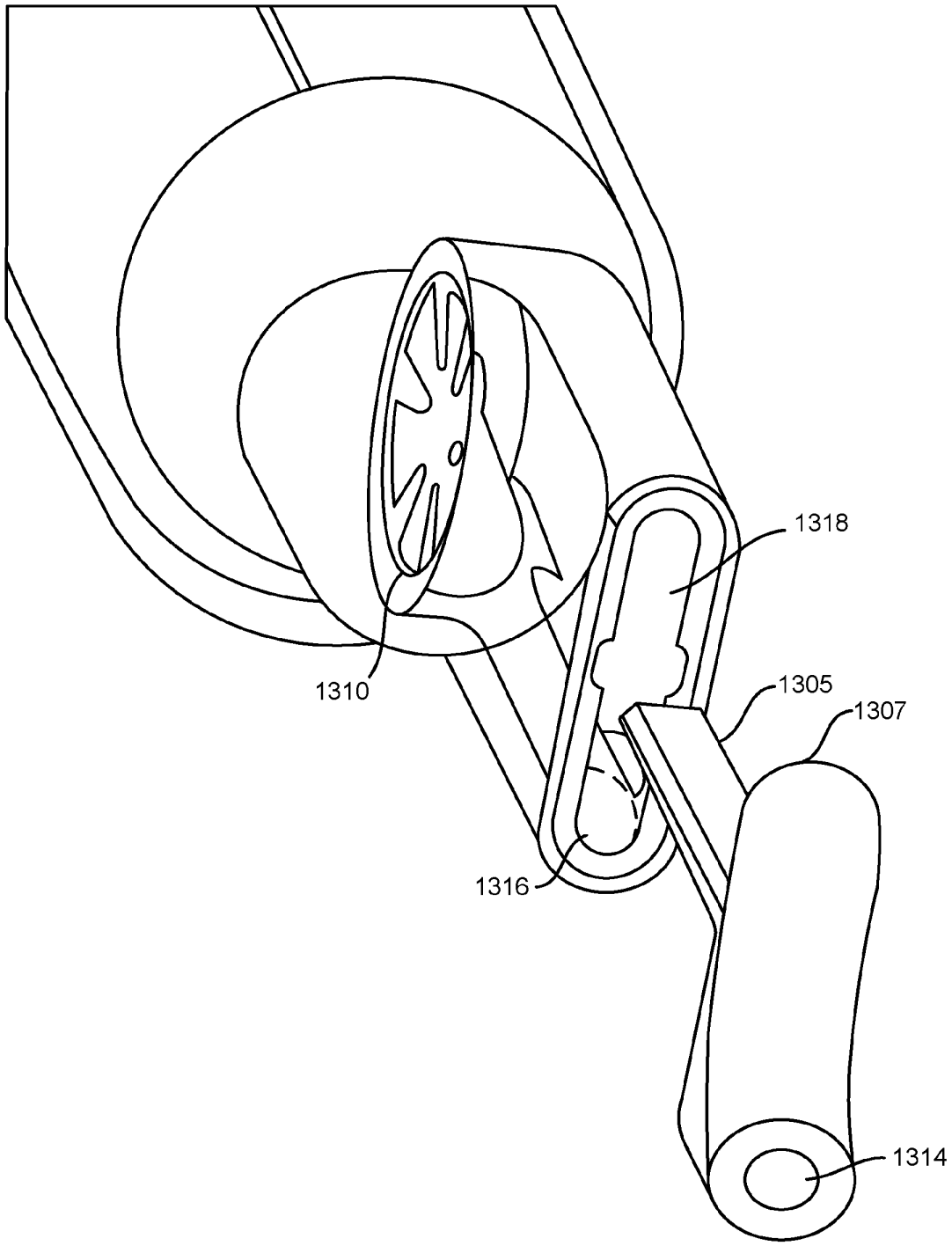


FIG. 13C

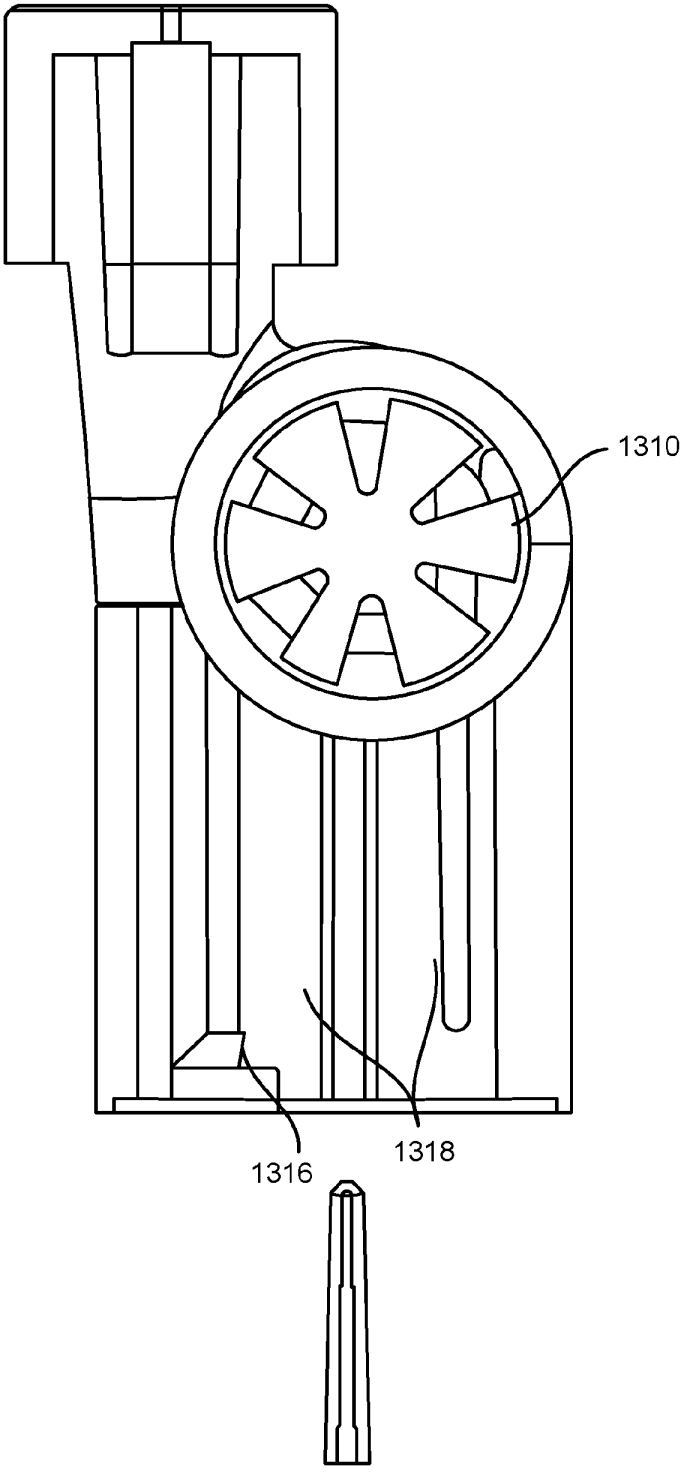


FIG. 13D

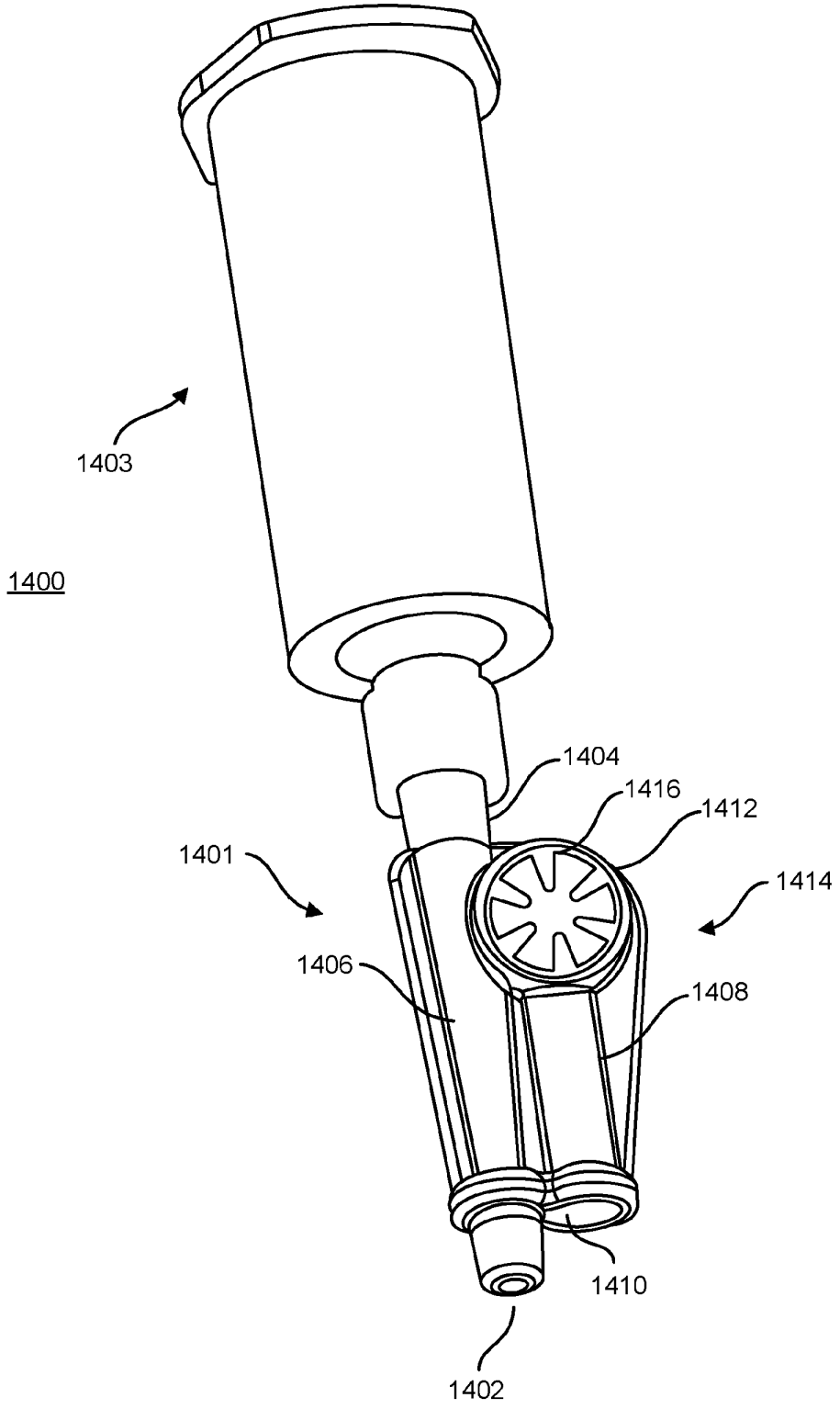


FIG. 14A

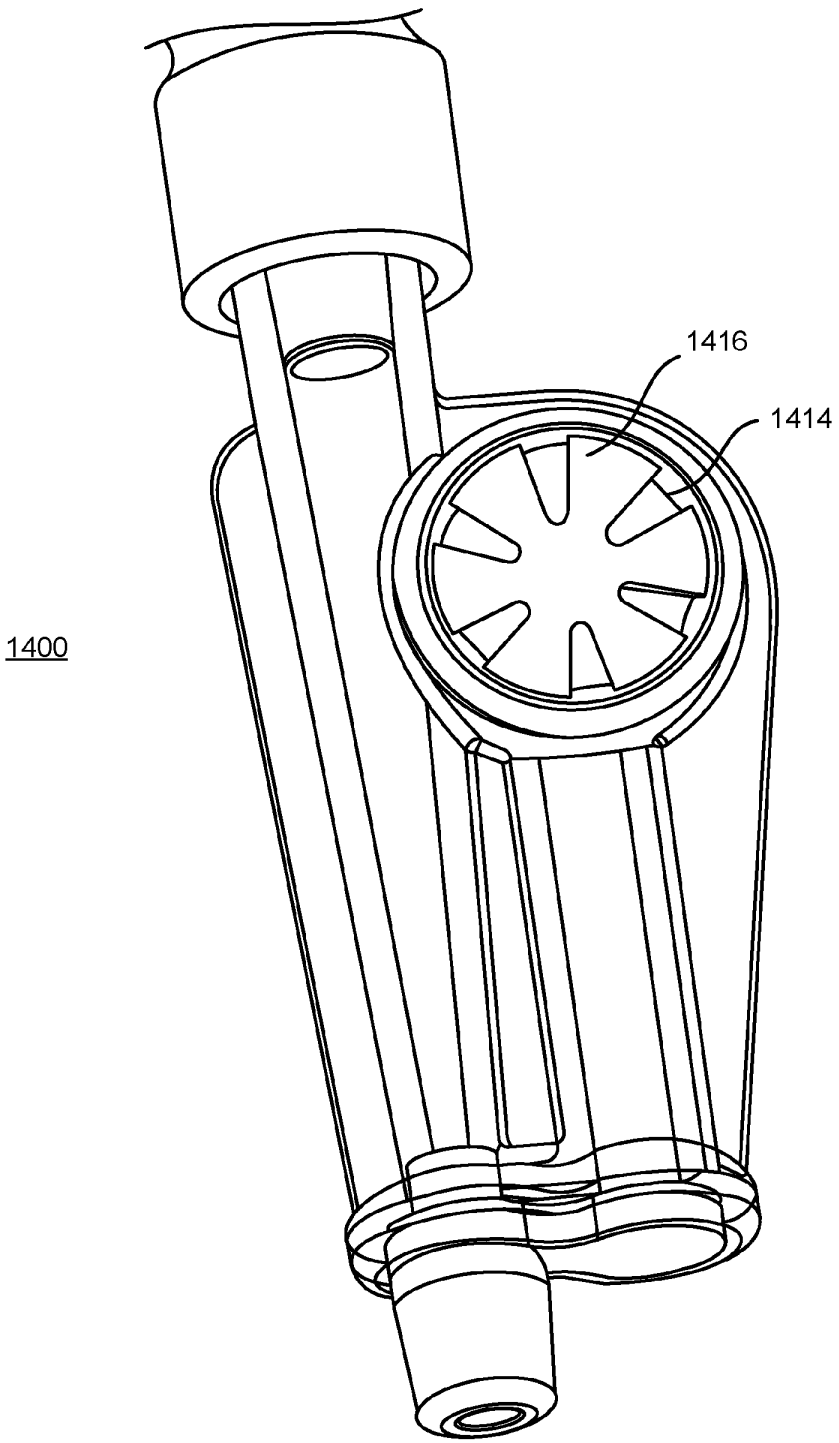


FIG. 14B

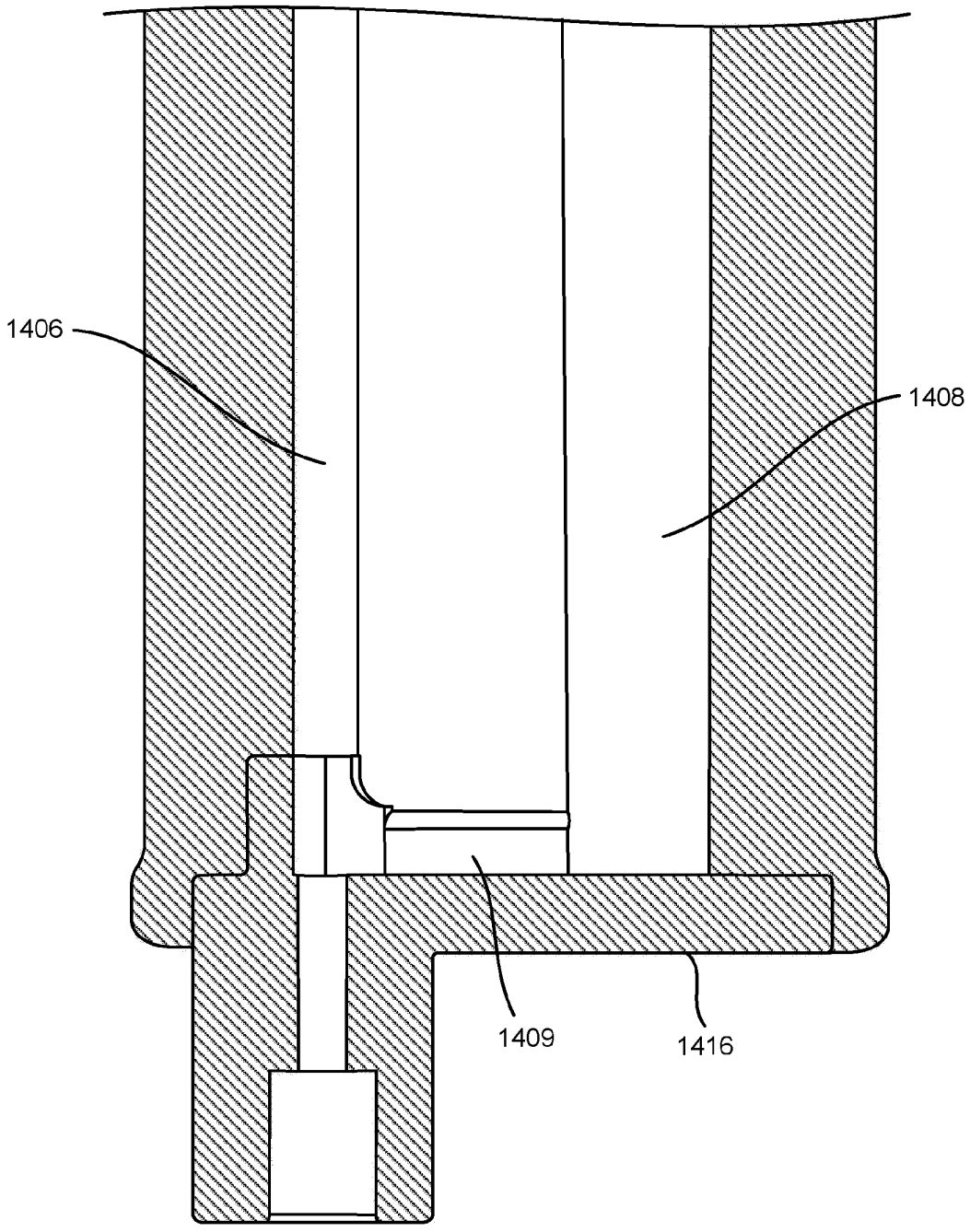


FIG. 14C

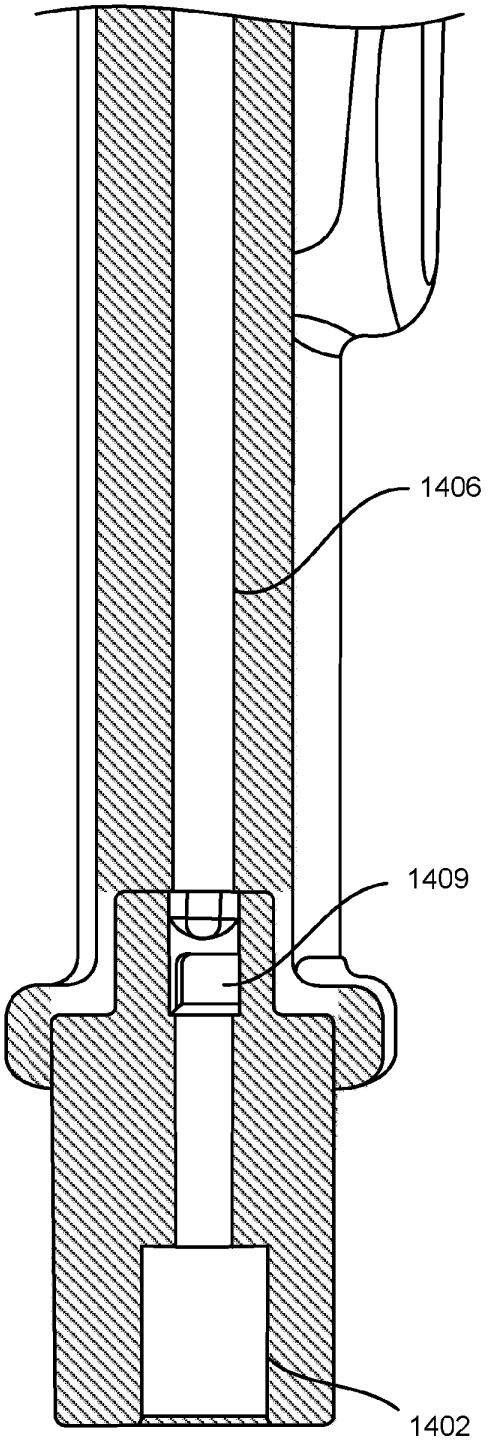


FIG. 14D

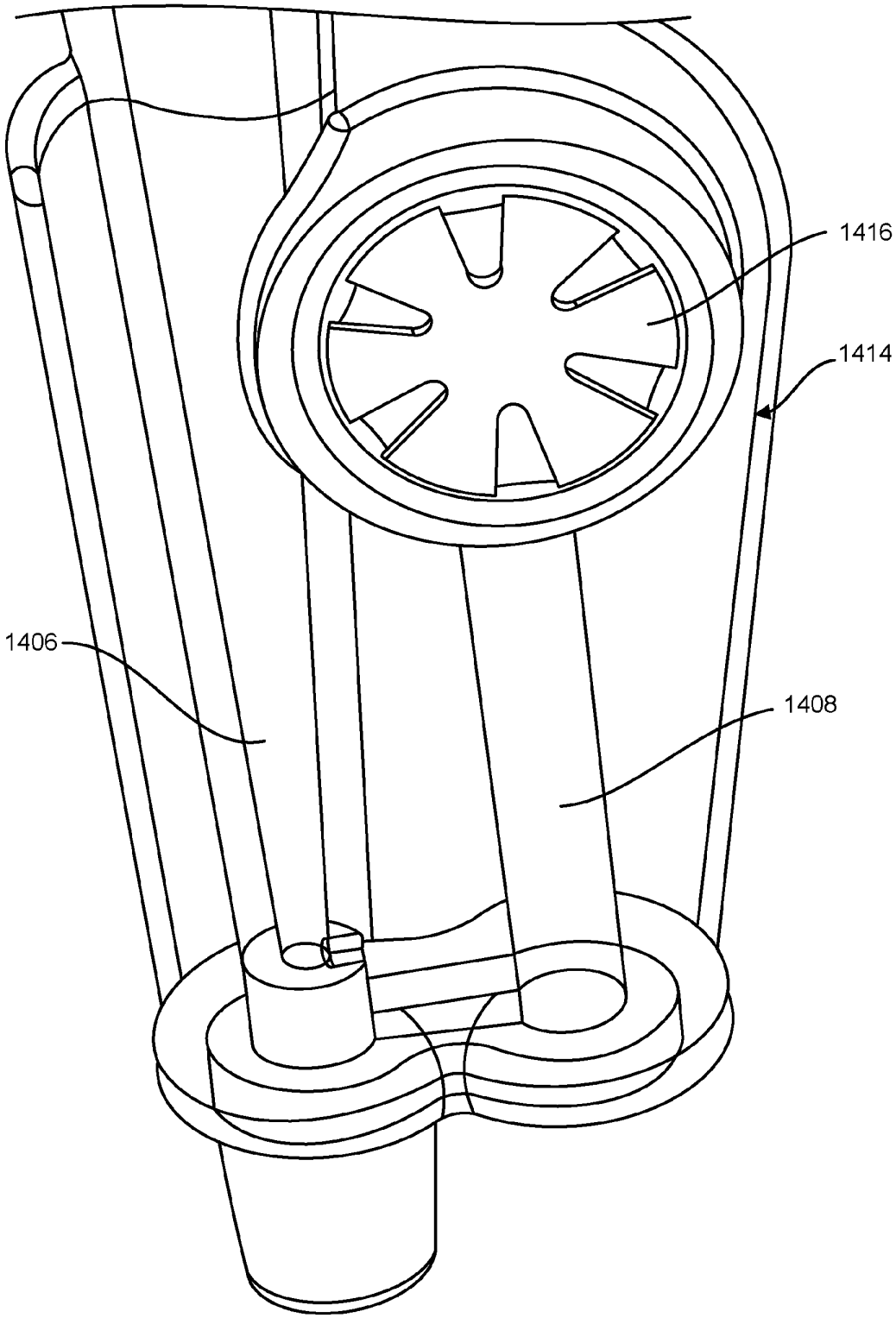


FIG. 14E

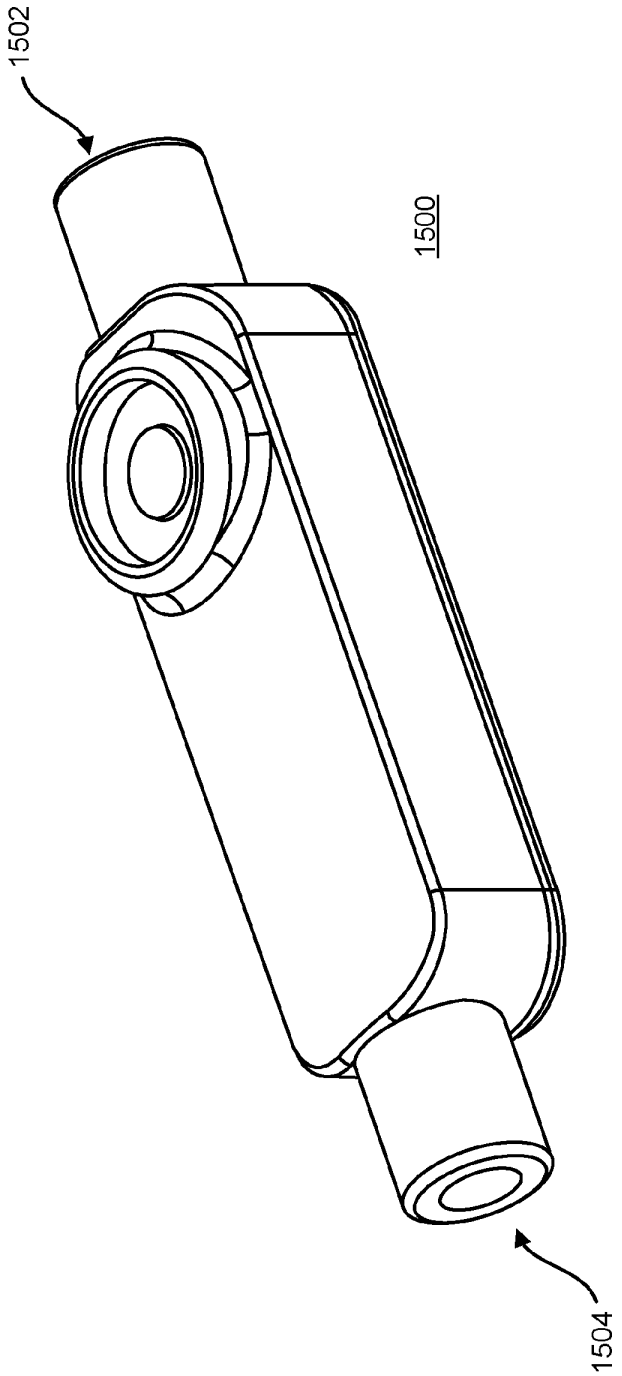


FIG. 15A

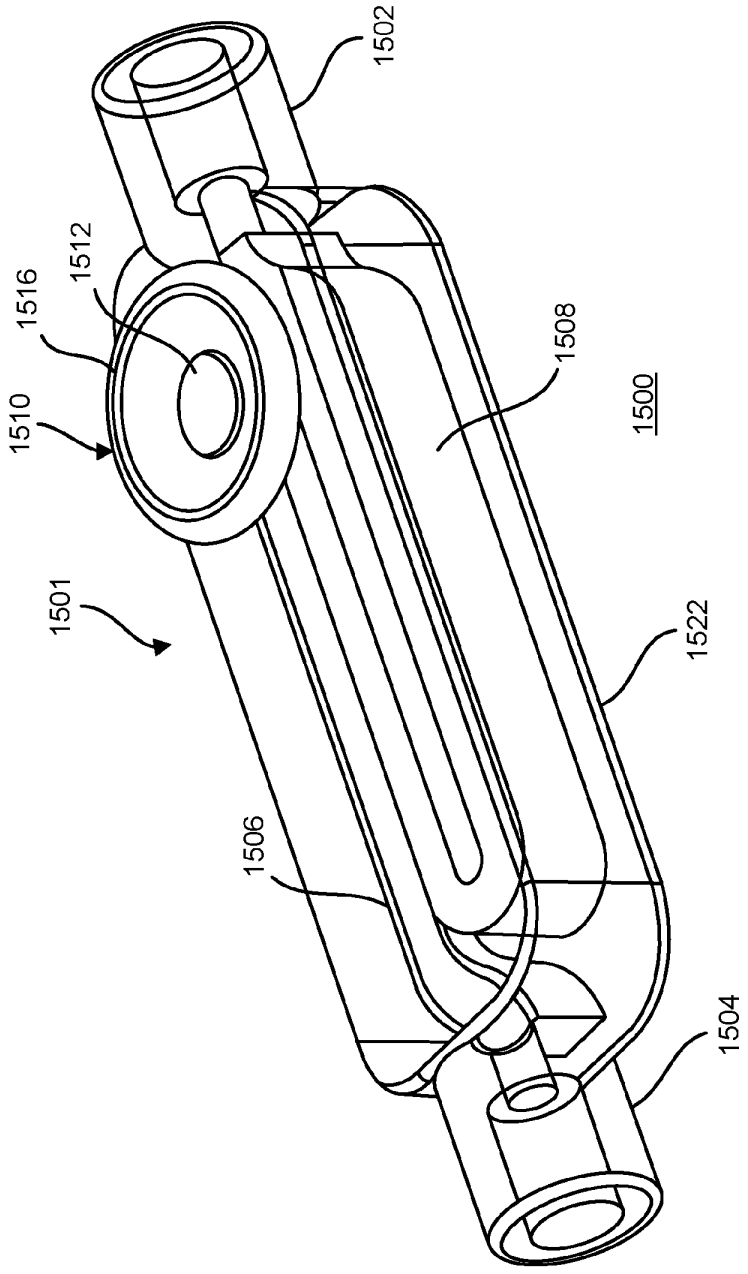


FIG. 15B

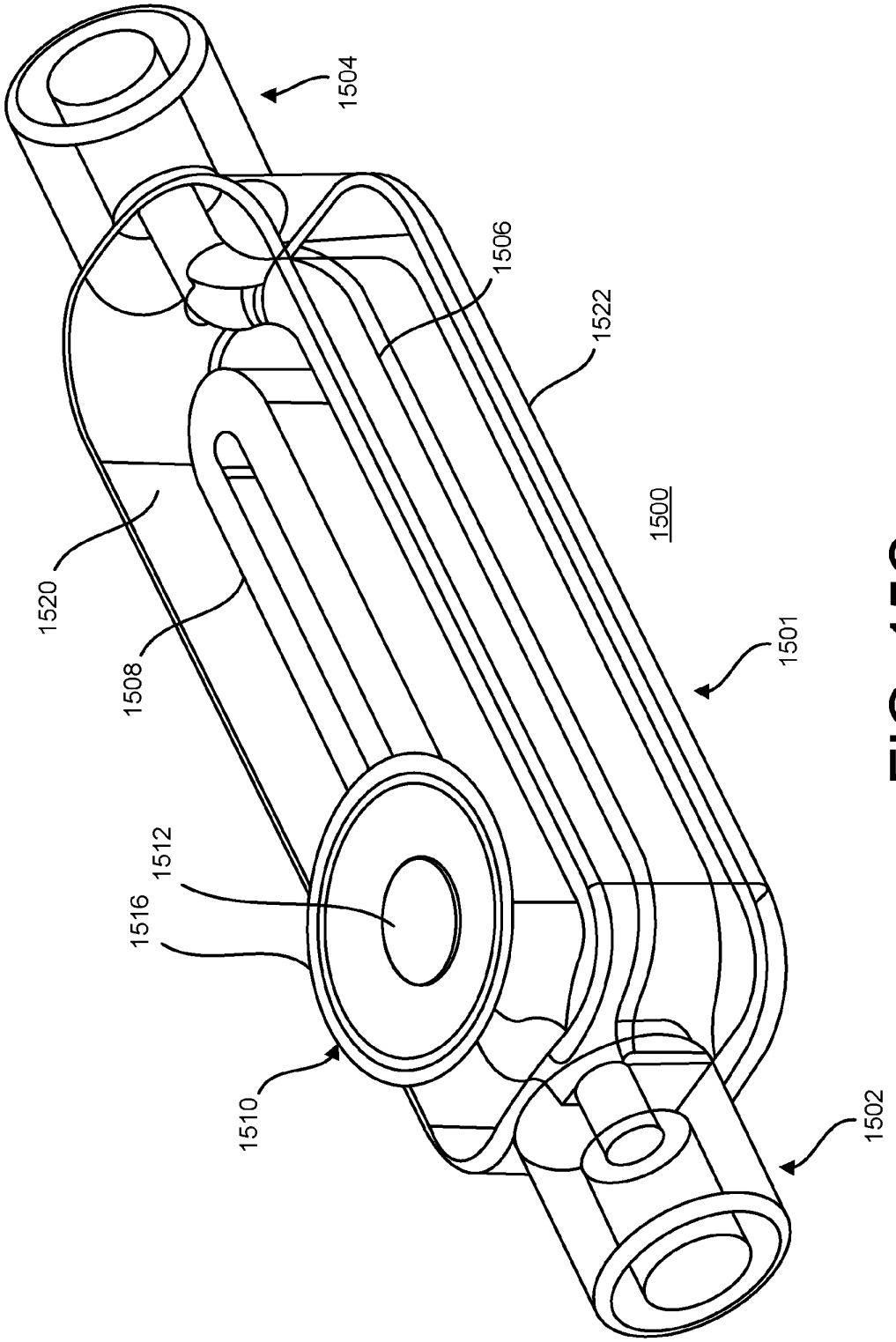


FIG. 15C

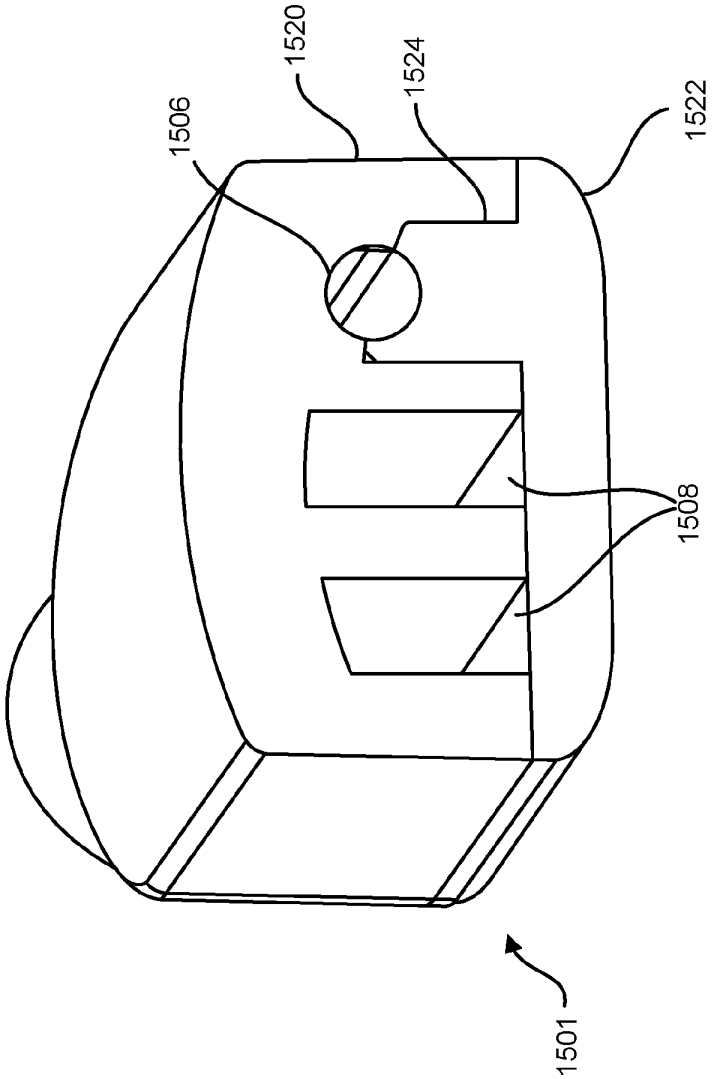


FIG. 15D

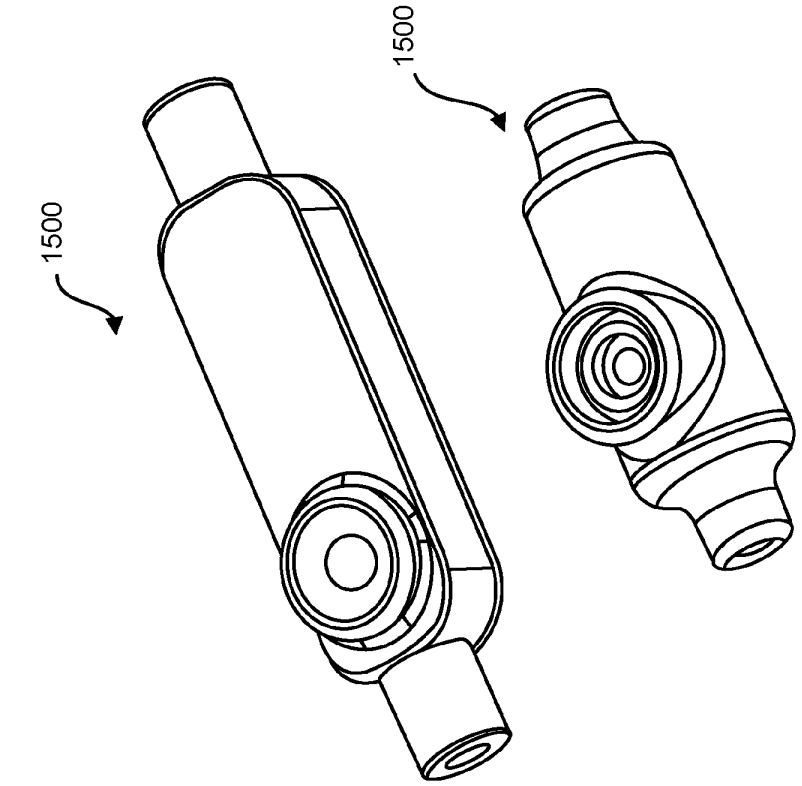


FIG. 15F

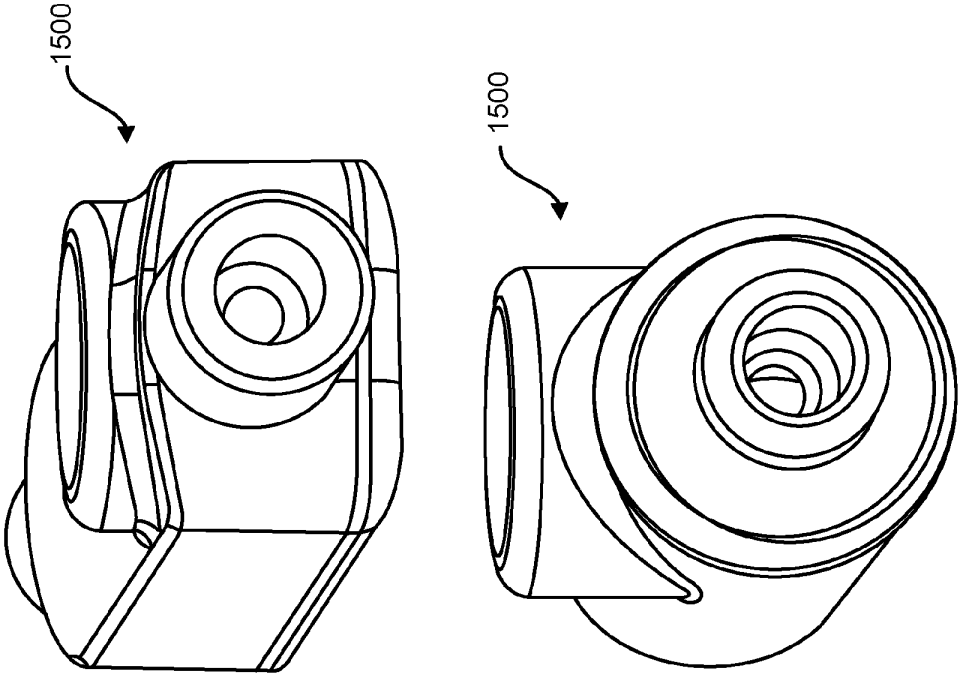


FIG. 15E

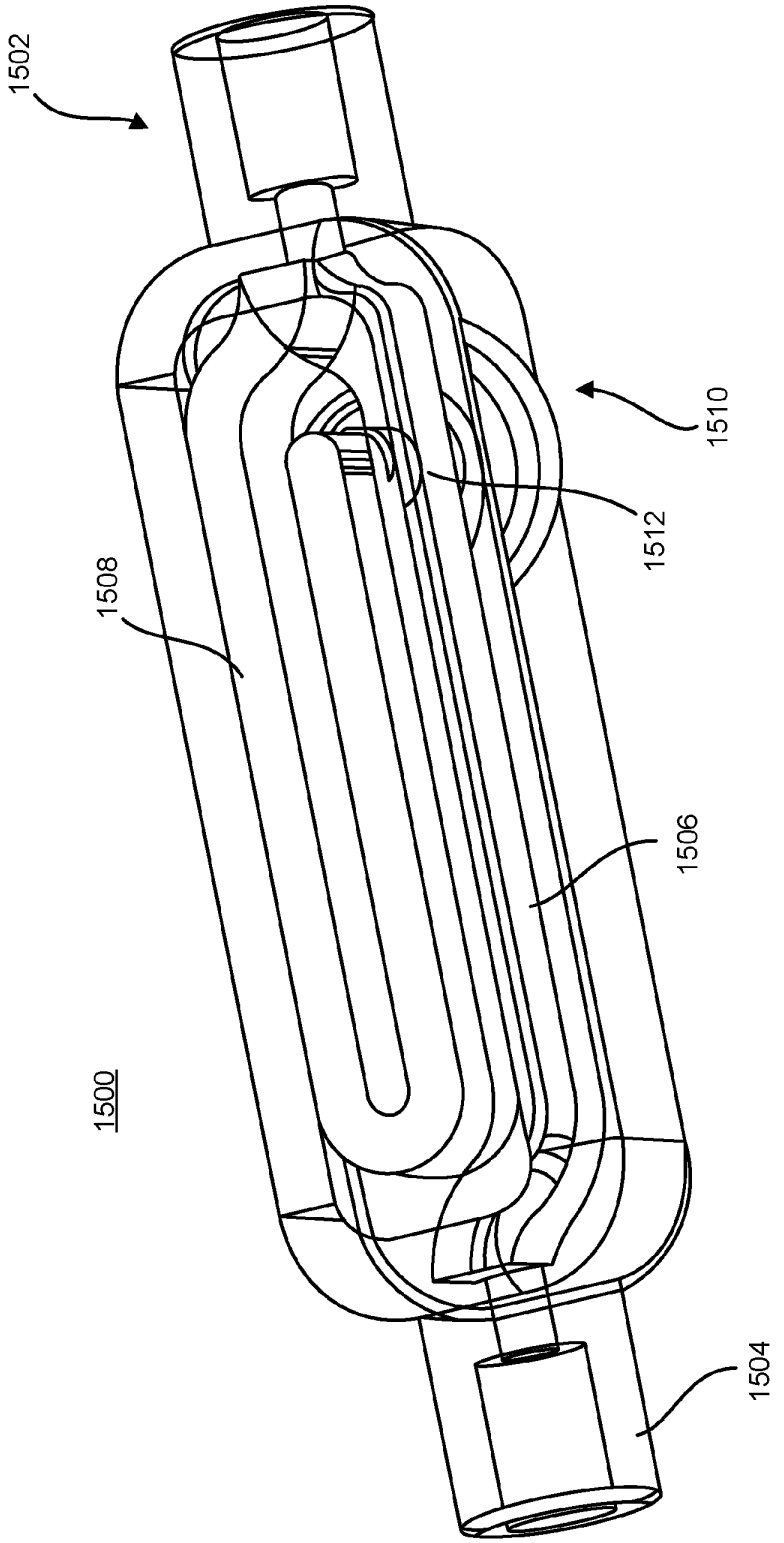


FIG. 15G

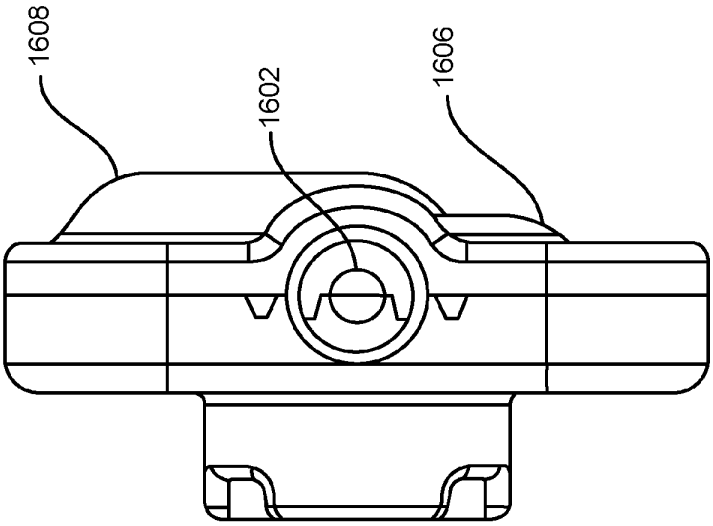


FIG. 16C

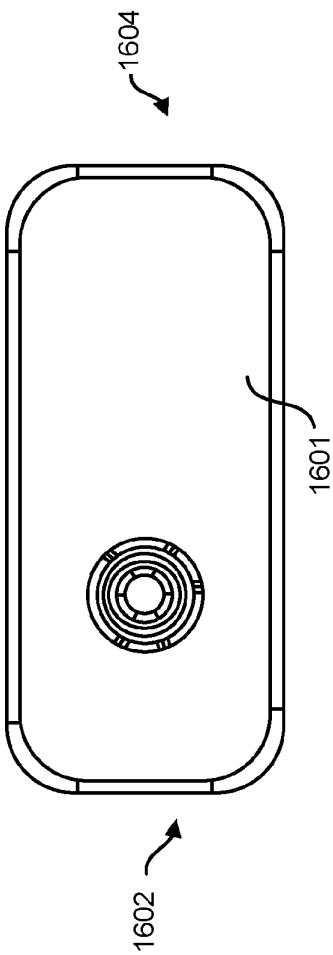


FIG. 16A

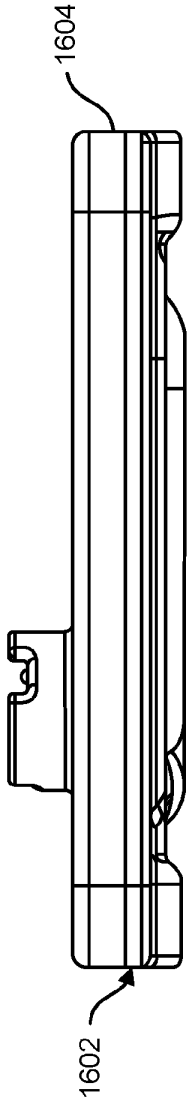


FIG. 16B

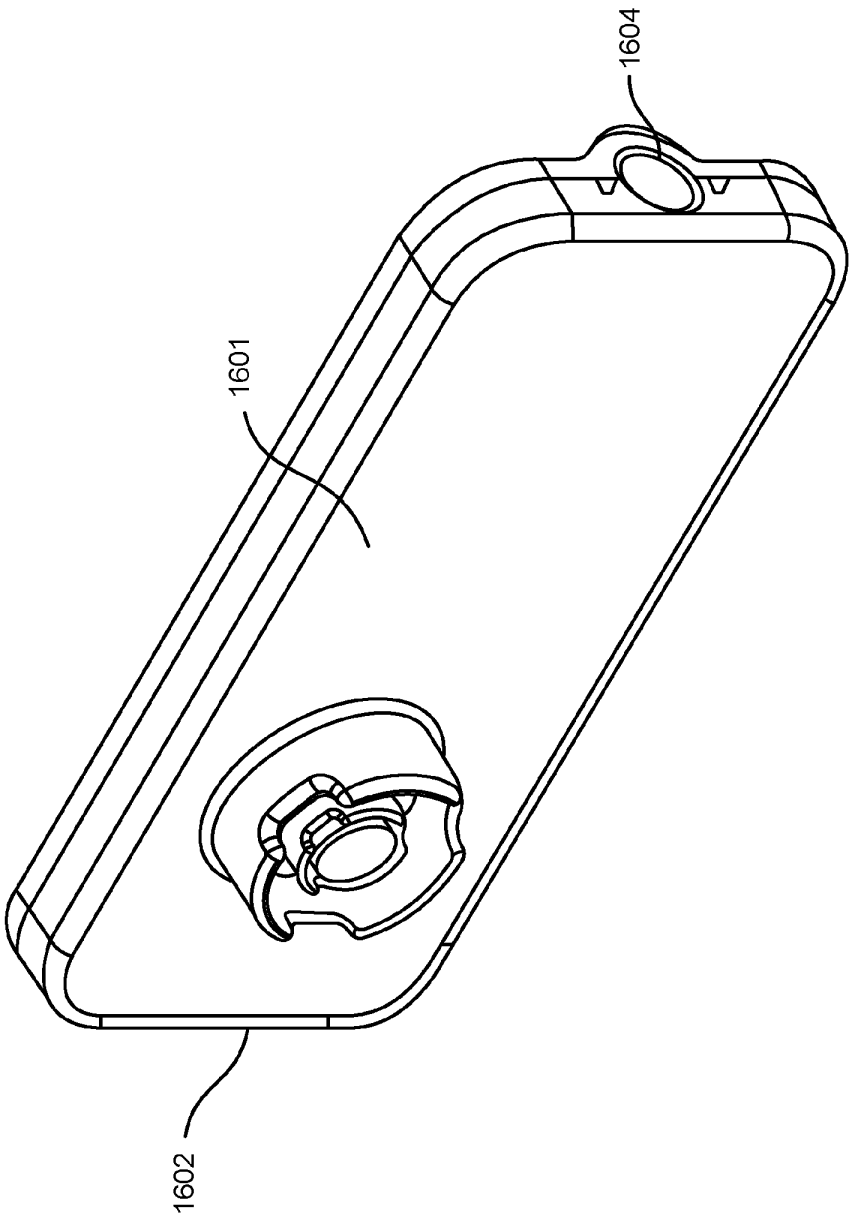


FIG. 16D

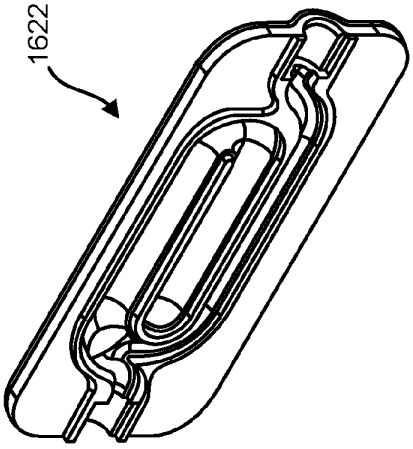


FIG. 17B



FIG. 17E

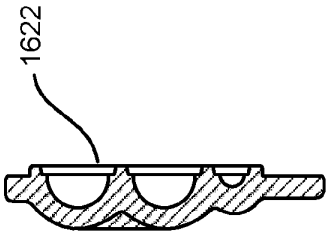


FIG. 17D

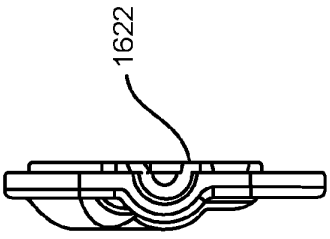


FIG. 17C

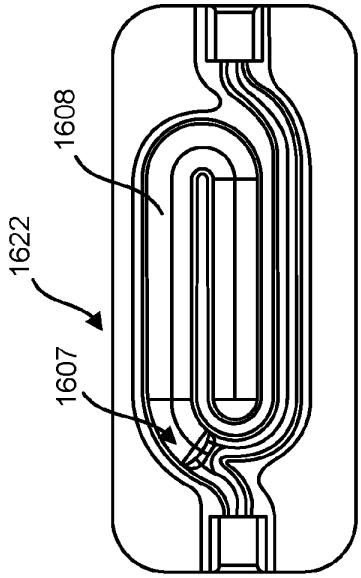


FIG. 17A

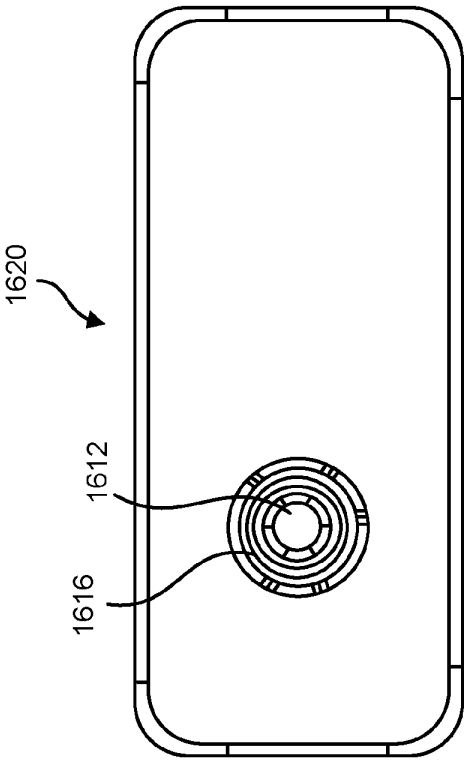


FIG. 18A

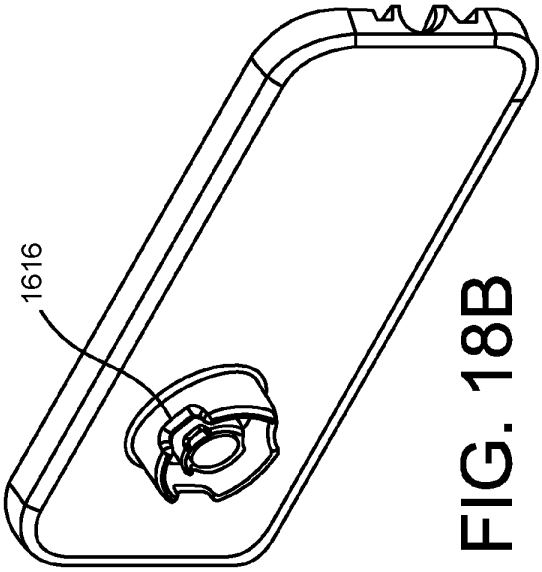


FIG. 18B



FIG. 18C

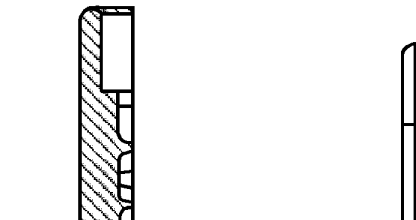


FIG. 18F

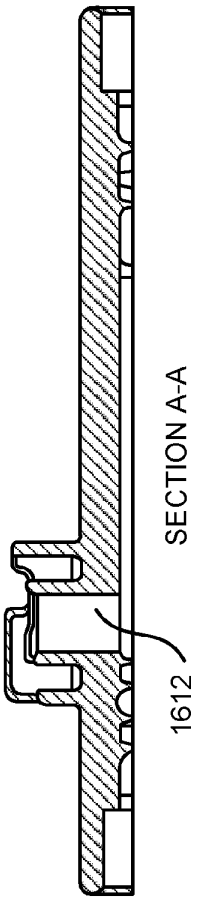


FIG. 18D

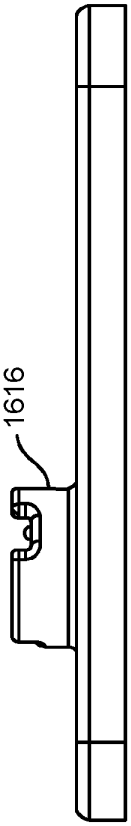


FIG. 18E

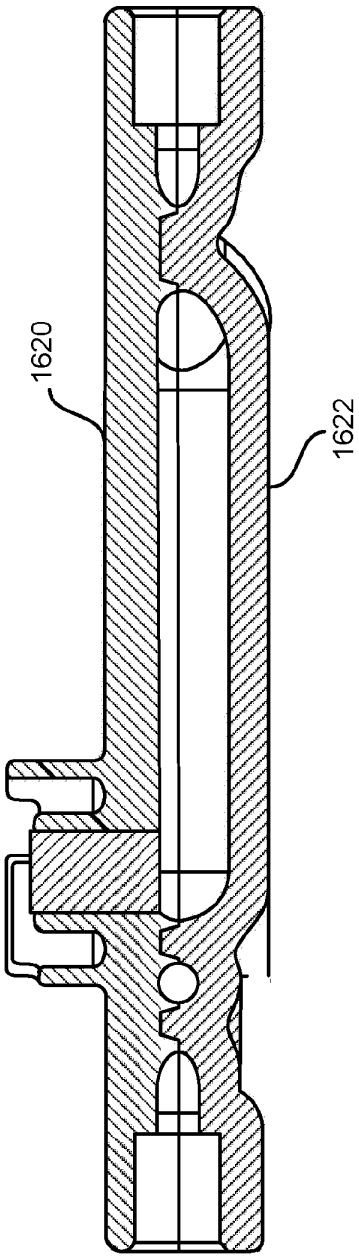


FIG. 19A

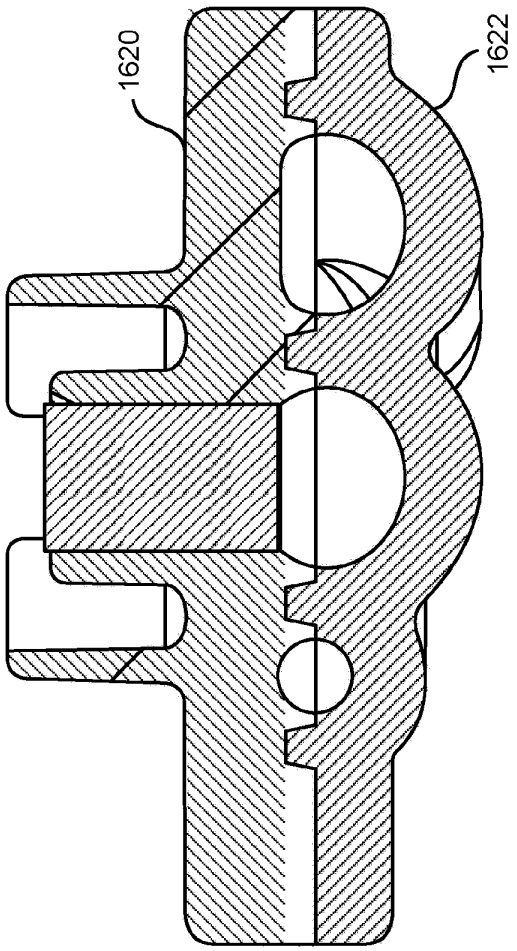


FIG. 19B

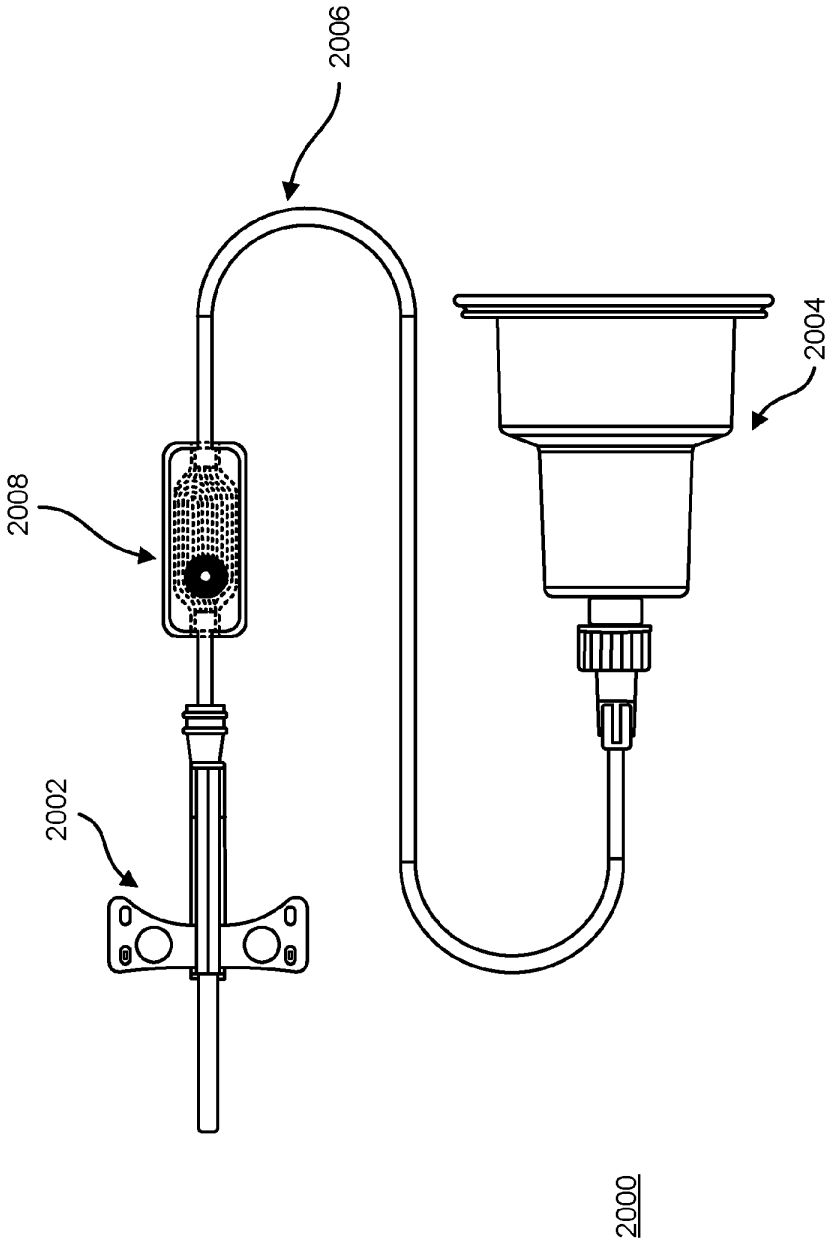


FIG. 20

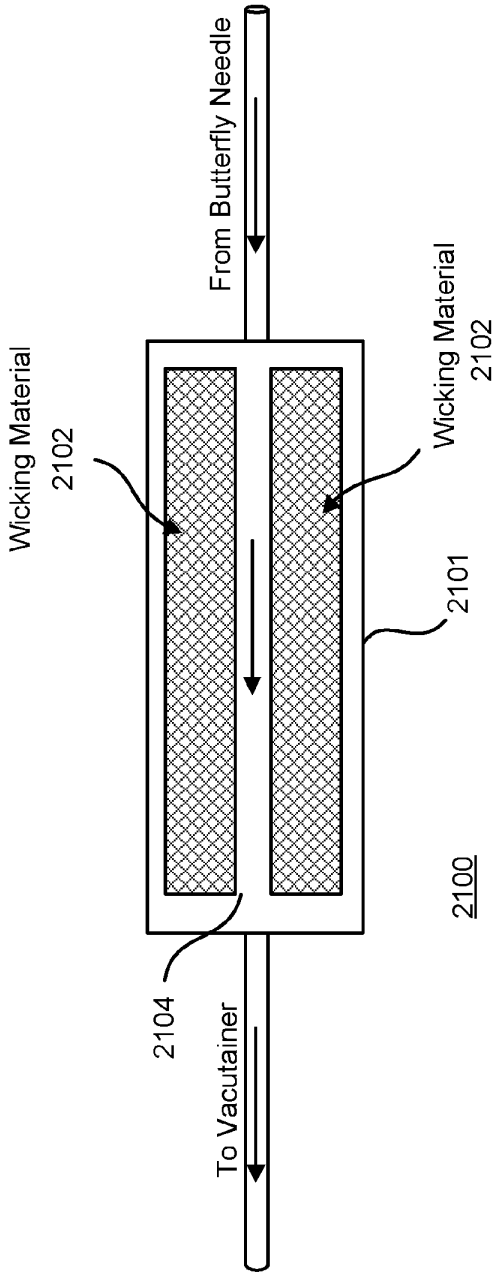

From Butterfly Needle
Wicking Material
2102
Wicking Material
2102
2101
2100
2104
To Vacutainer

FIG. 21

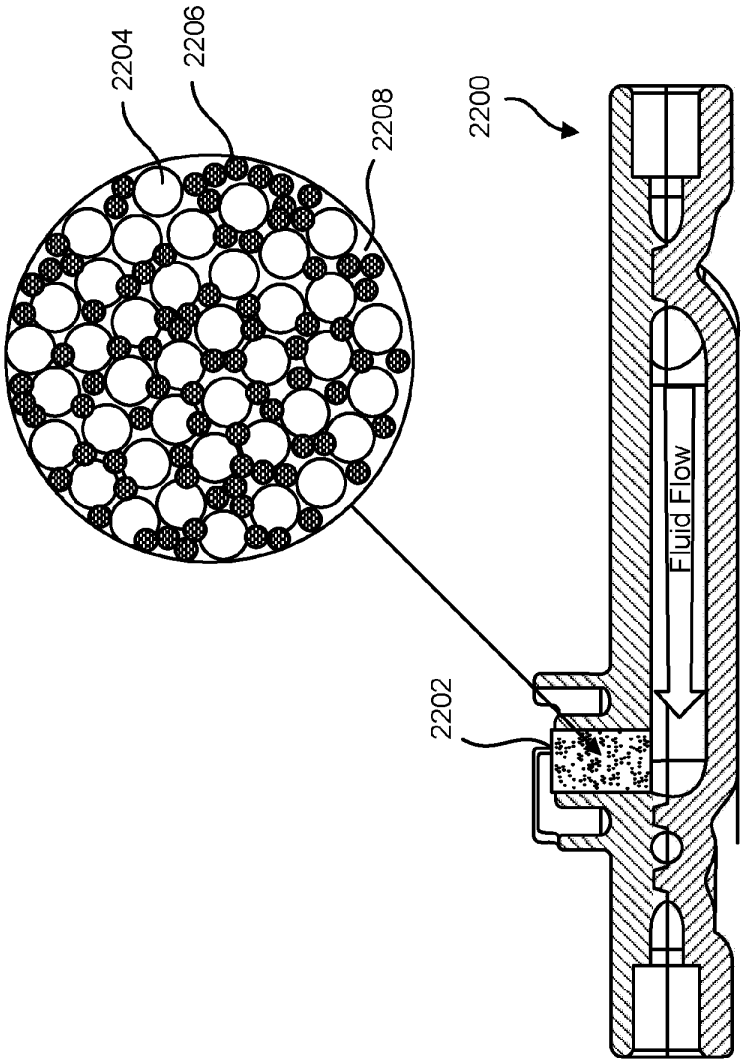


FIG. 22A

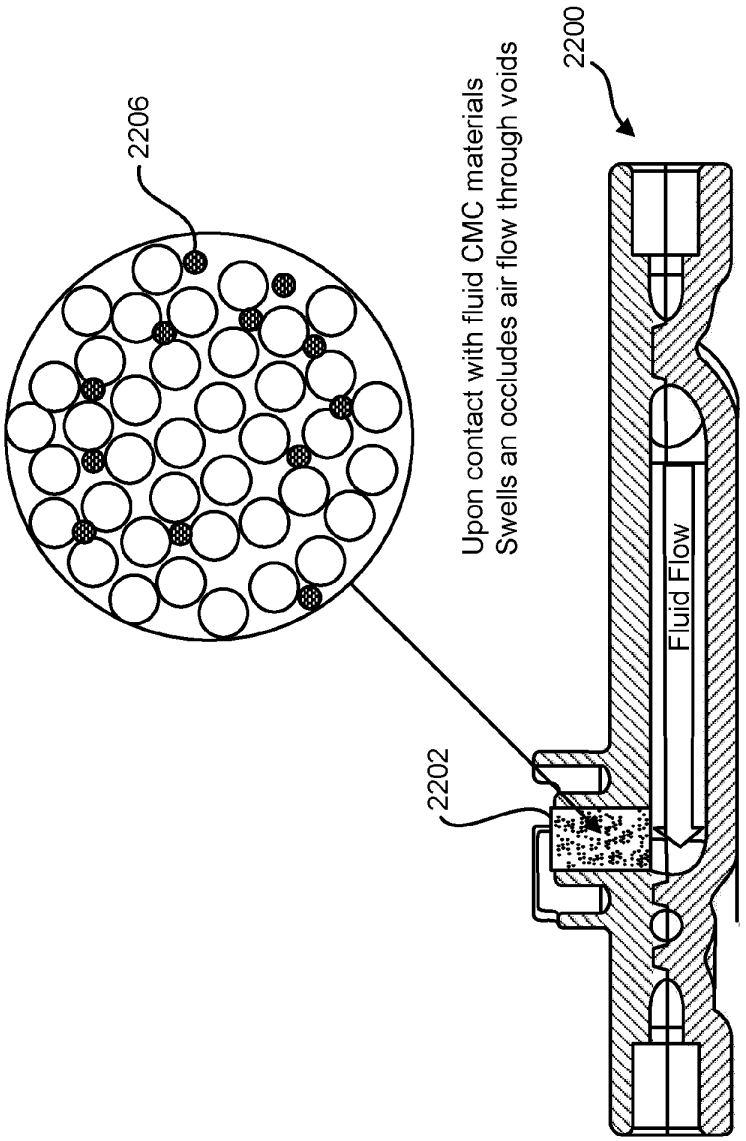

2206
2200
Upon contact with fluid CMC materials
Swells an occludes air flow through voids
Fluid Flow
2202

FIG. 22B

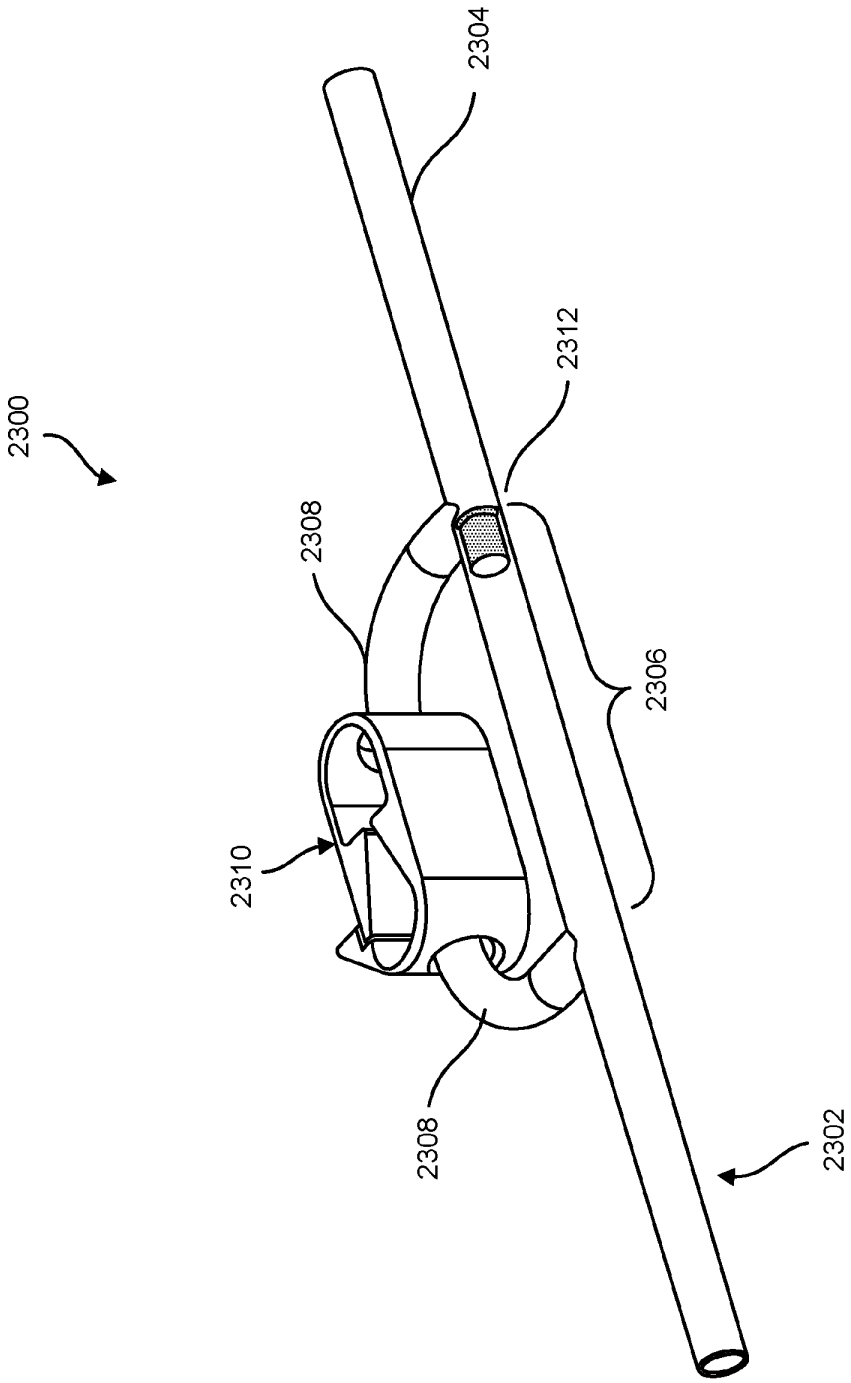


FIG. 23A

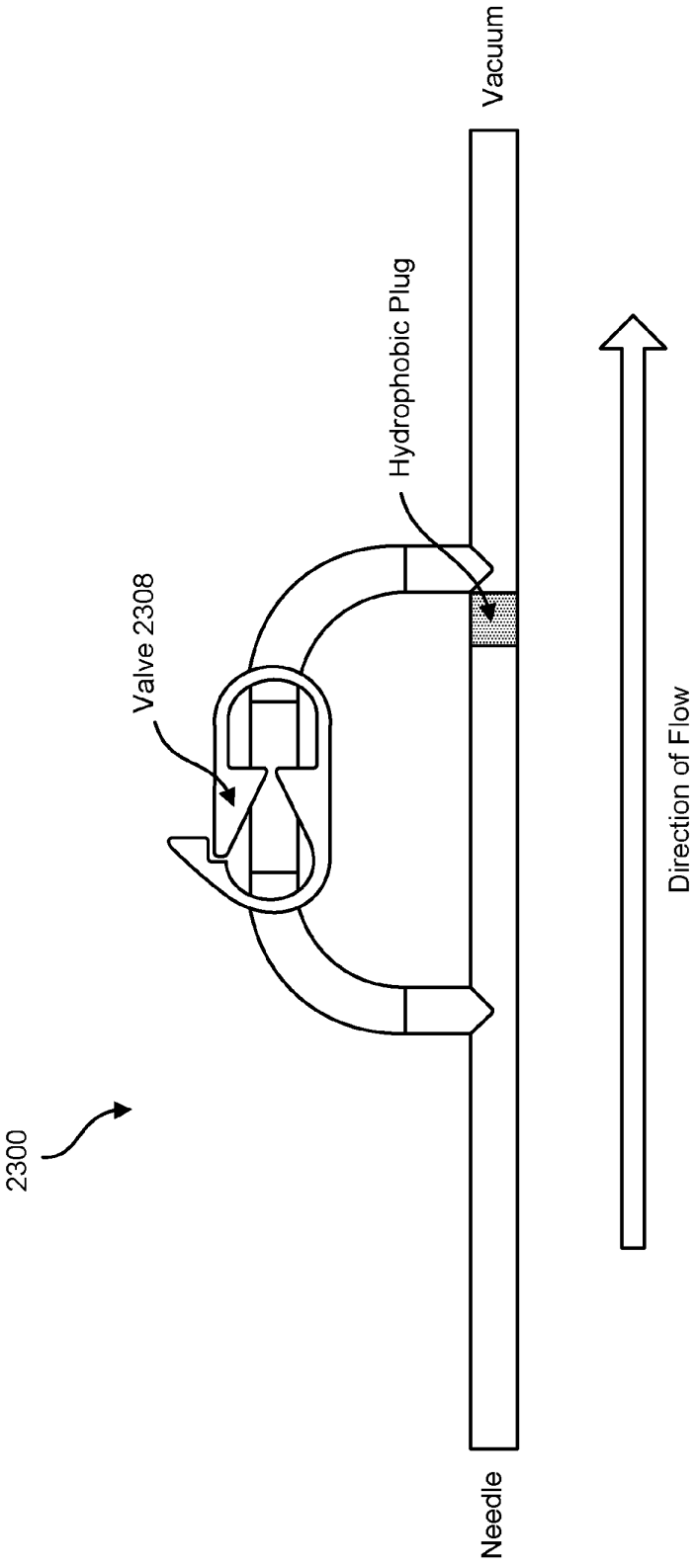

Vacuum
Hydrophobic Plug
Valve 2308
Direction of Flow
2300
Needle

FIG. 23B

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2016/043709

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.
X	WO 2011/162772 A1 (CLEARVIEW PATIENT SAFETY TECHNOLOGIES LLC [US]; FISCHEL LLOYD [US]; BR) 29 December 2011 (2011-12-29)	1-5, 7-13, 15-20
A	paragraph [0070] figure 15 abstract	6,14
A	US 2009/227953 A1 (TAN CHEE LEONG [SG] ET AL) 10 September 2009 (2009-09-10) the whole document	1-20
A	JP H08 257018 A (NISSHO KK) 8 October 1996 (1996-10-08) abstract; figures	1-20

-/--

[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

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"O" document referring to an oral disclosure, use, exhibition or other means

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"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

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Date of the actual completion of the international search	Date of mailing of the international search report
11 October 2016	19/10/2016

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/US2016/043709

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 4 416 290 A (LUTKOWSKI LAWRENCE [US]) 22 November 1983 (1983-11-22) abstract; figures	1-20
A	US 3 648 684 A (BARNWELL CLEORA W ET AL) 14 March 1972 (1972-03-14) abstract; figures	1-20
A	EP 1 665 986 A1 (BECTON DICKINSON CO [US]) 7 June 2006 (2006-06-07) figures 13,14	1-20
A	US 4 056 101 A (GEISSLER ULRICH C ET AL) 1 November 1977 (1977-11-01) abstract; figures	1-20
A	US 2013/317391 A1 (BULLINGTON GREGORY J [US] ET AL) 28 November 2013 (2013-11-28) paragraphs [0084] - [0094] figures 16-18	1-20

2

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2016/043709

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2011162772 A1	29-12-2011	NONE	
US 2009227953 A1	10-09-2009	US 2009227953 A1	10-09-2009
		US 2010262038 A1	14-10-2010
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US 4416290 A	22-11-1983	NONE	
US 3648684 A	14-03-1972	NONE	
EP 1665986 A1	07-06-2006	BR PI0505336 A	11-07-2006
		EP 1665986 A1	07-06-2006
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		US 2015099996 A1	09-04-2015
		US 2015351678 A1	10-12-2015

Form PCT/ISA/210 (patent family annex) (April 2005)

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
17 April 2014 (17.04.2014)

WIPO | PCT

(10) International Publication Number
WO 2014/058945 A1

(51) International Patent Classification:
A61M 5/168 (2006.01)

(21) International Application Number:
PCT/US2013/063975

(22) International Filing Date:
9 October 2013 (09.10.2013)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
61/712,468 11 October 2012 (11.10.2012) US

(72) Inventors; and
(71) Applicants : **BULLINGTON, Gregory J.** [US/US]; 5825 134th Place SE, Bellevue, Washington 98006 (US). **PATTON, Richard G.** [US/US]; 2561 Magnolia Blvd. W., Seattle, Washington 98199 (US). **GAW, Shan E.** [US/US]; 4027 Sunnyside Ave. N., Seattle, Washington 98103 (US).

(74) Agents: **TALBOT, C. Scott** et al.; Cooley LLP, 1299 Pennsylvania Ave., Suite 700, Washington, District of Columbia 20004 (US).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Published:

— *with international search report (Art. 21(3))*

— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))*

(54) Title: SYSTEMS AND METHODS FOR DELIVERING A FLUID TO A PATIENT WITH REDUCED CONTAMINATION

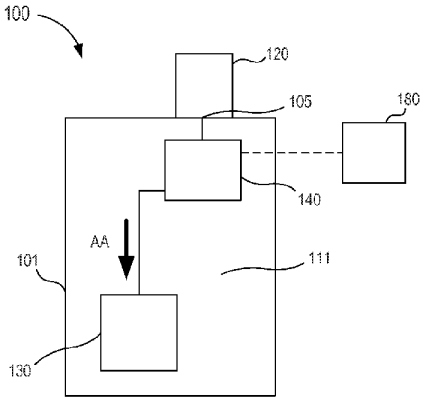


FIG. 1

(57) Abstract: An apparatus includes a cannula assembly, a housing, a fluid reservoir, a flow control mechanism, and an actuator. The housing includes an inlet port removably coupled to the cannula assembly and defines an inner volume. The fluid reservoir is fluidically coupled to the housing and configured to receive and isolate a volume of bodily fluid from a patient. The flow control mechanism is at least partially disposed in the inner volume. The actuator is operably coupled to the flow control mechanism and is configured to move the flow control mechanism between a first configuration, in which bodily fluid can flow, via a fluid flow path defined by the flow control mechanism, from the cannula assembly, through the inlet port and into the fluid reservoir, to a second configuration, in which the fluid reservoir is fluidically isolated from the cannula assembly.

WO 2014/058945 A1

SYSTEMS AND METHODS FOR DELIVERING A FLUID TO A PATIENT WITH REDUCED CONTAMINATION

Cross-Reference to Related Applications

[1001] This application claims priority to and the benefit of U.S. Provisional Patent Application Serial No. 61/712,468, filed October 11, 2012, entitled, "Systems and Methods for Delivering a Fluid to a Patient with Reduced Contamination," the disclosure of which is incorporated herein by reference in its entirety.

Background

[1002] Embodiments described herein relate generally to delivering a fluid to a patient, and more particularly to devices and methods for delivering a parenteral fluid to a patient with reduced contamination from microbes or other contaminants exterior to the body and/or the fluid source, such as dermally residing microbes.

[1003] Human skin is normally habituated in variable small amounts by certain bacteria such as coagulase-negative Staphylococcus species, Proprionobacterium acnes, Micrococcus species, Streptococci Viridans group, Corynebacterium species, and Bacillus species. These bacteria for the most part live in a symbiotic relationship with human skin but in some circumstances can give rise to serious infections in the blood stream known as septicemia. Septicemia due to these skin residing organisms is most often associated with an internal nidus of bacterial growth at the site of injured tissue, for example a damaged, scarred heart valve, or a foreign body (often an artificial joint, vessel, or valve). Furthermore, there are predisposing factors to these infections such as malignancy, immunosuppression, diabetes mellitus, obesity, rheumatoid arthritis, psoriasis, and advanced age. In some instances, these infections can cause serious illness and/or death. Moreover, these infections can be very expensive and difficult to treat and often can be associated with medical related legal issues.

[1004] In general medical practice, blood is drawn from veins (phlebotomy) for two main purposes; (1) donor blood in volumes of approximately 500mL is obtained for the treatment of anemia, deficient blood clotting factors including platelets and other medical conditions; and (2) smaller volumes (e.g., from a few drops to 10mL or more) of blood are obtained for testing purposes. In each case, whether for donor or testing specimens, a fluid communicator (e.g., catheter, cannula, needle, etc.) is used to penetrate and enter a vein (known as venipuncture) enabling withdrawing of blood into a tube or vessel apparatus in the desired

amounts for handling, transport, storage and/or other purposes. The site of venipuncture, most commonly the antecubital fossa, is prepared by cleansing with antiseptics to prevent the growth of skin residing bacteria in blood withdrawn from the vein. It has been shown venipuncture needles dislodge fragments of skin including hair and sweat gland structures as well as subcutaneous fat and other adnexal structures not completely sterilized by skin surface antisepsis. These skin fragments can cause septicemia in recipients of donor blood products, false positive blood culture tests and other undesirable outcomes. Furthermore, methods, procedures and devices are in use, which divert the initial portion of venipuncture blood enabling exclusion of these skin fragments from the venipuncture specimen in order to prevent septicemia in recipients of donor blood products, false positive blood culture tests and other undesirable outcomes.

[1005] Venipuncture is also the most common method of accessing the blood stream of a patient to deliver parenteral fluids into the blood stream of patients needing this type of medical treatment. Fluids in containers are allowed to flow into the patient's blood stream through tubing connected to the venipuncture needle or through a catheter that is placed into a patient's vasculature (e.g. peripheral IV, central line, etc.). During this process, fragments of incompletely sterilized skin can be delivered into the blood stream with the flow of parenteral fluids and/or at the time of venipuncture for introduction and insertion of a peripheral catheter. These fragments are undesirable in the blood stream and their introduction into the blood stream of patients (whether due to dislodging of fragments by venipuncture needle when inserting a catheter or delivered through tubing attached to needle or catheter) is contrary to common practices of antisepsis. Further, these microbes can be associated with a well-known phenomenon of colonization by skin residing organisms of the tubing and tubing connectors utilized to deliver parenteral fluids. The colonization is not typically indicative of a true infection but can give rise to false positive blood culture tests, which may result in unnecessary antibiotic treatment, laboratory tests, and replacement of the tubing apparatus with attendant patient risks and expenses. Furthermore, the risk of clinically significant serious infection due to skin residing organisms is increased.

[1006] As such, a need exists for improved fluid transfer devices, catheter introduction techniques and devices, as well as methods for delivering a parenteral fluid to a patient that reduce microbial contamination and inadvertent injection of undesirable external microbes into a patient's blood stream.

Summary

[1007] Devices and methods for delivering a fluid to a patient and/or introducing a peripheral catheter with reduced contamination from dermally residing microbes or other contaminants exterior to the body and/or an external fluid source are described herein. In some embodiments, an apparatus includes a cannula assembly, a housing, 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 includes an inlet port removably coupled to the cannula assembly. The fluid reservoir is fluidically coupled to the housing and configured to receive and isolate a first volume of bodily fluid withdrawn from a patient. The flow control mechanism is at least partially disposed in the inner volume and is configured to move relative to the housing between a first configuration and a second configuration. The flow control mechanism defines a fluid flow path between the cannula assembly and the fluid reservoir in the first configuration. The actuator is operably coupled to the flow control mechanism to move the flow control mechanism from the first configuration, in which the inlet port is placed in fluid communication the fluid reservoir such that bodily fluid can flow from the cannula assembly, through the inlet port via the fluid flow path and to the fluid reservoir, to the second configuration, in which the fluid reservoir is fluidically isolated from the cannula assembly.

Brief Description of the Drawings

[1008] FIGS. 1 and 2 are schematic illustrations of a fluid transfer device according to an embodiment.

[1009] FIG. 3 is a schematic illustration of a fluid transfer device according to an embodiment.

[1010] FIG. 4 is a perspective view of a fluid transfer device according to an embodiment.

[1011] FIG. 5 is an exploded view of the fluid transfer device of FIG. 4.

[1012] FIG. 6 is a cross-sectional view of the fluid transfer device taken along the line X_1-X_1 in FIG. 4, in a first configuration.

[1013] FIG. 7 is an enlarged view of a portion of the fluid transfer device labeled as region **A** in FIG. 6.

[1014] FIGS. 8 and 9 are cross-sectional views of the fluid transfer device taken along the line X_1-X_1 in FIG. 4, in a second and third configuration, respectively.

[1015] FIG. 10 is a side view of the fluid transfer device of FIG. 4 in a fourth configuration.

[1016] FIG. 11 is a perspective view of a fluid transfer device according to an embodiment.

[1017] FIG. 12 is an exploded view of the fluid transfer device of FIG. 11.

[1018] FIGS. 13 and 14 are cross-sectional views of the fluid transfer device taken along the line X_2-X_2 in FIG. 11, in a first and second configuration, respectively.

[1019] FIG. 15 is a side view of the fluid transfer device of FIG. 11 in a third configuration.

[1020] FIG. 16 is a perspective view of a fluid transfer device according to an embodiment.

[1021] FIG. 17 is an exploded view of the fluid transfer device of FIG. 16.

[1022] FIG. 18 is a cross-sectional perspective view of a housing included in the fluid transfer device taken along the line X_4-X_4 in FIG. 17.

[1023] FIG. 19 is a cross-sectional perspective view of a portion of a flow control mechanism included in the fluid transfer device taken along the line X_5-X_5 in FIG. 17.

[1024] FIG. 20 is a cross-sectional view of the fluid transfer device taken along the line X_3-X_3 in FIG. 16, in a first configuration.

[1025] FIG. 21 is a front view of the fluid transfer device of FIG. 16 in a second configuration.

[1026] FIG. 22 is a cross-sectional view of the fluid transfer device taken along the line X_3-X_3 in FIG. 16, in the second configuration.

[1027] FIG. 23 is a side view of the fluid transfer device of FIG. 16 in a third configuration.

[1028] FIG. 24 is a perspective view of a fluid transfer device according to an embodiment.

[1029] FIG. 25 is an exploded view of the fluid transfer device of FIG. 24.

[1030] FIG. 26 is a cross-sectional perspective view of a fluid reservoir included in the fluid transfer device taken along the line X_7-X_7 in FIG. 25.

[1031] FIG. 27 is a cross-sectional perspective view of a flow control mechanism included in the fluid transfer device taken along the line X_8-X_8 in FIG. 25.

[1032] FIGS. 28-30 are cross-sectional views of the fluid transfer device taken along the line X_6-X_6 in FIG. 24, in a first, second, and third configuration, respectively.

[1033] FIG. 31 is a perspective view of a fluid transfer device according to an embodiment.

[1034] FIG. 32 is an exploded view of the fluid transfer device of FIG. 31.

[1035] FIGS. 33 and 34 are cross-sectional views of the fluid transfer device taken along the line X_9-X_9 in FIG. 31, in a first configuration and a second configuration, respectively.

[1036] FIG. 35 is a perspective view of a fluid transfer device according to an embodiment.

[1037] FIG. 36 is an exploded view of the fluid transfer device of FIG. 35.

[1038] FIG. 37 is a cross-sectional view of the fluid transfer device taken along the line X_{10}-X_{10} in FIG. 35, in a first configuration.

[1039] FIG. 38 is a front view of the fluid transfer device of FIG. 35 in a second configuration.

[1040] FIG. 39 is a cross-sectional view of the fluid transfer device taken along the line X_{10}-X_{10} in FIG. 35, in the second configuration.

[1041] FIG. 40 is a flowchart illustrating a method of delivering a fluid to a patient using a fluid transfer device according to an embodiment.

Detailed Description

[1042] Devices and methods for delivering a fluid to a patient with reduced contamination from dermally residing microbes or other contaminants exterior to the body are described herein. In some embodiments, an apparatus includes a cannula assembly, a housing, 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 includes an inlet port configured to be removably coupled to the cannula assembly. The fluid reservoir is fluidically coupled to the housing and configured to receive and isolate a first volume of bodily fluid withdrawn from a patient. The flow control mechanism is at least partially disposed in the inner volume and is configured to move relative to the housing between a first configuration and a second configuration. The flow control mechanism defines a fluid flow path between the cannula assembly and the fluid reservoir in the first configuration. The actuator is operably coupled to the flow control mechanism to move the flow control mechanism from the first configuration, in which the inlet port is placed in fluid communication the fluid reservoir such that bodily fluid can flow from the cannula assembly, through the inlet port via the fluid flow path and to the fluid reservoir, to the second configuration, in which the fluid reservoir is fluidically isolated from the cannula assembly.

[1043] In some embodiments, a device for delivering a fluid to a patient with reduced contamination includes a housing, a fluid reservoir, and a flow control mechanism. The housing has a proximal end portion and a distal end portion and defines an inner volume therebetween. The housing includes a first port configured to be removably coupled to a cannula assembly, and a second port configured to be fluidically coupled to a fluid source. The fluid reservoir is fluidically coupleable to the cannula assembly and configured to receive and isolate a predetermined volume of bodily fluid withdrawn from the patient. The flow control mechanism is at least partially disposed in the inner volume of the housing and is configured to move between a first configuration and a second configuration. When in the first configuration, the first port is placed in fluid communication with the fluid reservoir such that bodily fluid can flow from the cannula assembly, through the first port and to the fluid reservoir. When in the second configuration, the fluid reservoir is fluidically isolated

from the cannula assembly and fluid can flow from the fluid source, in the second port, through the flow control mechanism, out the first port and to the cannula assembly.

[1044] In some embodiments, a method of delivering a fluid to a patient using a fluid transfer device includes establishing fluid communication between the patient and the fluid transfer device. Once in fluid communication, a predetermined volume of a bodily fluid is withdrawn from the patient. The predetermined volume of bodily fluid is transferred to a fluid reservoir. The fluid transfer device is fluidically isolated from the fluid reservoir to sequester the predetermined volume of bodily fluid in the fluid reservoir. The method further includes establishing fluid communication between the patient and a fluid source with the fluid transfer device.

[1045] In some embodiments, an apparatus includes a housing, a cannula assembly, a flow control mechanism, and a fluid reservoir. The flow control mechanism is configured to move relative to the housing between a first configuration and a second configuration. The cannula assembly is coupled to the housing and fluidically coupled to the fluid reservoir when the flow control mechanism is in the first configuration. The fluid reservoir is fluidically isolated from the cannula assembly when the flow control mechanism is in a second configuration such that the cannula assembly can be fluidically coupled to an external fluid reservoir and/or an external fluid source.

[1046] As referred to herein, "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.

[1047] 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).

[1048] As used in this specification, 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.

[1049] FIGS. 1 and 2 are schematic illustrations of a fluid transfer device 100 according to an embodiment, in a first and second configuration, respectively. Generally, the fluid transfer device 100 (also referred to herein as "transfer device") is configured to facilitate the insertion of a piercing member (e.g., a needle, a trocar, a cannula, or the like) into a patient to withdrawal and isolate a predetermined amount of bodily fluid from the patient containing, for example, dermally residing microbes. The fluid transfer device 100 is further configured to facilitate the delivery of parenteral fluid to the patient that does not substantially contain, for example, the dermally residing microbes. In other words, the transfer device 100 is configured to transfer and fluidically isolate the predetermined amount of bodily fluid, including dermally residing microbes dislodged from a venipuncture, within a collection reservoir and deliver parenteral fluids to the patient that are substantially free from the dislodged dermally residing microbes and/or other undesirable external contaminants.

[1050] The transfer device 100 includes a housing 101, a cannula assembly 120, a fluid reservoir 130, a flow control mechanism 140, and an actuator 180. The housing 101 can be any suitable shape, size, or configuration and is described in further detail herein with respect to specific embodiments. As shown in FIG. 1, the housing 101 defines an inner volume 111 that can movably receive and/or movably house at least a portion of the flow control mechanism 140, as described in further detail herein. A portion of the housing 101 can be, at least temporarily, physically and fluidically coupled to the cannula assembly 120. For example, in some embodiments, a distal end portion of the housing 101 can include an inlet port 105 or the like configured to physically and fluidically couple to a lock mechanism (not shown in FIGS. 1 and 2) included in the cannula assembly 120. In such embodiments, the lock mechanism can be, for example, a Luer-Lok® or the like that can engage the port. In some embodiments, the housing 101 can be monolithically formed with at least a portion of the cannula assembly 120. In other words, in some embodiments, the inlet port 105 can be monolithically formed with a portion of the cannula assembly 120 to define a fluid flow path between a portion of the housing 101 the cannula assembly 120. In this manner, a portion of the housing 101 can receive a bodily fluid from and/or deliver a parenteral fluid to a patient via a cannula included in the cannula assembly 120, as described in further detail herein.

[1051] The cannula assembly 120 can be any suitable configuration. For example, in some embodiments, the cannula assembly 120 includes an engagement portion and a cannula portion (not shown in FIGS. 1 and 2). In such embodiments, the engagement portion can physically and fluidically couple the cannula assembly 120 to the housing 101 (e.g., it can be the lock mechanism physically and fluidically coupled to the inlet port 105 as described above). The cannula portion can be configured to be inserted into a portion of a patient to deliver a fluid to or receive a fluid from the patient. For example, in some embodiments, the cannula portion can include a distal end with a sharp point configured to pierce a portion of the patient to dispose the cannula portion, at least in part, within a vein of the patient. In other embodiments, a piercing member (e.g., a lumen defining needle) can be movably disposed within the cannula assembly 120 to facilitate the insertion of the cannula portion 120 into the portion of the patient.

[1052] As shown in FIG. 1, the housing 101 can house and/or define the fluid reservoir 130. Similarly stated, in some embodiments, the fluid reservoir 130 can be disposed within and/or at least partially defined by the inner volume 111 of the housing 101. The fluid reservoir 130 can be configured to receive a predetermined amount of the bodily fluid and fluidically isolate the bodily fluid from a volume outside the fluid reservoir 130, as described in further detail herein. While shown in FIGS. 1 and 2 as being disposed within the inner volume 111 of the housing 101, in some embodiments, the fluid reservoir 130 can be disposed substantially outside the housing 101. In such embodiments, the fluid reservoir 130 can be physically and fluidically coupled to a portion of the housing 101. For example, in some embodiments, the fluid reservoir 130 can be coupled to an outlet port (not shown in FIGS. 1 and 2). In other embodiments, the fluid reservoir 130 can be operably coupled to the housing 101 via an intervening structure, such as, for example, a Luer-Lok® and/or flexible sterile tubing. In still other embodiments, the fluid reservoir 130 can be monolithically formed with at least a portion of the housing 101.

[1053] The flow control mechanism 140 included in the transfer device 100 is disposed, at least partially, within the inner volume 111 of the housing 101 and can be moved between a first configuration (FIG. 1) and a second configuration (FIG. 2). The flow control mechanism 140 can be any suitable mechanism configured to control or direct a flow of a fluid. For example, in some embodiments, the flow control mechanism 140 can include a valve (e.g., a check valve or the like) that allows a flow of a fluid in a single direction. In

other embodiments, a valve can selectively control a flow of a fluid in multiple directions. In still other embodiments, the flow control mechanism 140 can define one or more lumens configured to selectively receive a flow of a fluid. In such embodiments, the flow control mechanism 140 can be moved relative to the housing 101 to selectively place a lumen in fluid communication with a portion of the transfer device 100 (e.g., the housing 101, the cannula assembly 120, and/or the fluid reservoir 130). For example, in some embodiments, a portion of the flow control mechanism 140 can be movably disposed, at least temporarily, within the cannula assembly 120 to selectively place the fluid reservoir 130 in fluid communication with the cannula assembly 120. In some embodiments, the portion of the flow control mechanism 140 can include a piercing member such as, for example, a needle configured to extend beyond a distal end of the cannula assembly 120 (not shown in FIGS. 1 and 2) to pierce the skin of a patient and facilitate the insertion of the cannula assembly 120 into a vein of the patient.

[1054] In some embodiments, the transfer device 100 can include an actuator 180 operably coupled to the flow control mechanism 140 and configured to move the flow control mechanism 140 between the first and the second configuration. For example, in some embodiments, the actuator 180 can be a push button, a slider, a toggle, a pull-tab, a handle, a dial, a lever, an electronic switch, or any other suitable actuator. In this manner, the actuator 180 can be movable between a first position corresponding to the first configuration of the flow control mechanism 140, and a second position, different from the first position, corresponding to the second configuration of the flow control mechanism 140. In some embodiments, the actuator 180 can be configured for uni-directional movement. For example, the actuator 180 can be moved from its first position to its second position, but cannot be moved from its second position back to its first position. In this manner, the flow control mechanism 140 is prevented from being moved to its second configuration before its first configuration, as described in further detail herein.

[1055] In use, the flow control mechanism 140 can be in the first configuration to place the fluid reservoir 130 in fluid communication with the cannula assembly 120, as indicated by the arrow AA in FIG. 1. In this manner, the fluid reservoir 130 can receive a flow of bodily fluid that can include dermally residing microbes dislodged during a venipuncture event (e.g., when the cannula assembly 120 and/or the flow control mechanism 140 pierces the skin of the patient). In some embodiments, the fluid reservoir 130 can be configured to

receive a predetermined volume of the bodily fluid. With a desired amount of bodily fluid transferred to the fluid reservoir 130, a user (e.g., a doctor, physician, nurse, technician, phlebotomist, etc.) can manipulate the actuator 180 to move the flow control mechanism 140 from the first configuration to the second configuration. For example, the flow control mechanism 140 can be in the first configuration when the flow control mechanism 140 is in a distal position relative to the housing 101 (FIG. 1) and the actuator 180 can move the flow control mechanism 140 in a proximal direction relative to the housing 101 to place the flow control mechanism in the second configuration, as indicated by the arrow BB in FIG. 2. Moreover, when in the second configuration, the flow control mechanism 140 no longer facilitates the fluidic coupling of the fluid reservoir 130 to the cannula assembly 120. Thus, the fluid reservoir 130 is fluidically isolated from the cannula assembly 120.

[1056] While shown in FIGS. 1 and 2 as being moved in the proximal direction (e.g., in the direction of the arrow BB), in other embodiments, the actuator 180 can move the flow control mechanism 140 between the first configuration and the second configuration in any suitable manner or direction. For example, in some embodiments, the flow control mechanism 140 can be moved in a rotational motion between the first configuration and the second configuration. In other embodiments, the flow control mechanism 140 can be moved in a transverse motion (e.g., substantially perpendicular to the direction of the arrow BB). In such embodiments, the rotational or transverse motion can be such that the flow control mechanism 140 selectively defines one or more fluid flow paths configured to receive a fluid from a patient or to deliver a fluid to the patient, as described in further detail herein.

[1057] In some embodiments, the movement of the flow control mechanism 140 to the second configuration can substantially correspond to a physical and fluidic decoupling of at least a portion of the housing 101 from the cannula assembly 120 such that an external fluid reservoir 199 (e.g., also referred to herein as "fluid source") can be physically and fluidically coupled to the cannula assembly 120. For example, as shown in FIG. 2, in some embodiments, the housing 101 can be moved in the proximal direction (e.g., in the direction of the arrow BB) to be physically and fluidically decoupled from the cannula assembly 120. In some embodiments, the proximal movement of the flow control mechanism 140 urges the housing 101 to move in the proximal direction. In other embodiments, a user (e.g., a physician, phlebotomist, or nurse) can move the housing 101 in the proximal direction. In this manner, the external fluid reservoir 199 can be fluidically coupled to the cannula

assembly 120. Expanding further, with the predetermined amount of bodily fluid transferred to the fluid reservoir 130, the external fluid reservoir 199 can be fluidically coupled to the cannula assembly 120 to deliver a flow of a parenteral fluid that is substantially free from dermally residing microbes dislodged during the venipuncture event, as indicated by the arrow CC in FIG. 2. Similarly stated, the dermally residing microbes that are dislodged during the venipuncture event can be entrained in the flow of the bodily fluid delivered to the fluid reservoir 130. Thus, when the flow control mechanism 140 is moved to the second configuration and the fluid reservoir 130 is fluidically isolated from the cannula assembly 120, the external fluid reservoir 199 can deliver the flow of parenteral fluid substantially free from dermally residing microbes.

[1058] While the housing 101 is shown in FIG. 2 as being moved in the proximal direction such that the external fluid reservoir 199 can be physically and fluidically coupled to the cannula assembly 120, in other embodiments, a housing need not be decoupled from a cannula assembly. For example, FIG. 3 is a schematic illustration of a transfer device 200 according to an embodiment. The transfer device 200 includes a housing 201, a cannula assembly 220, a fluid reservoir 230, and a flow control mechanism 240.

[1059] As shown in FIG. 3, the housing 201 includes a proximal end portion 202 and a distal end portion 203 and defines an inner volume 211 therebetween. The distal end portion 203 can be physically and fluidically coupled to the cannula assembly 220, as described above in reference to FIG. 1. For example, in some embodiments, the distal end portion 203 can include an inlet port 205 (also referred to herein as "first port") or the like that can be physically and fluidically coupled to the cannula assembly 220. The proximal end portion 202 includes an outlet port 206 (also referred to herein as "second port") that can be physically and fluidically coupled to an external fluid reservoir 299. The external fluid reservoir 299 can be any suitable fluid reservoir and can be coupled to the second port 206 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. For example, in some embodiments, the external fluid reservoir 299 can be substantially similar to known fluid reservoirs configured to deliver a parenteral fluid (e.g., a fluid source). In some embodiments, the external fluid reservoir 299 is monolithically formed with the second port 206. In still other embodiments, the external fluid reservoir 299 can be operably coupled to the second port 206 via an intervening structure (not shown in FIG. 3), such as, for example,

a flexible sterile tubing. More particularly, the intervening structure can define a lumen configured to place the external fluid reservoir 299 in fluid communication with the second port 206.

[1060] The housing 201 can house or define at least a portion of the fluid reservoir 230. Similarly stated, the fluid reservoir 230 can be at least partially disposed within the inner volume 211 of the housing 201. The fluid reservoir 230 can receive and fluidically isolate a predetermined amount of the bodily fluid, as described above in reference to FIGS. 1 and 2. Similarly, the flow control mechanism 240 is at least partially disposed within the inner volume 211 of the housing 201 and can be moved between a first configuration and a second configuration. More specifically, the flow control mechanism 240 defines a first lumen 246 that fluidically couples the cannula assembly 220 to the fluid reservoir 230 when the flow control mechanism 240 is in the first configuration and a second lumen 247 that fluidically couples the cannula assembly 220 to the external fluid reservoir 299 when the flow control mechanism 240 is in the second configuration.

[1061] In use, the flow control mechanism 240 can be placed in the first configuration to fluidically couple the cannula assembly 220 to the fluid reservoir 230 via the first lumen 246. In this manner, a flow of a bodily fluid can be delivered to the fluid reservoir 230, as indicated by the arrow DD in FIG. 3. More specifically, the bodily fluid can flow from the cannula assembly 220, through the first port 205 (e.g., the inlet port) and into the fluid reservoir 230. As described above in the previous embodiment, the flow of the bodily fluid can contain dermally residing microbes dislodged by a venipuncture event (e.g., the insertion of a portion of the cannula assembly 220 into a vein of the patient).

[1062] With a predetermined amount of bodily fluid disposed within the fluid reservoir 230, the flow control mechanism 240 can be moved (e.g., by an actuator and/or manual intervention from the user) to the second configuration to fluidically isolate the fluid reservoir 230 from the cannula assembly 220. More specifically, the flow control mechanism 240 can be moved from the first configuration to fluidically isolate the first lumen 246 from the cannula assembly 220 and/or the fluid reservoir 230, thereby fluidically isolating the fluid reservoir 230 from the cannula assembly 220. In addition, the movement of the flow control mechanism 240 to the second configuration can place the second lumen 247 in fluid communication with the cannula assembly 220 and the outlet port 206 (e.g., the second port) disposed at the proximal end portion 202 of the housing 201. Thus, the external fluid

reservoir 299 can be fluidically coupled (as described above) to the second port 206 to deliver a flow of parenteral fluid to the patient via the second lumen 247 and the cannula assembly 220, as indicated by the arrow EE. For example, the flow of parenteral fluid can flow from the external fluid reservoir 299 (e.g., a fluid source), in the second port 206, through the second lumen 247 defined by the flow control mechanism 240, out the first port 205 and to the cannula assembly 220 to be delivered to the patient. Moreover, the flow of the parenteral fluid is substantially free from dermally residing microbes and/or other undesirable external contaminants.

[1063] In some embodiments, the transfer device 200 can be configured such that the first amount of bodily fluid needs to be conveyed to the fluid reservoir 230 before the transfer device 200 will permit the flow of the parenteral fluid to be conveyed through the transfer device 200 to the patient. In this manner, the transfer device 200 can be characterized as requiring compliance by a health care practitioner regarding the collection of the predetermined amount of bodily fluid prior to the delivery of the parenteral fluid. Similarly stated, the transfer device 200 can be configured to prevent a health care practitioner from delivering the parenteral fluid to the patient without first diverting or transferring the predetermined amount of bodily fluid to the fluid reservoir 230. In this manner, the health care practitioner is substantially prevented from introducing (whether intentionally or unintentionally) bodily surface microbes and/or other undesirable external contaminants into, for example, the flow of the parenteral fluid and/or the blood stream of the patient. In other embodiments, the fluid transfer device 200 need not include a forced-compliance feature or component.

[1064] FIGS. 4-10 illustrate a transfer device 300 according to an embodiment. The transfer device 300 includes a housing 301, a cannula assembly 320, a fluid reservoir 330, a flow control mechanism 340, and an actuator 380. The transfer device 300 can be any suitable shape, size, or configuration. For example, while shown in FIG. 4 as being substantially cylindrical, the transfer device 300 can be square, rectangular, polygonal, and/or any other non-cylindrical shape. Moreover, any portion of the transfer device 300 can include any feature or finish configured to enhance the ergonomics of the transfer device 300. For example, the housing 301 can include a portion configured to form a grip configured to be engaged by a user's hand.

[1065] The housing 301 includes a proximal end portion 302 and a distal end portion 303 and defines an inner volume 311 therebetween (see e.g., FIG. 6). As shown in FIG. 5, the proximal end portion 302 of the housing 301 includes a protrusion 304 that selectively engages a portion of the fluid reservoir 330, as described in further detail herein. The distal end portion 303 of the housing 301 is coupled to a port 305. More specifically, the port 305 can be coupled to the distal end portion 303 in any suitable manner such as, for example, via a friction fit, a threaded coupling, a mechanical fastener, an adhesive, any number of mating recesses, and/or any combination thereof. In other embodiments, the port 305 can be monolithically formed with the housing 301. Moreover, the port 305 can be coupled to the distal end portion 303 of the housing 301 such that a seal member 316 is disposed between the port 305 and a distal wall 308 of the housing 301. In this manner, when the port 305 is coupled to the housing 301, the seal member 316 can engage the distal wall 308 of the housing 301 and the port 305 to selectively form a substantially fluid tight seal, as described in further detail herein.

[1066] As shown in FIG. 6, the port 305 is removably coupled to a lock mechanism 321 of the cannula assembly 320. The lock mechanism 321 of the cannula assembly 320 can be, at least temporarily, coupled to the port 305 to selectively place the housing 301 in fluid communication with the cannula assembly 320. For example, in some embodiments, the lock mechanism 321 can be a Luer-Lok® that receives a portion of the port 305 to physically and fluidically couple the cannula assembly 320 to the housing 301. In other embodiments, the lock mechanism 321 and the port 305 can be removably coupled in any suitable manner.

[1067] As shown in FIGS. 5 and 6, the fluid reservoir 330 defines an inner volume 333 between a proximal end portion 331 and a distal end portion 332. More specifically, the inner volume 333 is closed at the proximal end portion 331 of the fluid reservoir 330 such that at the proximal end, the inner volume 333 is fluidically isolated from a volume outside the fluid reservoir 330. Conversely, the distal end portion 332 of the fluid reservoir 330 is open such that at the distal end, the inner volume 333 can be in fluid communication with a volume outside the fluid reservoir 330. The distal end portion 332 of the fluid reservoir 330 is movably disposed about the proximal end portion 302 of the housing 301, as shown in FIG. 6. Similarly stated, the proximal end portion 302 of the housing 301 is movably disposed within the inner volume 333 defined by the fluid reservoir 330 such that the inner volume 311 defined by the housing 301 is in fluid communication with the inner volume 333 of the fluid

reservoir 330. Moreover, the distal end portion 332 of the fluid reservoir 330 includes a protrusion 335 that can be placed in contact with the protrusion 304 disposed at the proximal end portion 302 of the housing 301 to substantially limit the movement of the fluid reservoir 330 relative to the housing 301, as described in further detail herein.

[1068] The flow control mechanism 340 included in the transfer device 300 is at least partially disposed within the inner volume 311 of the housing 301 and is configured to be moved between a first configuration and a second configuration. Expanding further, the flow control mechanism 340 is in the first configuration when disposed in a distal position relative to the housing 301 (see e.g., FIG. 6) and is in the second configuration when disposed in a proximal position relative to the housing 301 (see e.g., FIG. 9). As shown in FIGS. 6 and 7, the flow control mechanism 340 includes a first member 341 and a second member 360. The first member 341 includes a proximal end portion 342 and a distal end portion 343 and defines a lumen 346 therethrough. The first member 341 can be any suitable shape, size, or configuration. For example, as shown in FIG. 5, the first member 341 can be substantially cylindrical and can have a diameter substantially corresponding to the diameter of the inner volume 311 of the housing 301.

[1069] The second member 360 of the flow control mechanism 340 includes a proximal end portion 361 and a distal end portion 362 and defines a lumen 363 therethrough. As shown in FIG. 6, at least a portion of the second member 360 is movably disposed within the cannula assembly 320. More specifically, the second member 360 can be substantially cylindrical and can have a diameter substantially corresponding to the inner diameter of the cannula 324 included in the cannula assembly 320. As shown in the enlarged view of FIG. 7, the proximal end portion 361 of the second member 360 is configured to extend through the port 305 and the seal member 316 (described above), and through an opening 309 defined in the distal wall 308 to allow the second member 360 to be coupled to the first member 341. Expanding further, the proximal end portion 361 of the second member 360 is disposed within the lumen 346 defined by the first member 341. In some embodiments, the proximal end portion 361 of the second member 360 can form a friction fit with the walls of the first member 341 that define the lumen 346, thereby coupling the second member 360 to the first member 341. In other embodiments, the second member 360 can be coupled to the first member 341 via an adhesive or the like.

[1070] The distal end portion 362 of the second member 360 is configured to extend beyond a distal end of the cannula 324 included in the cannula assembly 320, when the flow control mechanism 340 is in the first configuration. Furthermore, the distal end portion 362 of the second member 360 can include a sharp point that can facilitate the insertion of the transfer device 300 (e.g., the flow control mechanism 340 and the cannula assembly 320) into a portion of a patient. For example, the distal end portion 362 of the second member 360 can be used to access a vein of the patient and facilitate the introduction of the cannula 324 into the vein. Moreover, with the cannula 324 and the distal end portion 362 of the second member 360 disposed within the vein of the patient the transfer device 300 can be configured to transfer a portion of a bodily fluid from the patient to the fluid reservoir 330 to prevent injection of dislodged dermally residing microbes that have been incompletely sterilized by surface antisepsis and/or other undesirable external contaminants.

[1071] As shown in FIG. 8, the transfer device 300 can be moved to a second configuration to begin a flow of bodily fluid (e.g., blood) from the patient to the transfer device 300. More specifically, the fluid reservoir 330 can be moved in the proximal direction relative to the housing 301 to place the transfer device 300 in the second configuration, as indicated by the arrow FF. The arrangement of the fluid reservoir 330 and the housing 301 is such that the proximal motion of the fluid reservoir 330, relative to the housing 301, increases the inner volume 333 defined by the fluid reservoir 330. Expanding further, the proximal end portion 302 of the housing 301 can be disposed within the inner volume 333 of the fluid reservoir 330 such that the protrusion 304 engages an inner surface of the fluid reservoir 330 to define a substantially fluid tight seal. In addition, the protrusion 335 of the fluid reservoir 330 can be placed in contact with the protrusion 304 of the housing 301 to limit the proximal motion of the fluid reservoir 330 relative to the housing 301. In this manner, the proximal motion of the fluid reservoir 330 relative to the housing 301 increases the collective volume of both the inner volume 311 defined by the housing 301 and the inner volume 333 of the fluid reservoir 330.

[1072] The increase of volume introduces a negative pressure within the inner volume 333 of the fluid reservoir 330 and within the inner volume 311 of the housing 301. Therefore, with the cannula 324 and the second member 360 of the flow control mechanism 340 disposed within the vein of the patient, the negative pressure urges a flow of bodily fluid (e.g., blood) through the lumen 363 and 346 defined by the second member 360 and first

member 341 of the flow control mechanism 340, respectively. As indicated by the arrow GG in FIG. 8, the bodily fluid can flow through the lumen 363 and 346 of the flow control mechanism 340 and enter the collective volume formed and/or defined by the inner volume 311 of the housing 301 and the inner volume 333 of the fluid reservoir 330.

[1073] As shown in FIG. 9, when a predetermined amount of bodily fluid is disposed within the fluid reservoir 330, the flow control mechanism 340 can be moved to its second configuration (e.g., the proximal position relative to the housing 301) to place the transfer device 300 a third configuration. More specifically, the flow control mechanism 340 includes a spring 349 that is in contact with the distal wall 308 of the housing 301 and the distal end portion 343 of the first member 341 included in the flow control mechanism 340. As shown in FIGS. 6-8, the spring 349 is maintained in a compressed configuration while the transfer device 300 is in the first and second configuration. As shown in FIG. 9, when the spring 349 is allowed to expand, the spring 349 exerts a force to move the flow control mechanism 340 in the proximal direction, as indicated by the arrow HH. In some embodiments, the expansion of the spring 349 can be in response to the actuator 380. The actuator 380 can be any suitable mechanism configured to selectively interact with the spring 349 such as, for example, a push button. In other embodiments, the actuator 380 can be a slider, a pull-tab, a lever, a toggle, an electronic switch, or the like.

[1074] The proximal motion of the flow control mechanism 340 can be such that both the first member 341 and the second member 360 of the flow control mechanism 340 are disposed within the collective volume defined by the fluid reservoir 330 and the housing 301. Similarly stated, the spring 349 moves the flow control mechanism 340 in the proximal direction a sufficient distance to move the distal end portion 362 of the second member 360 through the port 305, the seal member 316, and the distal wall 308 to be disposed within the housing 301. Furthermore, the seal member 316 can be configured such that as the distal end portion 362 passes beyond the distal wall 308 of the housing 301, the seal member 316 acts to seal the opening 309 through which the second member 360 was disposed. Thus, when the flow control mechanism 340 is completely disposed within the collective volume defined by the housing 301 and the fluid reservoir 330 (e.g., the combination of the inner volume 311 and the inner volume 333, respectively), the seal member 316 seals the distal end portion 303 of the housing 301 and the fluid reservoir 330 is substantially fluidically isolated from the cannula assembly 320.

[1075] With the fluid reservoir 330 fluidically isolated from the cannula assembly 320, the transfer device 300 can be placed in a fourth configuration, as shown in FIG. 10. More specifically, the housing 301 and the fluid reservoir 330 can be collectively moved in the proximal direction such that the port 305 is physically decoupled from the lock mechanism 321 of the cannula assembly 320, as indicated by the arrow II. In this manner, the fluid reservoir 330 can contain and fluidically isolate a portion of the bodily fluid (e.g., blood) that includes, for example, dermally residing microbes dislodged during the venipuncture event (e.g., the insertion of the distal end portion 362 of the second member 360 of the flow control mechanism 340). Furthermore, with the port 305 decoupled from the lock mechanism 321 of the cannula assembly 320, the cannula assembly 320 can be physically and fluidically coupled to an external fluid reservoir (not shown in FIG. 10) that can deliver a flow of a parenteral fluid that is substantially free from the dermally residing microbes.

[1076] While the fluid reservoir 330 is shown in FIGS. 4-10 as being disposed about a portion of the housing 301, in some embodiments, a transfer device can include a fluid reservoir the is substantially enclosed within a housing. For example, FIGS. 11-15 illustrate a transfer device 400 according to an embodiment. The transfer device 400 includes a housing 401, a cannula assembly 420, a fluid reservoir 430, a flow control mechanism 440, and an actuator 480. As shown in FIGS. 11 and 12, the overall size and shape of the transfer device 400 can be substantially similar to the overall size and shape of the transfer device 300 described above in reference to FIG. 4. In addition, the cannula assembly 420, the flow control mechanism 440, and the actuator 480 can be substantially similar in form and function to the cannula assembly 320, the flow control mechanism 340, and the actuator 380 included in the transfer device 300, described above in reference to FIGS. 4-10. Therefore, the cannula assembly 420, the flow control mechanism 440, and the actuator 480 are not described in further detail herein.

[1077] The housing 401 of the transfer device 400 includes a proximal end portion 402 and a distal end portion 403 and defines an inner volume 411 therebetween. More specifically, the housing 401 is substantially closed at the proximal end portion 402 such that at the proximal end, the inner volume 411 is fluidically isolated from a volume outside the housing 401. The distal end portion 403 of the housing 401 is coupled to a port 405. The port 405 is substantially similar to the port 305 described above, and can be coupled to the distal end portion 403 of the housing 401 such that a seal member 416 is disposed between

the port 405 and a distal wall 408 of the housing 401. In this manner, the seal member 416 can form a substantially fluid tight seal between the distal wall 408 and the port 405 (described in detail with reference the port 305 shown in FIGS. 6 and 7). Furthermore, the port 405 can be configured to removably couple the housing 401 to the cannula assembly 420. For example, the port 405 can be, at least temporarily, physically and fluidically coupled to a lock mechanism 421 included in the cannula assembly 420. In this manner, the housing 401 and the cannula assembly 420 can be selectively placed in fluid communication.

[1078] The fluid reservoir 430 included in the transfer device 400 is movably disposed within the inner volume 411 defined housing 401. More specifically, the fluid reservoir 430 is configured to move within the housing 401 between a first configuration (FIG. 13) and a second configuration (FIG. 14). The fluid reservoir 430 defines an inner volume 433 between a proximal end portion 431 and a distal end portion 432. The inner volume 433 is configured to selectively receive at least a portion of the flow control mechanism 440. Furthermore, the flow control mechanism 440 can moved between a first position and a second position to move the fluid reservoir 430 between the first configuration and the second configuration, as described in further detail herein.

[1079] As shown in FIG. 13, the flow control mechanism 440 is in the first position when disposed in a distal position relative to the housing 401. While in the first position, a first member 441 of the flow control mechanism 440 is completely contained within the inner volume 433 and a second member 460 is configured to extend from the first member 441 through the distal end portion 432 of the fluid reservoir 430. The second member 460 of the flow control mechanism 460 further extends through the housing 401 and the port 405 to be at least partially disposed within the cannula assembly 420 (as described above in detail with reference to the second member 360 shown in FIGS. 6 and 7). In this manner, a distal end portion 462 of the second member 460 can extend beyond a cannula 424 of the cannula assembly 420 to facilitate the insertion of the cannula 424 into a portion of a patient. Moreover, with the distal end portion 462 of the second member 460 disposed within the portion of the patient, a lumen 463 defined by the second member 460 and a lumen 446 defined by the first member 441 can place the fluid reservoir 430 in fluid communication with the portion of the patient.

[1080] In use, the transfer device 400 can be moved from the first configuration (FIG. 13) to the second configuration (FIG. 14) to facilitate the flow of a bodily fluid (e.g., blood) into

the fluid reservoir 430. More specifically, the flow control mechanism 440 includes a mechanical actuator 449 (e.g., a spring) that is in contact with the distal wall 408 of the housing 401 and the first member 441 of the flow control mechanism 440. As shown in FIG. 13, the mechanical actuator 449 is maintained in a compressed configuration while the transfer device 400 is in the first configuration. Similarly stated, the flow control mechanism 440 is in the first position relative to the housing 401 when the mechanical actuator 449 is in the compressed configuration. As shown in FIG. 14, when the mechanical actuator 449 is allowed to expand, the mechanical actuator 449 exerts a force to move the flow control mechanism 440 in the proximal direction, as indicated by the arrow JJ. In some embodiments, the expansion of the mechanical actuator 449 can be in response to an actuation of the actuator 480.

[1081] The proximal motion of the flow control mechanism 440 moves within the inner volume 433 to place the first member 441 in contact with the proximal end portion 441 of the fluid reservoir 430. In this manner, the flow control mechanism 440 urges the proximal end portion 431 of the fluid reservoir 430 to move in the direction of the arrow JJ (e.g., the proximal direction). Moreover, the distal end portion 432 of the fluid reservoir 430 can be coupled to the distal wall 408 of the housing 401 such that as the proximal end portion 431 moves in the proximal direction, the fluid reservoir 430 expands. Similarly stated, the fluid reservoir 430 can form a bellows in which the proximal motion of the flow control mechanism 440 moves the fluid reservoir 430 from a compressed configuration (e.g., the first configuration) to an expanded configuration (e.g., the second configuration).

[1082] The movement of the proximal end portion 431 relative to the distal end portion 432 increases the inner volume 433 defined by the fluid reservoir 430 and introduces a negative pressure within the inner volume 433. Moreover, with the lumen 446 of the first member 441 and the lumen 463 of the second member 460 in fluid communication with the fluid reservoir 430, at least a portion of the negative pressure is transferred through the flow control mechanism 440. Therefore, while the flow control mechanism 440 is being moved to the second position (FIG. 14), the negative pressure urges a flow of bodily fluid (e.g., blood) through the lumen 463 and 446 defined by the second member 460 and first member 441 of the flow control mechanism 440, respectively. Expanding further, as shown in FIG. 14, the proximal motion of the flow control mechanism 440 is such that the second member 460 is retracted to a proximal position relative to the distal wall 408 of the housing 401. Prior to

being disposed in the proximal position relative to the distal wall 408, however, the lumen 463 is maintained in fluid communication with the portion of the patient via the cannula 424. In this manner, the flow control mechanism 440 transfers the bodily fluid to the fluid reservoir 430 while being moved in the proximal direction and prior to being disposed in the second position. Thus, when the second member 460 is retracted to the proximal position relative to the distal wall 408, the flow control mechanism 440 has transferred a predetermined amount of bodily fluid to the fluid reservoir 430 and the seal member 416 can act to fluidically isolate the fluid reservoir 430. Similarly stated, the flow control mechanism 440 is configured to transfer the predetermined amount of bodily fluid to the fluid reservoir 430 concurrently with the proximal motion of both the flow control mechanism 440 and the fluid reservoir 430.

[1083] With the fluid reservoir 430 fluidically isolated from the cannula assembly 420, the transfer device 400 can be placed in a third configuration, as shown in FIG. 15. More specifically, the housing 401 and the fluid reservoir 430 can be collectively moved in the proximal direction to physically decouple the port 405 from the lock mechanism 421 of the cannula assembly 420, as indicated by the arrow KK. In some embodiments, the actuator 480 can facilitate the decoupling of the port 405 from the lock mechanism 421. In other embodiments, a second actuator (not shown) can be engaged to decouple the port 405 from the lock mechanism 421. In other embodiments, an actuator need not be engaged to decouple the port 405 from the lock mechanism 421.

[1084] With the port 405 decoupled from the lock mechanism 421, the fluid reservoir 430 can contain and fluidically isolate a portion of the bodily fluid (e.g., blood) that includes, for example, dermally residing microbes dislodged during the venipuncture event (e.g., the insertion of the distal end portion 462 of the second member 460 of the flow control mechanism 440). Furthermore, with the port 405 decoupled from the lock mechanism 421, the cannula assembly 420 can be physically and fluidically coupled to an external fluid reservoir (not shown in FIG. 15) that can deliver a flow of a parenteral fluid that is substantially free from the dermally residing microbes, as described above.

[1085] While the fluid reservoir 430 is shown in FIGS. 11-15 as being disposed within the inner volume 411 of the housing 401, in some embodiments, a fluid reservoir can be physically and fluidically coupled to a portion of the transfer device. For example, FIGS. 16-23 illustrate a transfer device 500 according to an embodiment. The transfer device 500

includes a housing 501, a cannula assembly 520, a flow control mechanism 540, and an actuator mechanism 580. As shown in FIGS. 16 and 17, the overall size and shape of the transfer device 500 can be substantially similar to the overall size and shape of the transfer device 300 described above in reference to FIG. 4. In other embodiments, the overall size and shape of the transfer device 500 can be square, rectangular, polygonal, and/or any other non-cylindrical shape. In addition, the cannula assembly 520 can be substantially similar in form and function to the cannula assembly 320 included in the transfer device 300, described above in reference to FIGS. 4-10. Therefore, the cannula assembly 520 is not described in further detail herein.

[1086] As shown in FIG. 18, the housing 501 of the transfer device 500 includes a proximal end portion 502 and a distal end portion 503 and defines an inner volume 511 therebetween. The housing 501 is substantially closed at the proximal end portion 502 such that at the proximal end, the inner volume 511 is fluidically isolated from a volume outside the housing 501. The distal end portion 503 of the housing 501 includes a distal wall 508 that defines an opening 509 configured to receive, at least temporarily, a portion of the flow control mechanism 540, as described in further detail herein. The housing 501 further defines an actuator chamber 510 configured to receive at least a portion of the actuator mechanism 580. As shown in FIG. 18, the walls of the housing 501 can be arranged such that the actuator chamber 510 is a bore with a centerline that is substantially perpendicular to a centerline defined by the inner volume 511.

[1087] Referring back to FIG. 17, the actuator mechanism 580 includes a first actuator member 581 and a second actuator member 585. As described in further detail herein, the actuator mechanism 580 can be moved between a first configuration (see e.g., FIG. 16) and a second configuration (see e.g., FIG. 21). The first actuator member 581 can be rotatably coupled to the walls of the housing 501 defining the actuator chamber 510. Similarly stated, the first actuator member 581 is configured to be disposed substantially outside the housing 501 and can be rotatably coupled to the walls of the housing 501 that define the actuator chamber 510. The first actuator member 581 includes an engagement portion 582 and a port 583 configured to be physically and fluidically coupled to a fluid reservoir, as described in further detail herein.

[1088] As shown in FIG. 19, the second actuator member 585 can be substantially cylindrical and is configured to be disposed within the actuator chamber 510 defined by the

housing 501. The second actuator member 585 defines a lumen 587 and a flow control channel 588. The lumen 587 is configured to be in fluid communication with the port 583 of the first actuator member 581. In this manner, the lumen 587 and the port 583 can receive a flow of a bodily fluid when the actuator mechanism 580 is in the first configuration, as described in further detail herein. The flow control channel 588 is configured to receive at least a portion of the flow control mechanism 540 when the actuator mechanism 580 is placed in the second configuration, as described in further detail herein.

[1089] The flow control mechanism 540 included in the transfer device 500 is at least partially disposed within the inner volume 511 of the housing 501 and is configured to be moved between a first position and a second position. Expanding further, the flow control mechanism 540 is in the first position when disposed in a distal position relative to the housing 501 (see e.g., FIG. 20) and is in the second position when disposed in a proximal position relative to the housing 501 (see e.g., FIG. 22). As shown in FIGS. 17 and 20, the flow control mechanism 540 includes a first member 541 and a second member 560. The first member 541 includes a proximal end portion 542 and a distal end portion 543 and defines a lumen 546 therethrough. The first member 541 can be any suitable shape, size, or configuration. For example, as shown in FIG. 17, the first member 541 can be substantially cylindrical with the proximal end portion 542 having a first diameter that substantially corresponds to the diameter of the flow control channel 588 defined by the second actuator member 585. As shown in FIG. 20, the first member 541 can be configured such that when the flow control mechanism 540 is in the first position, the lumen 546 defined by the first member 541 is in fluid communication with the lumen 587 defined by the second actuator member 585, as described in further detail herein.

[1090] The distal end portion 543 of the first member 541 can have a second diameter, smaller than the first diameter, substantially corresponding to an inner diameter of a lock mechanism 521 included in the cannula assembly 520. For example, in some embodiments, the distal end portion 543 can extend through the opening 509 defined by the distal wall 508 of the housing 501 to be disposed within the lock mechanism 521. In some embodiments, the distal end portion 543 can form a friction fit with an inner surface of the lock mechanism 521 to removably couple the flow control mechanism 540 to the cannula assembly 520. Furthermore, with the proximal end portion 542 of the first member 541 disposed in a proximal position relative to the distal wall 508 and with the diameter of the proximal end

portion 542 substantially larger than the diameter of the opening 509, the flow control mechanism 540 operatively couples the housing 501 to the cannula assembly 520.

[1091] The second member 560 of the flow control mechanism 540 includes a proximal end portion 561 and a distal end portion 562 and defines a lumen 563 therethrough. As shown in FIG. 20, at least a portion of the second member 560 is movably disposed within a cannula 524 of the cannula assembly 520. As described above with respect to the flow control mechanism 340, the proximal end portion 561 of the second member 560 is configured to extend through the lock mechanism 521 to be coupled to the first member 541. Expanding further, the proximal end portion 561 of the second member 560 is disposed within the lumen 546 defined by the first member 541. The distal end portion 562 of the second member 560 is configured to extend beyond a distal end of the cannula 524 included in the cannula assembly 520, when the flow control mechanism 540 is in the first configuration. In this manner, the second member 560 can facilitate the insertion of the transfer device 500 into a portion of a patient (e.g., the distal end can include a sharp point) and can further facilitate a transfer of a bodily fluid from the patient to a fluid reservoir (e.g., via the lumen 563).

[1092] For example, as shown in FIG. 20, the transfer device 500 can be in a first configuration when the flow control mechanism 540 is in the first position and the actuator mechanism 580 is in its first configuration. In this manner, the second member 560 of the flow control mechanism 540 and the cannula 524 of the cannula assembly 520 can be inserted into a portion of the patient, such as a vein, to place the transfer device 500 in fluid communication with the portion of the patient. Furthermore, a fluid reservoir (not shown in FIGS. 16-23) can be physically and fluidically coupled to the port 583 of the second actuator member 581. The arrangement of the flow control mechanism 540 and the actuator mechanism 580 is such that when the fluid reservoir is physically and fluidically coupled to the port 583, the fluid reservoir is in fluid communication with the lumen 587 defined by the second actuator member 585 and the two lumen 546 and 563 defined by the first member 541 and the second member 560 of the flow control mechanism 540, respectively. In some embodiments, the fluid reservoir can be, for example, a Vacutainer®. In such embodiments, the fluid reservoir can define a negative pressure such that when fluidically coupled to the port 583, the fluid reservoir introduces a suction force within the portion of the patient (e.g., via the lumen 587, 546, and 563). In this manner, a portion of the suction force can urge a

flow of bodily fluid through the lumen 563, 546, and 587 and into the fluid reservoir, as indicated by the arrow LL in FIG. 20. Moreover, the flow of bodily fluid can be such that dermally residing microbes dislodged during a venipuncture event (e.g., the insertion of the flow control mechanism 540 and the cannula 524) become entrained therein and are transferred to the fluid reservoir.

[1093] With a predetermined amount of bodily fluid transferred to the fluid reservoir, the fluid reservoir can be decoupled from the port 583 (e.g., physically and fluidically or only fluidically). In this manner, a user can engage the first actuator member 581 to move the actuator mechanism 580 to its second configuration and thereby place the transfer device in a second configuration. For example, as indicated by the arrow MM in FIG. 21, the user (e.g., a physician, a nurse, a phlebotomist, etc.) can rotate the first actuator member 581 in a clockwise direction relative to the housing 501.

[1094] The actuator mechanism 580 is such that the rotation of the first actuator member 581 urges the second actuator member 585 to also rotate relative to the housing 501. In this manner, a centerline defined by the flow control channel 587 is rotated from a first configuration in which the centerline is substantially perpendicular to the centerline defined by the inner volume 511 to a second configuration in which the centerline is substantially parallel to the centerline of the inner volume 511. Similarly stated, the second actuator member 585 is rotated such that the centerline defined by the flow control channel 587 is aligned with the centerline defined by the inner volume 511.

[1095] As shown in FIG. 22, the rotation of the actuator mechanism 580 toward the second configuration can facilitate the movement of the flow control mechanism 540 from the first position toward the second position. More specifically, the flow control mechanism 540 includes a spring 549 that is disposed about the distal end portion 543 of the first member 541 and is in contact with the distal wall 508 of the housing 501 and a surface of the first member 541. The spring 549 is maintained in a compressed configuration while the transfer device 500 is in the first configuration. For example, as shown in FIG. 20, a proximal surface of the first member 541 of the flow control mechanism 540 can be in contact with a surface of the second actuator mechanism 585 such that the second actuator mechanism 585 prevents proximal movement of the flow control mechanism 540. When the actuator mechanism 580 is moved to the second configuration and the flow control channel 587 is aligned with the inner volume 511 (as described above), however, the proximal surface of the first member

541 is no longer in contact with the surface of the second actuator member 585 and the spring 549 is allowed to expand.

[1096] The expansion of the spring 549 exerts a force on the first member 541 of the flow control mechanism 540 to move the flow control mechanism 540 in the proximal direction, as indicated by the arrow NN in FIG. 22. In this manner, the flow control mechanism 540 can pass through the flow control channel 587 defined by the second actuator member 585 to be disposed in the second position (e.g., the distal position). The proximal motion of the flow control mechanism 540 is such that both the first member 541 and the second member 560 of the flow control mechanism 540 are disposed within the inner volume 511 defined by the housing 501. Similarly stated, the spring 549 moves the flow control mechanism 540 in the proximal direction a sufficient distance to move the distal end portion 562 of the second member 560 through the opening 509 defined by the distal wall 508 to be disposed within the housing 501.

[1097] As shown in FIG. 23, with the flow control mechanism 540 disposed within the housing 501, the distal end portion 543 of the first member 541 is no longer disposed within the lock mechanism 521 of the cannula assembly 520. In this manner, the housing 501 is physically and fluidically decoupled from the cannula assembly 520 and can be moved away from the cannula assembly 520, as indicated by the arrow OO in FIG. 23. Furthermore, with the housing 501 decoupled from the lock mechanism 521, the cannula assembly 520 can be physically and fluidically coupled to an external fluid reservoir (not shown in FIG. 23) that can deliver a flow of a parenteral fluid to the portion of the patient that is substantially free from the dermally residing microbes.

[1098] While the transfer devices described above are configured to include a cannula assembly that is physically and fluidically decoupled from a portion of the transfer device to receive a parenteral fluid, in some embodiments, a transfer device can include a cannula assembly configured to remain physically coupled to a portion of the transfer device. For example, FIGS. 24-30 illustrate a transfer device 600 according to an embodiment. The transfer device 600 includes a housing 601, a cannula assembly 620, a fluid reservoir 630, and a flow control mechanism 640. In use, the transfer device 600 can be moved between a first, a second, and a third configuration to receive a predetermined amount of a bodily fluid from a patient and to deliver a flow of a parenteral fluid to the patient that is substantially free from, for example, dermally residing microbes.

[1099] As shown in FIGS. 24 and 25, the housing 601 includes a proximal end portion 602 and a distal end portion 603 and defines an inner volume 611 therebetween. The proximal end portion 602 is substantially open such that the inner volume 611 can selectively receive the fluid reservoir 630 and at least a portion of the flow control mechanism 640. In addition, the proximal end portion 602 includes a protrusion 604 configured to engage a portion of the flow control mechanism 640, as described in further detail herein.

[1100] The distal end portion 603 of the housing 601 includes a distal port 605 and a reservoir seat 618. The reservoir seat 618 is configured to engage, at least temporarily, a portion of the fluid reservoir 630, as described in further detail herein. The distal port 605 is configured to be physically and fluidically coupled to a lock mechanism 621 included in the cannula assembly 620. For example, in some embodiments, the lock mechanism 621 can be a Luer-Lok® configured to receive the port 605. In other embodiments, the port 605 and the lock mechanism 621 can be coupled in any suitable manner such as, for example, a threaded coupling, a friction fit, or the like. In still other embodiments, the port 605 and the lock mechanism 621 can be coupled via an adhesive or the like to fixedly couple the cannula assembly 620 to the housing 601. With the lock mechanism 621 coupled to the port 605, the inner volume 611 of the housing 601 is in fluid communication with a cannula 624 included in the cannula assembly 620, as further described herein.

[1101] As described above, the fluid reservoir 630 is disposed within the inner volume 611 of the housing 601. More particularly, the fluid reservoir 630 is movably disposed within the inner volume 611 between a first position in which the fluid reservoir 630 is in a distal position relative to the housing 601 (see e.g., FIG. 28) and a second position in which the fluid reservoir 630 is in a proximal position relative to the housing 601 (see e.g., FIG. 30). As shown in FIG. 26, the fluid reservoir 630 includes a proximal end portion 631 and a distal end portion 632 and defines an inner volume 633 therebetween. The proximal end portion 631 includes a flange 634 and a protrusion 635 and defines a set of openings 636. Furthermore, the proximal end portion 631 of the fluid reservoir 630 is substantially open to receive a portion of the flow control mechanism 640. In this manner, the proximal end portion 631 is configured to engage, interact, or otherwise correspond with a portion of the flow control mechanism 640, as further described herein.

[1102] The distal end portion 632 of the fluid reservoir 630 includes a valve seat 637. The valve seat 637 includes a port 638 and receives a valve 639 (see e.g., FIG. 28-30). The

valve seat 637 is selectively disposed about the reservoir seat 618 of the housing 601, as described in further detail herein. The valve 639 can be any suitable valve such as, for example, a check valve or the like. In this manner, the distal end portion 632 can be selectively placed in fluid communication with the inner volume 611 when the fluid reservoir 630 is disposed within the housing 601, as described in further detail herein.

[1103] As described above, the flow control mechanism 640 can be at least partially disposed within the housing 601. More particularly and as shown in FIG. 27, the flow control mechanism 640 includes an engagement portion 645 configured to be disposed outside the housing 601 and a plunger portion 650 configured to be at least partially disposed within the inner volume 611 defined by the housing 601. As described in further detail herein, the engagement portion 645 can be engaged by a user to move the flow control mechanism 640 between a first configuration and a second configuration.

[1104] The plunger portion 650 of the flow control mechanism 640 is configured to extend in a distal direction from a surface of the engagement portion 645. The plunger 650 includes a first surface 652, a second surface 655, a protrusion 653, a first seal member 658, and a second seal member 659. As shown in FIG. 27, the plunger portion 650 is substantially cylindrical and defines a channel 651 that receives, for example, a cannula 664 that defines a lumen 646. More particularly, the cannula 664 is configured to be disposed within an opening 654 defined by the first surface 652 to place the lumen 646 in fluid communication with an inner volume 656 defined between the first surface 652 and the second surface 655. The plunger 650 is further configured to define a set of openings 657 that can selectively place the inner volume 656 in fluid communication with a portion of the housing 601, as described in further detail herein.

[1105] In use, the transfer device 600 can be moved between a first configuration (FIG. 28), a second configuration (FIG. 29), and a third configuration (FIG. 30). Referring to FIG. 28, while in the first configuration, the cannula 624 of the cannula assembly 620 can be inserted into a portion of a patient to place the cannula 624 in fluid communication with, for example, a vein. In some embodiments, the cannula 624 can include a sharp point at a distal end such that the cannula 624 can pierce the portion of the patient. In other embodiments, the cannula assembly 620 can include a trocar (not shown) to facilitate the insertion of the cannula 624. As described above, the cannula assembly 620 is physically and fluidically coupled to the port 605 of the housing 601 such that when the cannula 624 is placed in fluid

communication with the vein of the patient, the port 605 is concurrently placed in fluid communication with the vein. With the port 605 in fluid communication with the portion of the patient (e.g., the vein), a user (e.g., a physician, nurse, technician, or the like) can engage the engagement portion 645 of the flow control mechanism 640 to place the transfer device 600 in the second configuration.

[1106] As shown in FIG. 29, the transfer device 600 is placed in the second configuration when the plunger portion 650 of the flow control mechanism 640 is moved within the fluid reservoir 630 from a first position (e.g., a distal position) to a proximal position (e.g., a proximal position), as indicated by the arrow PP. More specifically, the transfer device 600 includes a spring 649 configured to engage the protrusion 604 of the housing 601 and the flange 634 of the fluid reservoir 630 to maintain the fluid reservoir 630 in the first position while the flow control mechanism 640 is moved to its second position. Similarly, stated the flow control mechanism 640 is moved in a proximal direction relative to the fluid reservoir 630.

[1107] In addition, the first seal member 658 can engage an inner surface of the fluid reservoir 630 such that the proximal movement of the flow control mechanism 640 produces a negative pressure within a portion of the inner volume 633 of the fluid reservoir 630 (e.g., the portion of the inner volume 633 that is disposed distally relative to the first seal member 658). In this manner, the negative pressure introduces a suction force that can be operable placing the valve 639 in an open configuration. Thus, with the cannula 624 and the port 605 in fluid communication with the portion of the patient (e.g., the vein), a flow of bodily fluid (e.g., blood) can pass through the valve 639 and enter the inner volume 633 of the fluid reservoir 630, as indicated by the arrow QQ.

[1108] As shown in FIG. 29, the proximal movement of the flow control mechanism 640 relative to the fluid reservoir 630 is configured to stop when the flow control mechanism 640 is in the second position (e.g., the proximal position). More specifically, the protrusion 635 of the fluid reservoir 630 can engage the protrusion 653 of the plunger portion 650 to limit the proximal movement of the flow control mechanism 640 relative to the fluid reservoir 630. Furthermore, when the flow control mechanism 640 is in the second position relative to the fluid reservoir 630, the openings 657 of the plunger portion 650 are in fluid communication with the openings 636 defined by the fluid reservoir 630. Thus, the inner volume 656 defined by the plunger portion 650 of the flow control mechanism 640 is placed in fluid

communication with the inner volume 611 of the housing 601, as described in further detail herein.

[1109] With the transfer device 600 in the second configuration, a flow of a predetermined amount of bodily fluid can be transferred to the inner volume 633 of the fluid reservoir 630 that can include, for example, dermally residing microbes dislodged during a venipuncture event (e.g., the insertion of the cannula 624 into the vein and/or otherwise accessing the vasculature of the patient). In addition, when the predetermined amount of bodily fluid is transferred to the inner volume 633 of the fluid reservoir 630, the valve 639 can be placed in a closed configuration. For example, in some embodiments, the transfer of the predetermined amount of bodily fluid can be such that the negative pressure within the inner volume 633 is brought into equilibrium with the pressure of the vein, thus allowing the valve 639 to move to the closed configuration. In other embodiments, the valve 639 can be manually actuated by user interference (e.g., engagement of an actuator, a switch, a button, a toggle, or the like). In this manner, the bodily fluid disposed in the inner volume 633 between the first seal member 658 and the distal end portion 632 of the fluid reservoir 630 can be fluidically isolated from a volume outside the inner volume 633. Expanding further, the first seal member 658 prevents a flow of the bodily fluid in the proximal direction and the valve 639, being in the closed configuration, prevents a flow of the bodily fluid in the distal direction. Thus, the predetermined amount of bodily fluid is fluidically isolated from a volume outside the inner volume 633 of the fluid reservoir 630 defined between the first seal member 658 and the distal end portion 632.

[1110] As indicated by the arrow RR in FIG. 30, the user can continue to move the flow control mechanism 640 in the proximal direction to place the transfer device 600 in the third configuration. More specifically, with the protrusion 653 of the flow control mechanism 640 in contact with the protrusion 635 of the fluid reservoir 630, the proximal movement of the flow control mechanism 640 is such that the flow control mechanism 640 and the fluid reservoir 630 move, concurrently, in the proximal direction relative to the housing 601. Furthermore, the proximal movement is such that the valve seat 637 is moved in the proximal direction relative to the reservoir seat 618. Similarly stated, the proximal movement of the fluid reservoir 630 is such that the valve seat 637 is no longer disposed about the reservoir seat 618 of the housing 601. In this manner, the port 605 is placed in fluid communication with the inner volume 611 of the housing 601.

[1111] With the transfer device 600 in the third configuration, an external fluid source (not shown in FIG. 30) can be placed in fluid communication with a portion of the transfer device 600 to transfer a flow of parenteral fluid to the portion of the patient. For example, in some embodiments, the transfer device 600 can include a proximal lock mechanism 613 that can physically and fluidically couple the transfer device 600 to the external fluid source. The proximal lock mechanism 613 can be any of those described herein. In this manner, the external fluid source can deliver a flow of parenteral fluid to the lumen 646, as indicated by the arrow SS. Moreover, with the lumen 646 in fluid communication with the inner volume 656 defined between the first surface 652 and the second surface 655, the flow of the parenteral fluid can pass through the openings 657 defined by the plunger portion 650 of the flow control mechanism 640. In addition, the first seal member 658 and the second seal member 659 can act to define a fluid flow path that directs the flow of the parenteral fluid to the openings 636 defined by the fluid reservoir 630. In this manner, the flow of parenteral fluid can pass through the openings 636 of the fluid reservoir 630 to enter the inner volume 611 defined by the housing 601. Similarly stated, upon exiting the openings 636, the parenteral fluid can flow within the inner volume 611 defined by the housing 601 and outside of the fluid reservoir 630, as indicated by the arrows SS. Expanding further, the parenteral fluid can flow within the housing 601 in the distal direction and enter the port 605 to transfer the flow parenteral fluid to the cannula assembly 620. Therefore, the external fluid source can deliver a flow of parenteral fluid to the patient that is fluidically isolated from the predetermined amount of bodily fluid disposed in the fluid reservoir 630 and is thus, substantially free from dermally residing microbes and/or other undesirable external contaminants.

[1112] In some embodiments, user intervention maintains the transfer device 600 in the third configuration. Expanding further and as described above, the proximal movement of the fluid reservoir 630 is such that a portion of the force applied by the user (e.g., the physician, nurse, technician, or the like) to move the flow control mechanism 640 and fluid reservoir 630 is used to move the spring 649 to a compressed configuration. In such embodiments, the removal of the portion of the force would allow the spring 649 to expand and thereby move the fluid reservoir 630 in the distal direction. In other embodiments, a transfer device can include a catch, protrusion, latch or the like configured to maintain the spring in the compressed configuration.

[1113] While the transfer device 600 is shown in FIGS. 24-30 as including a fluid reservoir 630, in other embodiments, a transfer device can include a flow control mechanism with an integrated fluid reservoir. For example, FIGS. 31-34 illustrate a transfer device 700 according to an embodiment. The transfer device 700 includes a housing 701, a cannula assembly 720, and a flow control mechanism 740. In use, the transfer device 700 can be moved between a first configuration and a second configuration to receive a predetermined amount of a bodily fluid from a patient and to deliver a flow of a parenteral fluid to the patient that is substantially free from, for example, dermally residing microbes and/or other undesirable external contaminants.

[1114] As shown in FIGS. 31 and 32, the housing 701 includes a proximal end portion 702 having a proximal port 706 and a distal end portion 703 having a distal port 705. The proximal port 706 is configured to be physically and fluidically coupled to an external fluid source, as described in further detail herein. The distal port 705 is configured to be physically and fluidically coupled to a lock mechanism 721 included in the cannula assembly 720. For example, in some embodiments, the lock mechanism 721 can be a Luer-Lok® configured to receive the distal port 705. In other embodiments, the distal port 705 and the lock mechanism 721 can be coupled in any suitable manner such as, for example, a threaded coupling, a friction fit, or the like. In still other embodiments, the distal port 705 and the lock mechanism 721 can be coupled via an adhesive or the like to fixedly couple the cannula assembly 720 to the housing 701. With the lock mechanism 721 coupled to the distal port 705, the distal port 705 is placed in fluid communication with a cannula 724 included in the cannula assembly 720, as further described herein.

[1115] The housing 701 defines an inner volume 711 and a set of recess 710. The inner volume 711 is configured to receive at least a portion of the flow control mechanism 740. As shown in FIG. 31, the set of recesses 710 are defined by the housing 701 in a perpendicular orientation relative to the proximal port 706 and distal port 705. Similarly stated, the recesses 710 are perpendicular to a centerline defined by the proximal port 706 and the distal port 705. In this manner, a portion of the flow control mechanism 740 can extend through the recesses 710 when the flow control mechanism 740 is disposed within the inner volume 711 of the housing 701, as described in further detail herein.

[1116] The flow control mechanism 740 defines a first lumen 746, a second lumen 747, and a fluid reservoir 730. The first lumen 746 extends though a portion of the flow control

mechanism 740 and is in fluid communication with the fluid reservoir 730. Similarly stated, the first lumen 746 extends through a portion of the flow control mechanism 740 to selectively place the fluid reservoir 730 in fluid communication with a volume substantially outside of the flow control mechanism 740, as described in further detail herein. As shown in FIG. 33, the second lumen 747 extends through the flow control mechanism 740 and is fluidically isolated from the fluid reservoir 730. In this manner, the second lumen 747 can be selectively placed in fluid communication with the proximal port 706 and the distal port 705 of the housing 701 to deliver a flow of parenteral fluid, as described in further detail herein.

[1117] The flow control mechanism 740 has a circular cross-sectional shape such that when the flow control mechanism 740 is disposed within the inner volume 711, a portion of the flow control mechanism 740 forms a friction fit with the walls of the housing 701 defining the inner volume 711. For example, in some embodiments, the flow control mechanism 740 is formed from silicone and has a diameter larger than the diameter of the inner volume 711. In this manner, the diameter of the flow control mechanism 740 is reduced when the flow control mechanism 740 is disposed within the inner volume 711. Thus, the outer surface of the flow control mechanism 740 forms a friction fit with the inner surface of the walls defining the inner volume 711. In other embodiments, the flow control mechanism 740 can be any suitable elastomer configured to deform when disposed within the inner volume 711 of the housing 701.

[1118] In use, while in the first configuration, the cannula 724 of the cannula assembly 720 can be inserted into a portion of a patient to place the cannula 724 in fluid communication with, for example, a vein. In some embodiments, the cannula 724 can include a sharp point at a distal end such that the cannula 724 can pierce the portion of the patient. In other embodiments, the cannula assembly 720 can include a trocar (not shown) to facilitate the insertion of the cannula 724. As described above, the cannula assembly 720 is physically and fluidically coupled to the distal port 705 of the housing 701 such that when the cannula 724 is placed in fluid communication with the vein of the patient, the distal port 705 is placed in fluid communication with the vein.

[1119] As shown in FIG. 33, when the transfer device 700 is in the first configuration, the first lumen 746 of the flow control mechanism 740 is in fluid communication with the distal port 705 of the housing 701. In this manner, the fluid reservoir 730 defined by the flow control mechanism 740 is placed in fluid communication with the vein of the patient and can

rcccivc a flow of a bodily fluid (c.g., blood). Morcovcr, with thc flow control mcchanism 740 forming a friction fit with the inner surface of the housing 701 (as described above), the flow control mechanism 740 and the housing 701 can form a substantially fluid tight seal about an inlet of the first lumen 746. In this manner, the cannula assembly 720, the distal port 705, and the first lumen 746 collectively define a flow path configured to deliver a flow of bodily fluid from the portion of the patient to the fluid reservoir 730, as indicated by the arrow TT. In addition, the flow of bodily fluid can be such that dermally residing microbes dislodged during a venipuncture event (e.g., the insertion of the cannula 724) are entrained in the flow of bodily fluid and are transferred to the fluid reservoir 740.

[1120] With a desired amount of bodily fluid transferred to the fluid reservoir 730, a user can engage the transfer device 700 to move the transfer device 700 from the first configuration to the second configuration. In some embodiments, the desired amount of bodily fluid transferred to the fluid reservoir 730 is a predetermined amount of fluid. For example, in some embodiments, the transfer device 700 can be configured to transfer bodily fluid until the pressure within the fluid reservoir 730 is equilibrium with the pressure of the portion of the body in which the cannula 724 is disposed (e.g., the vein). In some cmbodimcnts, at lcast a portion of thc flow control mcchanism 740 can bc transparcnt to allow visualization of the bodily fluid flowing into the fluid reservoir 730. The flow control mechanism 740 can include indicators (e.g., 0.1 mL, 0.5 mL, 1 mL, 1.5 mL, 2 mL, 3 mL, 4 mL, 5 mL, etc. graduation marks) to the user can visualize the volume of bodily fluid that has been received in the fluid reservoir 730.

[1121] As shown in FIG. 34, the transfer device 700 can be moved from the first configuration to the second configuration by moving the flow control mechanism 740 in the direction of the arrow UU. In this manner, the first lumen 746 is fluidically isolated from the distal port 705. While not shown in FIGS. 31-34, the first lumen 746 can include a valve or seal configured to fluidically isolate the bodily fluid disposed within the fluid reservoir 730 from a volume outside the flow control mechanism 740. In some embodiments, the valve can be, for example, a one-way check valve. Thus, the fluid reservoir 730 can receive the flow of fluid from a volume outside the fluid reservoir 730 but prevent a flow of fluid from the fluid reservoir 730.

[1122] When moved to the second configuration, the second lumen 747 defined by the flow control mechanism 740 is placed in fluid communication with the distal port 705 and the

proximal port 706 of the housing 701. As described above, the proximal port 706 can be physically and fluidically coupled to an external fluid source (not shown in FIGS. 31-34) such that when the transfer device 700 is in the second configuration, the proximal port 706, the second lumen 747, the distal port 705, and the cannula assembly 720 collectively define a fluid flow path. In this manner, the transfer device 700 can facilitate the delivery of a flow of parenteral fluid from the external fluid source to the portion of the patient (e.g., the vein), as indicated by the arrow VV in FIG. 34. Expanding further, with the predetermined amount of bodily fluid fluidically isolated within the fluid reservoir 730, the transfer device 700 can facilitate the delivery of the flow of parenteral fluid to the patient that is substantially free from, for example, the dermally residing microbes dislodged during the venipuncture event.

[1123] While the flow control mechanism 740 is shown in FIGS. 31-34 as including the integrated fluid reservoir 730, in other embodiments, a transfer device can be configured to be physically and fluidically coupled to an external fluid reservoir. For example, FIGS. 35-39 illustrate a transfer device 800 according to an embodiment. As shown in FIGS. 35 and 36, the transfer device 800 includes a housing 801, a cannula assembly 820, and a flow control mechanism 880. In use, the transfer device 800 can be moved between a first configuration and a second configuration to receive a predetermined amount of a bodily fluid from a patient and to deliver a flow of a parenteral fluid to the patient that is substantially free from, for example, dermally residing microbes.

[1124] The housing 801 includes a proximal end portion 802, a distal end portion 803, and defines an inner volume 811. The inner volume 811 can receive at least a portion of the flow control mechanism 880 and the actuator 880, as further described herein. As shown in FIG. 37, the distal end portion 803 of the housing 801 defines a distal port 805 and the proximal end portion 802 of the housing 801 defines a first proximal port 806, and a second proximal port 807. The distal port 805, the first proximal port 806, and the second proximal port 807 are configured to be in fluid communication with the inner volume 811 defined by the housing 801.

[1125] The distal port 805 is configured to receive a distal cannula 817. The distal cannula 817 (e.g., a lumen defining cannula) is configured to be physically and fluidically coupled to a port 822 included in the cannula assembly 820. The port 822 can be any suitable port. For example, in some embodiments, the distal cannula 817 and the port 822 can be coupled via an adhesive or the like to fixedly couple the cannula assembly 820 to the housing

801. With the port 822 of the cannula assembly 820 coupled to the distal cannula 817 and with the distal cannula 817 coupled to the distal port 805, the distal port 805 is in fluid communication with a cannula 824 included in the cannula assembly 820, as further described herein.

[1126] The first proximal port 806 and the second proximal port 807 are configured to receive a first proximal cannula 812 and a second proximal cannula 814, respectively (e.g., lumen defining cannulas). Furthermore, the first proximal cannula 812 is physically and fluidically coupled to a first lock mechanism 813 that can further be physically and fluidically coupled to an external fluid reservoir (not shown in FIGS. 35-39). Similarly, the second proximal cannula 814 is physically and fluidically coupled to a second lock mechanism 815 that can further be physically and fluidically coupled to an external fluid source (not shown in FIGS. 35-39). In this manner, the cannula assembly 820, the external fluid reservoir (not shown), and the external fluid source (not shown) can be selectively placed in fluid communication with the inner volume 811 defined by the housing 801, as described in further detail herein.

[1127] Referring back to FIG. 36, the actuator mechanism 880 includes an engagement portion 882 and an activation surface 884. The activation surface 844 is configured to contact, mate, or otherwise engage the flow control mechanism 840. The engagement portion 882 can be engaged by a user to rotate the actuator mechanism 880 relative to the housing 801 to move the transfer device 800 between a first configuration and a second configuration, as described in further detail herein.

[1128] The flow control mechanism 840 defines a first lumen 846 and a second lumen 847 and is disposed within the inner volume 821 defined by the housing 801. The flow control mechanism 840 defines a circular cross-sectional shape such that when the flow control mechanism 840 is disposed within the inner volume 821, a portion of the flow control mechanism 840 forms a friction fit with the walls of the housing 801 defining the inner volume 821, as described in detail above. The flow control mechanism 840 is operably coupled to and/or otherwise engages the actuator 880. For example, in some embodiments, the actuator mechanism 880 can be coupled to the flow control mechanism 840 via a mechanical fastener and/or adhesive. In other embodiments, the actuator mechanism 880 and the flow control mechanism 840 can be coupled in any suitable manner. Therefore, the flow control mechanism 840 is configured to move concurrently with the actuator mechanism 880

when the actuator mechanism 880 is rotated relative to the housing 801. In this manner, the flow control mechanism 840 can be moved to place the first lumen 846 or the second lumen 847 in fluid communication with the distal port 805, the first proximal port 806, and/or the second proximal port 807, as described in further detail herein.

[1129] In use, while in the first configuration, the cannula 824 of the cannula assembly 820 can be inserted into a portion of a patient to place the cannula 824 in fluid communication with, for example, a vein. In some embodiments, the cannula 824 can include a sharp point at a distal end such that the cannula 824 can pierce the portion of the patient. In other embodiments, the cannula assembly 820 can include a trocar (not shown) to facilitate the insertion of the cannula 824. As described above, the cannula assembly 820 is physically and fluidically coupled to the distal port 805 of the housing 801 such that when the cannula 824 is placed in fluid communication with the vein of the patient, the distal port 805 is placed in fluid communication with the vein.

[1130] Furthermore, a user (e.g., a physician, a nurse, a technician, or the like) can engage the transfer device 800 to physically and fluidically couple the first lock mechanism 813 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. In this manner, the external fluid reservoir can define a negative pressure within an inner volume of the reservoir. Therefore, when the flow control mechanism 840 is in the first configuration, a negative pressure differential introduces a suction force within the first proximal cannula 812, the first lumen 846 defined by the flow control mechanism 840, the distal cannula 817, and the cannula assembly 820. In this manner, the first proximal cannula 812, the first lumen 846 defined by the flow control mechanism 840, the distal cannula 817, and the cannula assembly 820 collectively define a fluid flow path configured to transfer a flow of a bodily fluid to the external fluid reservoir, as indicated by the arrow WW in FIG. 37. In addition, the flow of bodily fluid can be such that dermally residing microbes dislodged during a venipuncture event (e.g., the insertion of the cannula 824) are entrained in the flow of bodily fluid and are transferred to the external fluid reservoir.

[1131] As shown in FIG. 38, in some embodiments, the magnitude of the suction force can be modulated by moving the actuator mechanism 880 in the direction of the arrow XX. For example, in some instances, it can be desirable to limit the amount of suction force

introduced to a vein. In such instances, the user can move the actuator mechanism 880 and the flow control mechanism 840 to reduce the size of the fluid pathway (e.g., an inner diameter) between the distal port 805 of the housing 801 and the first lumen 846 of the flow control mechanism 840, thereby reducing the suction force introduced into the vein of the patient.

[1132] With the desired amount of bodily fluid transferred to the external fluid reservoir, a user can engage the actuator mechanism 880 to move the transfer device 800 from the first configuration to the second configuration. In some embodiments, the desired amount of bodily fluid transferred to the external fluid reservoir is a predetermined amount of fluid. For example, in some embodiments, the transfer device 800 can be configured to transfer bodily fluid until the pressure within the external fluid reservoir is equilibrium with the pressure of the portion of the body in which the lumen-defining device is disposed (e.g., the vein), as described above. In some embodiments, at least a portion of the external fluid reservoir can be transparent to allow visualization of the bodily fluid flowing into the fluid reservoir. The external fluid reservoir can include indicators (e.g., 0.1 mL, 0.5 mL, 1 mL, 1.5 mL, 2 mL, 3 mL, 4 mL, 5mL, etc. graduation marks to accommodate identification of diversion volumes ranging from just a few drops or centiliters of blood to a larger volumes) so the user can visualize the volume of bodily fluid that has been received in the external fluid reservoir.

[1133] The transfer device 800 can be moved from the first configuration to the second configuration by further moving the actuator mechanism 880 in the direction of the arrow XX in FIG. 38. As the actuator mechanism 880 is moved from the first configuration toward the second configuration, the actuator mechanism 880 rotates the flow control mechanism 840 toward its second configuration. In this manner, the first lumen 846 is fluidically isolated from the distal port 805 and the first proximal port 806 and the external fluid reservoir can be physically and fluidically decoupled from the transfer device 800. In addition, the second lumen 847 defined by the flow control mechanism 840 is placed in fluid communication with the distal port 805 and the second proximal port 807, as shown in FIG. 39.

[1134] With the transfer device in the second configuration, the second proximal lock mechanism 815 can be physically and fluidically coupled to the external fluid source (not shown in FIGS. 35-39). In this manner, the second proximal cannula 814, the second lumen 847 of the flow control mechanism 840, the distal cannula 817, and the cannula assembly 820 collectively define a fluid flow path. Thus, the transfer device 800 can facilitate the delivery

of a flow of parenteral fluid from the external fluid source to the portion of the patient (e.g., the vein), as indicated by the arrow YY in FIG. 39. Expanding further, with the predetermined amount of bodily fluid transfer to the external fluid reservoir and with the external fluid reservoir decoupled from the transfer device 800, the transfer device 800 can facilitate the delivery of the flow of parenteral fluid to the patient that is substantially free from, for example, the dermally residing microbes dislodged during the venipuncture event or otherwise introduced to the fluid flow path to the patient.

[1135] FIG. 40 is a flowchart illustrating a method 990 of delivering a fluid to a patient using a fluid transfer device, according to an embodiment. The method 990 includes establishing fluid communication between the patient and the fluid transfer device, at 991. The fluid transfer device can be any of those described herein. As such, the fluid transfer device can include a cannula assembly or the like that can be inserted percutaneously to place the fluid transfer device in fluid communication with the patient (e.g., inserted into a vein of the patient). More specifically, in some embodiments, the cannula assembly of the fluid transfer device can include a sharpened distal end configured to pierce the skin of the patient. In other embodiments, the transfer device can include a flow control mechanism that can include a sharpened distal end portion that is configured to extend beyond a distal end portion of the cannula assembly to pierce the skin of the patient. For example, in some embodiments, the fluid transfer device can include a flow control mechanism that is substantially similar to the flow control mechanism 340 of the transfer device 300 described above with reference to FIGS. 4-10.

[1136] With the cannula assembly in fluid communication with the patient, a predetermined volume of a bodily fluid is withdrawn from the patient, at 991. For example, in some embodiments, the fluid transfer device can include a flow control mechanism, such as those described above, that can be moved between a first configuration and a second configuration. In some embodiments, flow control mechanism can be configured to define a fluid flow path between, for example, the cannula assembly and a fluid reservoir included in and/or fluidically coupled to the fluid transfer device. In other embodiments, any portion of fluid transfer device can define at least a portion of the fluid flow path. For example, the fluid transfer device can include a housing or the like that can define at least a portion of the fluid flow path. Thus, the predetermined volume of the bodily fluid is transferred to the fluid reservoir, at 993. In some embodiments, the predetermined volume of the bodily fluid can

include, for example, dermally residing microbes that were dislodged during, for example, the venipuncture event (e.g., inserting the cannula assembly into the patient).

[1137] Once the predetermined volume of bodily fluid is disposed in the fluid reservoir, the fluid transfer device is fluidically isolated from the fluid reservoir to sequester the predetermined volume of bodily fluid in the fluid reservoir, at 994. For example, in some embodiments, once the predetermined volume of bodily fluid is disposed in the fluid reservoir, the fluid transfer device can be physically and/or fluidically decoupled from the fluid reservoir. In other embodiments, the flow control mechanism (as described above) can be moved from the first configuration to the second configuration to fluidically isolate the fluid reservoir from a volume outside of the fluid reservoir. For example, in some embodiments, the flow control mechanism can define a lumen or the like that can define a fluid flow path between the cannula assembly and the fluid reservoir when in the first configuration. In such embodiments, the flow control mechanism can be transitioned (e.g., moved, rotated, and/or otherwise reconfigured) from the first configuration to the second configuration in which the lumen is removed from fluid communication with the cannula assembly and/or the fluid reservoir, thereby fluidically isolating the fluid reservoir from the cannula assembly. In some embodiments, the flow control mechanism can be configured to transition from the first configuration to the second configuration automatically once the predetermined volume of bodily fluid is disposed in the fluid reservoir.

[1138] With the fluid reservoir fluidically isolated from at least a portion of the fluid transfer device, fluid communication is established between the patient and a fluid source via the fluid transfer device, at 995. For example, in some embodiments, the fluid source can be operably coupled to the fluid transfer device to place the fluid source in fluid communication with at least a portion of the fluid transfer device. In some embodiments, the flow control mechanism (described above) can define a second lumen that can place the fluid source in fluid communication with the cannula assembly when in the second configuration. In other embodiments, with the fluid reservoir decoupled from the fluid transfer device that fluid source can be placed in fluid communication with the cannula assembly via any other portion of the fluid transfer device (e.g., a portion of a housing and/or the like). In this manner, a fluid can flow from the fluid source, through the fluid transfer device and into the patient. Moreover, by fluidically isolating the predetermined volume of bodily fluid the flow of fluid

from the fluid source can be substantially free of contaminants such as, for example, the dermally residing microbes, as described above.

[1139] 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 before proceeding to subsequent steps.

[1140] While various embodiments have been particularly shown and described, various changes in form and details may be made. For example, while the actuator 580 is shown and described with respect to FIG. 21 as being rotated in a single direction, in other embodiments, an actuator can be rotated in a first direction (e.g., in the direction of the arrow MM in FIG. 21) and a second direction, opposite the first. In such embodiments, the rotation in the second direction can be configured to move a transfer device through any number of configurations. In other embodiments, the rotation of the actuator in the second direction can be limited.

[1141] 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.

[1142] 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 of bodily fluid flow into a fluid reservoir or for a desired rate of parenteral fluid flow into the patient.

Claims

1. An apparatus, comprising:

a cannula assembly;

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 removably coupled to the cannula assembly;

a fluid reservoir fluidically coupled to the housing and configured to receive and isolate a first volume of bodily fluid withdrawn from the patient;

a flow control mechanism at least partially disposed in the inner volume of the housing and configured to move relative to the housing between a first configuration and a second configuration, the flow control mechanism defining a fluid flow path between the cannula assembly and the fluid reservoir in the first configuration; and

an actuator operably coupled to the flow control mechanism and configured to move the flow control mechanism from 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 cannula assembly, through inlet port via the fluid flow path and to the fluid reservoir, to the second configuration, in which the fluid reservoir is fluidically isolated from the cannula assembly.

2. The apparatus of claim 1, wherein the flow control mechanism includes a fluid communicator configured to be moved from a first position to a second position to place the flow control mechanism in the second configuration.

3. The apparatus of claim 2, wherein the fluid communicator is configured to extend through the inlet port and beyond the distal end portion of the housing in the first position.

4. The apparatus of claim 2, wherein the fluid communicator is retracted into the inner volume of the housing in the second position.

5. The apparatus of claim 1, wherein the flow control mechanism includes a first member movably disposed in the inner volume of the housing, and a second member coupled to the first member and configured to extend through the inlet port and beyond the distal end portion of the housing in the first configuration.

6. The apparatus of claim 5, wherein the first member includes a proximal end portion and a distal end portion, and defines a lumen therethrough.

7. The apparatus of claim 6, wherein the second member includes a proximal end portion and a distal end portion, and defines a lumen therethrough.

8. The apparatus of claim 7, wherein the proximal end portion of the second member is configured to be disposed in the lumen defined by the first member.

9. The apparatus of claim 7, wherein the distal end portion of the second member is configured to extend beyond a distal end of the cannula assembly when the flow control mechanism is in the first configuration.

10. The apparatus of claim 9, wherein the second member is a needle configured to be inserted into the patient

11. The apparatus of claim 1, wherein the cannula assembly is removably coupled to the housing.

12. The apparatus of claim 1, wherein the flow control mechanism includes a spring configured to expand and move the flow control mechanism from the first configuration to the second configuration.

13. The apparatus of claim 12, wherein the actuator is configured to release the spring from a compressed state when actuated by a user.

14. The apparatus of claim 1, wherein the fluid reservoir is movably coupled to the housing and configured to be moved from a first position to a second position, the movement from the first position to the second position configured to create a negative pressure in the fluid reservoir.

15. The apparatus of claim 1, wherein the fluid reservoir is movably disposed within the inner volume of the housing, the fluid reservoir including a proximal end portion and a

distal end portion and defining an inner volume therebetween, the inner volume configured to selectively receive at least a portion of the flow control mechanism.

16. The apparatus of claim 15, wherein the proximal end portion of the fluid reservoir is configured to move relative to the distal end portion of the fluid reservoir to increase the inner volume defined by the fluid reservoir and create a negative pressure within the inner volume.

17. The apparatus of claim 1, wherein the fluid reservoir is movably disposed within the inner volume of the housing and configured to move from a first configuration to a second configuration to create a negative pressure in the fluid reservoir.

18. The apparatus of claim 17, wherein the actuator is configured to move the fluid reservoir from the first configuration to the second configuration when actuated by a user.

19. The apparatus of claim 1, wherein the actuator includes an outlet port configured to be fluidically coupled to the fluid reservoir.

20. The apparatus of claim 19, wherein the actuator defines a lumen configured to allow fluid communication between the fluid flow path and the outlet port when the flow control mechanism is in the first configuration.

21. The apparatus of claim 20, wherein the actuator is configured to rotate from a first position in which bodily fluid can flow from the flow control mechanism, through the outlet port and to the fluid reservoir, to a second position, in which the flow control mechanism is placed in the second configuration and the fluid reservoir is fluidically isolated from the cannula assembly.

22. A device for delivering a fluid to a patient with reduced contamination, the device comprising:

a housing including a proximal end portion and a distal end portion and defining an inner volume therebetween, the housing having a first port configured to be removably coupled to a cannula assembly, and a second port configured to be fluidically coupled to a fluid source;

a fluid reservoir fluidically couplcablc to a cannula assembly and configured to receive and isolate a predetermined volume of bodily fluid withdrawn from the patient; and

a flow control mechanism at least partially disposed in the inner volume of the housing and configured to move relative to the housing between a first configuration in which the first port is placed in fluid communication with the fluid reservoir such that bodily fluid can flow from the cannula assembly, through first port and to the fluid reservoir, and a second configuration in which (a) the fluid reservoir is fluidically isolated from the cannula assembly, and (b) fluid can flow from the fluid source, in the second port, through the flow control mechanism, out the first port and to the cannula assembly.

23. The device of claim 22, wherein the fluid reservoir is disposed in the inner volume of the housing and is at least partially defined by the flow control mechanism.

24. The device of claim 23, wherein the fluid reservoir includes an inlet port configured to be fluidically coupled to the first port of the housing.

25. The device of claim 24, further comprising a valve disposed in the inlet port of the fluid reservoir.

26. The device of claim 25, wherein the valve is a check valve.

27. The device of claim 24, wherein the fluid reservoir is configured to move relative to the housing from a first position in which the inlet port is fluidically coupled to the first port of the housing, to a second position in which the inlet port is fluidically isolated from the first port of the housing.

28. The device of claim 22, wherein the flow control mechanism includes a first sealing member and a second sealing member spaced apart from the first sealing member, the first sealing member at least partially defining the fluid reservoir.

29. The device of claim 28, wherein the flow control mechanism is configured to move the first sealing member and the second sealing member from a first position to a second position to place the flow control mechanism in the second configuration.

30. The device of claim 29, wherein the movement of the first sealing member from the first position to the second position is configured to create a negative pressure in the fluid reservoir.

31. The device of claim 22, wherein the fluid reservoir is defined by the flow control mechanism.

32. The device of claim 31, wherein the fluid reservoir includes an inlet port configured to be fluidically coupled to the first port of the housing in the first configuration, and fluidically isolated from the first port of the housing in the second configuration.

33. The device of claim 22, wherein the flow control mechanism defines a lumen, the lumen configured to be fluidically isolated from the first port and the second port of the housing in the first configuration, and in fluid communication with the first port and the second port of the housing in the second configuration such that fluid can flow from the fluid source, in the second port of the housing, through the lumen of the flow control mechanism, and out the first port of the housing.

34. The device of claim 22, wherein the flow control mechanism is configured to rotate from a first position in which the flow control mechanism is in the first configuration, to a second position in which the flow control mechanism is placed in the second configuration.

35. A method of delivering a fluid to a patient using a fluid transfer device, the method comprising:

establishing fluid communication between the patient and the fluid transfer device;

withdrawing a predetermined volume of a bodily fluid from the patient;

transferring the predetermined volume of the bodily fluid to a fluid reservoir;

fluidically isolating the fluid transfer device from the fluid reservoir to sequester the predetermined volume of bodily fluid in the fluid reservoir; and

establishing fluid communication between the patient and a fluid source with the fluid transfer device.

36. The method of claim 35, whereby sequestering the predetermined volume of the bodily fluid in the fluid reservoir establishes a sterile fluid flow path between the fluid source and the patient.

37. The method of claim 35, wherein the fluid transfer device includes a flow control mechanism, the method further comprising:

disposing the flow control mechanism in a first configuration prior to withdrawing the predetermined volume of bodily fluid from the patient, the first configuration establishing fluid communication between the patient and the fluid reservoir.

38. The method of clam 37, further comprising:

after the predetermined volume of bodily fluid has been transferred the fluid reservoir, moving the flow control mechanism to a second configuration, the second configuration establishing fluid communication between the fluid source and the patient.

39. The method of claim 38, wherein the flow control mechanism is automatically moved from the first configuration to the second configuration after the predetermined volume of bodily fluid has been transferred to the fluid reservoir.

40. The method of claim 35, further comprising:

delivering fluid from the fluid source to the patient.

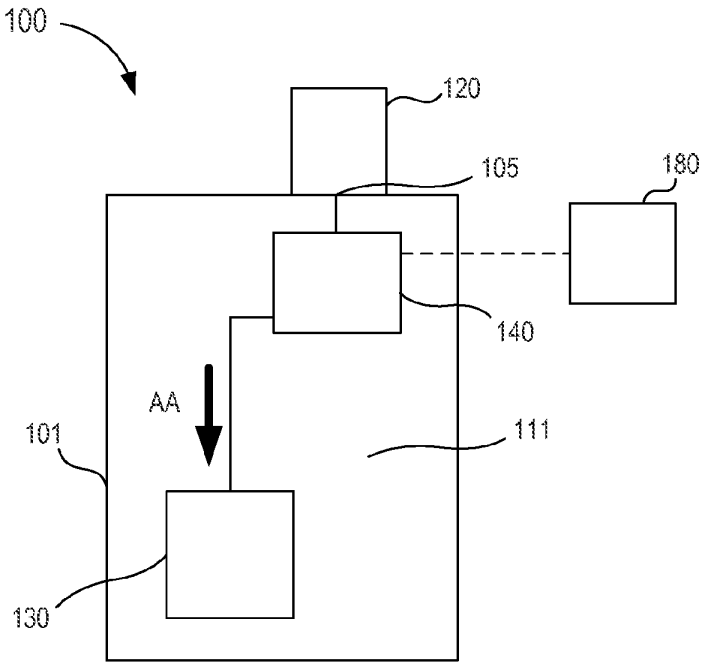

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FIG. 1

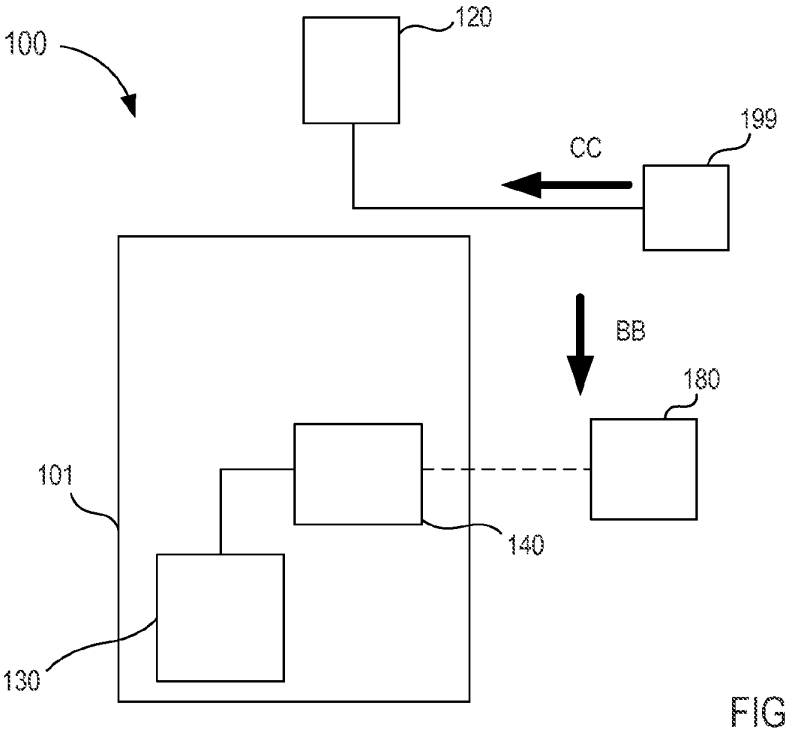

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FIG. 2

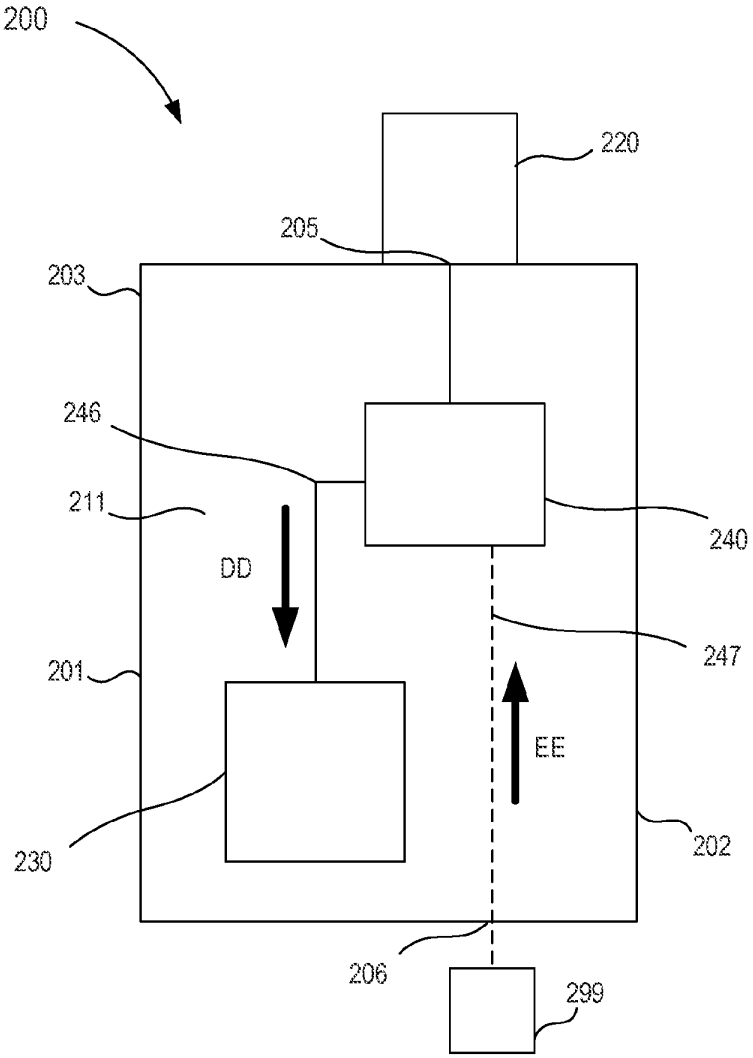


FIG. 3

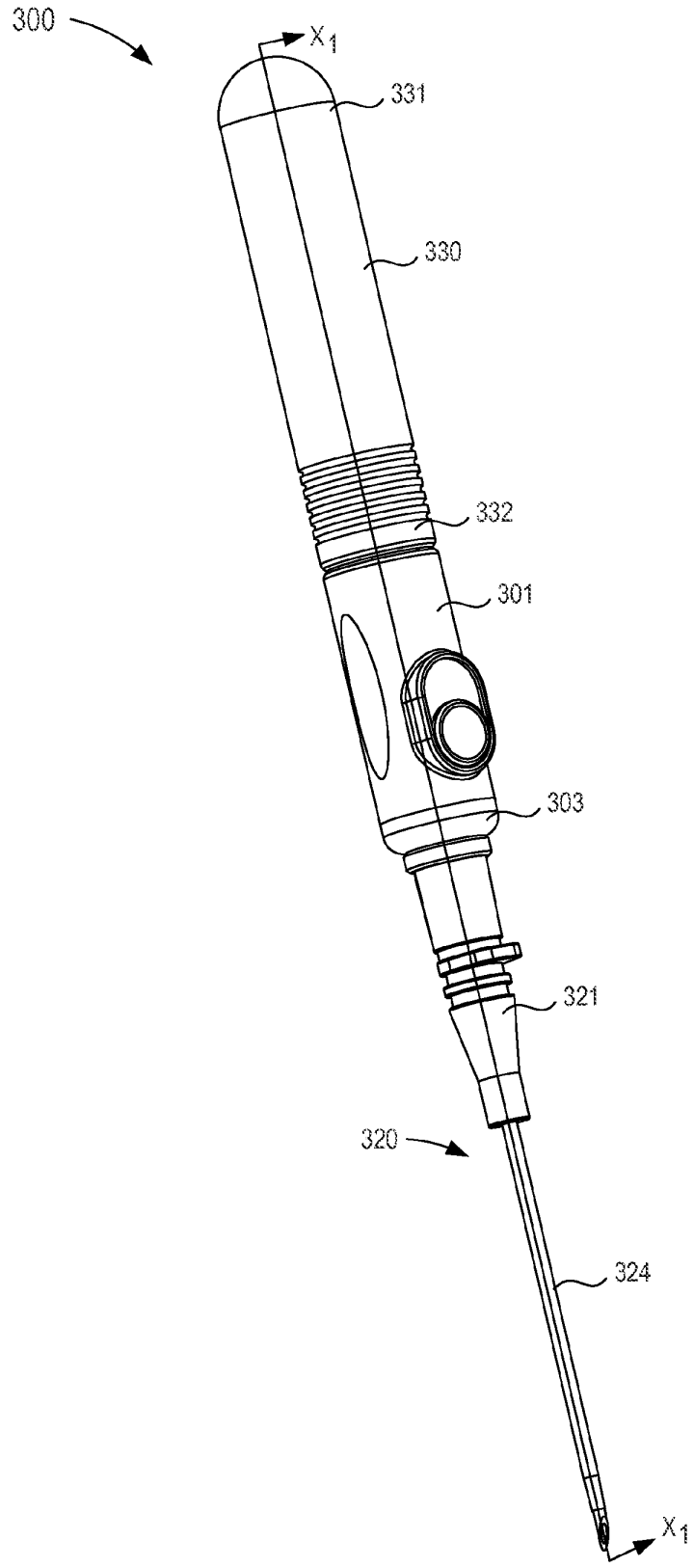


FIG. 4

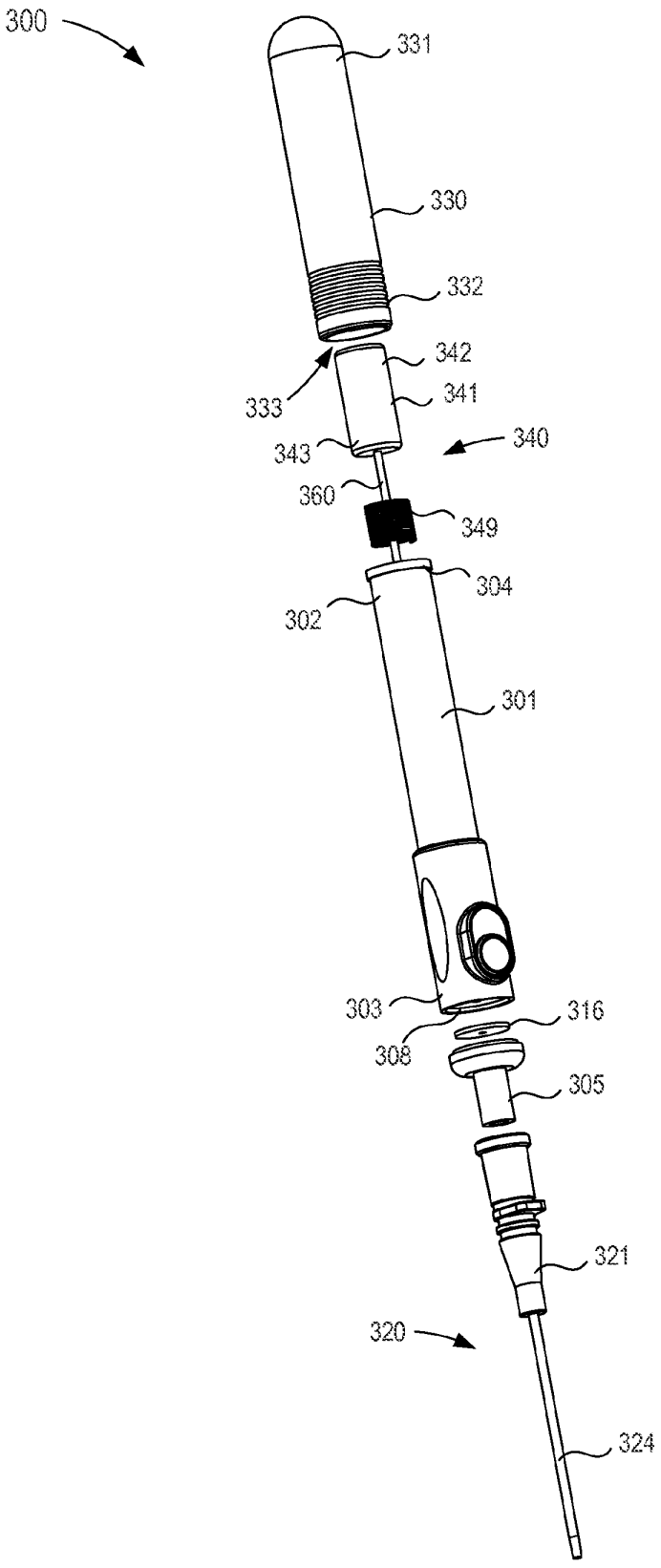

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FIG. 5

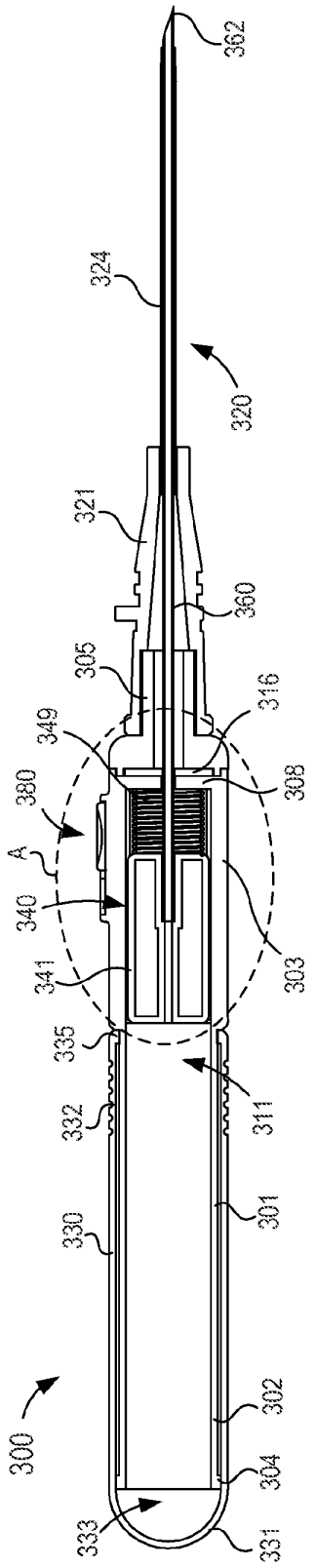

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FIG. 6

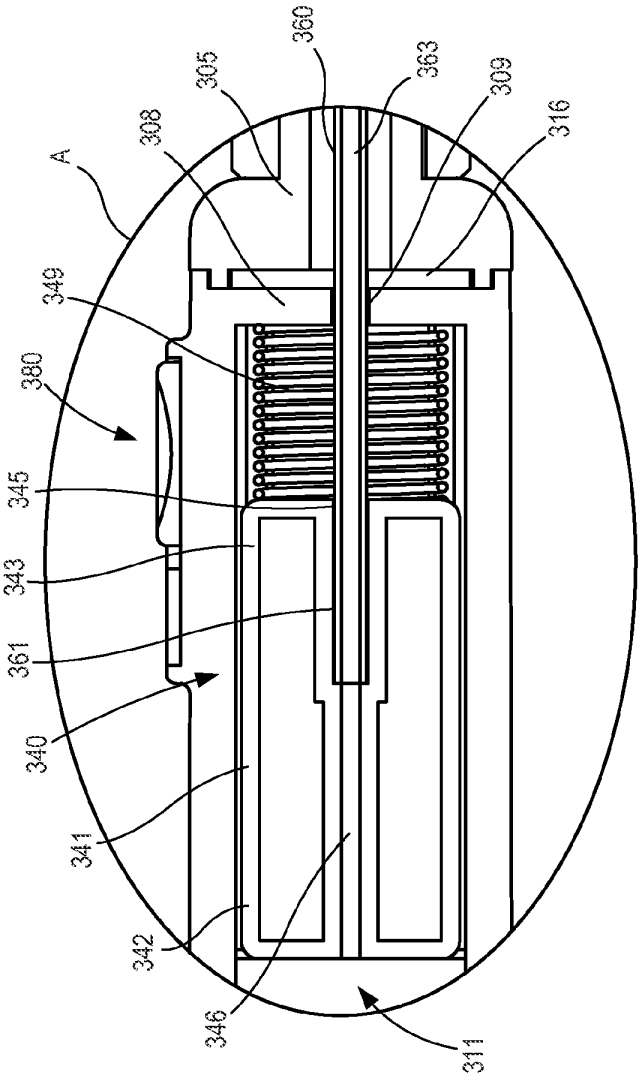

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FIG. 7

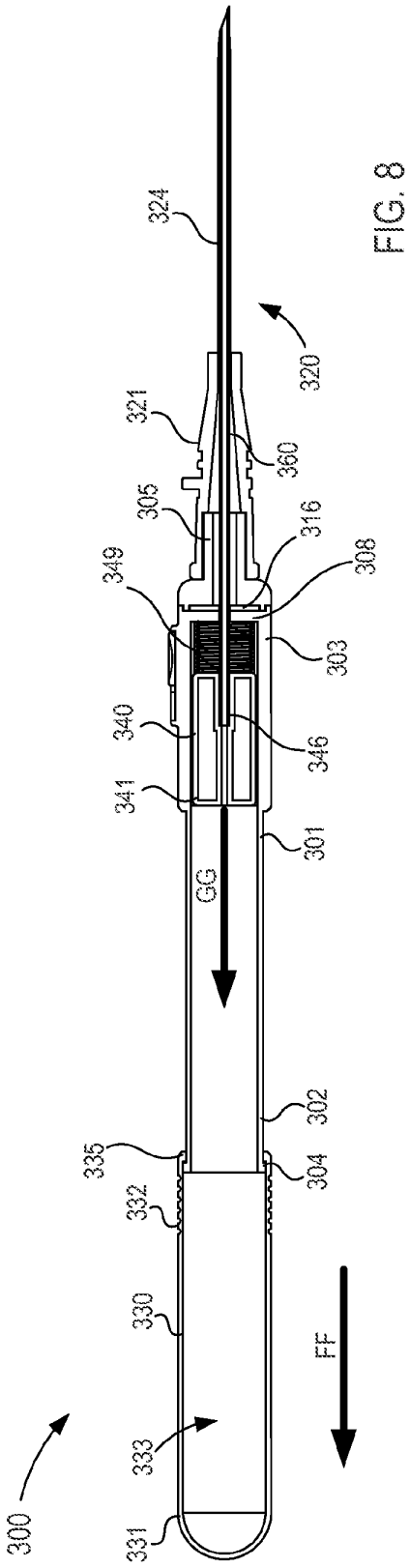

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FIG. 8

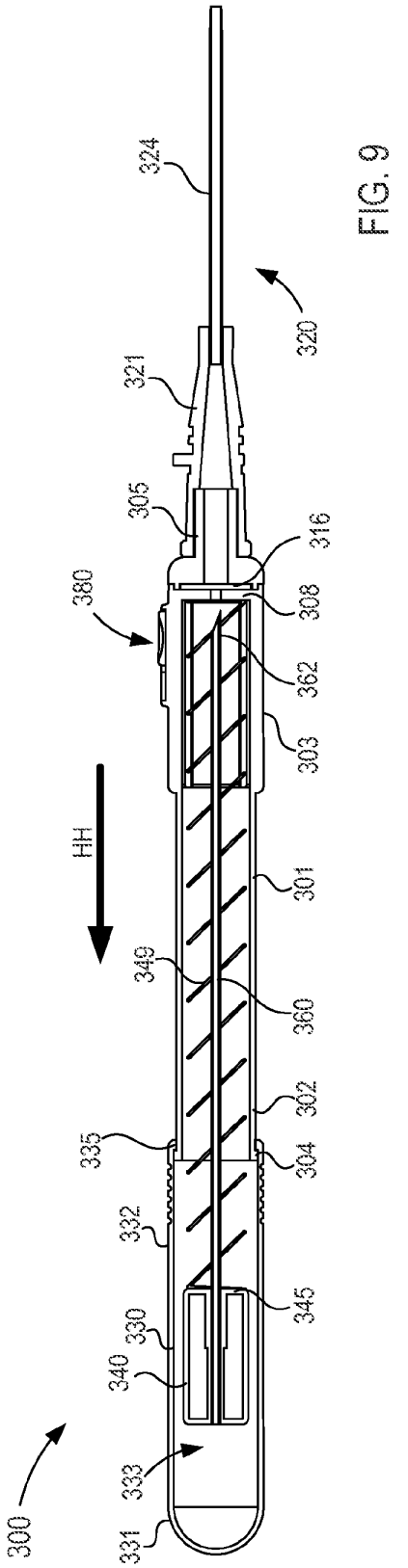

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FIG. 9

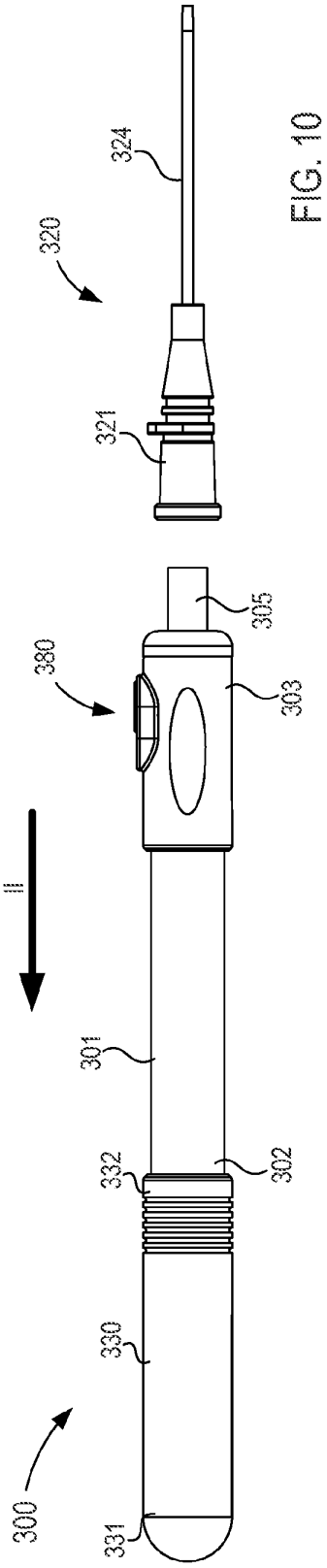


FIG. 10

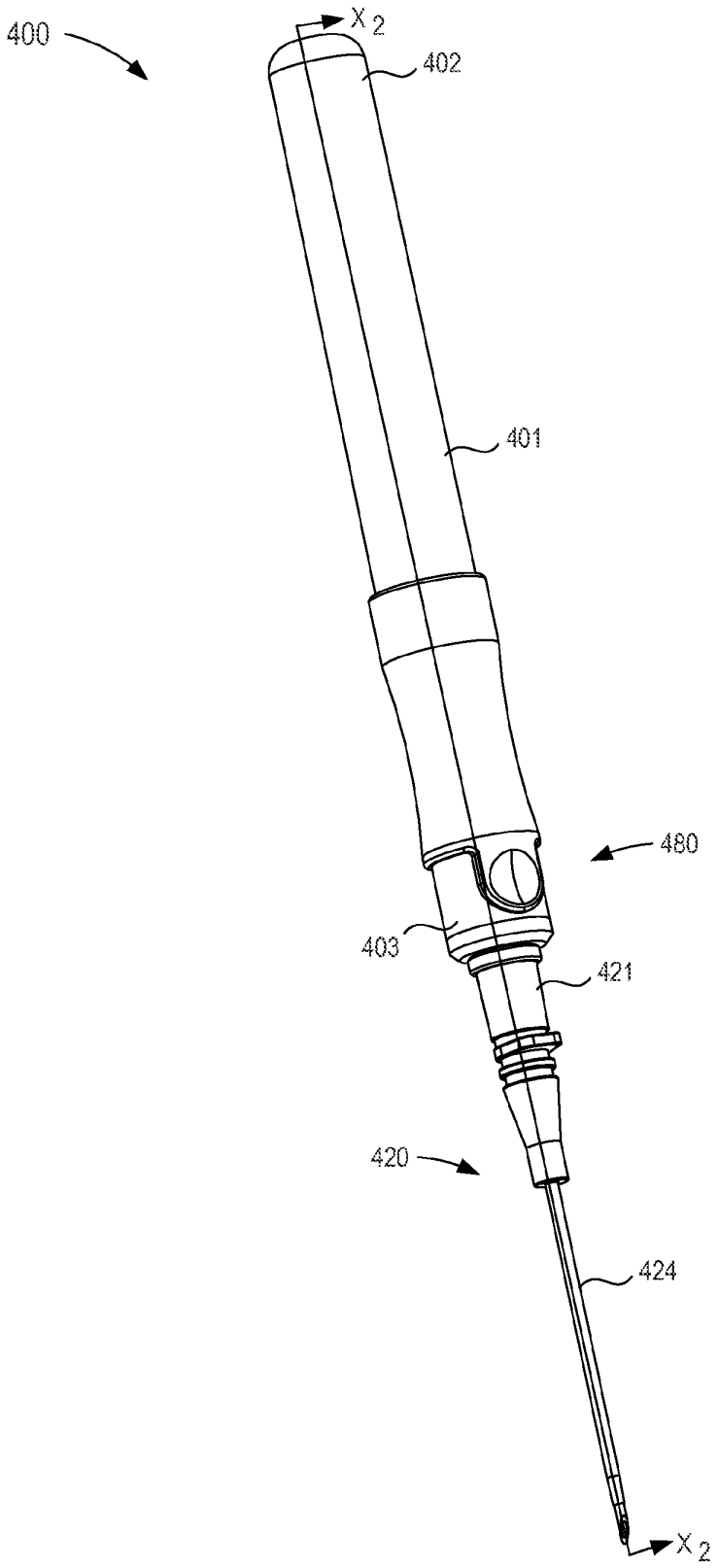


FIG. 11

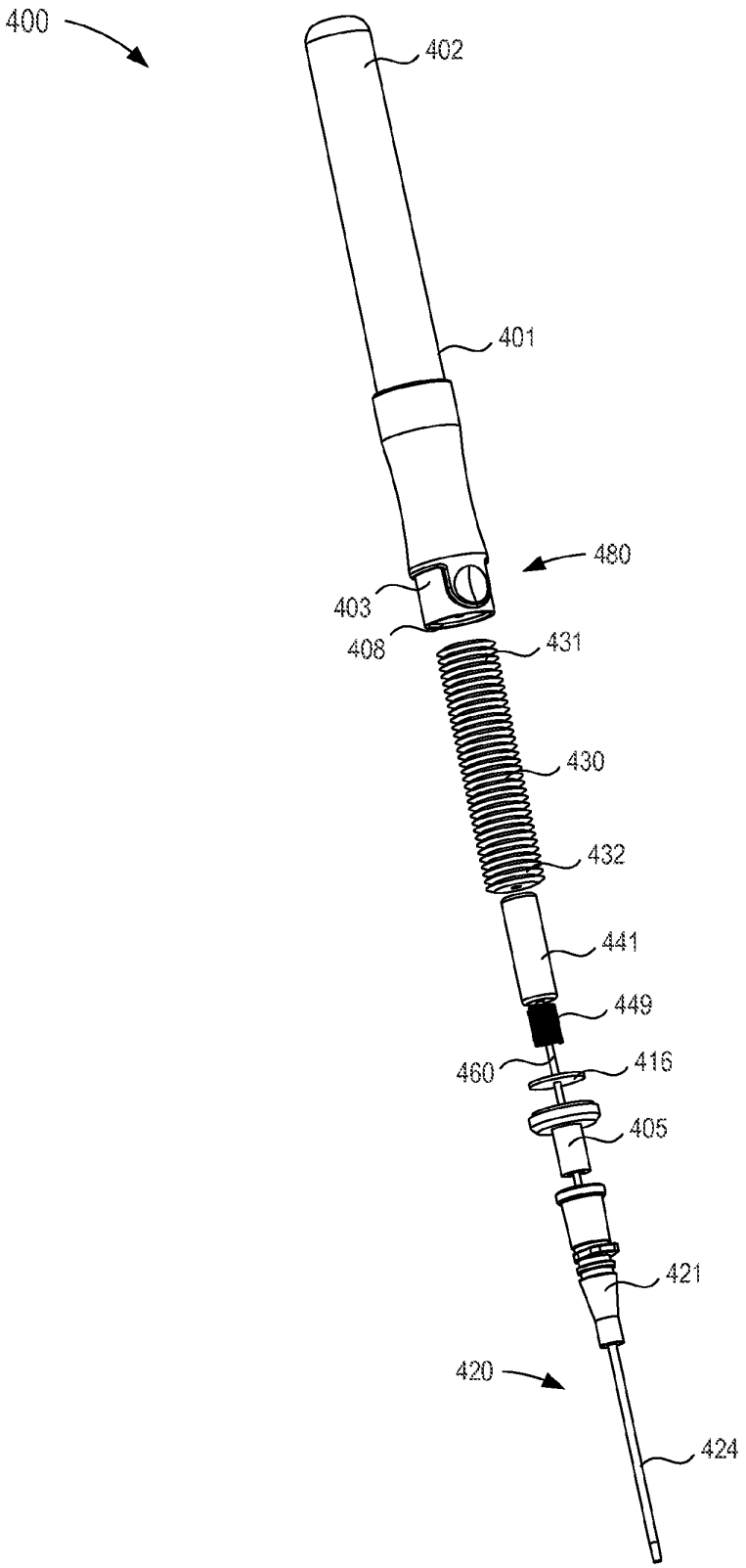

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FIG. 12

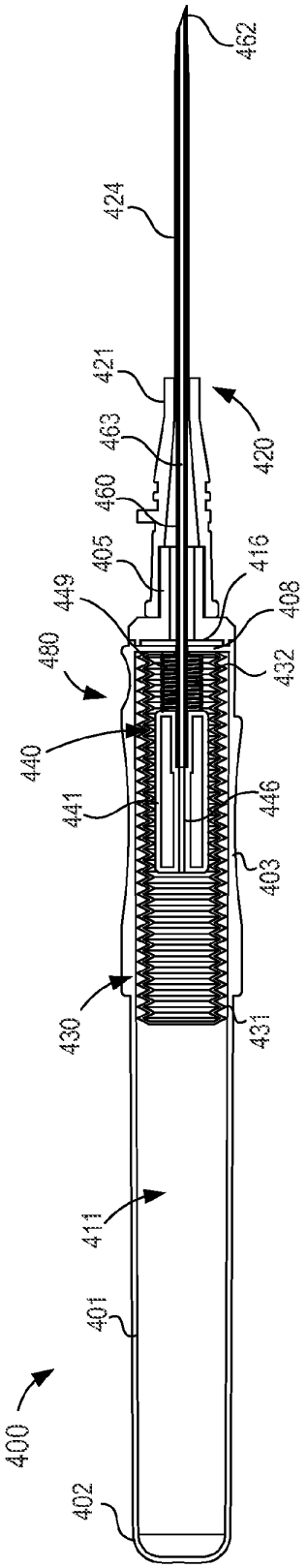

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FIG. 13

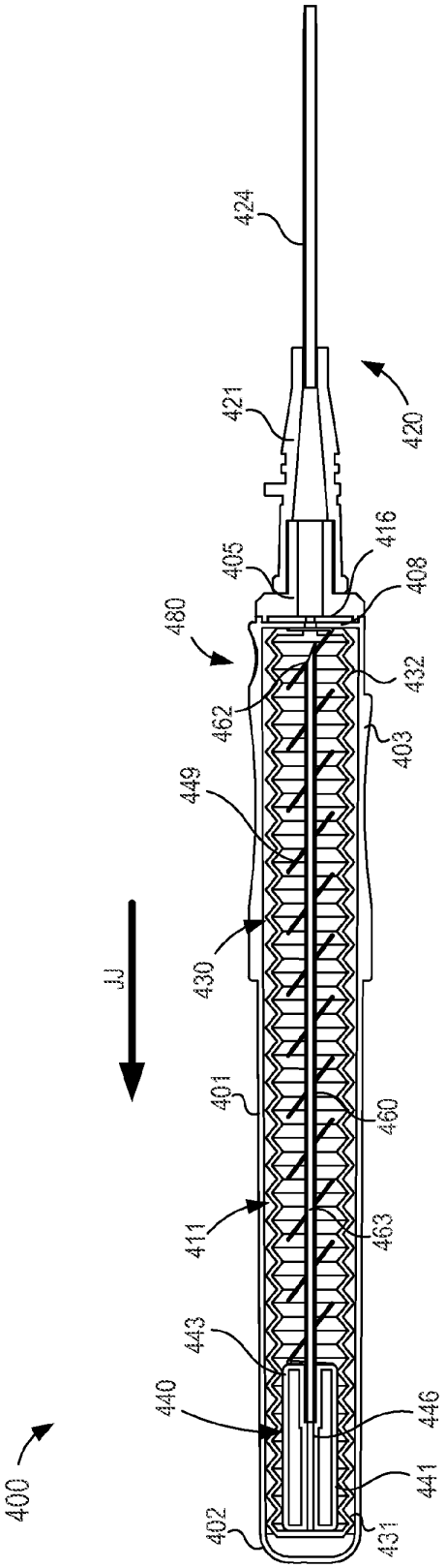

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FIG. 14

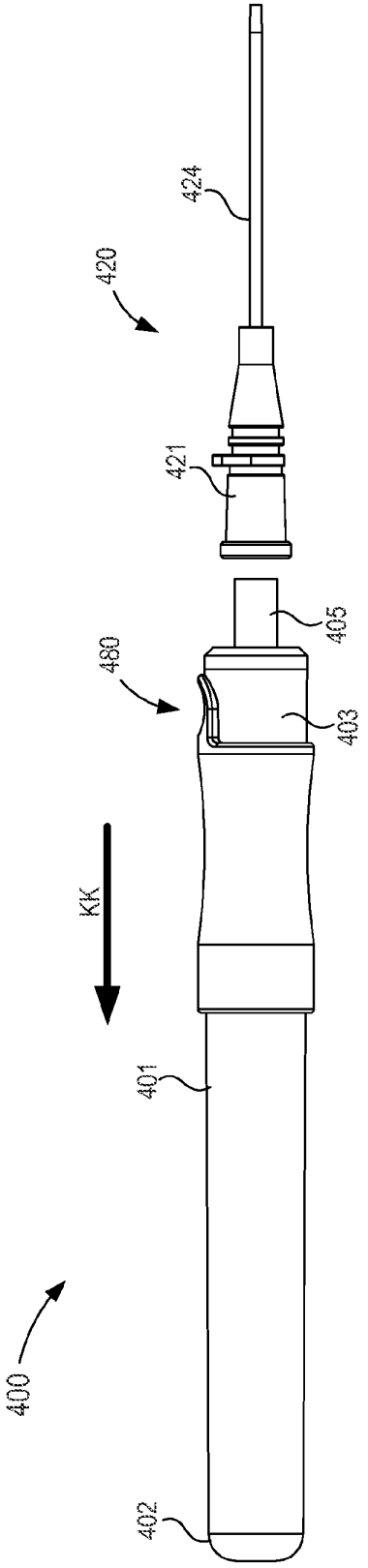


FIG. 15

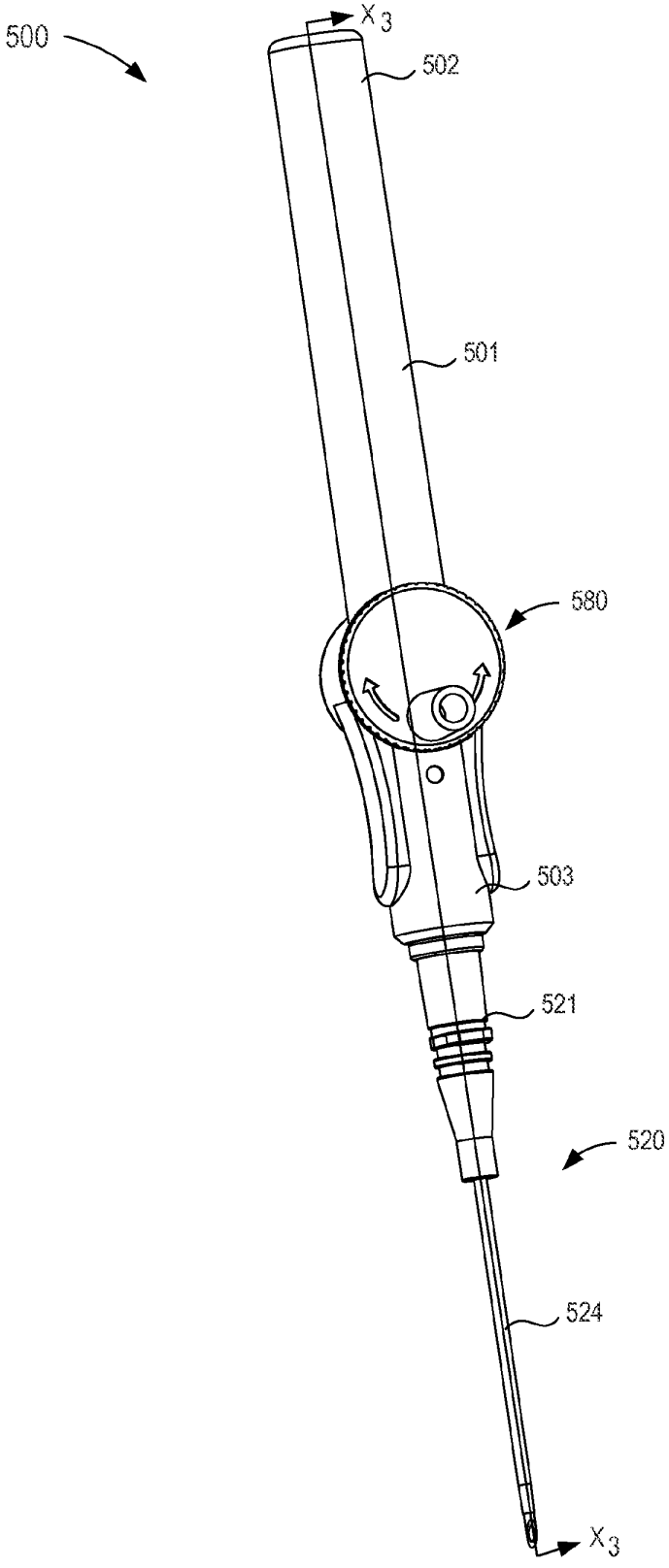


FIG. 16

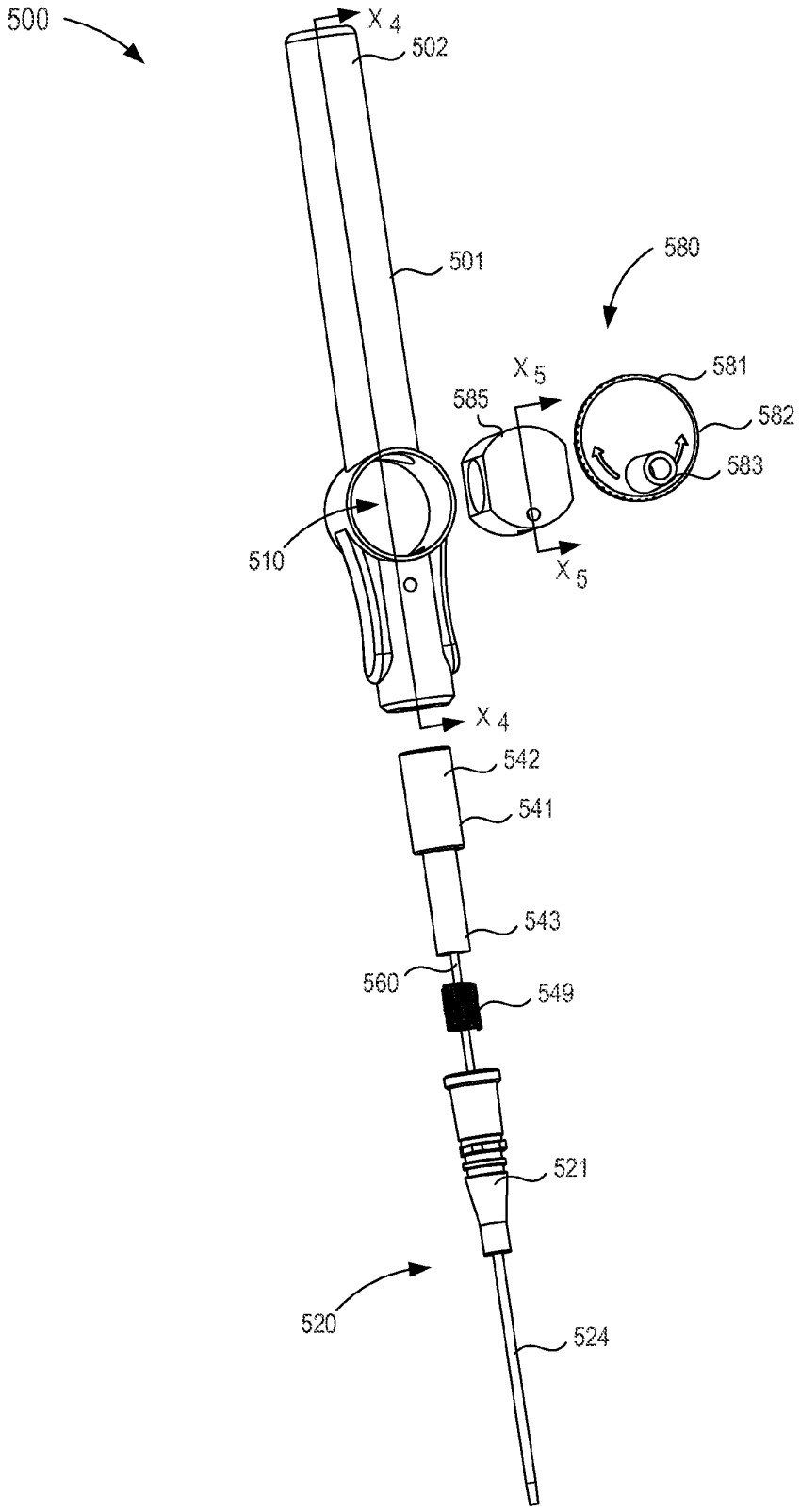

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FIG. 17

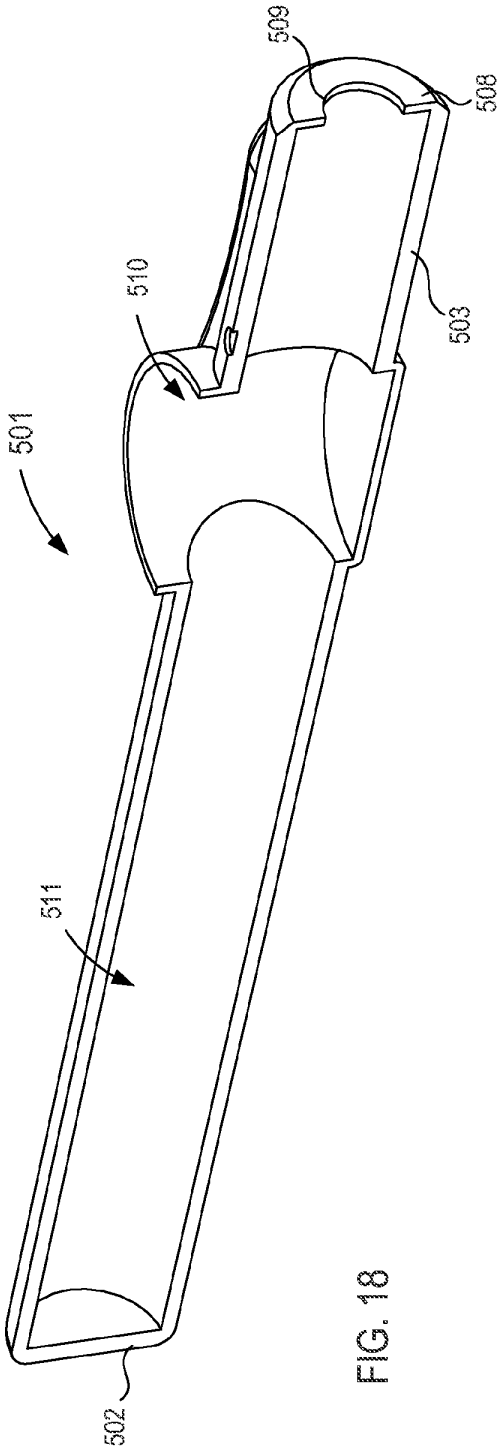


FIG. 18

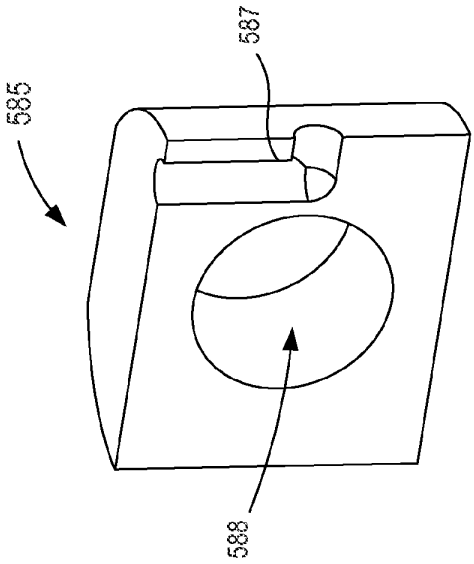


FIG. 19

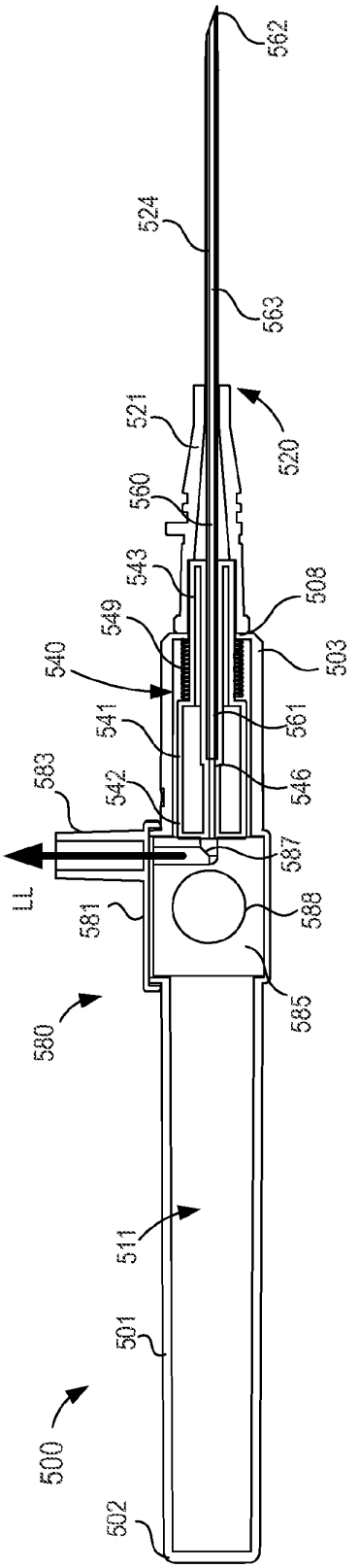

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FIG. 20

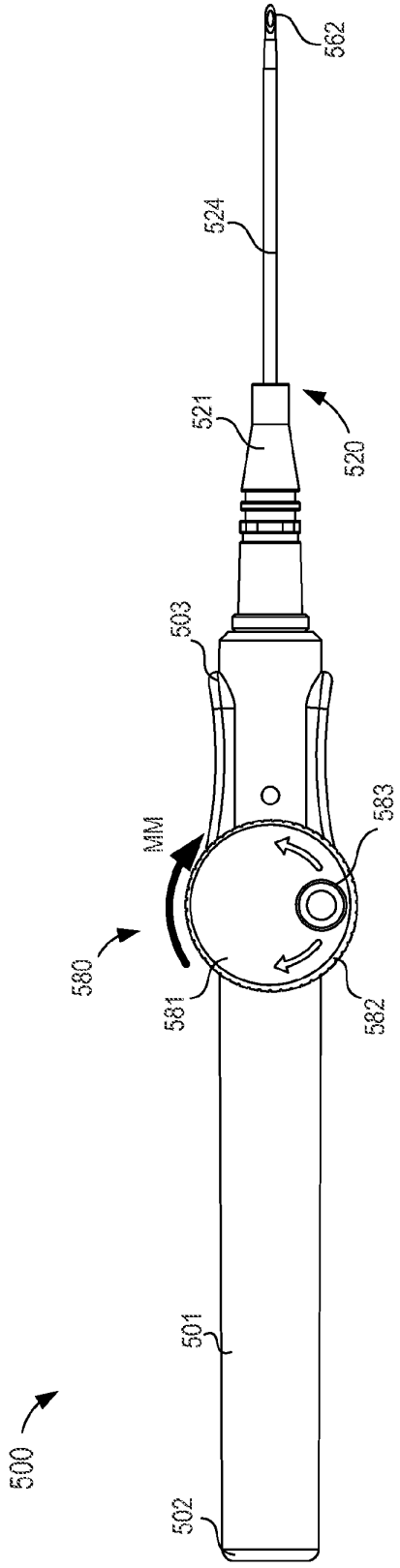

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FIG. 21

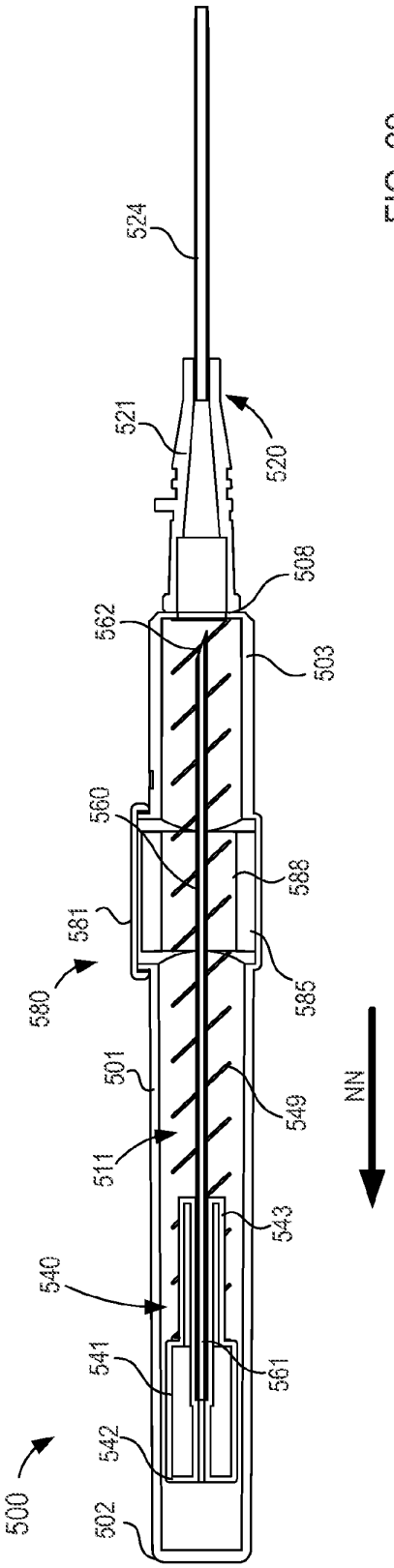

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FIG. 22

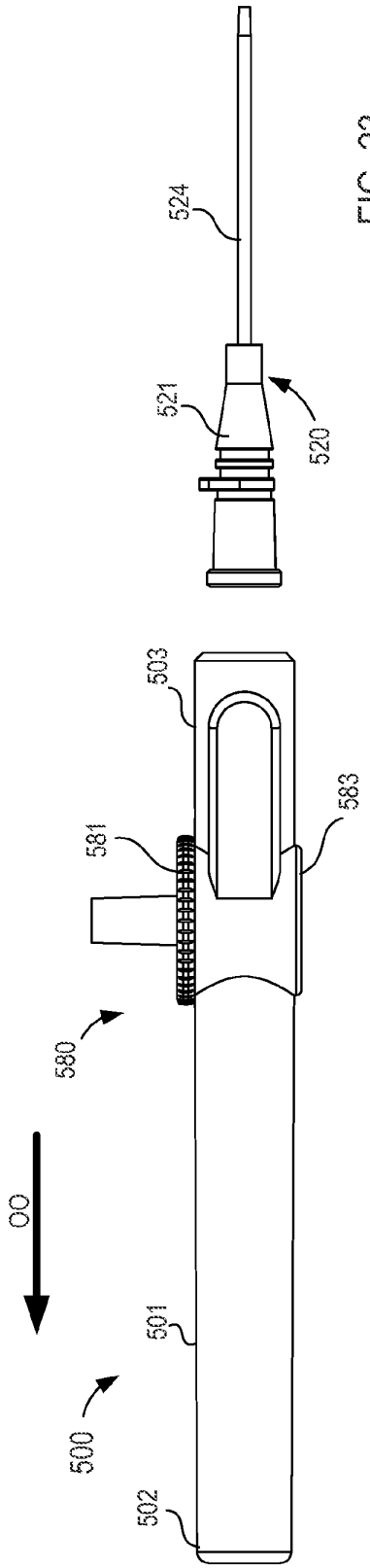

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FIG. 23

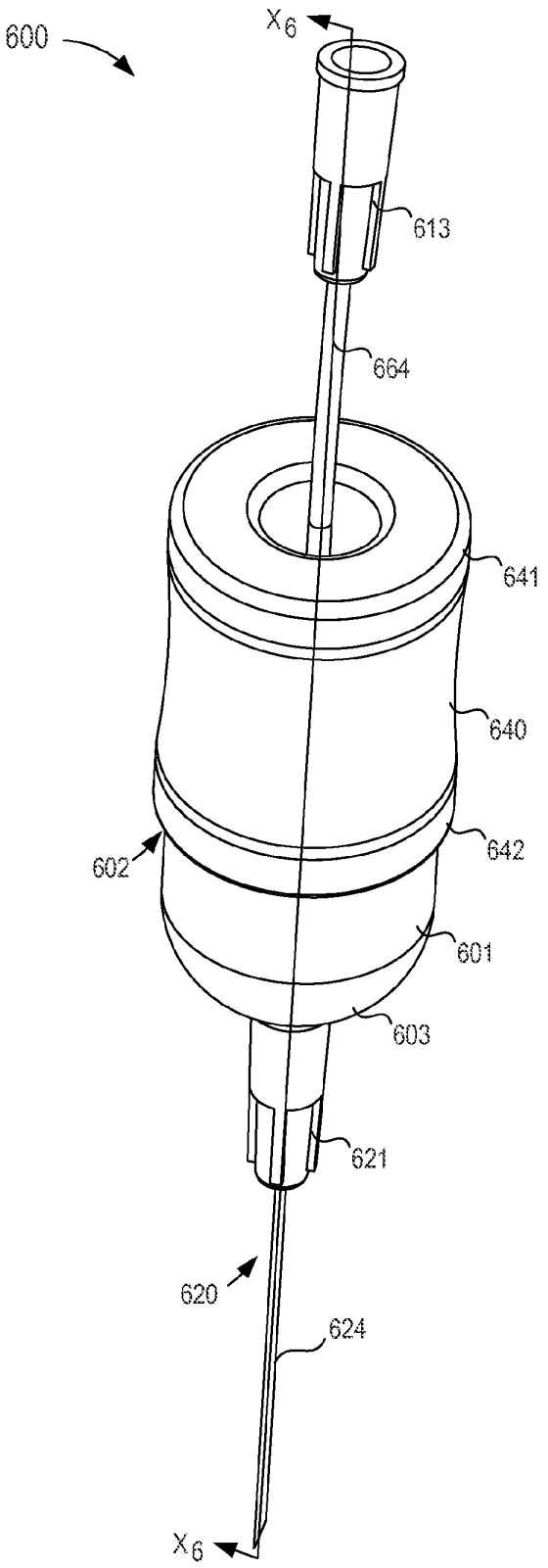


FIG. 24

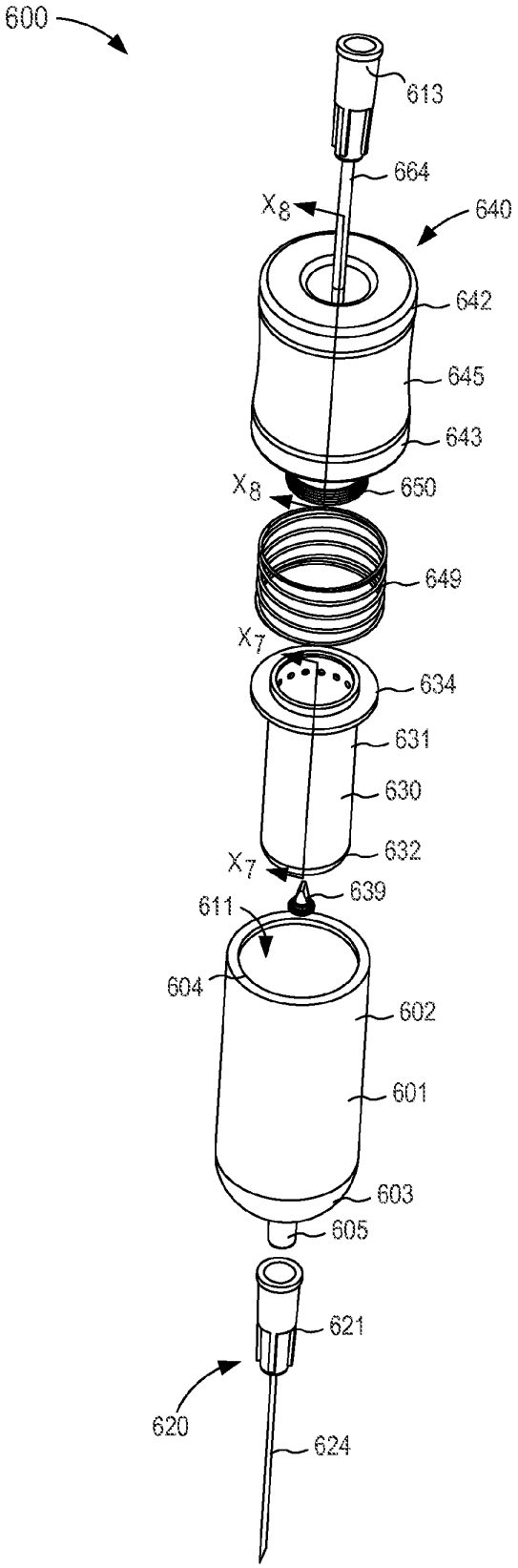

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FIG. 25

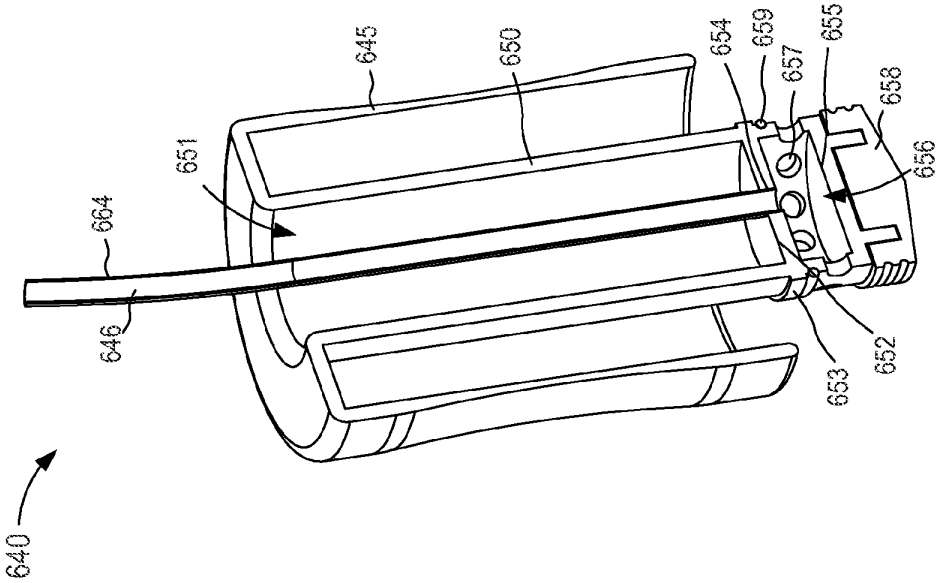

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FIG. 27

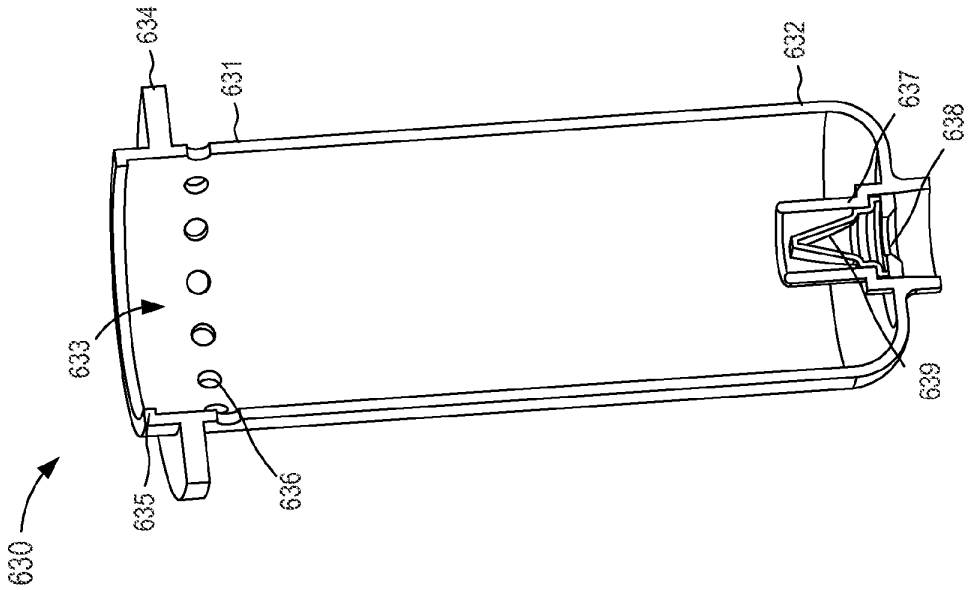

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FIG. 26

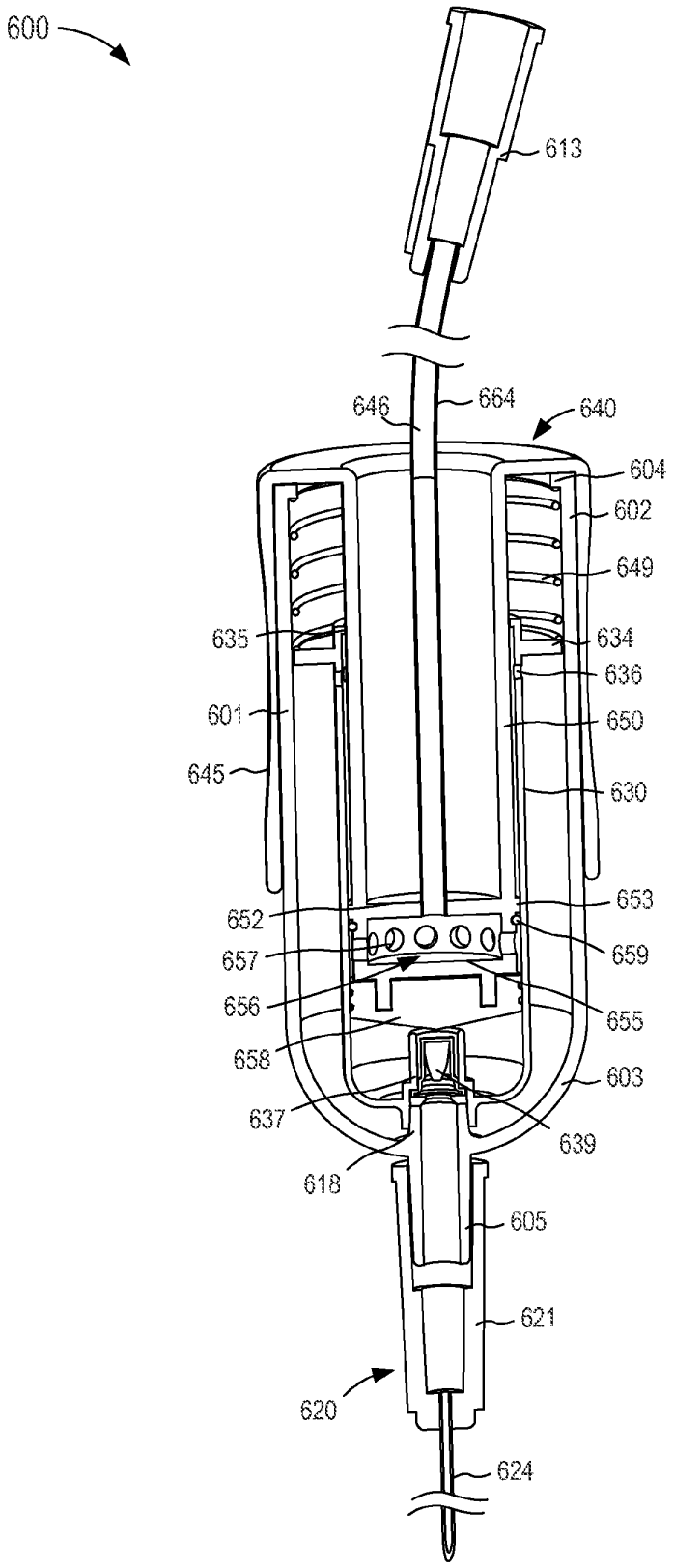

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FIG. 28

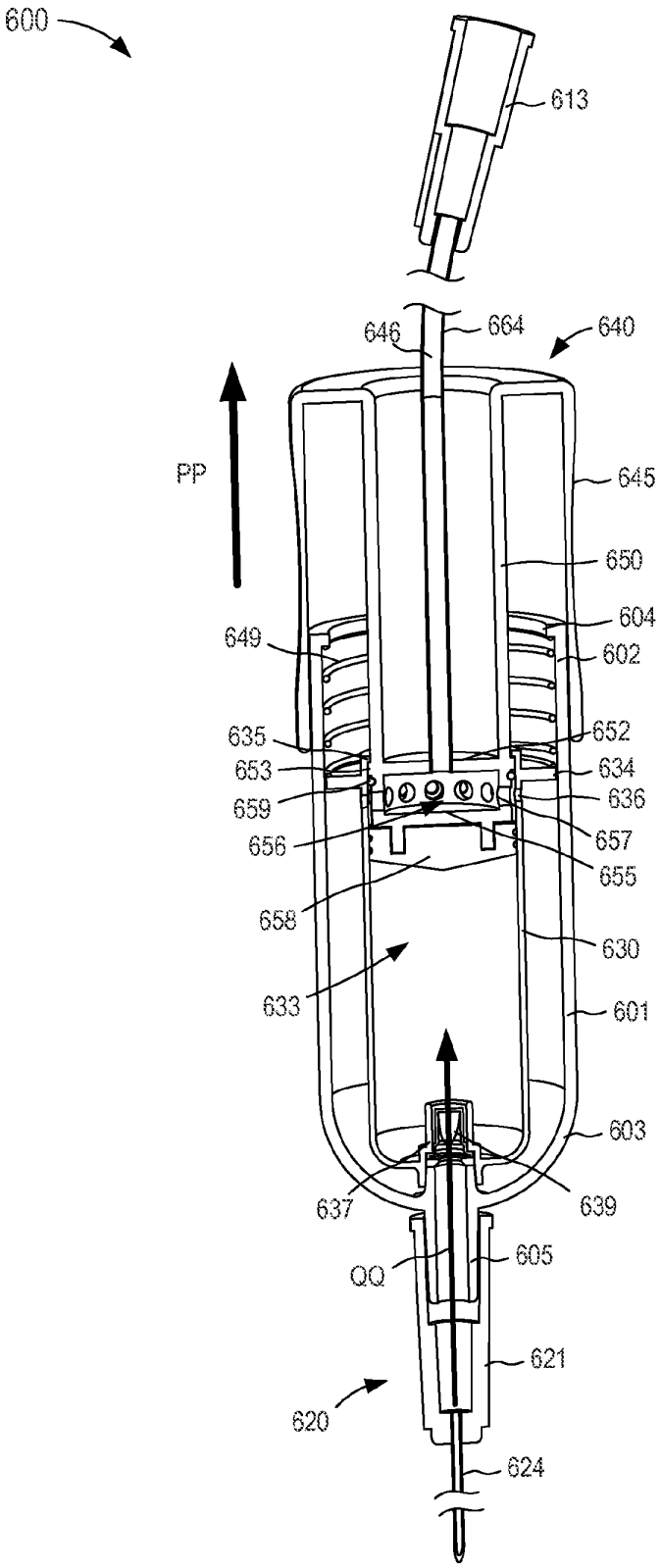

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FIG. 29

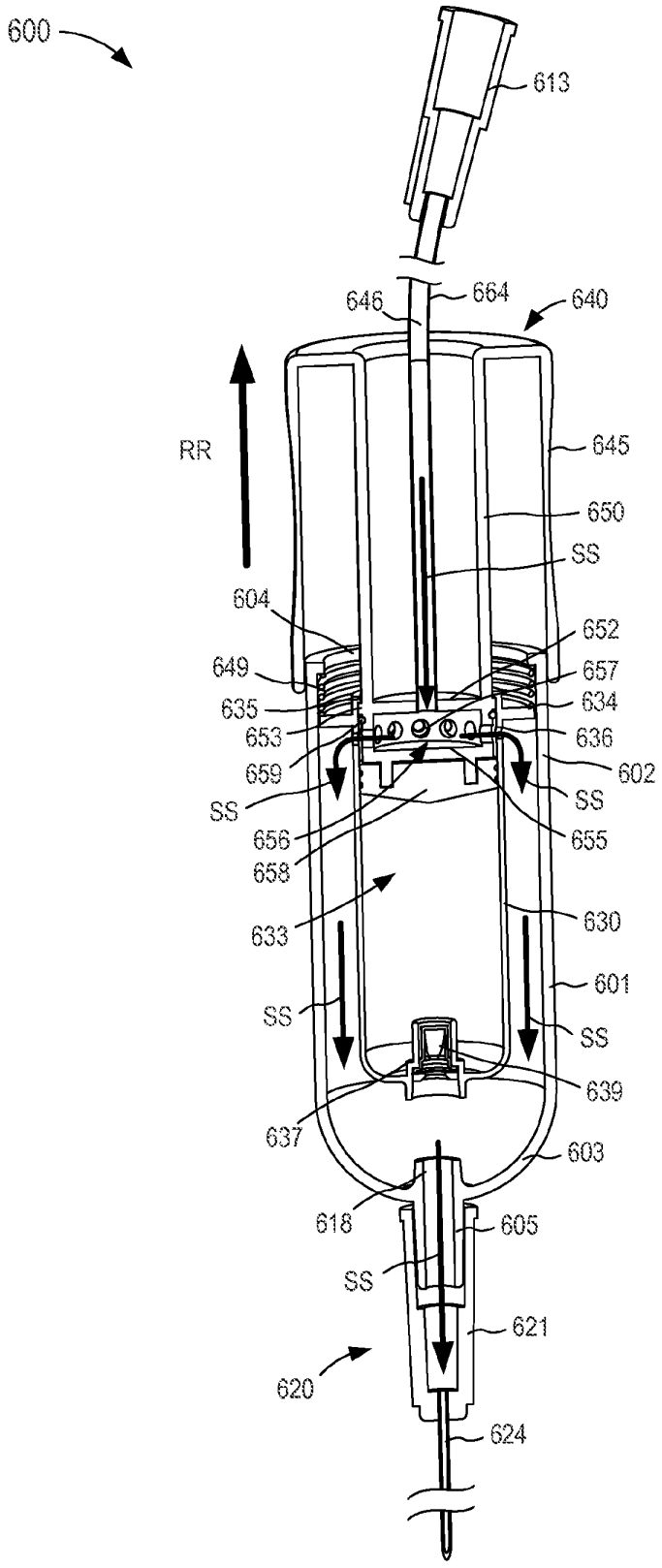

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FIG. 30

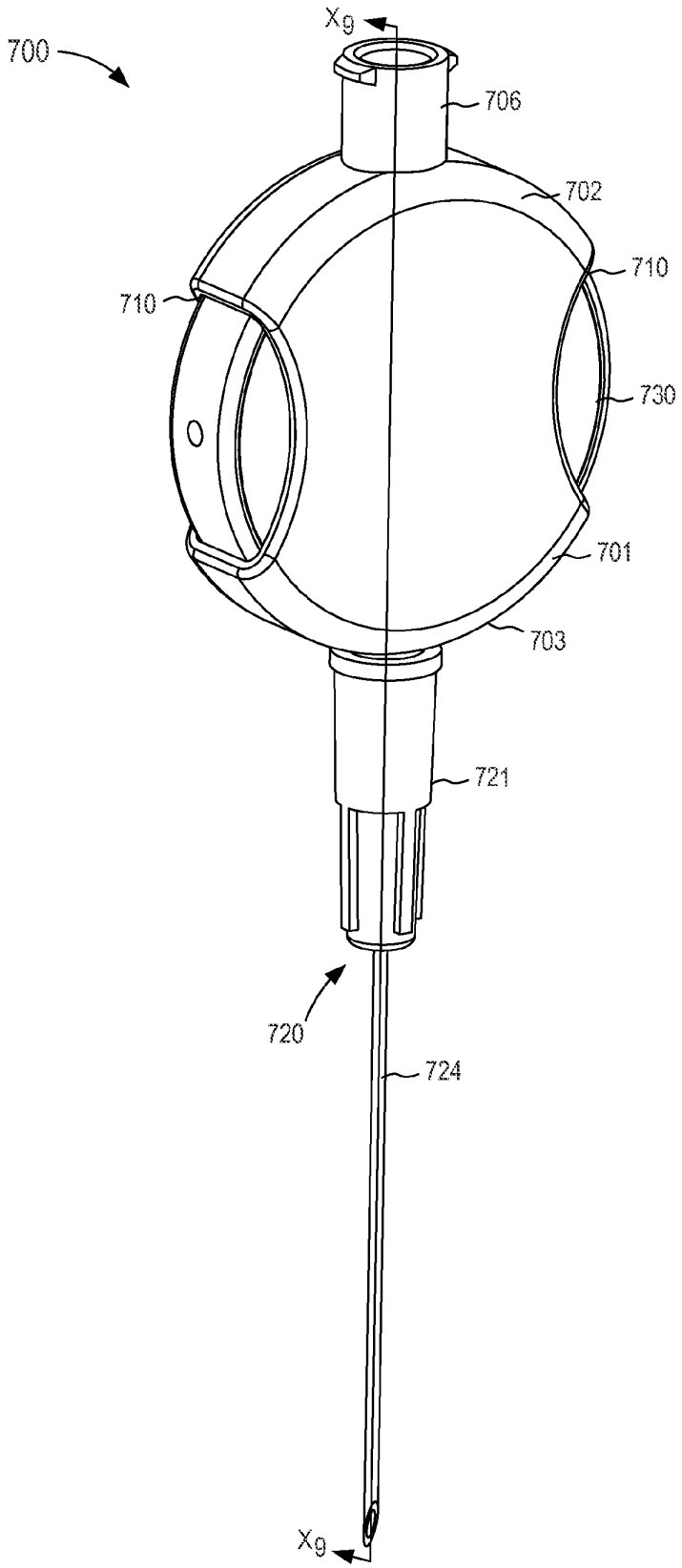


FIG. 31

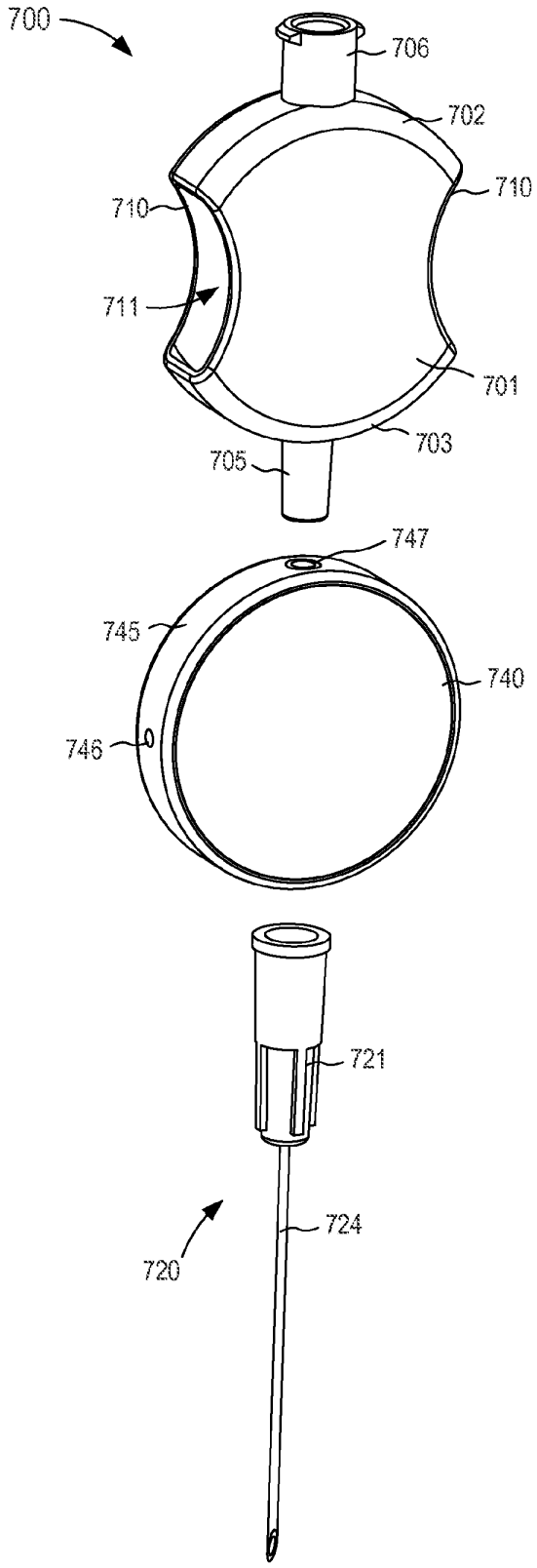


FIG. 32

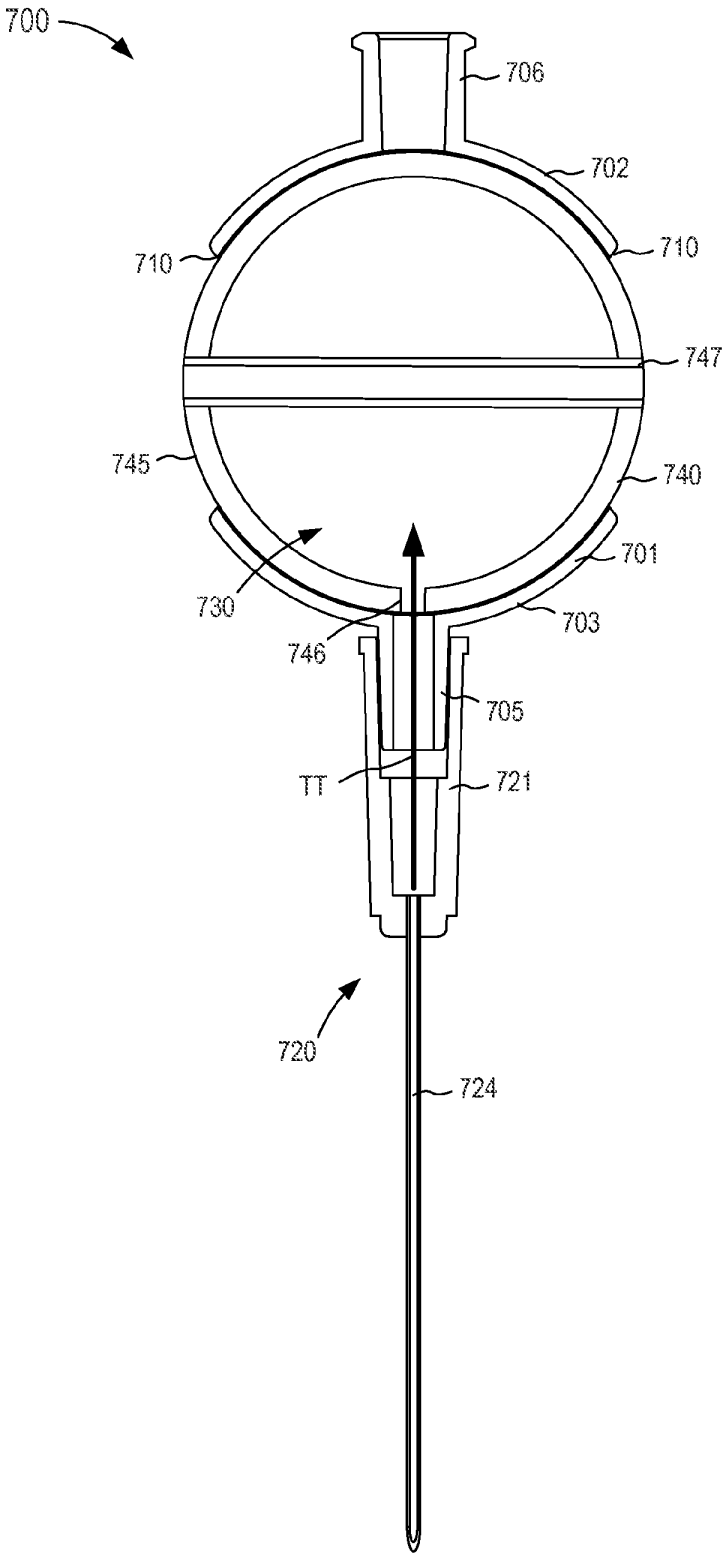

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FIG. 33

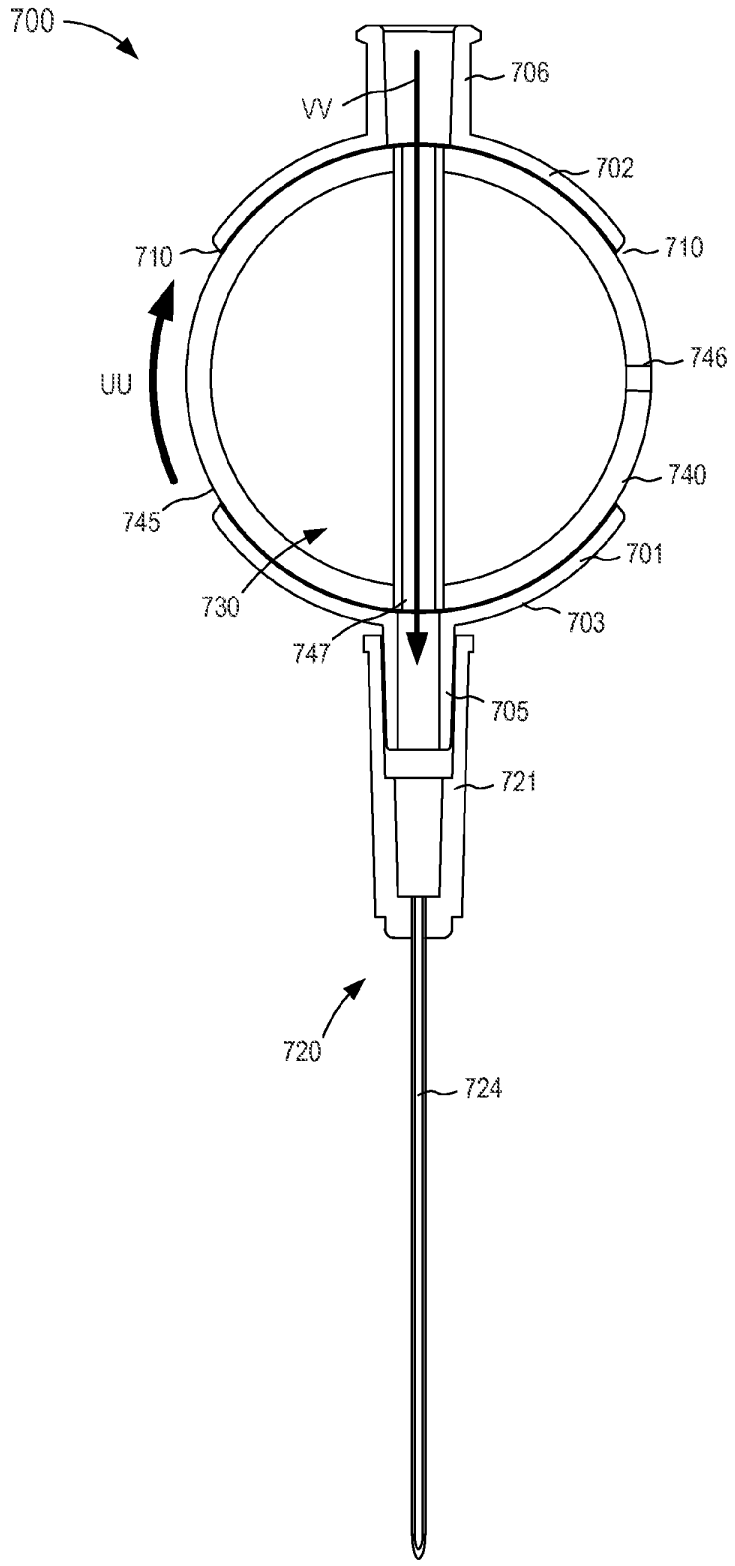

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FIG. 34

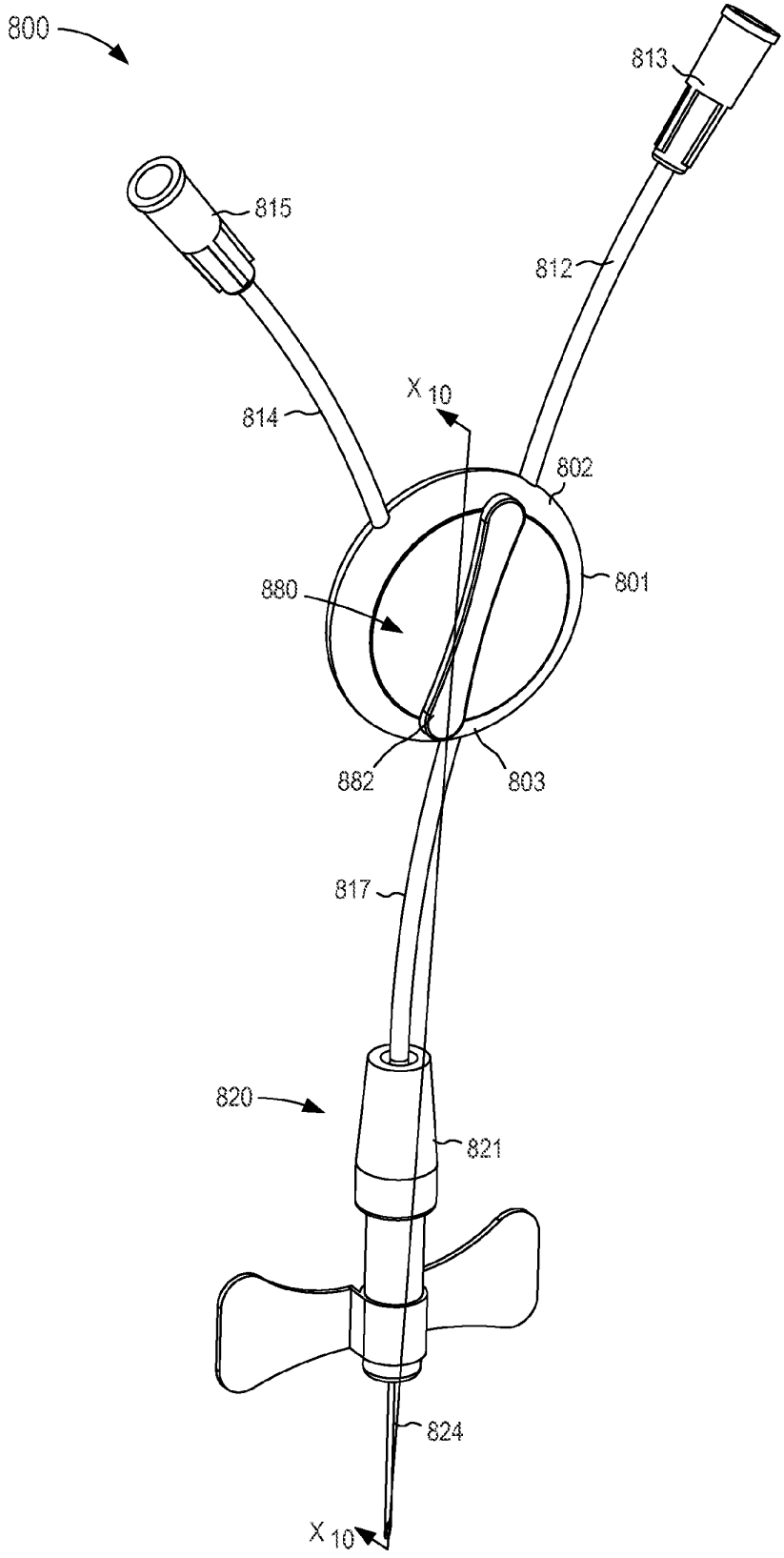


FIG. 35

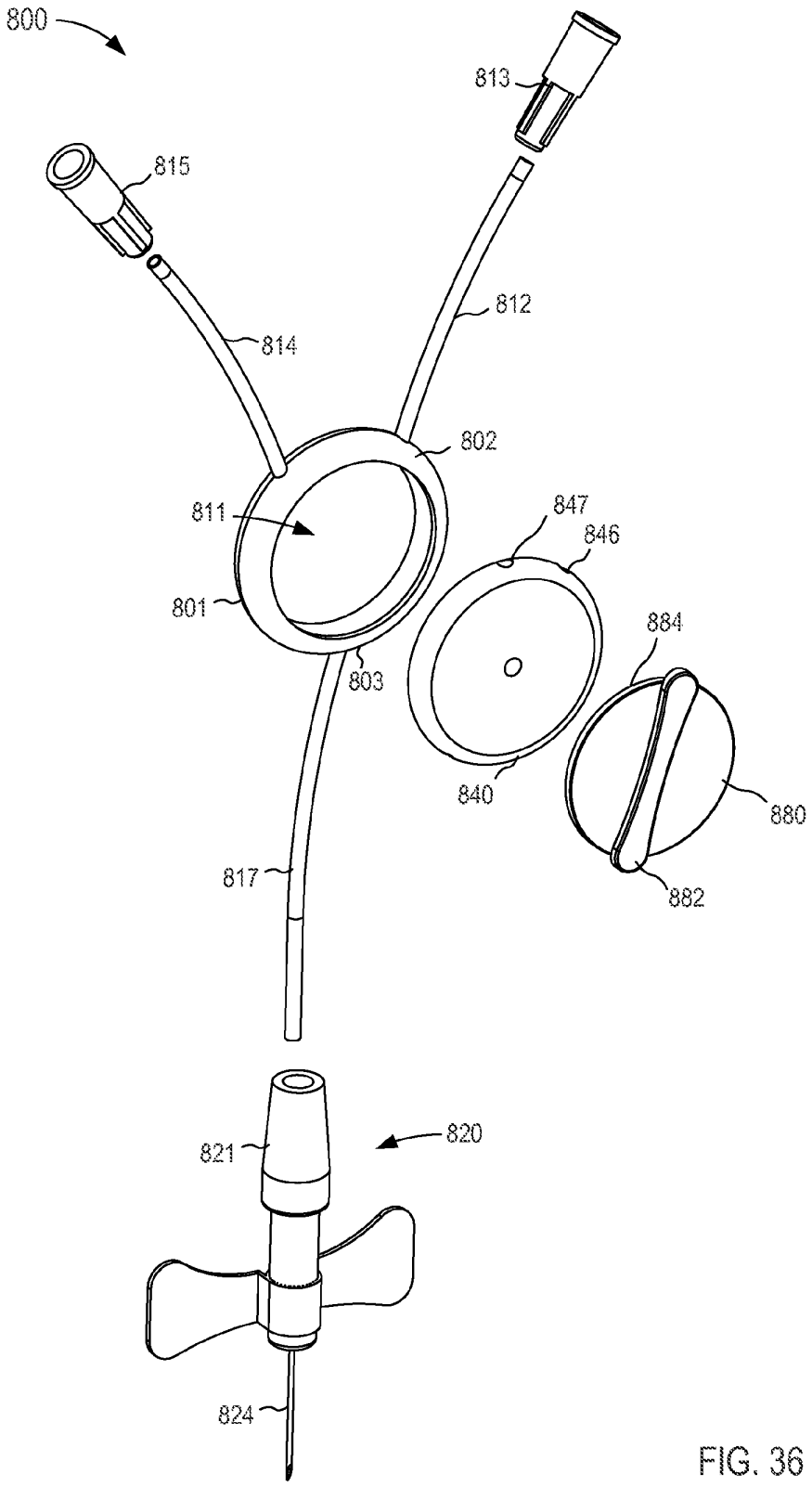

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FIG. 36

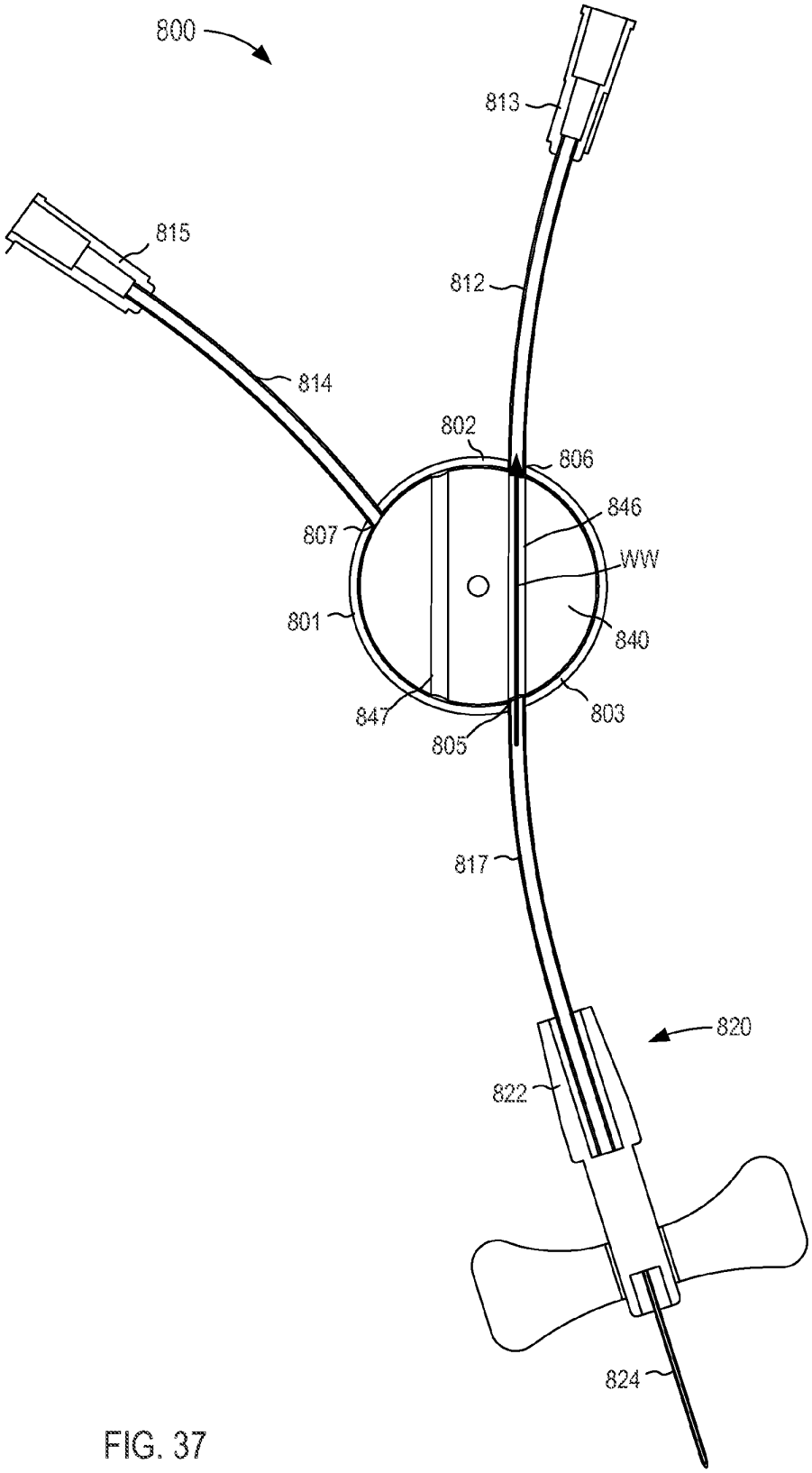

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FIG. 37

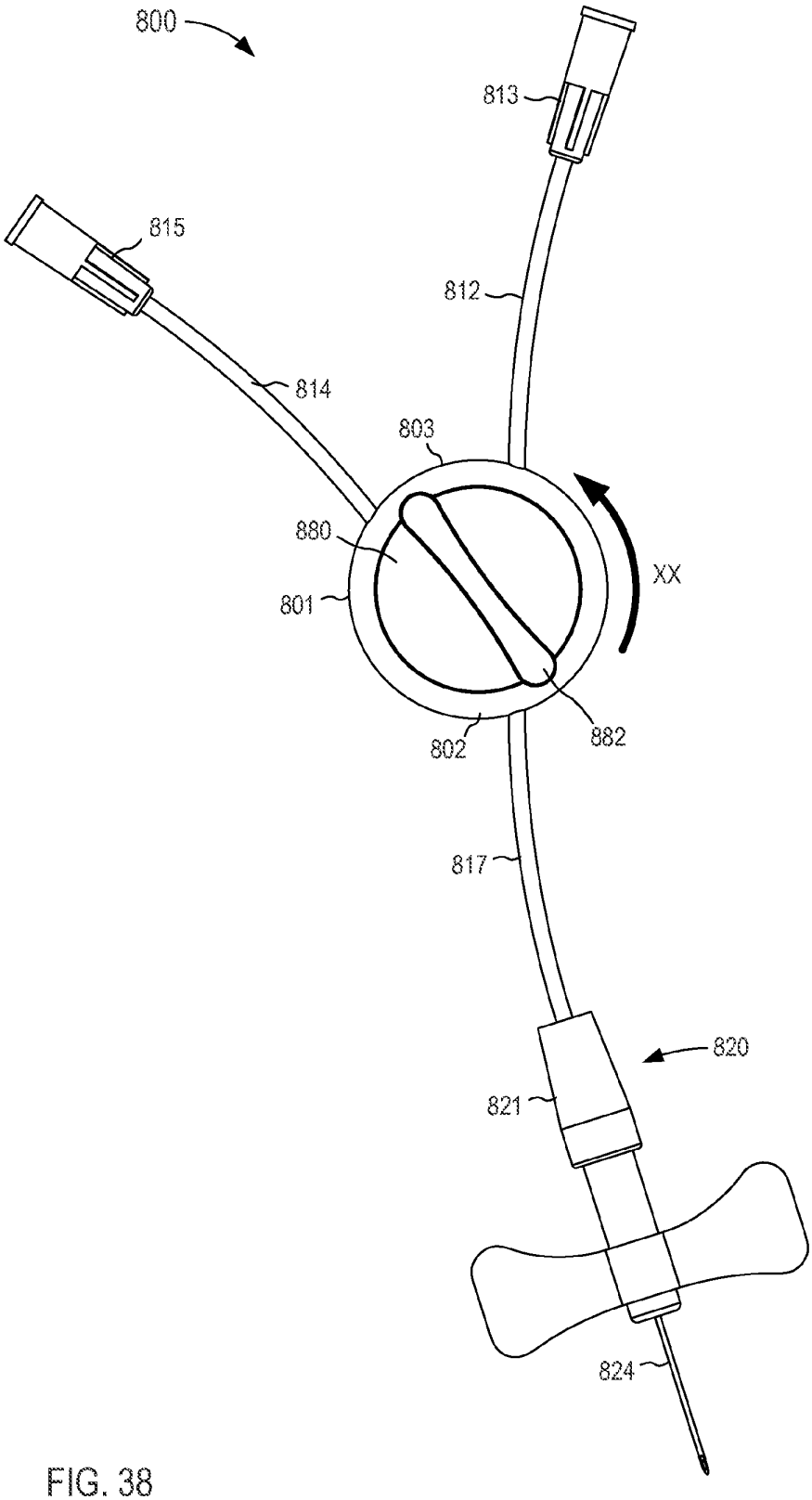


FIG. 38

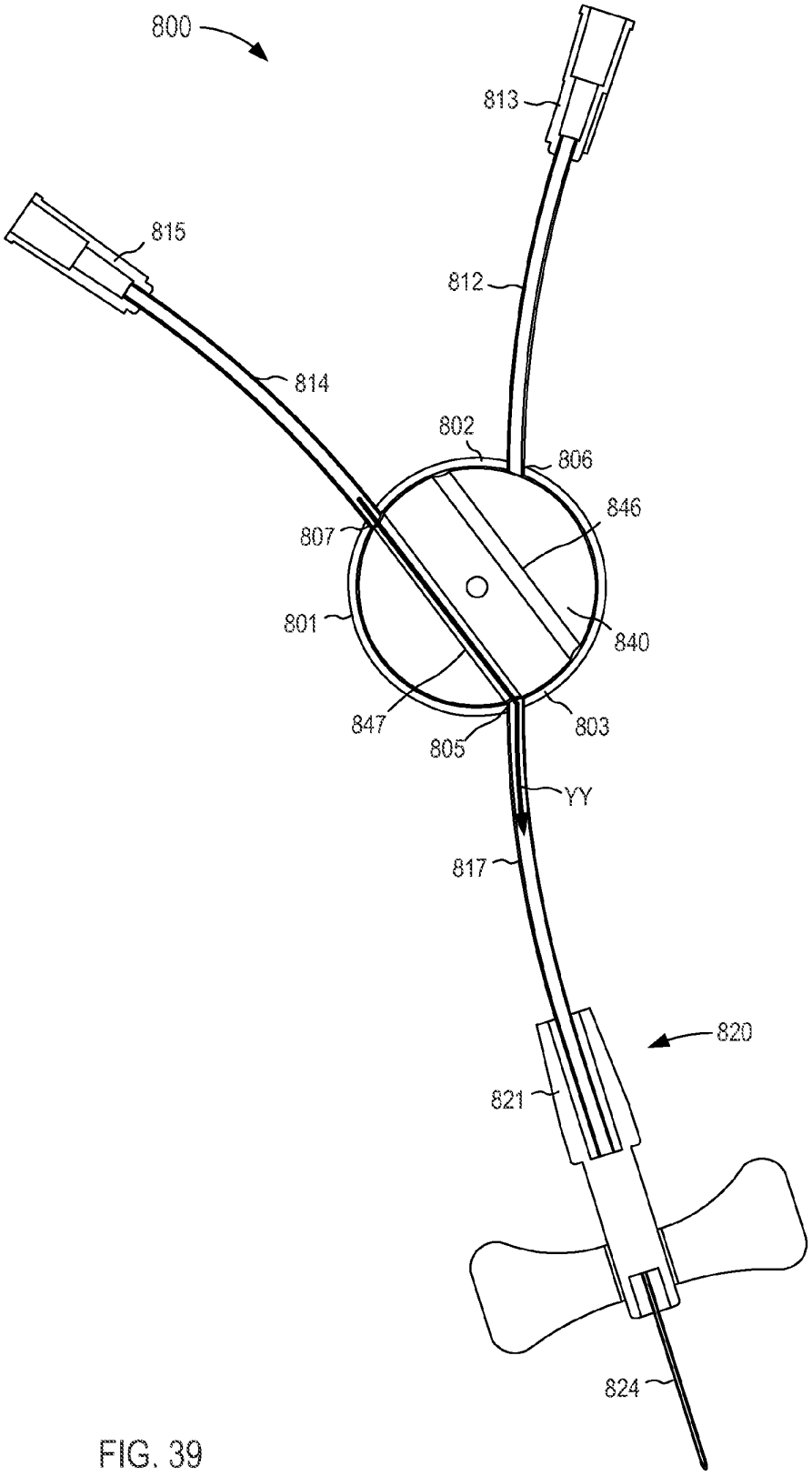

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FIG. 39

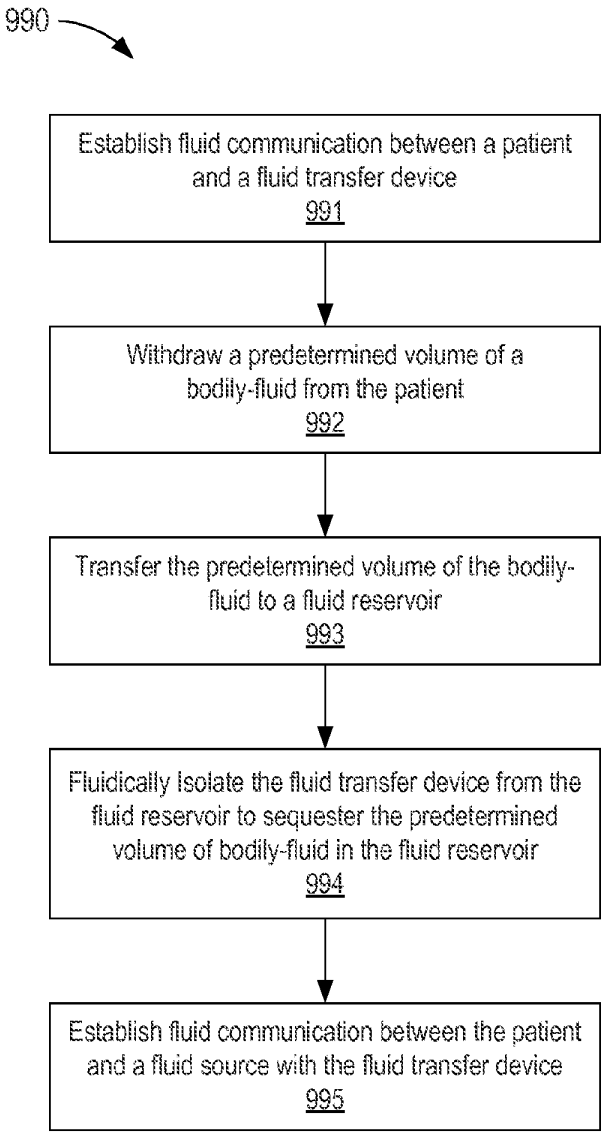

990
Establish fluid communication between a patient and a fluid transfer device
991
Withdraw a predetermined volume of a bodily-fluid from the patient
992
Transfer the predetermined volume of the bodily-fluid to a fluid reservoir
993
Fluidically isolate the fluid transfer device from the fluid reservoir to sequester the predetermined volume of bodily-fluid in the fluid reservoir
994
Establish fluid communication between the patient and a fluid source with the fluid transfer device
995

FIG. 40

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2013/063975

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 5/15, 5/155; A61M 1/00, 5/00, 5/31, 5/32, 5/178, 5/315, 25/06; B01L 3/14 (2014.01)
USPC - 600/573, 575, 576, 577, 578, 579; 604/110, 164.01, 164.08, 191, 228, 246, 403, 411

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
CPC - A61B 5/1405, 5/1427, 5/1428 (2013.01)

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
PatBase, Google Patents, Google

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 2009/0306601 A1 (SHAW et al) 10 December 2009 (10.12.2009) entire document	1-30, 33, 34
Y	US 2012/0215131 A1 (PATTON) 23 August 2012 (23.08.2012) entire document	1-30, 33, 34
Y	US 5,573,510 A (ISAACSON) 12 November 1996 (12.11.1996) entire document	14-18, 23-27
Y	US 4,988,339 A (VADHER) 29 January 1991 (29.01.1991) entire document	14-17, 28-30
Y	US 2002/0193751 A1 (THEEUWES et al) 19 December 2002 (19.12.2002) entire document	22-30, 33, 34
Y	US 6,016,712 A (WARDEN et al) 25 January 2000 (25.01.2000) entire document	26
Y	US 2003/0208151 A1 (KRAUSE et al) 06 November 2003 (06.11.2003) entire document	33

☐ 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
06 March 2014	20 MAR 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)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2013/063975

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:

SEE CONTINUATION SHEET ATTACHED

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.:
1-34

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
Information on patent family members

International application No.
PCT/US2013/063975

CONTINUATION OF BOX III

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 1-34 are drawn to an apparatus.

Group II, claims 35-40 are drawn to a method of delivering a fluid to a patient using a fluid transfer device.

The inventions listed as Groups I - II 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, housing including a proximal end portion and a distal end portion; a fluid reservoir fluidically coupled to the housing; and a flow control mechanism, are not present in Group II; and the special technical features of Group II, establishing fluid communication between the patient and the fluid transfer device; fluidically isolating the fluid transfer device from the fluid reservoir to sequester the predetermined volume of bodily fluid in the fluid reservoir, are not present in Group I.

Further, Groups I and II share the technical features of a fluid reservoir fluidically coupled and configured to receive and isolate a first volume of bodily fluid withdrawn from a patient.
However, these technical features do not represent a contribution over the prior art. Specifically, US 2011/0306853 A1 to Black et al teaches a body fluid sampling system (10; Abstract; Fig. 2A) comprising a fluid reservoir (18) fluidically coupled to an array of microchannels (16; para. [00060]) and configured to receive and isolate a first volume of bodily fluid withdrawn from a patient (paras. [0061] and [0062]).

Since none of the special technical features of the Groups I - II inventions is found in more than one of the inventions, unity is lacking.

J-PlatPat 特許情報プラットフォーム

English close

Literature display help

1 / 1 display

JP 2020-000340

Document unit PDF | progress information | OPD | search key | URLs

Display format of the document display screen:

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primary literature | PAJ

bibliography close

(19) [Country of issue] Japan Patent Office (JP)

(12) [Type of publication] Published patent publication (A)

(11) [Publication number] JP 2020-340 (P2020-340A)

(43) [Published date] January 9, 2020 (2020.1.9)

(54) [Title of the invention] Drug packaging device and method for manufacturing a packaged drug

(51) [International patent classification]

A61J 3/00 (2006.01)

B65B 61 /00 (2006.01)

B26F 1/18 (2006.01)

[FI]

A61J 3/00 310E

B65B 61/00

B26F 1/18

[Request for examination] Unclaimed

[Number of claims] 7

[Application form] OL

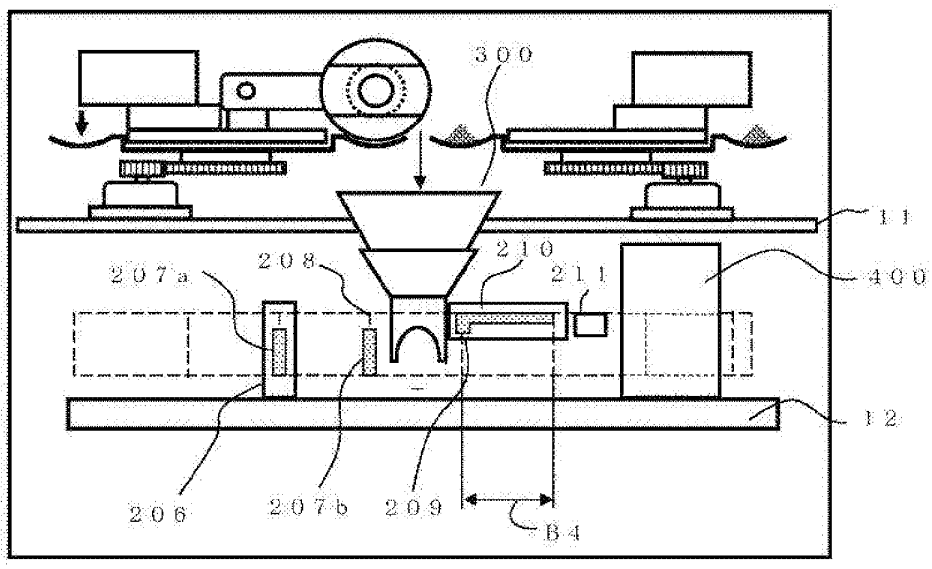
[Total number of pages]] 15

(21) [Application number] Patent application 2018-120789 (P2018-120789)
(22) [Application date] June 26, 2018 (2018.6.26)
(71) [Applicant]
[Identification number] 000151472
[Name] Tosho Co., Ltd.
(74) [Agent]
[Identification number] 100107928
[Patent attorney]
[Name] Masanori Inoue
(72) [Inventor]
[Name] Shiro Omura
(72) [Inventor]
[Name] Shigeyuki Yamamoto
(72) [Inventor]
[Name] Taku Yamamoto
(72) [Inventor]
[Name] Kunio Fukatsu
[Theme code (reference)]
3C060
3E056
4C047
[F term (参考）】
3C060AA01
3C060AB01
3C060BA08
3C060BB08
3C060BB19
3C060BD01
3C060BE08
3C060BF01
3C060BG08
3C060BG18
3C060BH01
3E056AA02
3E056BA11
3E056CA02
3E056CA14
3E056DA05
3E056EA03

3E056FA03
3E056FB03
3E056FB08
4C047AA17
4C047CC14
4C047CC15
4C047JJ03
4C047JJ13
4C047JJ15
4C047JJ24
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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 forming 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 apparatus 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 be torn at the perforations. In addition, since the drug is enclosed in the lower portion 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 that separates the packaging paper into individual packages, and a heat seal portion provided in the middle of th e transport path. , a medicine supply unit for supplying the medicine one package at a time b etween the packaging papers; a driving roller for pinching and driving the packaging paper co ntaining the medicine supplied by the medicine supply unit; and the driving roller. a perforatio n creating section provided downstream in the conveying direction of the packaging paper and forming 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 packin g machine, and can also be applied to an automatic tablet packing machine. Further, it is need less to say that the present invention can also be applied to a medicine packaging device for p ackaging 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 intermed iate table 11 of the housing 10 is arranged a disk distribution section 100 as a drug supply sec tion, and below the intermediate table 11 is arranged a printing packaging machine 200 as a drug packaging section. A drop hopper 300 serves to introduce the powdered medicine discha rged 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 medicin e in the amount necessary for the prescription at another place in advance, and manually ope rated by a staff member or by an automatic device such as a robot arm (not shown). It is plac ed 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 po wdered medicine cassette 101, the powdered medicine in the powdered medicine cassette 10 1 is transported by vibration, and the powdered medicine is dropped little by little in the direct ion of the arrow 103. It is.

Reference

numeral 104 denotes a horizontally arranged distribution disk, a large wheel of which is rotat ed by a stepping motor 105 via a gear 106 in the direction of an arrow 104a. Further, an arc-s haped 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 mot or 105 is continuously rotated, the powdered medicine falls little by little onto the arcuate con cave 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 shaf t 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 1 11. 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 th e 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 "single package distribution operation", when the stepping motor 105 is rotated by 10 degrees while the disc 110 is being rotated, one package of 1 g of powdered medicine can be correctly dispensed to the drop hop per 300. be. The disc distribution unit 100 and the drop hopper 300 constitute a medicine sup ply unit.

Two pairs 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 describe d with reference to FIGS. 4 and 5. FIG. FIG. 4 is a cross-sectional view of the front of the pow der medicine packaging machine, showing a state in which the drop hopper 300 positioned ab ove in FIG. 2 has moved downward. FIG. 5 is a top cross-sectional view of the printing and pa ckaging machine 200. As shown in FIG. Reference numeral 201 denotes a packing paper roll a s a packing paper storage unit, which is formed by winding a double-folded paper having ther mal adhesiveness on a reel with the valley-fold side facing downward, and is placed on the lo wer stage 12. It is The packaging paper pulled out from the leading end of the paper on the o uter peripheral side of the reel is conveyed along the conveying path along a route such as th e one-dotted chain line B2 to B3. A printing unit 202 is composed of an ink ribbon 203, a ther mal printing head 204, a platen roller 205, etc., and prints prescription information on the surf ace 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 lo wer table 12. By pressing the packing paper B from the front and back (top and bottom in FI G. 5) with a hot plate, the vertical sealing mechanism 207a is classified into individual packag es by performing the sealing. 207b shows vertical sealing at a position moved by one packag e, but the upper open end 208 of the packaging paper B is not sealed. This is so that the pack ing sheets B can be transported in a state in which the claw portions 305a and 305b of the dr op hopper 300 are inserted between the packing sheets B as shown in FIG. 3(a). The drop ho ok 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 descr iption thereof will be omitted.

Next , reference

numeral 209 denotes a horizontal sealing mechanism, which presses the packing paper B fro m 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 s eal 210, the packaging paper B is sealed as a single package. Although not shown in the draw ing, the vertical seal 7 does not seal the perforated portion but seals both sides of the perfora ted 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 figure by a cam follower (not show n). Since the supporting portion 424 to which the blade receiving portion 404 is fixed is conne cted to the slide shaft 422, the blade receiving portion 404 is also drawn rightward in the figur e. A second cam plate 418 on the second stage from the bottom drives the blade housing po rtion 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 protrud ed 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. T he insertion position and the number of horizontal blades 432g are not limited to the above ex amples, and they can be inserted at any position between blades 432d

.

Especially when the amount of powdered medicine stored in each individual packet is small, 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 pair of rubber rollers 529 is means for pinching and conveying the packin g paper B, and by installing them at a plurality of locations on 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 similar to the perforation forming device 400 described as the first embodiment is provide d downstream of the driving roller 529 on the downstream side

. [0057] In the operation of creating a medicine package, the transported packaging paper B is longitudinally sealed by the heat seal portion 522 to separate one package. At this time, the previous individual package is laterally sealed at the same time. Next, one package of medicin e is supplied between the packaging sheets B from the medicine supply 519 via the drop hopp er 518 . The packaging paper B to which the medicine is supplied is conveyed by the drive roll er 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

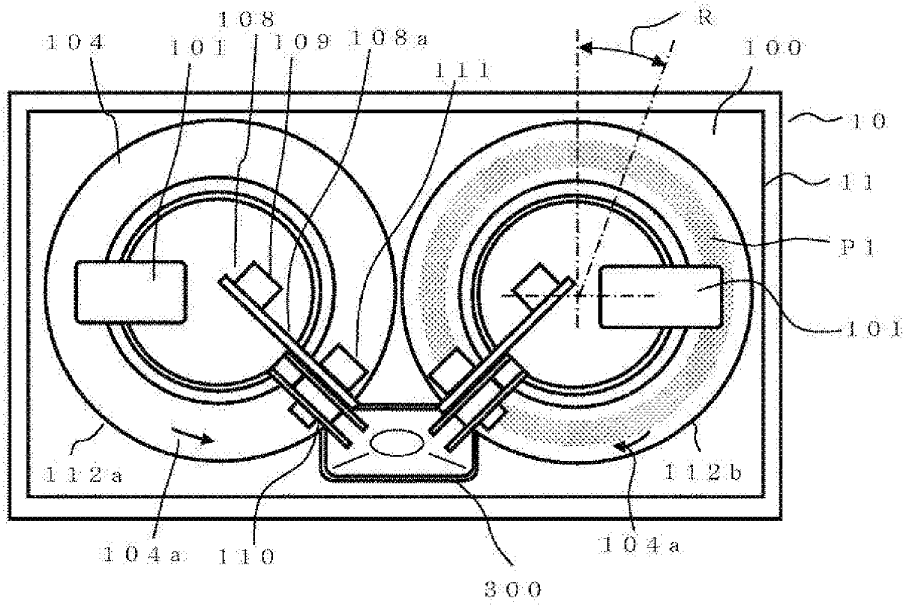
432c Perforating blade tip

B Packaging paper

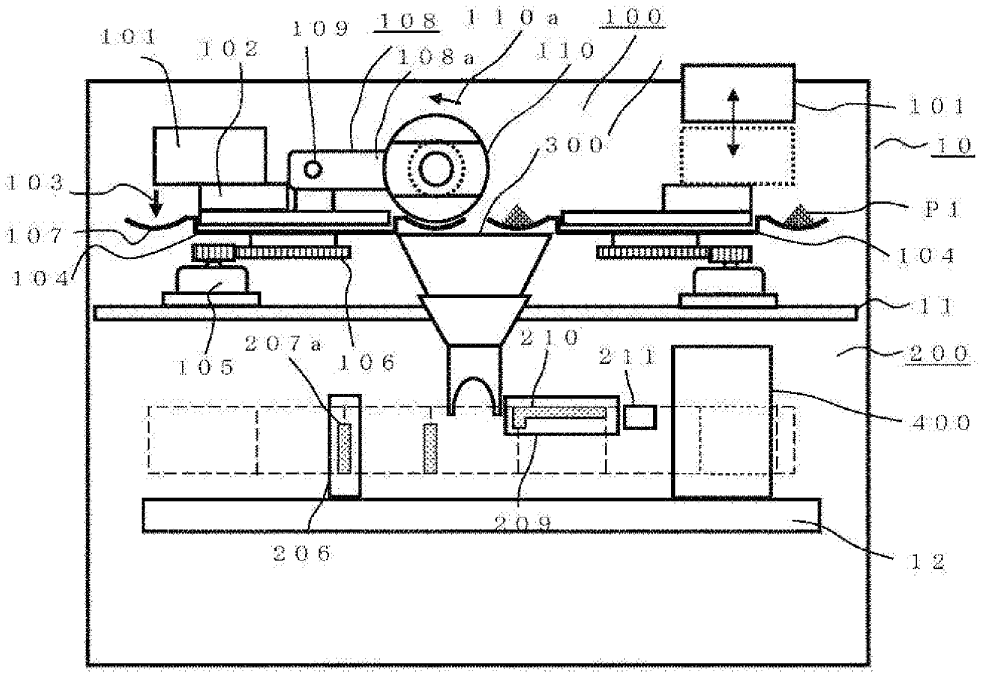
B2, B3 Conveyance path (conveyance path)

drawing open —

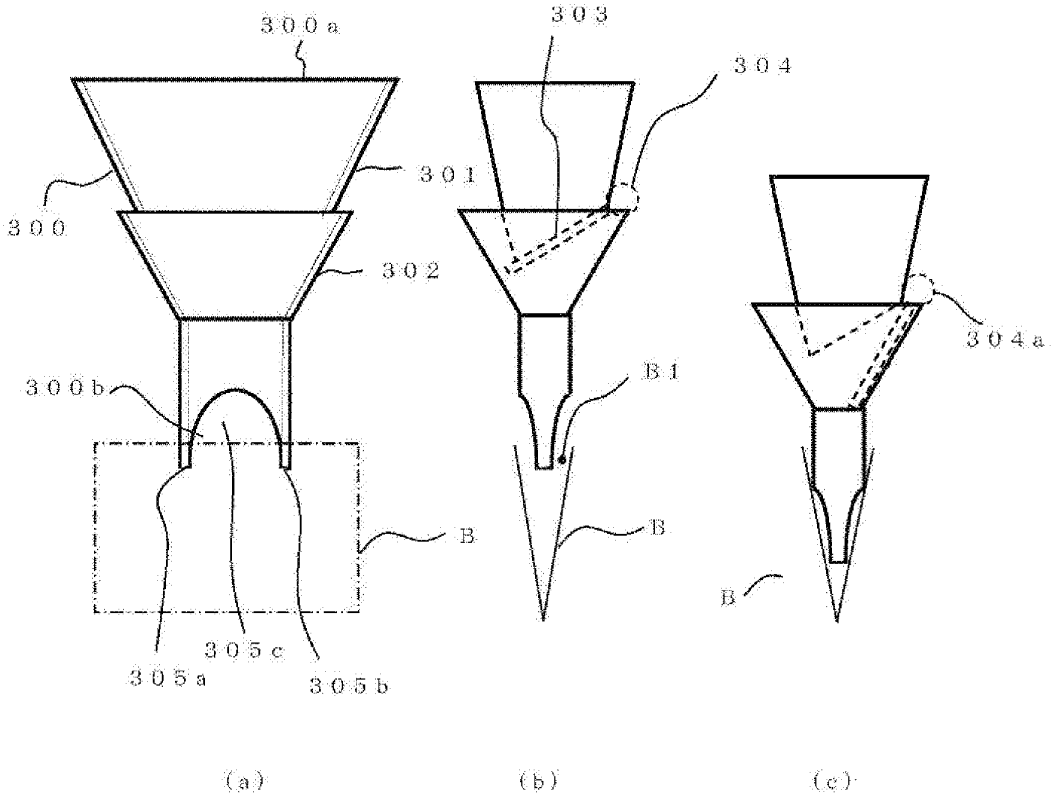
[Fig. 1]



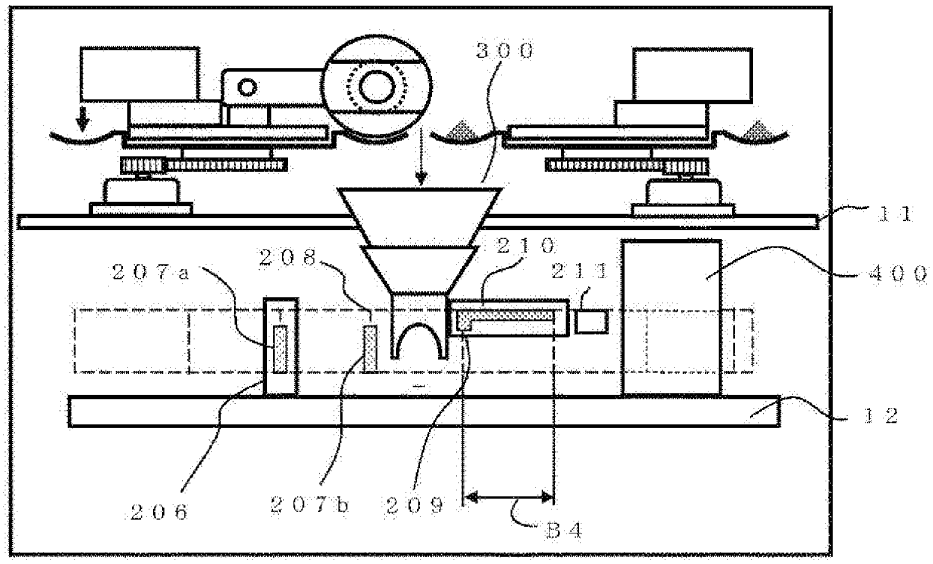
[Figure 2]



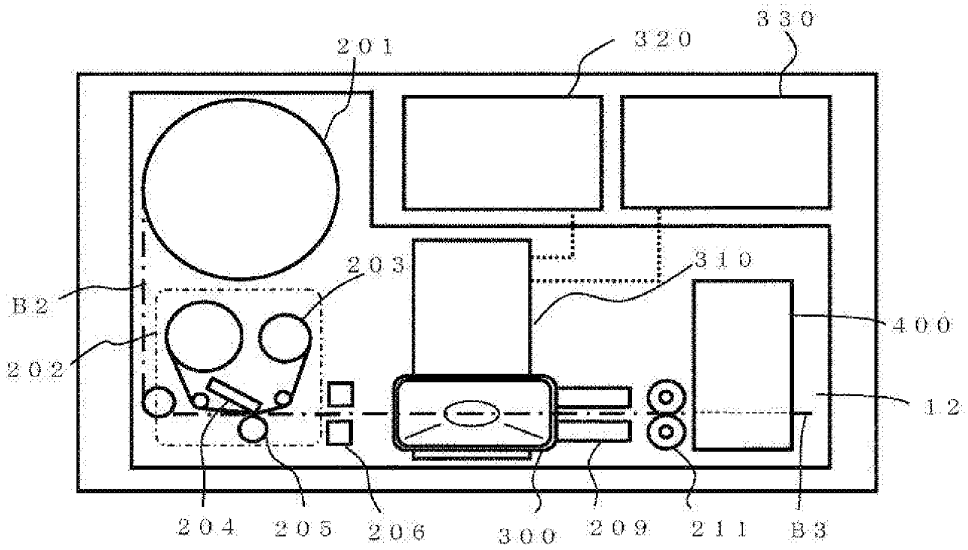
[Figure 3]



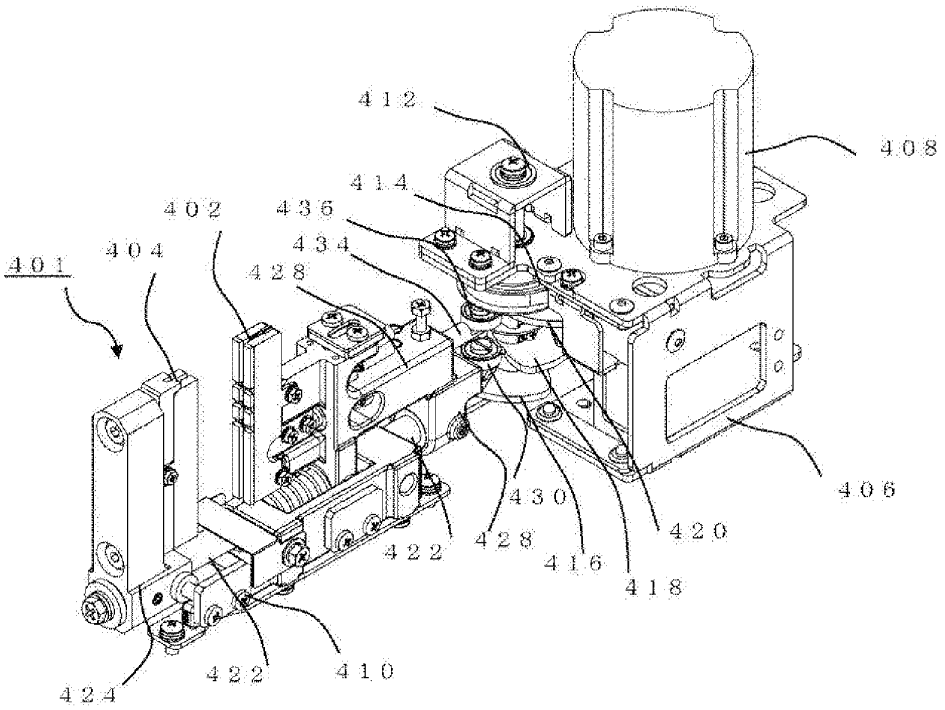
[Figure 4]



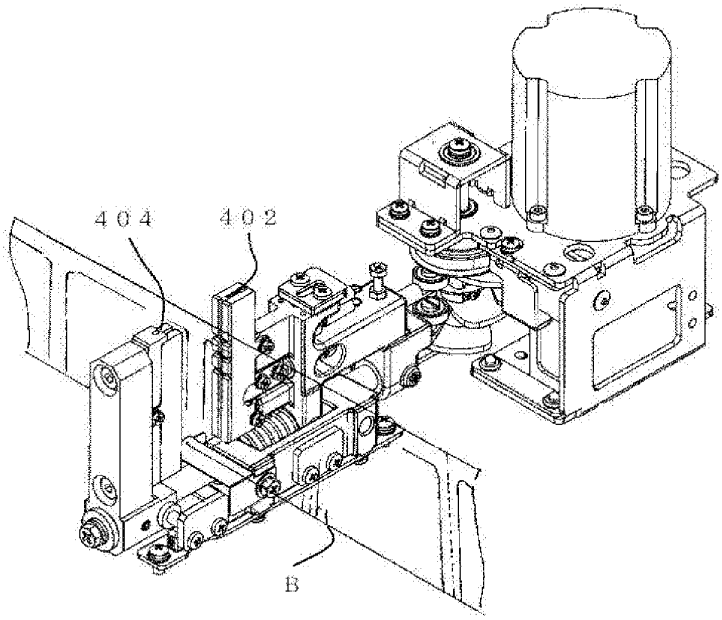
[Figure 5]



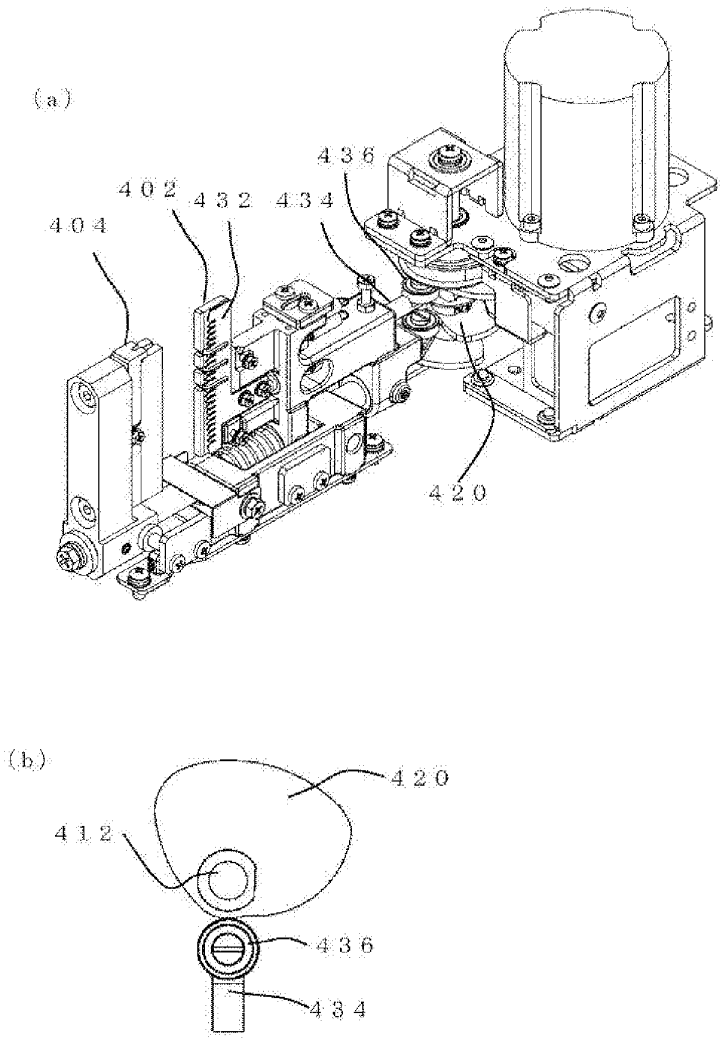
[Fig. 6]


412
408
414
402
436
434
401
404
428
406
430
420
422
428
416
418
422
410
424

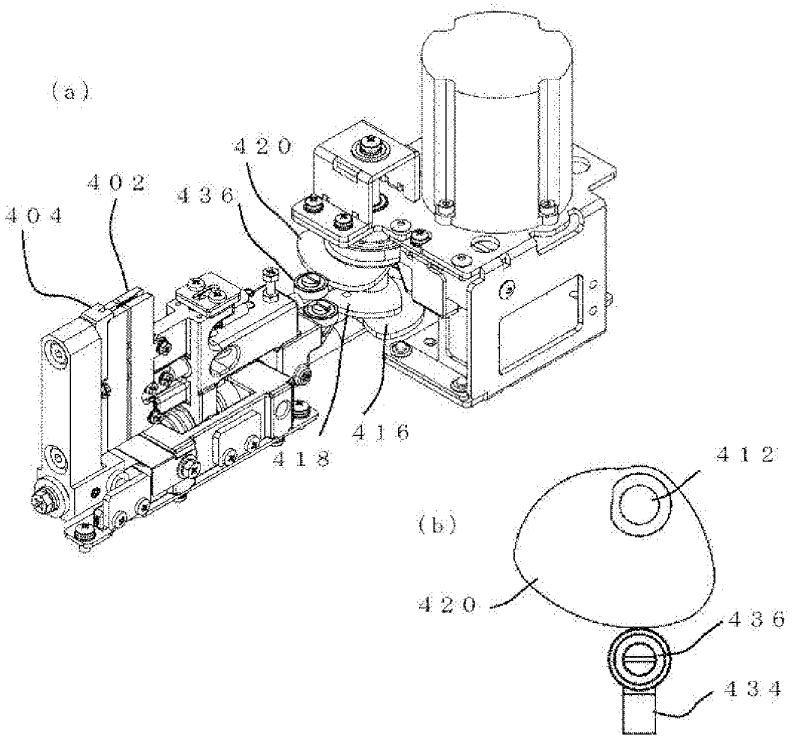
[Fig. 7]


404
402
B

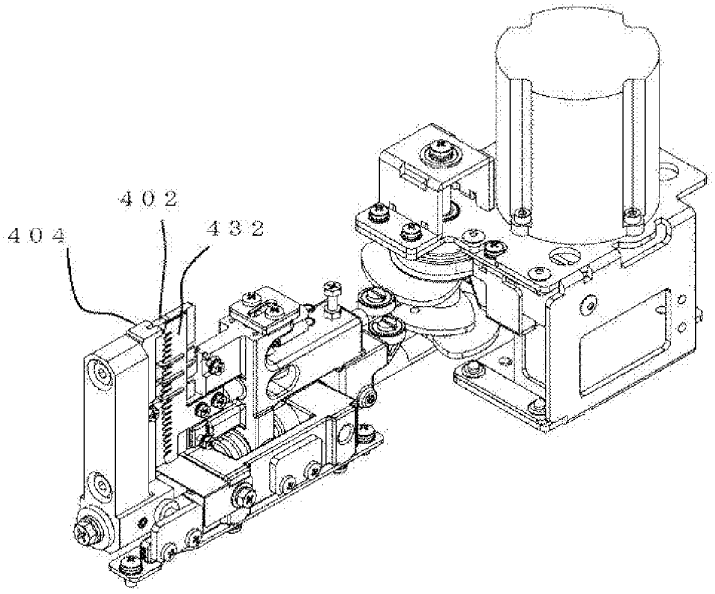
[Fig. 8]



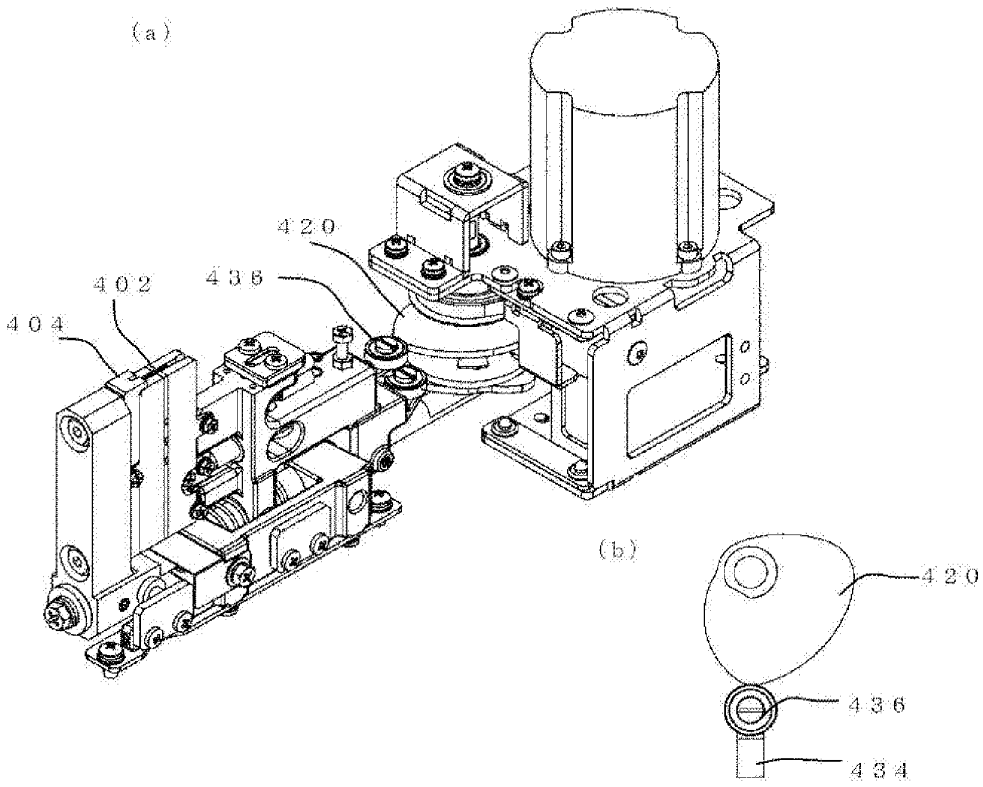
[Fig. 9]



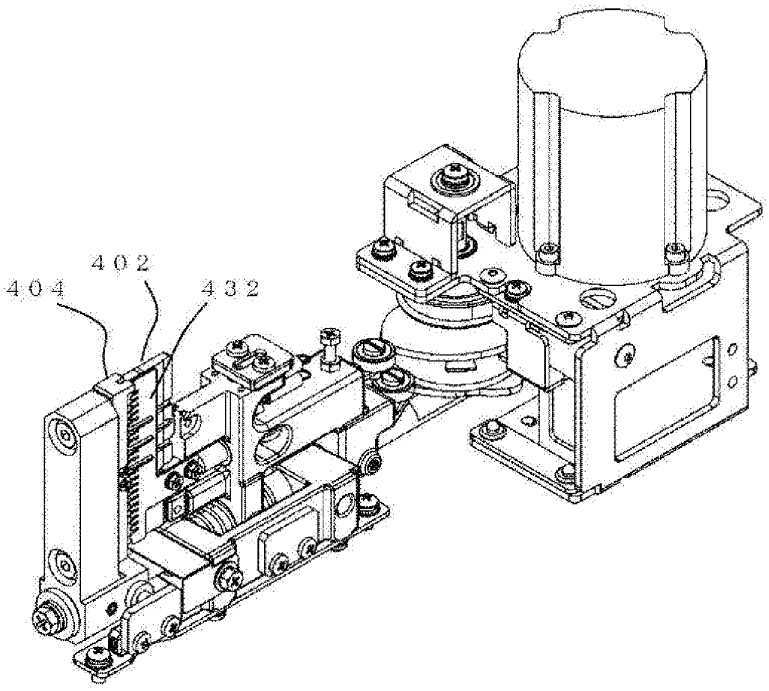
[Fig. 10]



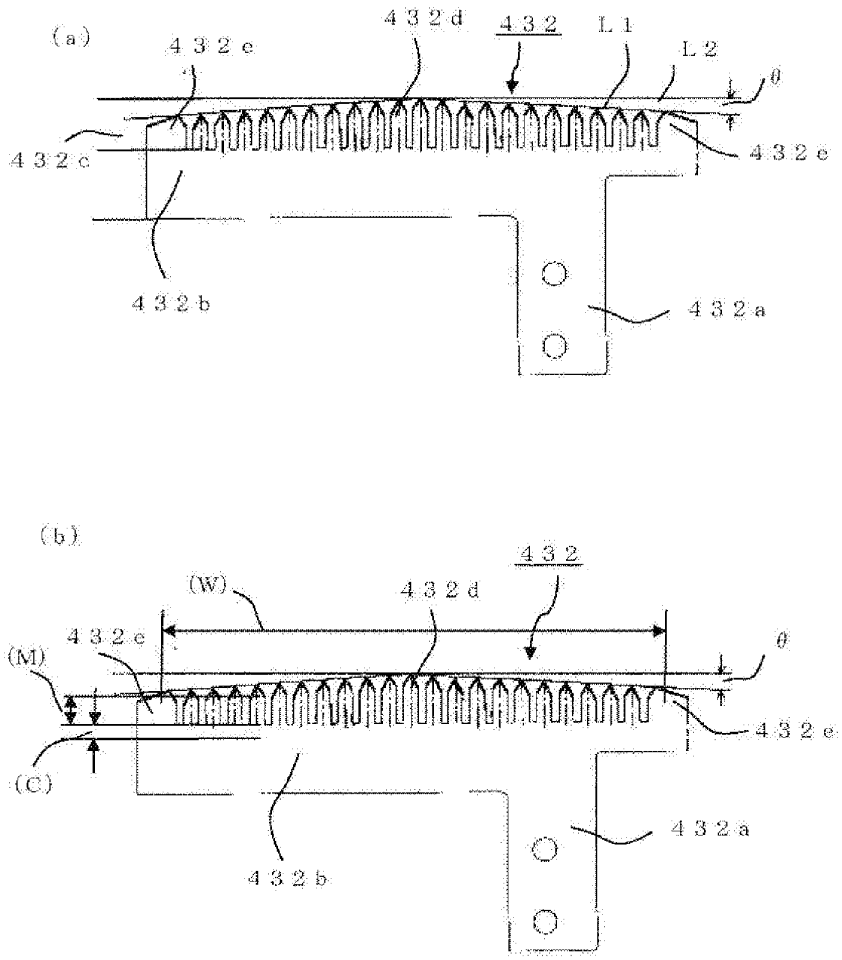
[Fig. 11]



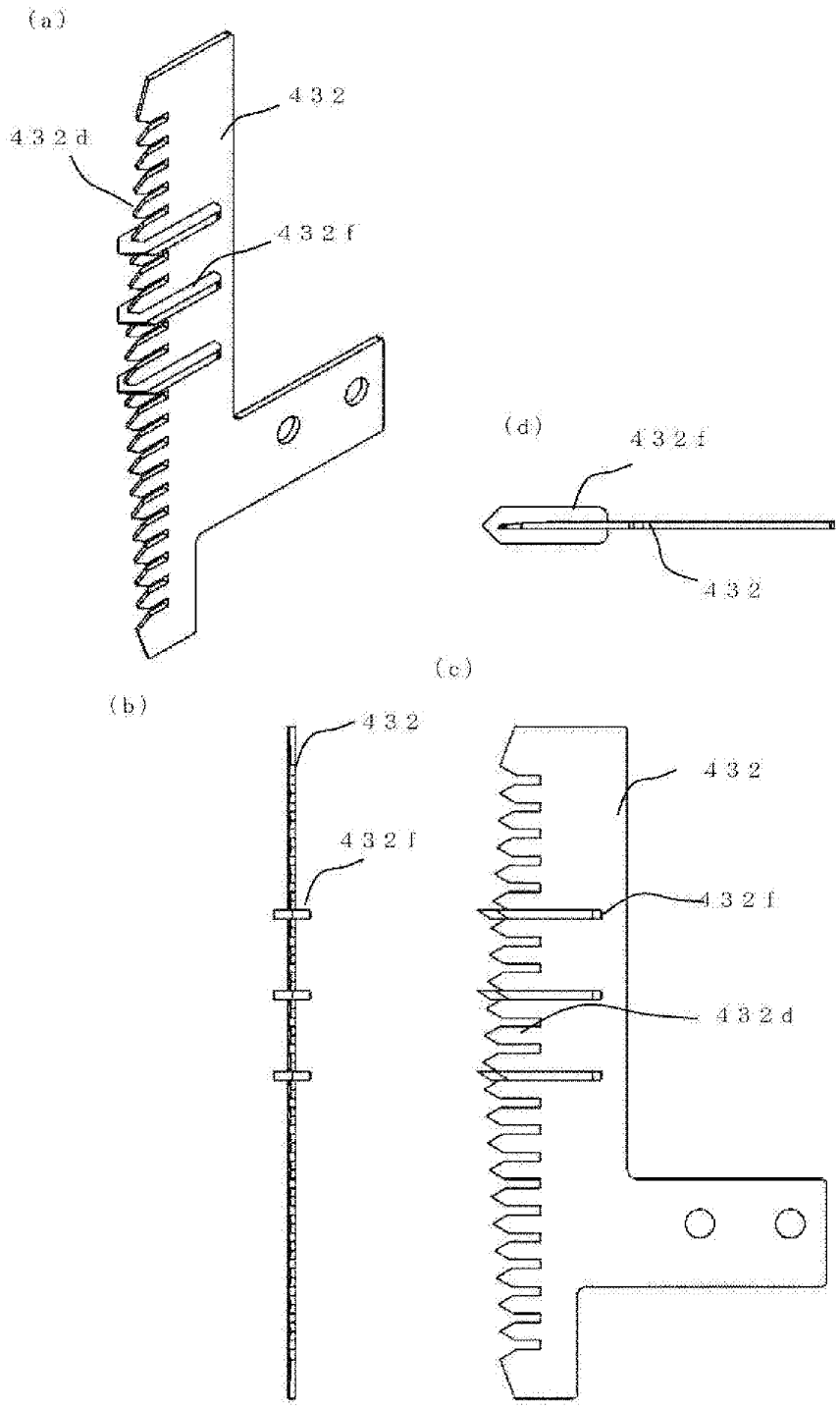
[Fig. 12]



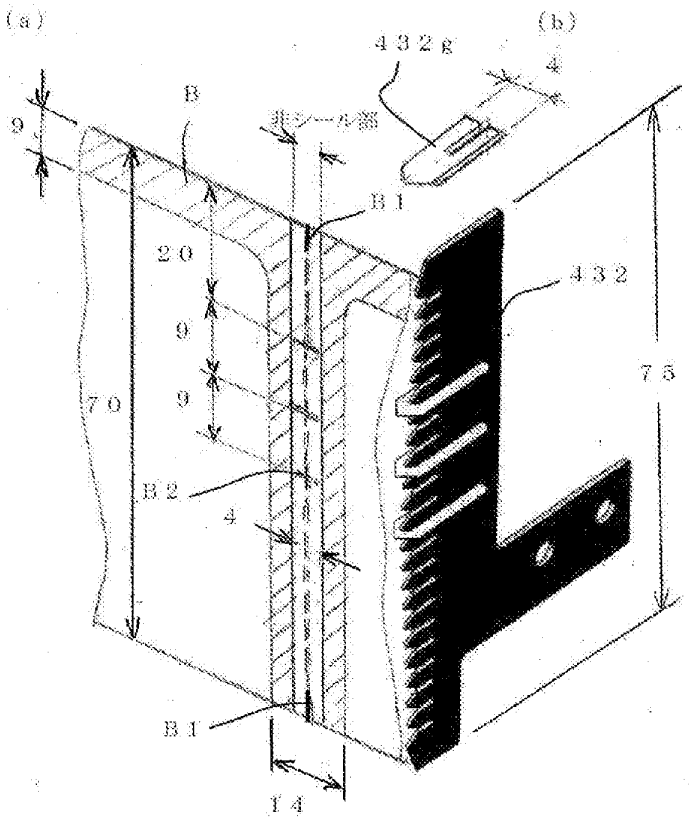
[Fig. 13]


(a)
432e
432d
432
L1
L2
θ
432c
432e
432b
432a
(b)
432
(W)
432d
432e
θ
(M)
432e
(C)
432a
432b

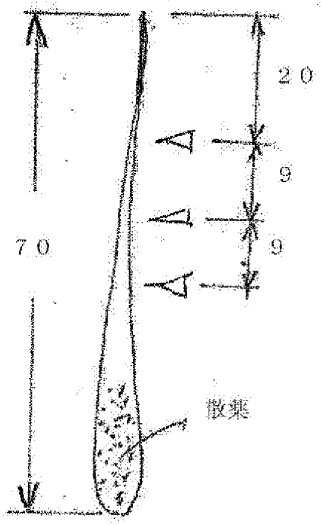
[Fig. 14]



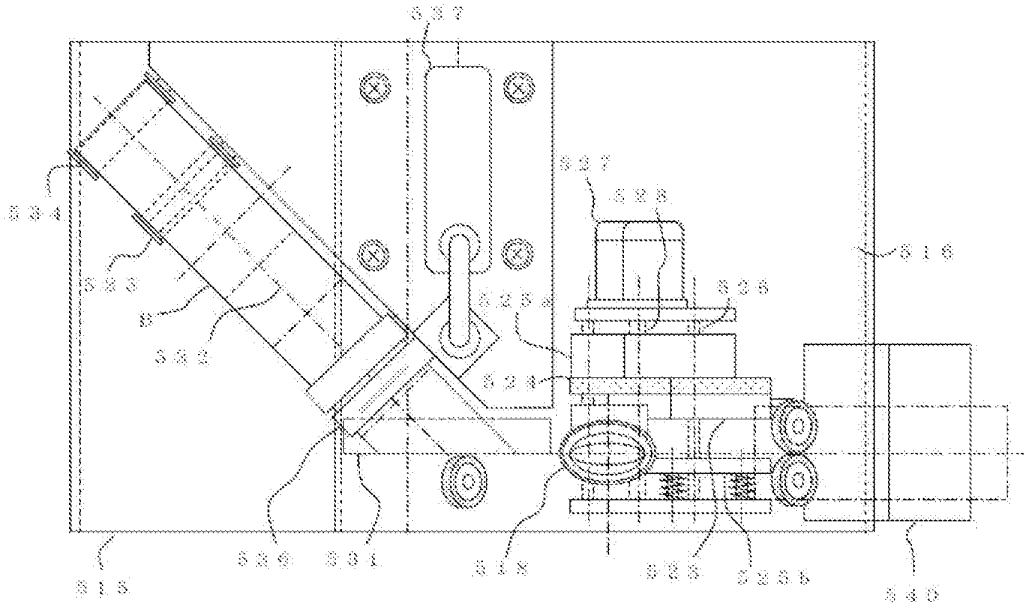
[Fig. 15]



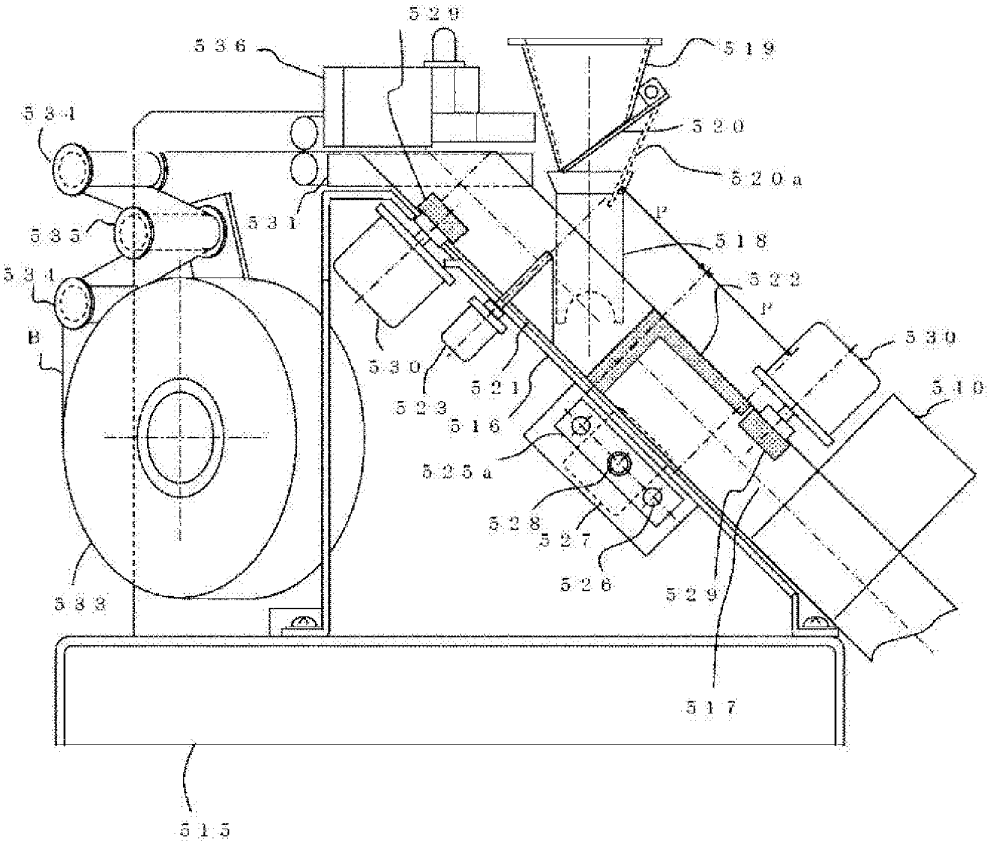
[Fig. 16]



[Fig. 17]



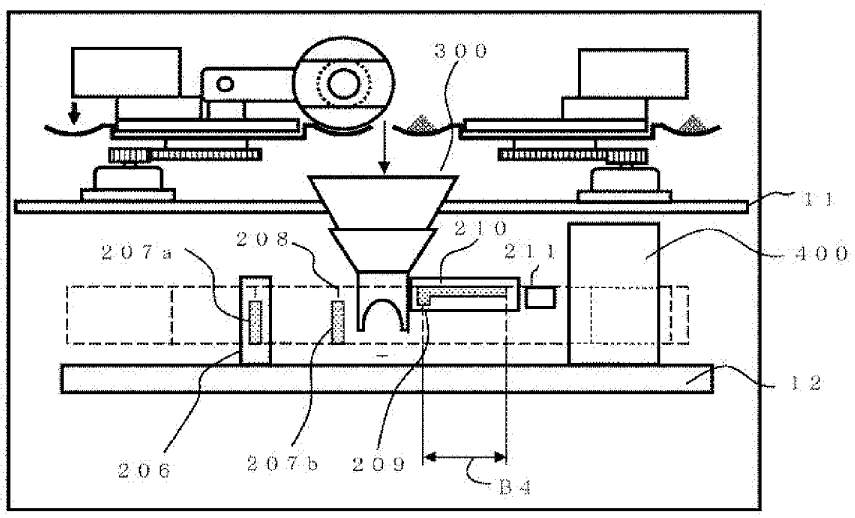
[Fig. 18]



drawing	open	—

Representative drawing | 1 | 2 | 3 | Four | Five | 6 | 7 | 8 | 9 | ...

Magnify and Rotate



Representative drawing

1 / 1 display

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Bibliographic data: JP2020000340 (A) — 2020-01-09

MEDICINE DISPENSING/PACKAGING DEVICE AND PRODUCTION METHOD OF DISPENSING/PACKAGING MEDICINE

Inventor(s): OMURA SHIRO; YAMAMOTO SHIGEYUKI; YAMAMOTO TAKU; FUKATSU KUNIO ± (大村 司郎, ; 山本 繁幸, ; 山本 拓, ; 深津 邦夫)

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

(19)日本国特許庁(JP)　(12)公開特許公報(A)　(11)特許出願公開番号
特開2020-340
(P2020-340A)
(43)公開日　令和2年1月9日(2020.1.9)

(51)Int.Cl.			F I			テーマコード（参考）
A61J	3/00	(2006.01)	A61J	3/00	310E	3C060
B65B	61/00	(2006.01)	B65B	61/00		3E056
B26F	1/18	(2006.01)	B26F	1/18		4C047

審査請求 未請求　請求項の数 7　OL　（全 15 頁）

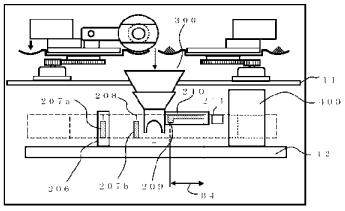
(21)出願番号　特願2018-120789 (P2018-120789)
(22)出願日　平成30年6月26日 (2018.6.26)

(71)出願人　000151472
株式会社トーショー
東京都大田区東糀谷３丁目１３番７号
(74)代理人　100107928
弁理士　井上　正則
(72)発明者　大村　司郎
東京都大田区東糀谷三丁目８番８号
(72)発明者　山本　繁幸
東京都大田区東糀谷三丁目８番８号
(72)発明者　山本　拓
東京都大田区東糀谷三丁目８番８号
(72)発明者　深津　邦夫
東京都大田区東糀谷三丁目８番８号

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(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刃部（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。

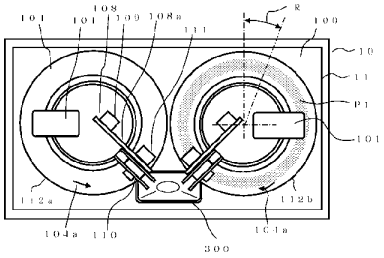
【符号の説明】

【００６１】

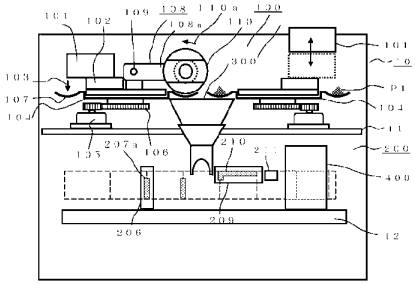
１００・・・円盤配分部（薬剤供給部）
２００・・・印刷包装機
２０１・・・分包用紙ロール（分包用紙収納部）
２０６・・・縦シール機構
２０９・・・横シール機構
２１１・・・駆動ローラ
３００・・・落下ホッパ（薬剤供給部）
４００・・・ミシン目作成装置
４０２・・・刃収納部
４０４・・・刃受け部
４１６，４１８・・・カム板
４２０・・・カム板

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）

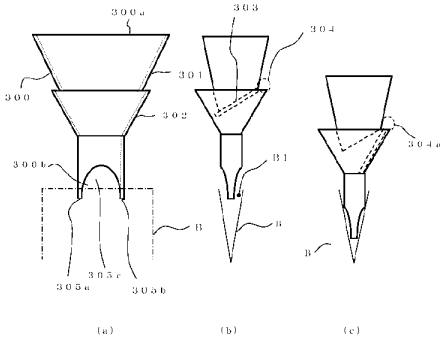
【図１】



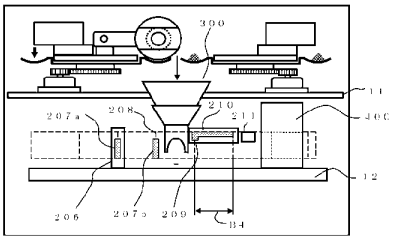
【図２】



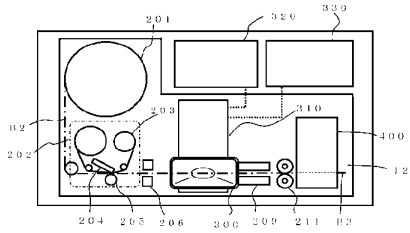
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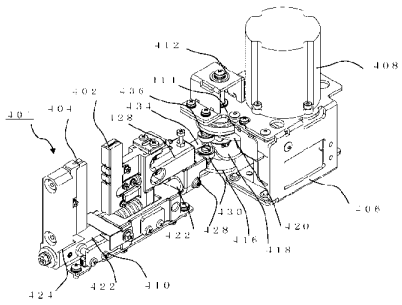
【図４】



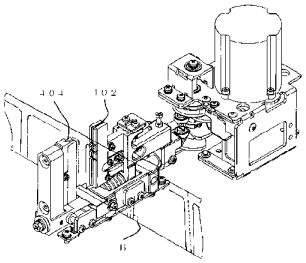
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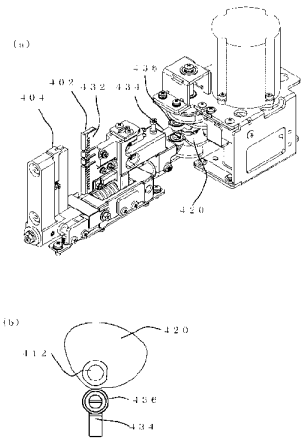
【図６】



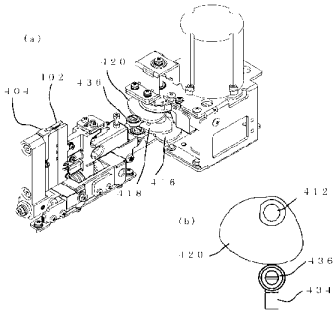
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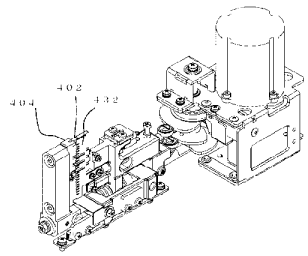
【図８】



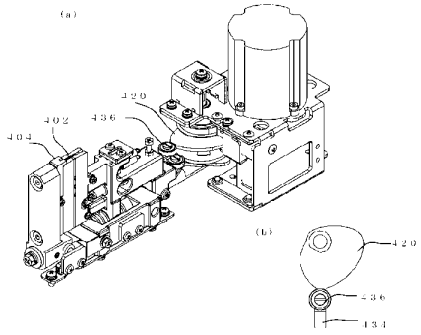
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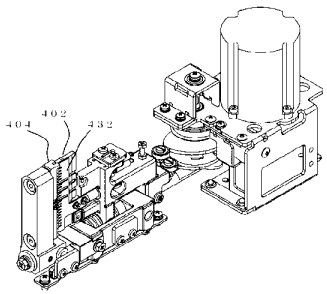
【図１０】



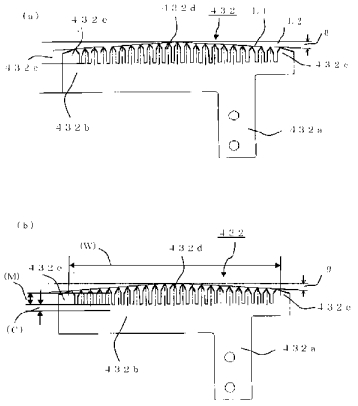
【図１１】



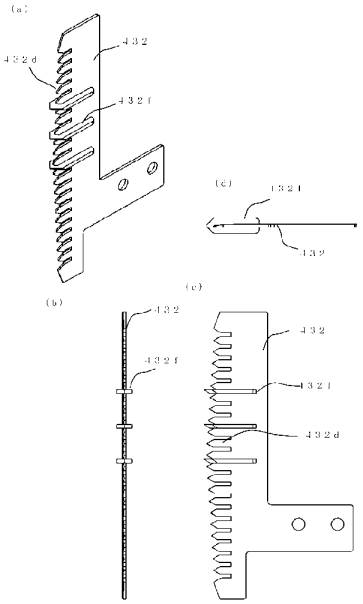
【図１２】



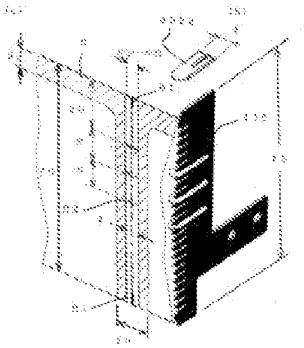
【図１３】



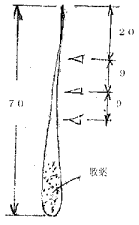
【図１４】



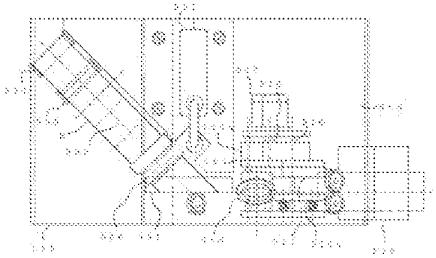
【図１５】



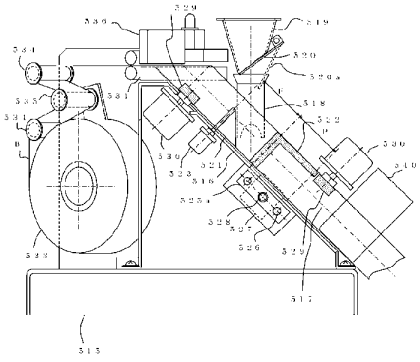
【図１６】



【図１７】



【図１８】



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The scope of the claims

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[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 device is communicable with the vacuum collecti on device. 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 needle assembly 10 include a housing 12, a first puncture needle 14 for insertion into the patient, and a second puncture needle 15 for puncturing a vac uum vessel 16 on the opposite side of housing 12 from which a blood sample is collected. incl ude. A threaded portion 18 of the housing 12 is adjacent to the second puncture needle 15 an d threads into internal threads 20 at the front end of the container holder 19 . By slidingly eng aging the vacuum container 16 within the holder 19 the second puncture needle 15 penetrate s the pierceable stopper 21 at the front end of the container 16 . Blood sample collection in th e 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 portion 24 is cylindrical in the illustrated example, and a hole 29 into which the puncture needle 14 is slidably fitted extends from the front end to a partial depth. Hole 29 does not ext end through front end 24, but a small diameter passageway 30 extends from hole 29 to form an opening 31 at the trailing edge of front end 24. As shown in FIG. A shoulder 33 is formed b etween the hole 29 and the passageway 30 . The puncture needle 14 comes into contact with the shoulder 33 and comes to a predetermined position. After the puncture needle 14 is at a p redetermined 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-outer ribs between the needle shield and the ne edle assembly facilitate attachment and detachment of the needle assembly from the holder 1 9 by the user. An annular flange 32 formed on the front end 24 forms a joining surface for the housing halves. Both parts 24, 25 are secured together using any desired attachment means, such 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 chamber 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 the example shown, the spacing between the lateral holes 48, 49 is greater than the longitudinal 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 hole 49 furthest from the hole 41 in the rear end 25. FIG. The plug 26 is in fluid tight sliding contact 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 construction 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 illustrated 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 chamber 40 . Since only the flange 52 contacts the housing inner wall 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 member 51 made of an impermeable material is combined with an inner space 54 , with openings 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 opening 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 plug. A plurality of openings 59 are formed in the outer wall of outer member 51 as longitudinal slots in the illustrated example. Although four openings 59 are shown in the illustrated example, any desired number may be used. Apertures 59 allow air communication between chamber 40 and interior space 54 .

The second member of combination plug 26 is a generally cylindrical member 60 made of a material that is permeable to gases such as air and impermeable to liquids such as blood. A passageway 61 extends longitudinally through the member 60 and passes through the inner portion 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-fitted within the inner space 54 of the outer member 61 so that the plug 26 is impermeable to fluids such as blood. The member 60 is pushed into the space 54 through the opening 56 using the 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. FIG. 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 inner wall of the housing, and the air permeable member 6 0 is fluid impermeable. Blood in the anterior chamber 40a is visible to the user through the tr ansparent material 42, indicating that the first needle 14 has entered the blood vessel. The th rust 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 towards the tube 16 . Although FIG. 7 shows the cross-bore 48 completely covered b y the sliding of the plug 26, some or all of the cross-bore 48 may be uncovered depending on the vacuum conditions at work. This sliding creates communication between the lateral hole 4 9 and the front portion 40a of the chamber, and blood in the front chamber 40a is free to flow into the second needle 15. As shown in FIG. Blood flows through the second needle into tube 16 and the first needle 14 is withdrawn from the patient when the desired amount of blood sa mple 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 that can be easily installed and entered the vessel upon the first vessel puncture allowing air to escape. I can confirm that. Because this air escape is allowed, blood will immed iately flow into the chamber once the needle punctures the blood vessel, providing a visual in dicator for the user to see that it has entered the blood vessel. Based on this visualization, a b lood collection tube can be attached to facilitate the collection of a blood sample from the pati ent.

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

Inventor(s): JIYOSEFU KOOFUMAN ± (JIYOSEFU KOOFUMAN, ; JOSEFU KOOFUMAN)

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.

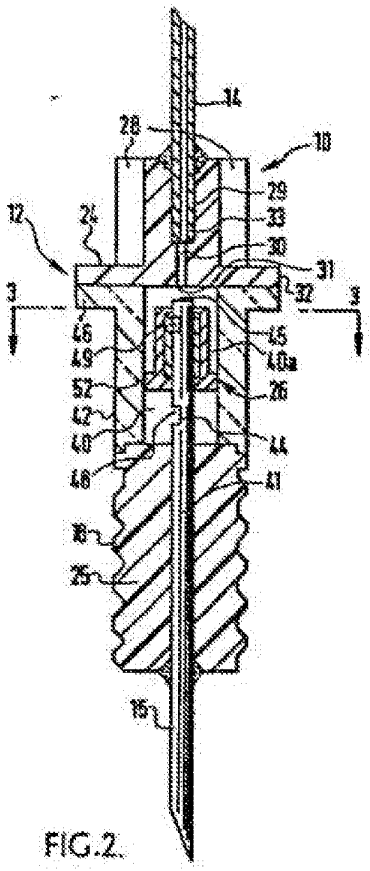

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FIG.2.

⑲ 日本国特許庁（JP）　　⑪ 特許出願公開

⑫ 公開特許公報（A）　　昭57—89869

⑤1Int. Cl.³	識別記号	庁内整理番号	⑬公開　昭和57年(1982)6月4日
A 61 M 5/18		6408—4C	
A 61 B 5/14		6530—4C	発明の数　4
A 61 M 5/32		6408—4C	審査請求　未請求

（全 8 頁）

⑤4単一サンプル針組立体

⑳特　　願　昭56—157375
㉒出　　願　昭56(1981)10月2日
優先権主張　㉜1980年10月12日㉝米国(US)
㉛193054

⑦2発 明 者　ジヨセフ・コーフマン
アメリカ合衆国ニユージヤージー州07630エマーソン・クレスト・ロード10
⑦1出 願 人　ベクトン・デイツキンソン・アンド・カンパニー
アメリカ合衆国ニユージヤージー州07652パラマス・マツク・センター・ドライブ（番地なし）
⑦4代 理 人　弁理士　湯浅恭三　　外2名

明　　細　　書

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を滑動嵌合させる孔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。

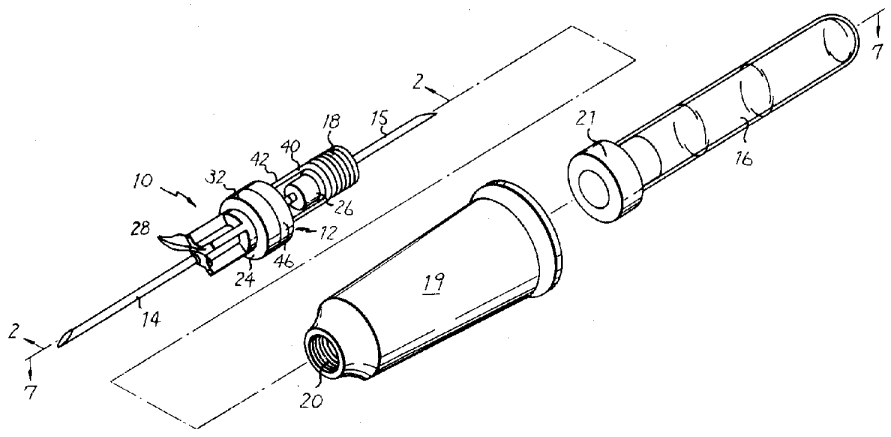
10---針組立体　12---ハウジング
14、15---針　16---真空容器
19---ホルダ　24---前端部
25---後端部　26---プラグ
40---室　44---内方部分
48、49---横孔　51---外側部材
59---開口　60---空気透過部材

特許出願人　ベクトン・ディッキンソン・アンド・カンパニー

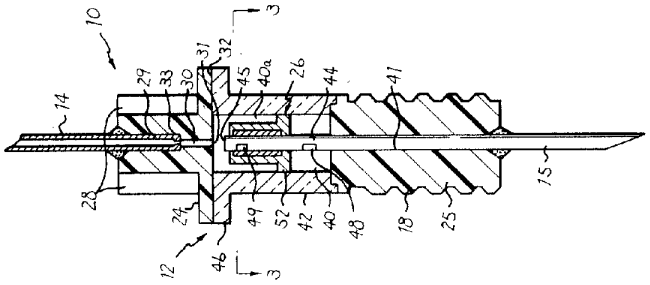
代理人　弁理士　湯浅恭三

（外2名）

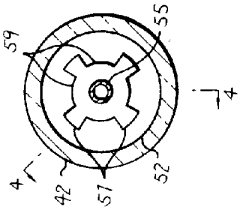
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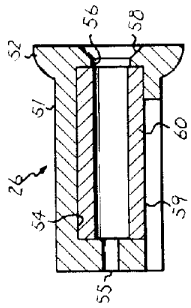
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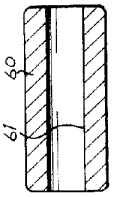
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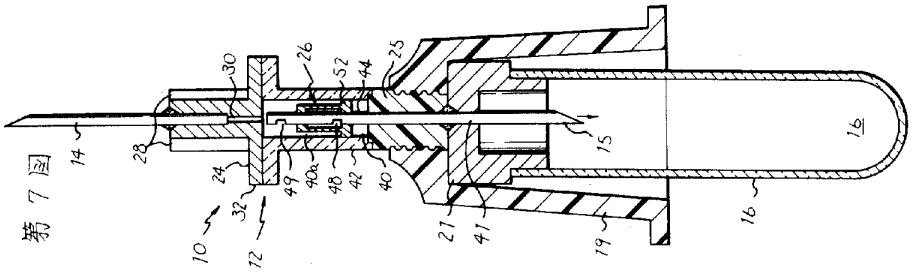
第4図



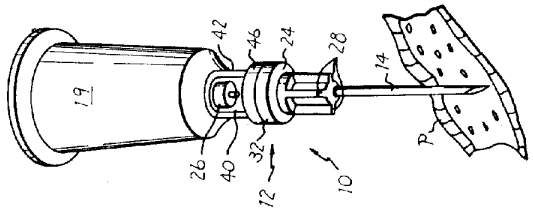
第5図



第7図



第6図



Abstract of DE 29913417 (A1)

Device for taking blood from a blood vessel5 (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, 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) of 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 position into 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]

26 dr Peter Zierden, Rudolf-Harbig-Weg 6
27 D - 40764 Langenfeld
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]

51 D-40239 DÜSSELDORF ;1\1uLVAnYs1iU*£.2 jTELEFON*49 \1Vl / 9*(J 145 -ö TljLEi1AX 49 / 211 / 96 145 - 20

[0009]

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

57 J^LEFflN^V 201 \ 84 2}Q - j FAX 4$y 201 / 84 230 - 20

[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.

(19) BUNDESREPUBLIK DEUTSCHLAND

DEUTSCHES PATENT- UND MARKENAMT

(12) **Gebrauchsmusterschrift**

(10) **DE 299 13 417 U 1**

(51) Int. Cl.[7]:
A 61 B 5/15
A 61 J 1/05

(21) Aktenzeichen: 299 13 417.2
(22) Anmeldetag: 6. 8. 1999
(47) Eintragungstag: 28. 12. 2000
(43) Bekanntmachung im Patentblatt: 1. 2. 2001

DE 299 13 417 U 1

(73) Inhaber:
Zierden, Peter, Dr., 40764 Langenfeld, DE

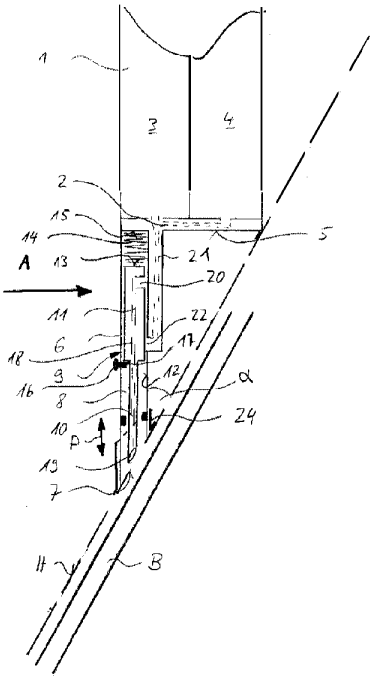
(74) Vertreter:
Palgen und Kollegen, 40239 Düsseldorf

(56) Recherchenergebnisse nach § 7 Abs. 2 GbmG:

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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.



DE 299 13 417 U 1

PALGEN, SCHUMACHER & KLUIN
PATENTANWÄLTE
DÜSSELDORF · ESSEN

UNSER ZEICHEN: 99 328 K/at

Düsseldorf, den 5. August 1999

Dr. Peter Zierden
Rudolf-Harbig-Weg 6

D - 40764 Langenfeld

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.

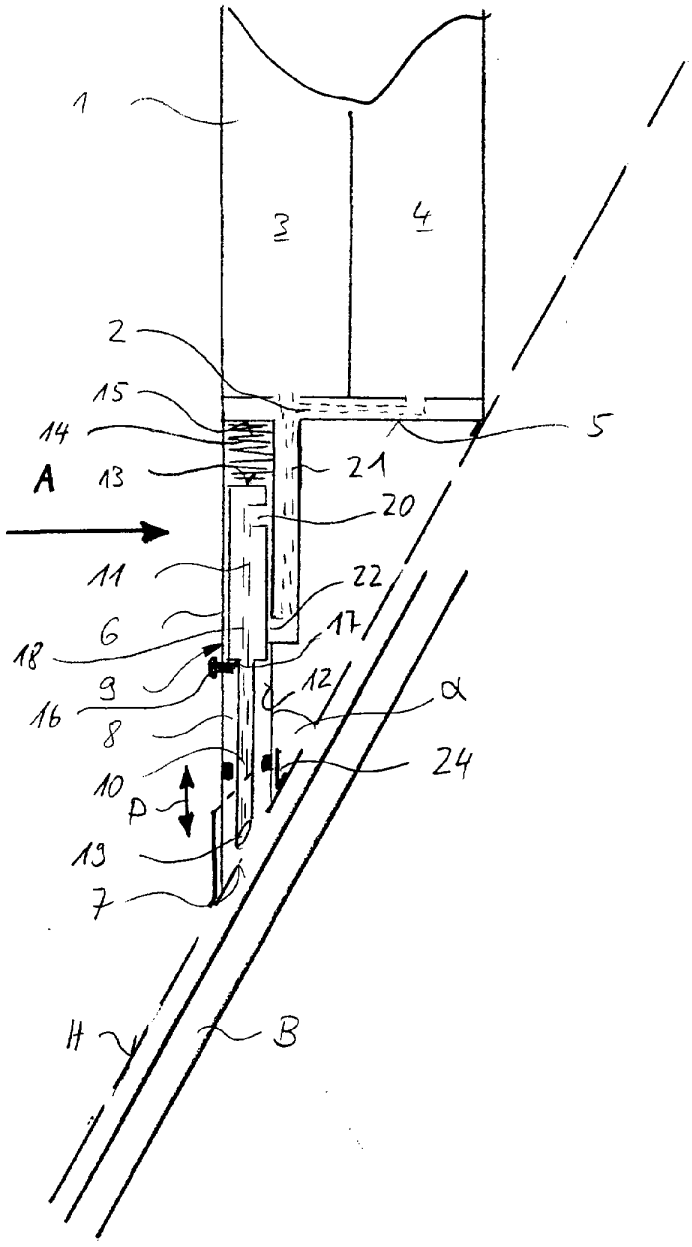
15. Vorrichtung nach einem der Ansprüche 1 bis 14, **dadurch gekennzeichnet**, daß die Vorrichtung eine Mehrzahl von einander getrennter Innenvolumina (3, 4, 28 - 33) zur Aufnahme des entnommenen Bluts umfaßt oder eine Adapteranordnung (39) zum Anschluß mehrerer Behälter zur Aufnahme entnommenen Blutes 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.

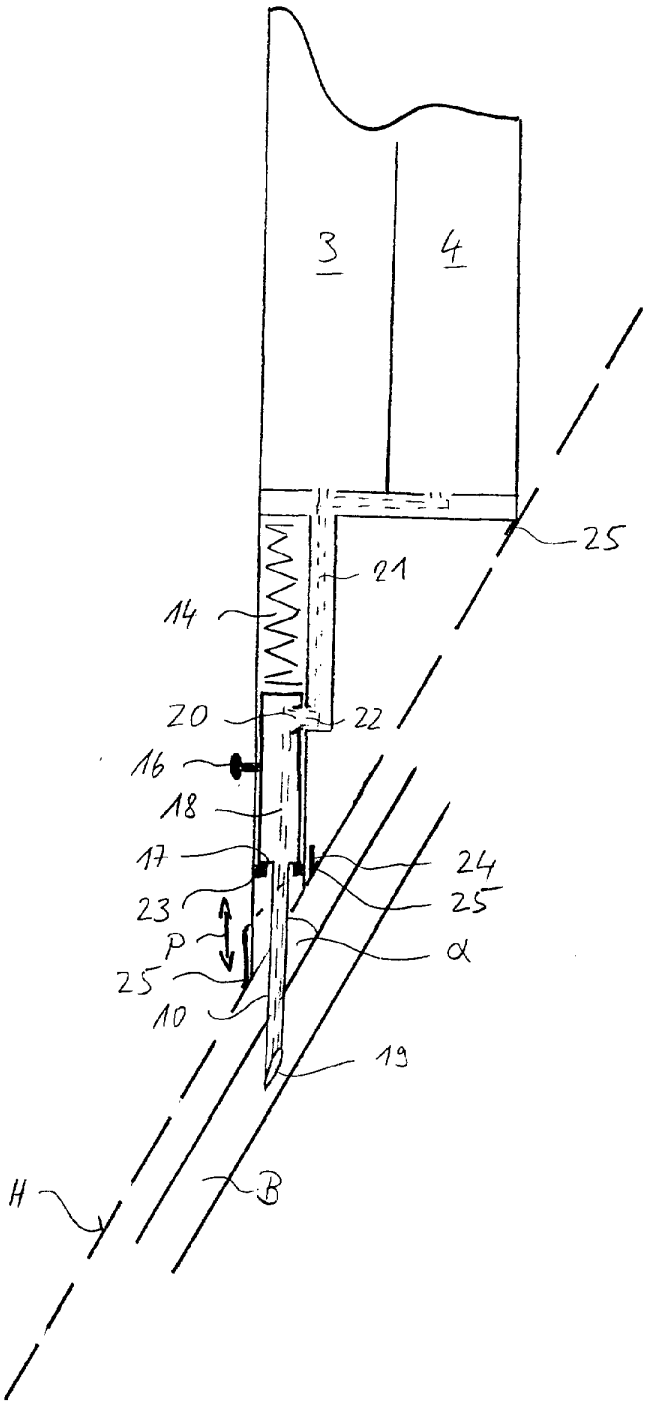
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Fig. 1



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Fig. 2



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Fig.3

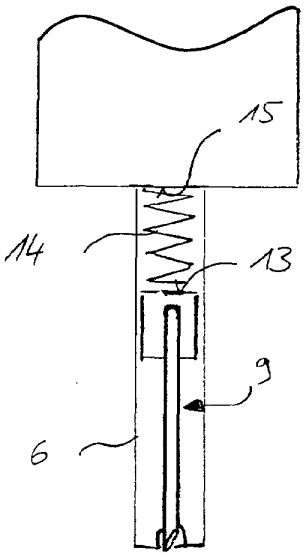
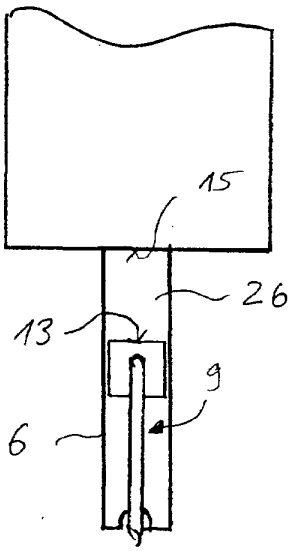


Fig.4



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Fig. 5

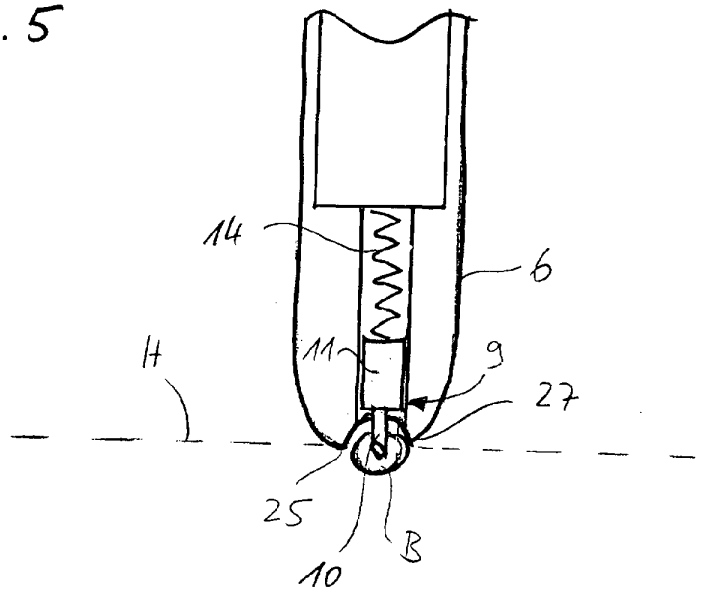
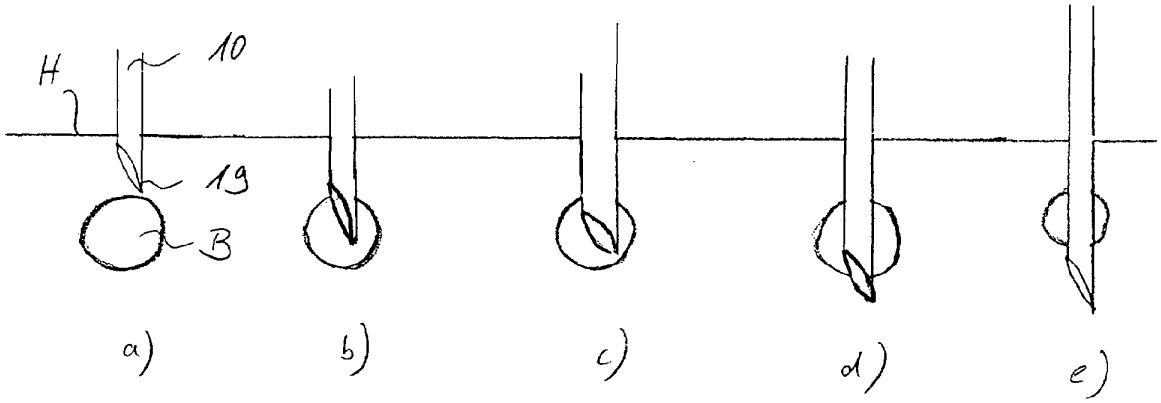


Fig. 6



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Fig. 7

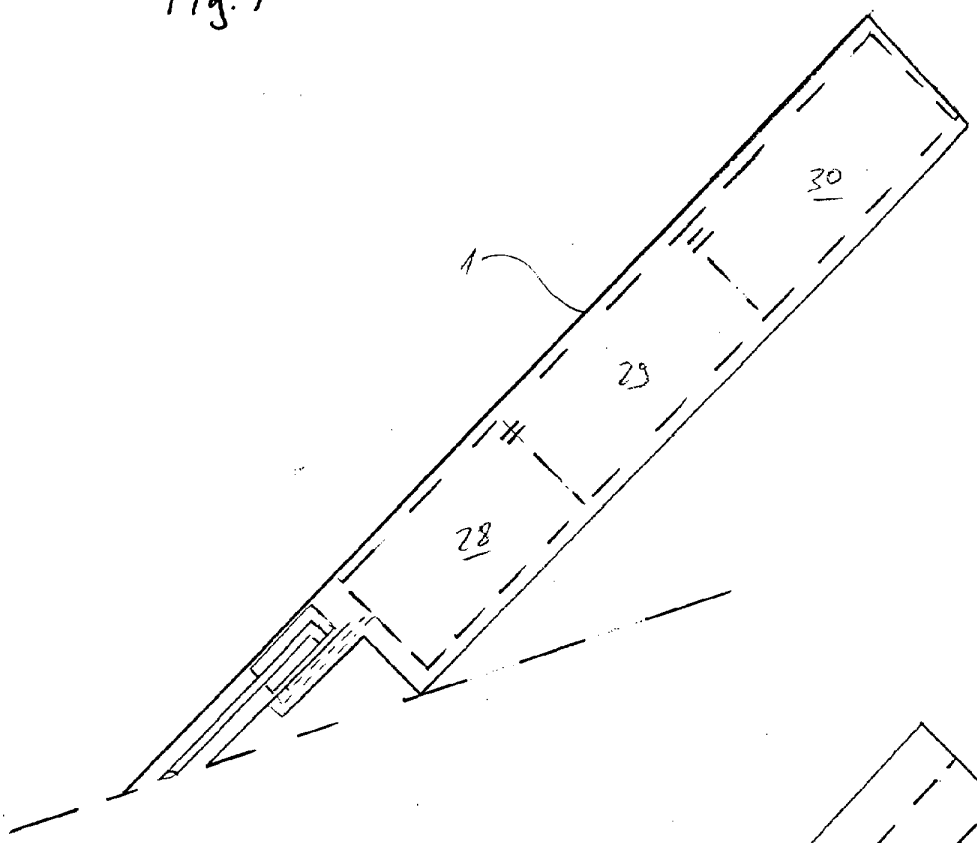
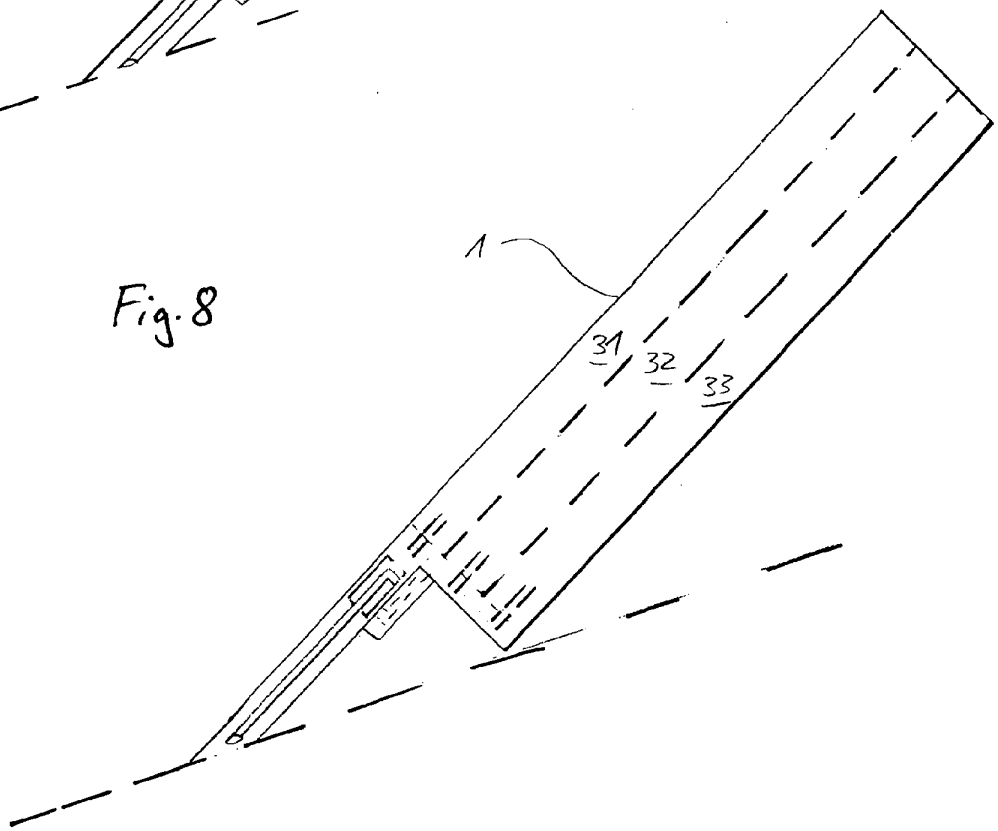
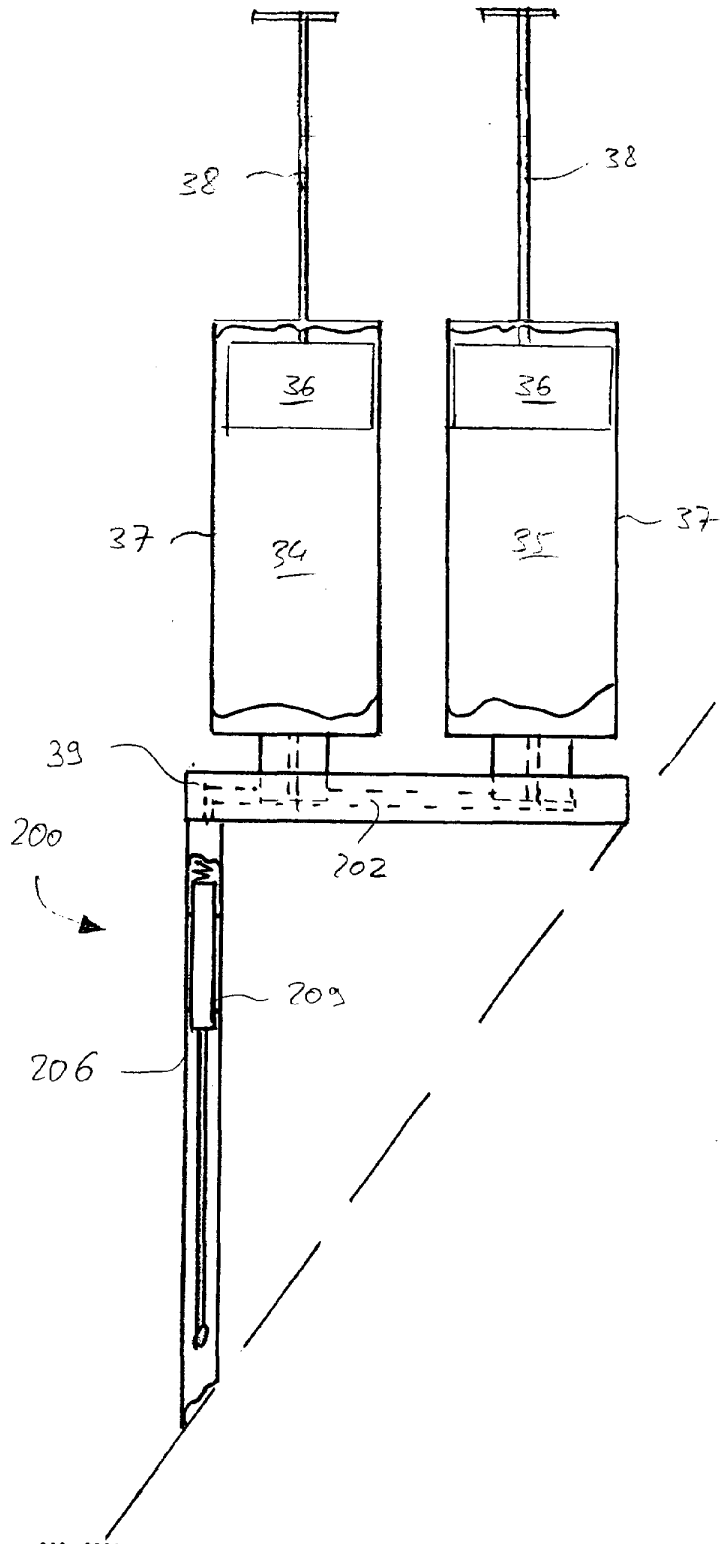


Fig. 8



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Fig. 9



DE 299 13 417 U1

Espacenet

Bibliographic data: DE10134913 (A1) — 2003-02-20

DEVICE AND METHOD FOR PREPARING BLOOD

Inventor(s): ECK MICHAEL [DE] ± (ECK, MICHAEL)

Applicant(s): HIBERNA AG [DE] ± (HIBERNA AG)

Classification: **- international:** ***A61M1/02;*** (IPC1-7): A61J1/00; A61M1/00; A61M1/36; B04B5/04
- cooperative: **A61M1/0209 (EP)**; **A61M1/029 (EP, US)**

Application number: DE20011034913 20010718

Priority number(s): DE20011034913 20010718

Also published as: DE10134913 (C2) AU2002331254 (A1) WO03008012 (A2) WO03008012 (A3) WO03008012 (A8)

Abstract not available for DE10134913 (A1)
Abstract of corresponding document: WO03008012 (A2)

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 DE10134913C2

[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, as well as a preparation station and a method 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. 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]

35 A major problem relates to the handling of the blood bags.

36 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]

48 Further disadvantages result from sterility problems when handling the blood bags.

49 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.

[0005]

56 The conventional blood bag preparation is also problematic because of the risk of mix-ups.

57 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.

[0006]

64 Another disadvantage of the technique described in WO 00/38762 is its specific tailoring to stem cell preparation.

66 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.

[0007]

72 In modern medicine and in civil protection there is an interest in enlarged blood banks with a wide range of different blood types.

74 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.

[0008]

80 The problems illustrated in handling blood samples are not unique to the preparation of preserves for cryopreservation.

82 A corresponding need for sterile, automated and safe sample handling also exists when processing biological cell suspensions for therapeutic purposes.

[0009]

87 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.

90 Furthermore, an improved system for the preparation of cryopreserves such.

91 B. cryopreserved blood can be created, as well as a new method for handling biological suspended samples, which can be automated and carried out safely in particular.

[0010]

96 These objects are achieved with a preparation device, a preparation station and a method having the features according to patent claims 1, 9 and 11.

98 Advantageous embodiments and applications of the invention result from the dependent claims.

[0011]

102 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.

106 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.

109 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.

112 According to a second embodiment, the preparation device comprises a framework into which the chambers can be inserted individually.

114 The connection pieces of the individual chambers are all on one (e.g.

115 B. lower) side of the rack arranged.

116 Depending on requirements, the connecting pieces, which are initially sealed with a septum, are opened and connected in pairs via line connections.

118 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.

121 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.

127 When using the preparation device according to the invention for the production of blood samples for cryopreservation, at least three chambers are preferably provided.

[0012]

132 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.

135 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.

138 A further advantage is the high stability of the preparation device, particularly during centrifugation processes.

[0013]

143 The second and third embodiments of the invention mentioned each represent a modular structure.

145 The chambers can be used as disposable products.

146 An additional advantage is the relatively low weight of the frame construction.

[0014]

150 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.

152 Alternatively, it is possible to transfer the pressure with a mechanically actuated piston (e.g.

153 B. with a connecting rod rod).

154 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.

[0015]

160 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.

162 If non-transparent material is used, the chambers preferably have at least one transparent window for optical detection.

164 A reliable and reproducible optical detection of sample properties, in particular the position of the phase boundary after centrifugation, is made possible.

[0016]

169 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.

[0017]

176 The invention also relates to a method for the preparation of suspensions containing biologically relevant components, such as e.g.

178 B. cells, cell components or macromolecules, using the preparation device according to the invention.

180 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.

[0018]

186 The invention has the following advantages for sample preparation, particularly for the manufacture of cryopreserved blood.

188 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.

191 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.

[0019]

197 The preparation device according to the invention is completely closed off from the outside during the preparation procedure.

199 It only comes into contact with the environment once during filling and emptying.

200 For example, the pre-treatment of a preserve is absolutely sterile until it is ready for freezing.

201 Advantageously, the opening, connecting and closing of bags and connecting tubes according to the conventional systems is avoided.

203 The suspension sample does not leave the preparation device during the preparation steps.

204 A mix-up e.g.

205 B. blood from different donors or contamination by foreign blood or microorganisms are

excluded.

207 The identity of the donor blood is guaranteed.

208 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.

210 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.

[0020]

216 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.

219 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.

222 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.

224 The construction of the device enables a defined positioning of the at least one connecting line.

225 Accidental connection of currently non-cooperating chambers is excluded.

226 Deformation or squeezing of the chambers is avoided according to the invention.

227 a z.

228 B. set by centrifugation phase separation of sample components can not be blurred by a gripping process.

[0021]

233 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.

236 All sensors and actuators are automatically positioned correctly.

237 Increased, error-free throughput is achieved.

238 For example, with a preparation device according to the invention, around three times as many cryopreserves can be prepared per unit of time.

240 The preparation device allows a free choice of material and dimensioning of the outer shape of the chamber arrangement.

242 Advantageously, the device can be readily used with conventional centrifuge equipment.

[0022]

246 By manufacturing the preparation device from inexpensive plastic materials, large numbers of the device can be manufactured using injection molding or extrusion techniques.

248 This is advantageous for the use according to the invention of the solidly walled chambers as disposable products.

[0023]

253 The following additional advantages result in particular in the preparation of blood samples.

254 When using the preparation device according to the invention, there is no significant additional effort for blood donation services.

256 No multiple bag systems are required.

257 The preparation device can be coupled directly to a simple donation bag (single blood bag).

258 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.

261 The preparation device also provides advantages when filling freezing bags after preparation.

262 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.

[0024]

267 Further advantages and details of the invention result from the following description of the accompanying drawings.

269 Show it:

[0025]

273 1 shows a schematic phantom view of an embodiment of a preparation device according to the invention in a partially expanded state,

[0026]

278 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,

[0027]

283 3 shows an enlarged partial view of a chamber end of the preparation device according to FIG. 1,

[0028]

288 4 illustration of a modified embodiment of a preparation device according to the invention,

[0029]

292 5 shows a schematic sectional view of a single chamber used according to the invention, and

[0030]

296 6 shows an illustration of a conventional preparation technique (prior art).

[0031]

300 1 shows an embodiment of a preparation device 100 according to the invention in a schematic phantom view.

302 The preparation device 100 comprises a chamber body 10, in which three chambers for receiving suspension samples are formed, a transmission device 20, consisting of a valve plate 22 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.

306 The chamber body 10 is integrally formed of a transparent plastic material (e.g.

307 B. PMMA, cycloolefin copolymers, polyamide, polycarbonate, PCHP, polyester or polysulfone).

308 It has the external shape of a right circular cylinder with a flat upper side 11 and a flat lower side 12.

310 In the interior of the chamber body 10, the three cylindrical chambers 13, 14 and 15 for receiving samples are formed.

312 At the upper end of the chamber body 10, the chambers open out freely into the top 11.

313 At the lower end, each chamber has a taper 16 with a connecting piece 17, as illustrated in FIG. 3 on an enlarged scale.

315 The connecting piece 17 opens into the underside 12 of the chamber body 10.

[0032]

319 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.

323 A chamber preferably has a volume in the range 400 ml to 600 ml.

324 The chambers 13 to 15 are preferably distributed symmetrically relative to the axis of the chamber body 10 .

[0033]

329 The transfer device 20 is set up to transfer samples between the chambers 13 to 15 .

330 The valve plate 21 is rotatably attached to the bottom 12 of the chamber body 10 .

331 The connecting line 22, which forms an overflow channel, is integrated into the valve plate 21,

which is also made of plastic material.

333 Sealing rings made of an elastic material (e.g.

334 B. PTFE) attached.

335 In addition to the sealing function, the sealing rings (not shown) can also serve as latching devices.

337 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.

[0034]

343 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.

345 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 .

348 This device includes, for example, teeth that prevent reverse rotation and/or an additional locking aid.

[0035]

353 The structure of the valve plate 21 can be modified depending on the application (see FIG. 4).

354 Several connecting lines can be provided.

355 The at least one connecting line can be equipped with a blocking or valve device.

356 Additional through-openings for charging the chambers can preferably be provided in the valve plate.

358 However, loading can also take place from the top.

[0036]

362 Pressure is applied to the samples to transport the samples between the chambers.

363 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.

365 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.

367 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 .

369 The plunger 31 to 33 consist of plastic bodies z.

370 B. in the form of a cylinder, which are fitted in a form-fitting manner into the respective chamber.

372 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.

374 The sealing lips prevent the piston from passing through the liquid samples when pressure is applied.
376 The pistons with the sealing lips are made of a plastic material (e.g.
377 e.g. PTFE).
378 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.
381 After a centrifugation, the phase boundary between the fractions is advantageously avoided.

[0037]

385 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.
387 B. a septum).
388 This allows access to the samples or supplemental liquids in the chambers from the top of the device 100.

[0038]

393 According to a modified embodiment of the invention, the use of the plunger can also be dispensed with.
395 In this case, the transfer pressure is applied directly to the liquid surface in the respective chamber.
397 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.
399 B. air, inert gas) is permeable.
400 The structure without a plunger has the advantages of an increased internal volume and a simplified structure of the chambers and thus cost savings.

[0039]

405 The upper cover plate 40 serves to close off the preparation device 100.
406 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.
408 The connecting pieces 41 serve to connect individual chambers or all chambers at the same time to the pressure device and/or charging devices.

[0040]

413 The process sequence for producing a blood cryopreservation using a preparation device according to the invention is explained below with reference to FIG.
415 FIG. 2 shows the preparation device 100 analogous to the representation according to FIG. 1 in

combination with parts of the preparation station.

[0041]

420 The components of the preparation device 100 are provided with the same reference symbols as in FIG. 1 .

[0042]

425 The preparation station includes, in particular, the printing device 50, a detector device 60, an actuating device 70 and a control device 80.

427 The pressure device 50 preferably comprises a pressure generator 51 with a motor 52 and a pump part 53.

429 Alternatively, the pressure device 50 comprises a lever device with a connecting rod.

430 The mechanical power transmission has the advantage that the positioning of the plunger can be done with increased precision.

432 According to alternative embodiments of the invention, the pressure generator can also be supplied by a pressure source (e.g.

434 B. compressed gas cylinder) are formed with a control valve.

[0043]

438 The detector device 60 comprises, in particular, at least one light-sensitive element 61 for detecting the phase boundary.

440 Depending on the application, the light-sensitive element 61 can be equipped with filter devices (not shown).

442 A plurality of light-sensitive elements can also be arranged corresponding to the positions of the chambers.

444 Depending on the application, other detectors for detecting sample properties can also be provided, as are known from analytics (e.g.

446 B. spectrophotometer, resistivity meter for density determination).

447 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.

449 The detectors can also be attached to other components of the preparation device, e.g.

450 B. be provided on a connecting line in the valve plate.

[0044]

454 To adjust the valve plate 21 explained above, the adjusting device 70 comprises an actuating element 71 and a servomotor 72.

456 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.

459 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.

[0045]

465 The control device 80 is connected to the components 50, 60 and 70 of the preparation system.

466 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.

468 In the case of semi-automatic or manual operation, the corresponding steps are at least partially carried out by an operator.

[0046]

473 In a starting state, the chambers of the preparation device 100 according to the invention are loaded as follows.

475 In the first chamber 13 there is a blood donation.

476 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.

478 The second chamber 14 is filled with a wash solution.

479 A cryoadditive is located in the third chamber 15 .

480 In the starting state, the first chamber 13 is completely filled, while the remaining chambers 14, 15 are only partially filled.

482 There is as much free volume in these chambers as is required to take over the erythrocyte suspension after centrifugation (see below).

484 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.

486 Advantageously, there is essentially no liquid exchange via the connecting line despite the connection in the pressure-free state.

[0047]

491 In a first preparation step, the chamber body with the filled chambers is centrifuged using a centrifugation device.

493 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.

496 During centrifugation, the blood donation is only separated into fractions.

497 The plungers 31 to 33 are not shifted.

498 The chambers are sealed during centrifugation.

[0048]

502 The state of the preparation device after centrifugation is shown in FIG.

503 In the first chamber 13, the formed fractions of the blood donation with the erythrocyte sediment 1 of the so-called

505 "Buffy Coat" layer 2 and the plasma supernatant 3 illustrated.

506 Depending on the operation, the erythrocyte sediment 1 comprises a volume proportion of approx. 45% of the chamber 13.

508 The volume fraction depends in particular on the centrifugation speed.

509 A higher speed results in a higher packing density of the erythrocytes and thus a lower volume fraction.

511 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.

[0049]

517 After the centrifugation, the preparation device 100 is inserted into the preparation station.

518 The valve plate 21 is rotated between the first and second chambers 13, 14 in the passage direction.

520 This is done manually, e.g.

521 B. with a knob wrench or with the adjusting device 70 (see above).

522 The first chamber 13 is pressurized.

523 Under the action of hydrostatic or mechanical pressure, the plunger 31 moves downwards and the plunger 32 moves upwards.

525 The separated blood donation is transferred to the second chamber 14 .

526 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 .

528 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.

530 When the buffy coat layer 2 has been detected, the print transfer is stopped.

531 Then the valve plate is brought into the closed position.

532 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.

[0050]

537 The erythrocytes transferred to the second chamber 14 mix with the washing solution.

538 The washing solution includes, for example, physiological saline.

539 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.

[0051]

545 In a further preparation step, the washed erythrocyte sediment is transferred to the third chamber 15 analogously to the manner described.

547 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 .

549 In addition, the pressure distributor 56 is adjusted accordingly.

550 The pressure transmission is in turn controlled as a function of the detector signal from the detector device 60 .

552 A further sensor (not shown) can be provided on the second chamber 14 .

553 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.

[0052]

558 After the washed erythrocyte sediment has been transferred to the third chamber 15, it is mixed with the cryoadditive there.

560 The additives known per se are used as cryoadditive.

561 For example, the cryoadditive comprises a solution of water-soluble starch derivative.

[0053]

565 After the washed erythrocytes have been transferred to the third chamber 15 and mixed with the cryoadditive, the cryopreserve is ready to be frozen.

567 This is followed by the transfer to the container selected depending on the application, e.g.

568 B. a cryobag in which the freezing process takes place.

569 After completion of the preparation, the plasma supernatant is advantageously present in the first chamber 13 as a donor-specific residual product.

571 Depending on the application, the plasma can be used for other purposes.

[0054]

575 Details of a design of the preparation device according to the invention that is modified compared to FIG. 1 are shown in FIG.

577 The differences relate to the design of the valve plate 21.

578 The lower side 12 of the chamber body 10 with the chambers 13 to 15 is illustrated in the top partial image of FIG.

580 Each chamber has an inlet and outlet opening in the form of a connecting piece 17 (see FIG. 3).

582 An O-ring seal 18 is provided on each connecting piece 17 .

583 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.

[0055]

588 In the middle part of Fig. 4, the valve plate 21 is shown individually.

589 In this design, two connecting lines (or overflow channels) 22, 23 are provided, which are arranged in such a way 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.

592 The use of two connecting lines has the advantage of shorter adjustment paths when setting the chamber connections in the individual preparation steps.

594 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.

[0056]

600 The valve plate 21 has a circumferential O-ring 25 which provides an additional seal against the underside 12 of the chamber body 10.

602 The reference number 26 refers to the axis of rotation and the bearing of the valve plate 21.

[0057]

606 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.

608 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.

611 The two preparation steps explained above can thus be carried out with a short travel distance.

[0058]

615 The embodiment of the invention illustrated in FIGS. 1 to 4 can be modified in many ways depending on the task at hand.

617 For example, further chambers for accommodating further additives can be provided in the chamber body in order to carry out further preparation steps.

619 Instead of the 120° arrangement, the chambers can also be arranged differently in the chamber body or a frame (see below).

621 Depending on the application, the chambers can be loaded from the top or bottom.

622 This is preferably done using tubing or pipetting systems.

623 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.

626 Depending on the application, the size of the preparation device can be scaled as desired.
627 The transmission device with the valve plate can be replaced by a fixed arrangement of several connecting lines with valves that can be actuated.

[0059]
632 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.

[0060]
637 According to the invention, the chamber body with the integrated chambers can be replaced by an arrangement of individual chambers in a frame.
639 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.
641 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.
644 Depending on the design of the chambers, the structure of the frame is adjusted.

[0061]
648 If ready-made plunger syringes with suitable plunger diameters are used as chambers, then the frame has recesses to accommodate the syringe plunger.
650 If the individual chambers are formed by straight tubular bodies, the recesses in the framework are adjusted accordingly.
652 If necessary, conically preformed chamber floors are provided on the floor of the framework, as illustrated in FIG.

[0062]
657 5 shows a single chamber in a schematic sectional view.
658 Two or more such individual chambers (e.g.
659 B. according to the above design three individual chambers) are provided on a frame (not shown).
661 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.
664 Inside the single chamber 90 is the plunger (see above).
665 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.
667 The stamp plate 94 consists of PMMA, for example. The sealing ring 97 is a z.

668 B. made of PTFE molded part that is pulled positively over the outer edge of the stamp plate 94.

670 The cross section of the sealing ring 97 has a U-shape, the open ends of which form two sealing lips.

672 This shape ensures that the sealing lips lie tightly against the chamber wall.

673 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.

[0063]

678 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.

681 The partial area 92 delimits a partial volume of approximately 30 ml.

[0064]

685 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.

688 The individual chamber of interest (e.g.

689 B. according to FIG. 5) removed from the frame and centrifuged separately.

690 Before or after centrifugation, the individual chamber is arranged in the frame for carrying out the remaining steps of sample preparation.

692 This method is particularly advantageous if no suitable centrifuge is available for centrifugation.

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CLAIMS DE10134913C2

1.

13 Preparation device (100) for the treatment of suspension samples, in particular for the preparation of cryopreserved blood, with an arrangement of at least two containers for receiving the suspension samples, sample parts and/or additives, characterized in that the containers as chambers (13 to 15, 90) are formed with solid walls and are arranged stationary relative to each other and a transmission device (20) is provided with at least one connecting line (22) via which the chambers (13 to 15) can be connected to one another.

2.

22 Preparation device according to Claim 1, characterized in that the chambers (13 to 15) are formed in a one-piece chamber body (10).

3.

27 Preparation device according to Claim 1, characterized in that the chambers (90) are detachably fastened as individual chambers in a framework.

4.

32 Preparation device according to one of the preceding claims, characterized in that the walls of the chambers or the chamber bodies (10) consist of a transparent material.

5.

37 Preparation device according to one of the preceding claims 1 or 2, characterized in that 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), with the underside (12) of 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, characterized in that a pressure plunger (31 to 33) is provided in each chamber.

7.

50 Preparation device according to Claim 6, characterized in that each pressure plunger (31 to 33) has a circumferential sealing lip.

8.

55 Preparation device according to one of the preceding claims, characterized in that 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 rotatably arranged.

9.

61 Preparation station for the preparation of suspension samples, having: at least one preparation device (100) according to one of the preceding claims, a pressure device (50) which is set up to generate an overpressure or underpressure in one of the chambers (13 to 15), a detector device (60) for detecting a phase boundary in one of the chambers (13 to 15), an actuating device (70) which has an actuating element (71) with which the transmission device (20) can be adjusted in such a way that two chambers each via the at least one connecting line (22) and a control device which is connected to the printing device (50), the detector device (60) and the actuating device (70) and for actuating the printing device (50) and the actuating device (70) as a function of a detector signal from the detector device (60) is established.

10.

73 Preparation station according to Claim 9, characterized in that the pressure device (50) has a pneumatic pressure generator or a mechanical pressure generator with connecting rods.

11.

78 Method for preparing suspension samples or cryopreserved blood using a preparation device (100) according to one of Claims 1 to 8, characterized in that a treatment of a sample in at least

one of the chambers (13 to 15, 90) and a transfer at least part of the sample between two chambers.

12.

Method according to Claim 11, characterized in that the sample treatment comprises centrifugation of the sample and/or treatment of the sample with additives.

13.

Method according to Claim 12, characterized in that the entire preparation device (100) or an individual chamber (90) is centrifuged during the centrifugation of the sample.

(19) BUNDESREPUBLIK DEUTSCHLAND

DEUTSCHES PATENT- UND MARKENAMT

(12) **Patentschrift**

(10) **DE 101 34 913 C 2**

(51) Int. Cl.[7]:
A 61 M 1/00
A 61 M 1/36
A 61 J 1/00
B 04 B 5/04

(21) Aktenzeichen: 101 34 913.0-35
(22) Anmeldetag: 18. 7. 2001
(43) Offenlegungstag: 20. 2. 2003
(45) Veröffentlichungstag der Patenterteilung: 26. 6. 2003

Innerhalb von 3 Monaten nach Veröffentlichung der Erteilung kann Einspruch erhoben werden

(73) Patentinhaber:
Hiberna AG, 97232 Giebelstadt, DE

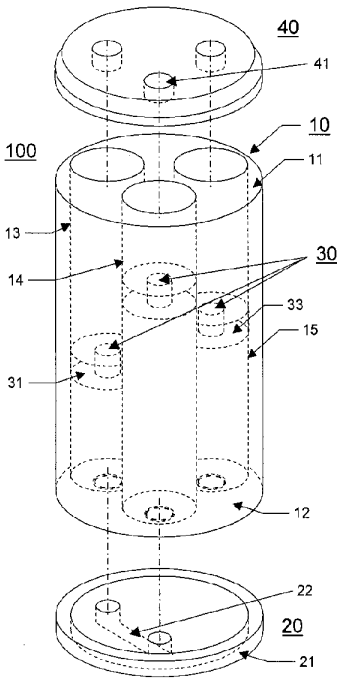
(74) Vertreter:
v. Bezold & Sozien, 80799 München

(72) Erfinder:
Eck, Michael, 97074 Würzburg, DE

(56) Für die Beurteilung der Patentfähigkeit in Betracht gezogene Druckschriften:
DE 298 05 538 U1
WO 00 38 762

(54) Vorrichtung und Verfahren zur Blutpräparation

(57) Präparationsvorrichtung (100) zur Behandlung von Suspensionsproben, insbesondere zur Präparation von Blut-Kryokonserven, mit einer Anordnung von mindestens zwei Behältnissen zur Aufnahme der Suspensionsproben, von Probenteilen und/oder von Zusatzstoffen, dadurch gekennzeichnet, dass die Behältnisse als Kammern (13 bis 15, 90) mit festen Wänden gebildet und relativ zueinander ortsfest angeordnet sind und eine Übertragungseinrichtung (20) mit mindestens einer Verbindungsleitung (22) vorgesehen ist, über die die Kammern (13 bis 15) miteinander verbindbar sind.



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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 sowie eine Präparationsstation und ein 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.

[0005] 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.

[0006] 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.

[0007] 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.

[0008] 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 Zellsuspensionen für therapeutische Zwecke.

[0009] Die Aufgabe der Erfindung ist es, eine verbesserte Vorrichtung zur Präparation suspendierter biologischer Proben bereitzustellen, mit der die Nachteile herkömmlicher Systeme überwunden werden und die insbesondere für eine automatisierbare und sichere Handhabung einer Vielzahl von Proben geeignet ist. Ferner soll ein verbessertes System zur Präparation von Kryokonserven, wie z. B. Blut-Kryokonserven geschaffen werden sowie ein neuartiges Verfahren zur Handhabung biologischer suspendierter Proben, das insbesondere automatisierbar und sicher durchführbar ist.

[0010] Diese Aufgaben werden mit einer Präparationsvorrichtung, eine Präparationsstation und einem Verfahren mit den Merkmalen gemäß den Patentansprüchen 1, 9 und 11 gelöst. Vorteilhafte Ausführungsformen und Anwendungen der Erfindung ergeben sich aus den abhängigen Ansprüchen.

[0011] 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 Herstellung von Blutproben für die Kryokonservierung sind

vorzugsweise mindestens drei Kammern vorgesehen.

[0012] 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.

[0013] 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.

[0014] 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.

[0015] 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.

[0016] 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.

[0017] 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.

[0018] 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.

[0019] 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.

[0020] 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.

[0021] 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.

[0022] 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.

[0023] 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.

[0024] Weitere Vorteile und Einzelheiten der Erfindung ergeben sich aus der folgenden Beschreibung der beigefügten Zeichnungen. Es zeigen:

[0025] **Fig.** 1 eine schematische Phantomansicht einer Ausführungsform einer erfindungsgemäßen Präparationsvorrichtung in teilweise auseinander gezogenem Zustand,

[0026] **Fig.** 2 eine Illustration der Einbindung der Präparationsvorrichtung gemäß **Fig.** 1 in eine Vorrichtung zur Herstellung von Blutkonserven,

[0027] **Fig.** 3 eine vergrößerte Teilansicht eines Kammerendes der Präparationsvorrichtung gemäß **Fig.** 1,

[0028] **Fig.** 4 Illustration einer abgewandelten Ausführungsform einer erfindungsgemäßen Präparationsvorrichtung,

[0029] **Fig.** 5 eine schematische Schnittansicht einer erfindungsgemäß verwendeten Einzelkammer, und

[0030] **Fig.** 6 eine Illustration einer herkömmlichen Präparationstechnik (Stand der Technik).

[0031] 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 **22** 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**.

[0032] 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.

[0033] 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.

[0034] 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.

[0035] 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 Beschickung kann aber auch von der oberen Seite her erfolgen.

[0036] 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.

[0037] 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.

[0038] 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.

[0039] 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.

[0040] 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.

[0041] Die Komponenten der Präparationsvorrichtung **100** sind mit den gleichen Bezugszeichen wie in **Fig.** 1 versehen.

[0042] 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.

[0043] 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.

[0044] 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.

[0045] 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.

[0046] 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.

[0047] 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.

[0048] 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.

[0049] 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.

[0050] Die in die zweite Kammer **14** übertragenen Erythrozyten vermengen sich mit der Waschlösung. Die Wasch-

lösung 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.

[0051] 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.

[0052] 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.

[0053] 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.

[0054] 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**.

[0055] 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.

[0056] 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**.

[0057] 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.

[0058] 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.

[0059] An der Außenseite des Kammerkörpers können zusätzliche Greif- oder Befestigungseinrichtungen zur Handhabung des Kammerkörpers und/oder zum Einsatz in eine Zentrifuge vorgesehen sein.

[0060] 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.

[0061] 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.

[0062] **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.

[0063] 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.

[0064] 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.

Patentansprüche

1. Präparationsvorrichtung (**100**) zur Behandlung von Suspensionsproben, insbesondere zur Präparation von Blut-Kryokonserven, mit einer Anordnung von mindestens zwei Behältnissen zur Aufnahme der Suspensionsproben, von Probenteilen und/oder von Zusatzstoffen, **dadurch gekennzeichnet**, dass die Behältnisse als Kammern (**13** bis **15**, **90**) mit festen Wänden gebildet und relativ zueinander ortsfest angeordnet sind und eine Übertragungseinrichtung (**20**) mit mindestens einer Verbindungsleitung (**22**) vorgesehen ist, über die die Kammern (**13** bis **15**) miteinander verbindbar sind.

2. Präparationsvorrichtung nach Anspruch 1, dadurch gekennzeichnet, dass die Kammern (**13** bis **15**) in einem einstückigen Kammerkörper (**10**) gebildet sind.

3. Präparationsvorrichtung nach Anspruch 1, dadurch gekennzeichnet, dass die Kammern (**90**) als Einzelkammern lösbar in einem Rahmengestell befestigt sind.

4. Präparationsvorrichtung nach einem der vorhergehenden Ansprüche, dadurch gekennzeichnet, dass die Wände der Kammern oder der Kammerkörper (**10**) aus einem transparenten Material bestehen.

5. Präparationsvorrichtung nach einem der vorhergehenden Ansprüche 1 oder 2, dadurch gekennzeichnet, dass 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 nach einem der vorhergehenden Ansprüche, dadurch gekennzeichnet, dass in jeder Kammer ein Druckstempel (**31** bis **33**) vorgesehen ist.

7. Präparationsvorrichtung nach Anspruch 6, dadurch gekennzeichnet, dass jeder Druckstempel (**31** bis **33**) eine umlaufende Dichtlippe aufweist.

8. Präparationsvorrichtung nach einem der vorhergehenden Ansprüche, dadurch gekennzeichnet, dass die Übertragungseinrichtung (**20**) durch eine Ventilplatte (**21**) gebildet ist, in der mindestens eine Verbindungsleitung (**22**) integriert ist, wobei die Ventilplatte (**21**) verdrehbar angeordnet ist.

9. Präparationsstation zur Präparation von Suspensionsproben, mit:
mindestens einer Präparationsvorrichtung (**100**) nach einem der vorhergehenden Ansprüche,
einer Druckeinrichtung (**50**), die zur Erzeugung eines Über- oder Unterdruckes in einer der Kammern (**13** bis **15**) eingerichtet ist,
einer Detektoreinrichtung (**60**) zur Erkennung einer Phasengrenze in einer der Kammern (**13** bis **15**),
einer Stelleinrichtung (**70**), die ein Betätigungselement (**71**) aufweist, mit dem die Übertragungseinrichtung (**20**) derart einstellbar ist, dass jeweils zwei Kammern über die mindestens eine Verbindungsleitung (**22**) verbunden sind, und
einer Steuereinrichtung, die mit der Druckeinrichtung (**50**), der Detektoreinrichtung (**60**) und der Stelleinrichtung (**70**) verbunden und zur Betätigung der Druckeinrichtung (**50**) und der Stelleinrichtung (**70**) in Abhängigkeit von einem Detektorsignal der Detektoreinrichtung (**60**) eingerichtet ist.

10. Präparationsstation nach Anspruch 9, dadurch gekennzeichnet, dass die Druckeinrichtung (**50**) einen pneumatischen Druckerzeuger oder einen mechanischen Druckerzeuger mit Pleuelstangen aufweist.

11. Verfahren zum Präparieren von Suspensionsproben oder von Blut-Kryokonserven unter Verwendung einer Präparationsvorrichtung (**100**) nach einem der Ansprüche 1 bis 8, dadurch gekennzeichnet, dass 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.

12. Verfahren nach Anspruch 11, dadurch gekennzeichnet, dass die Probenbehandlung eine Zentrifugation der Probe und/oder eine Behandlung der Probe mit Zusatzstoffen umfasst.

13. Verfahren nach Anspruch 12, dadurch gekennzeichnet, dass bei der Zentifugation der Probe die gesamte Präparationsvorrichtung (**100**) oder eine Einzelkammer (**90**) zentrifugiert wird.

Hierzu 5 Seite(n) Zeichnungen

Nummer: **DE 101 34 913 C2**
Int. Cl.[7]: **A 61 M 1/00**
Veröffentlichungstag: 26. Juni 2003

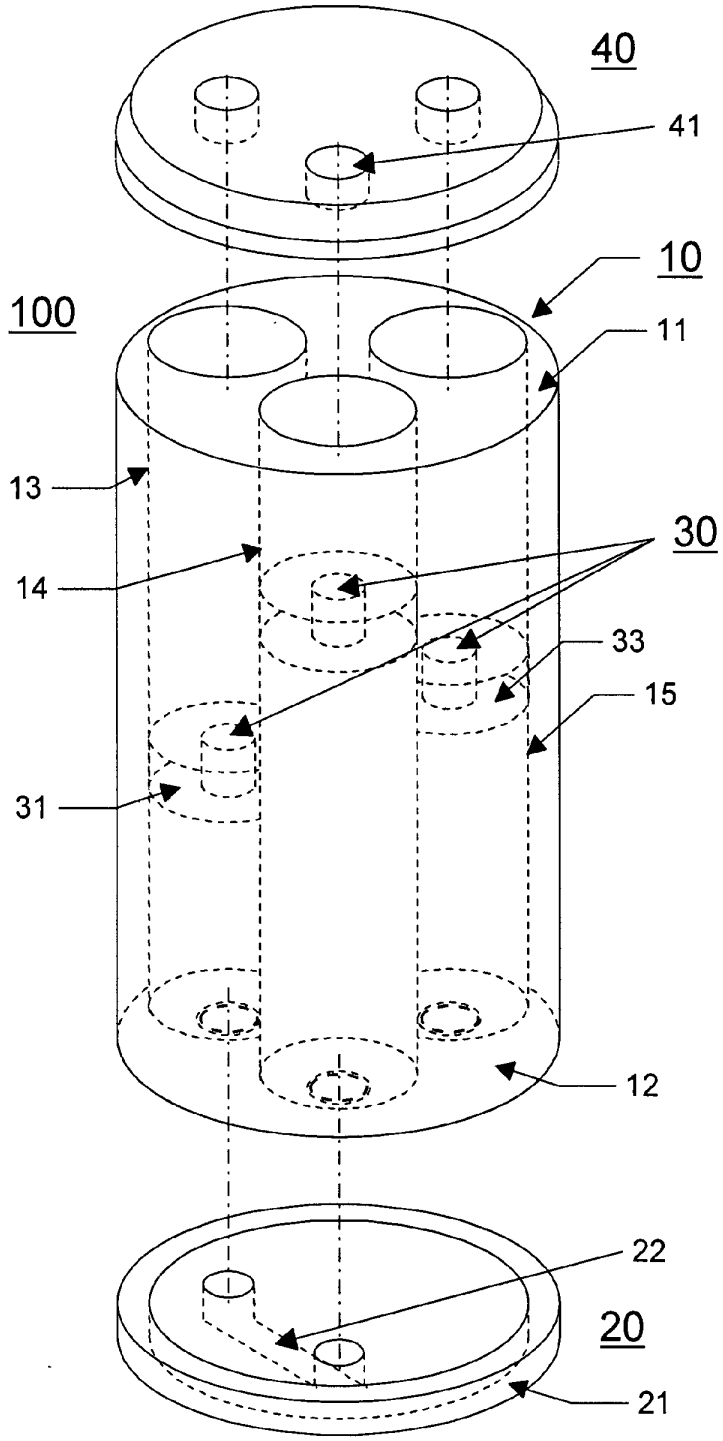


Fig. 1

Nummer: DE 101 34 913 C2
Int. Cl.[7]: A 61 M 1/00
Veröffentlichungstag: 26. Juni 2003

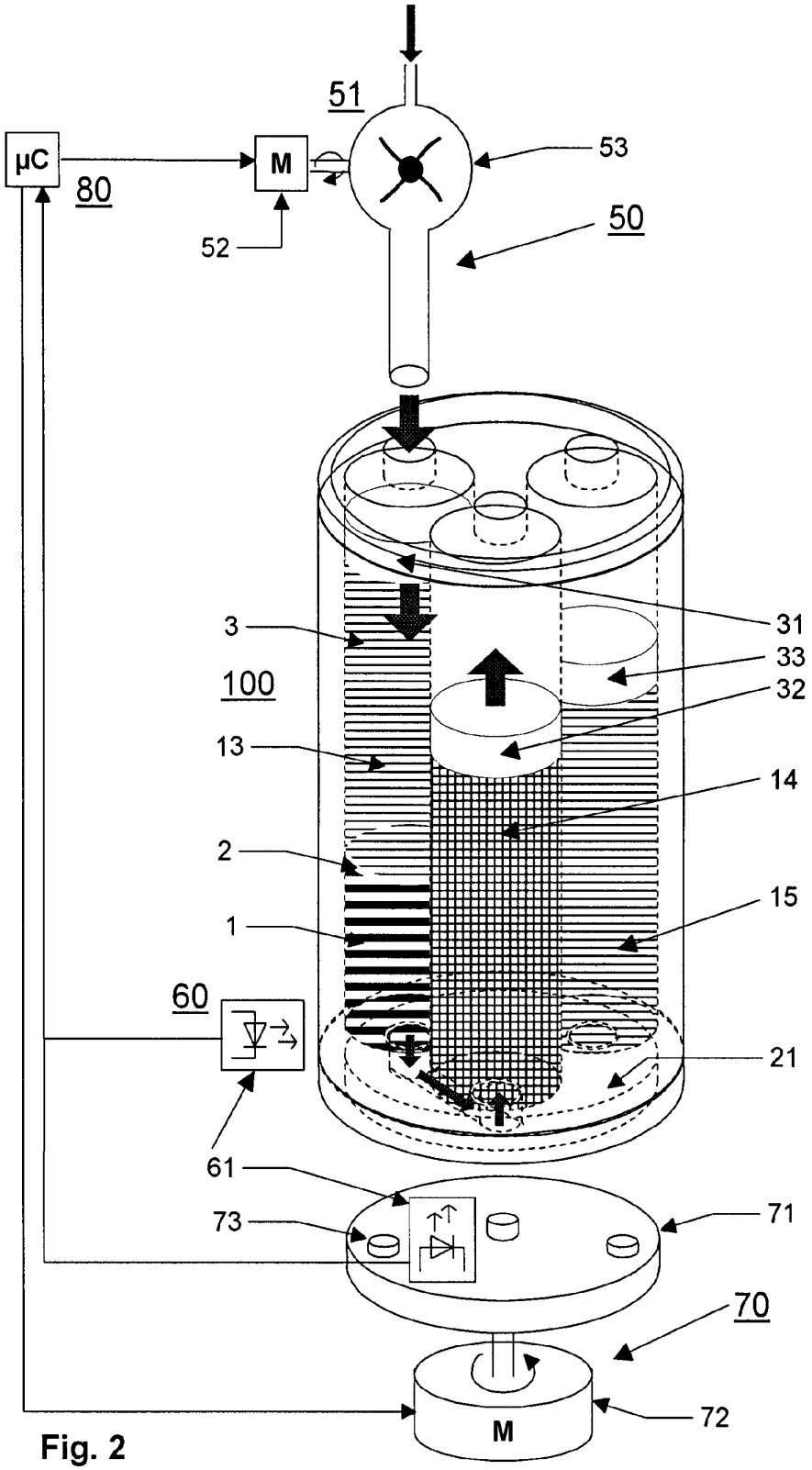


Fig. 2

Nummer: DE 101 34 913 C2
Int. Cl.[7]: A 61 M 1/00
Veröffentlichungstag: 26. Juni 2003

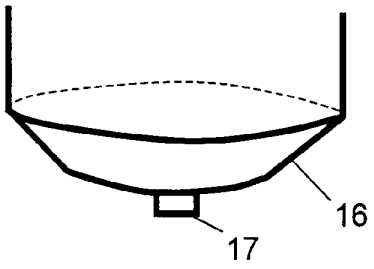


Fig. 3

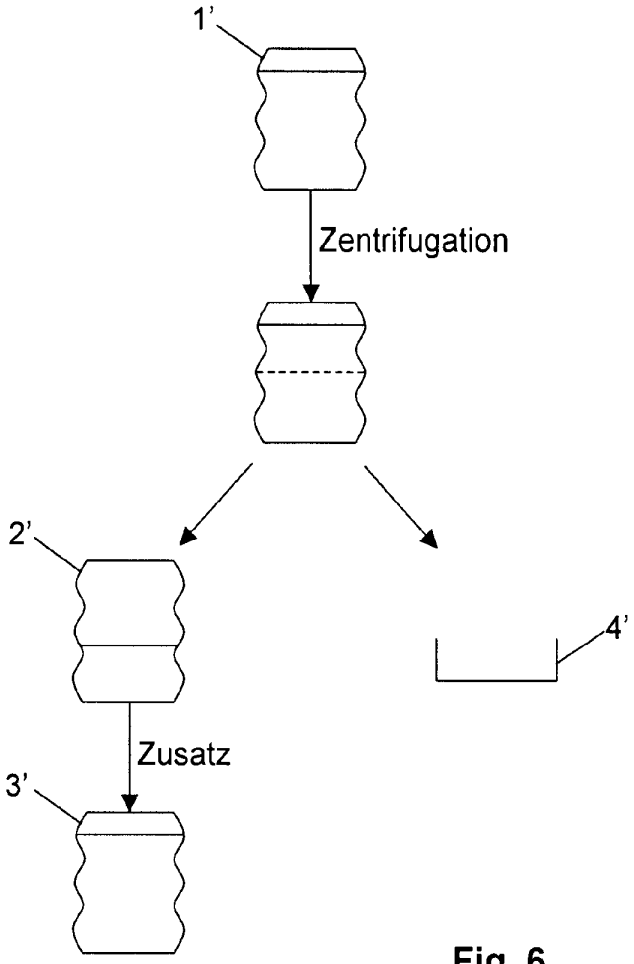
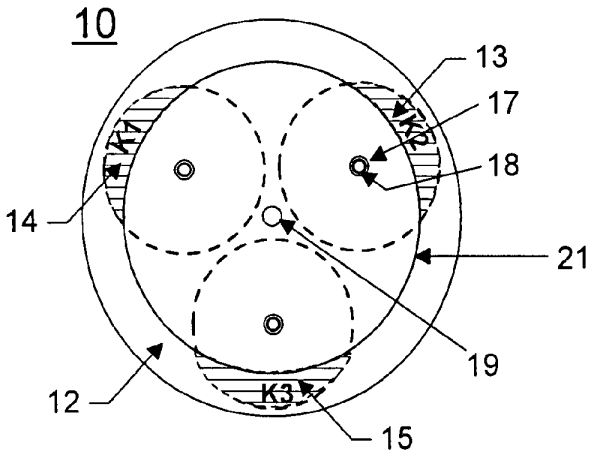
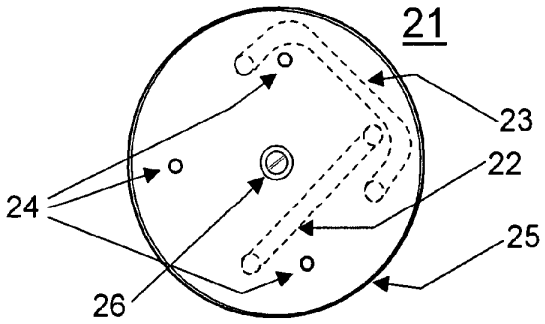


Fig. 6
(Stand der Technik)

Nummer: **DE 101 34 913 C2**
Int. Cl.[7]: **A 61 M 1/00**
Veröffentlichungstag: 26. Juni 2003





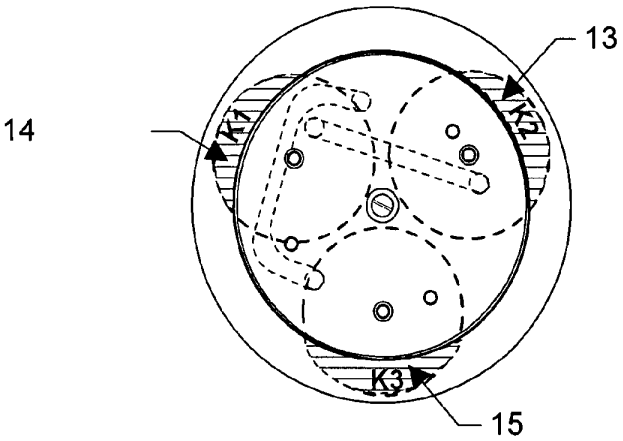


Fig. 4

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Nummer: **DE 101 34 913 C2**
Int. Cl.[7]: **A 61 M 1/00**
Veröffentlichungstag: 26. Juni 2003

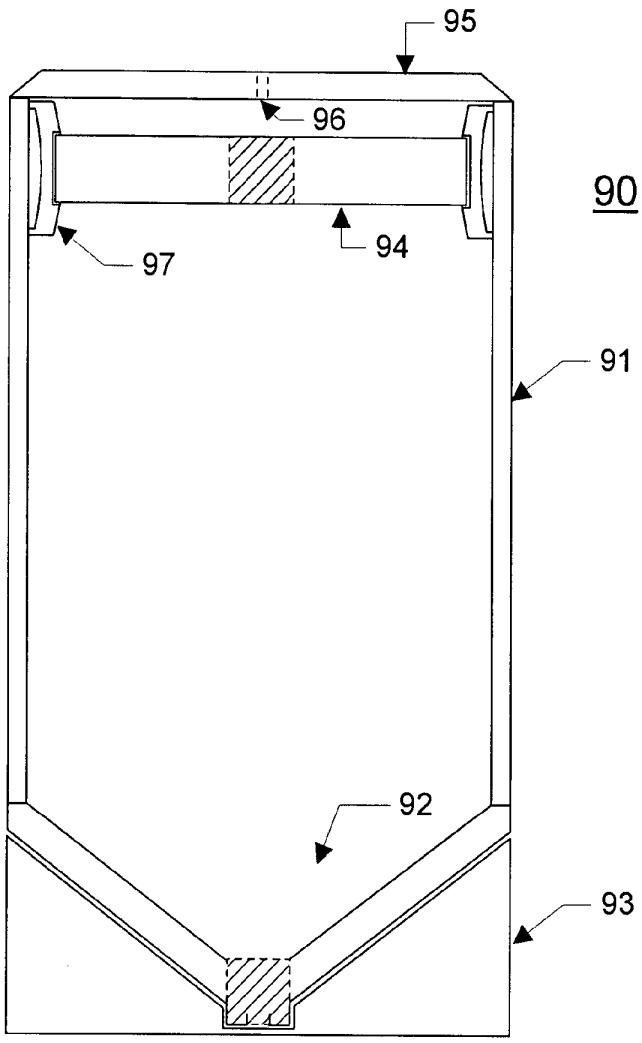


Fig. 5

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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 5 :		(11) International Publication Number:	WO 92/16144
A61B 5/14	A1	(43) International Publication Date:	1 October 1992 (01.10.92)

(21) International Application Number: PCT/AU92/00105

(22) International Filing Date: 10 March 1992 (10.03.92)

(30) Priority data:
PK 5140 15 March 1991 (15.03.91) AU

(71) Applicant *(for all designated States except US)*: GOLDSPILL PTY. LTD. [AU/AU]; 8 Eagle Street, Alderley, QLD 4051 (AU).

(72) Inventor; and
(75) Inventor/Applicant *(for US only)* : ROBB, Darryl, Gordon [AU/AU]; 10 Chapple Lane, Gympie, QLD 4570 (AU).

(74) Agent: F.B. Rice & Co.; 28A Montague Street, Balmain, NSW 2041 (AU).

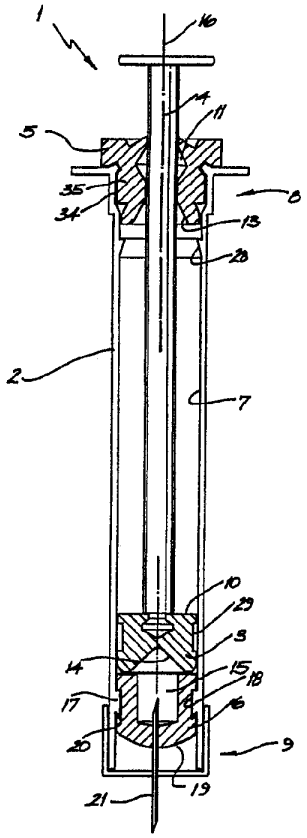
(81) Designated States: AT, AT (European patent), AU, BB, BE (European patent), BF (OAPI patent), BG, BJ (OAPI patent), BR, CA, CF (OAPI patent), CG (OAPI patent), CH, CH (European patent), CI (OAPI patent), CM (OAPI patent), CS, DE, DE (European patent), DK, DK (European patent), ES, ES (European patent), FI, FR (European patent), GA (OAPI patent), GB, GB (European patent), GN (OAPI patent), GR (European patent), HU, IT (European patent), JP, KP, KR, LK, LU, LU (European patent), MC (European patent), MG, ML (OAPI patent), MN, MR (OAPI patent), MW, NL, NL (European patent), NO, PL, RO, RU, SD, SE, SE (European patent), SN (OAPI patent), TD (OAPI patent), TG (OAPI patent), US.

Published
With international search report.

(54) Title: BODY FLUID EXTRACTION DEVICE

(57) Abstract

A device (1) for extracting body fluid in which depression of a plunger (4) into a tubular body (2) during a preparatory stroke creates a pressure reduction in a first chamber (12). After the preparatory stroke, the pressure reduction in the first chamber (12) exerts a force on a piston (3) to cause it to move and thereby to draw body fluid into a second chamber (15). The rate of extraction of the body fluid is governed by a frictional force on the plunger (4) which can be controlled by a cam arrangement (5).



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BODY FLUID EXTRACTION DEVICE

Field of the Invention

The present invention relates to devices for extracting body fluid, and more particularly to a device for extracting body fluid in which a pressure reduction is created by depression of a piston into a tubular body, and the pressure reduction so created is used to draw fluid into the tubular body.

Background

A conventional apparatus for extracting a body fluid, such as blood from a patient, usually comprises a cannula and an evacuated vial which is sealed with a rubber-like membrane. It is common practice to extract the body fluid by inserting a first end of the cannula into a part of the patient's body which contains the body fluid, followed by piercing the rubber-like membrane with a second end of the cannula. Body fluid is then drawn through the cannula into the evacuated vial.

A first disadvantage of the conventional apparatus for body fluid extraction is that the rate of flow of body fluid into the evacuated vial cannot be accurately and easily controlled, but depends on such parameters as the diameter of the cannula and the pressure inside the evacuated tube. In the case of blood extraction, it is desirable to control the rate of extraction, especially from weak patients, to avoid causing the patient's blood vessels to collapse.

A second disadvantage of the conventional apparatus for body fluid extraction is that it is potentially hazardous. In order that they may have sufficient strength to sustain a required low internal pressure, the evacuated vials are usually constructed from glass. However, this presents a potential hazard because glass vials can be shattered easily to expose sharp edges which can cut workers or technicians. This can be especially

dangerous when the vials contain hazardous substances such as blood infected with viruses.

A third disadvantage of the conventional apparatus for body fluid extraction is that it requires the maintenance of a stock of evacuated vials. Over time, the low pressures in such vials may degrade such that the vials may not be effective in receiving body fluid.

A fourth disadvantage of the conventional apparatus for body fluid extraction is that the evacuated vial cannot be pre-filled easily and accurately to predetermined levels with such fluids as anticoagulants or agents for separating red and white blood cells.

A fifth disadvantage of the conventional apparatus for body fluid extraction is that, once the body fluid is extracted, withdrawal of a sample of the body fluid from the evacuated vial for analysis can be difficult or dangerous. To withdraw a sample from the conventional apparatus, one end of the evacuated vial is usually removed, and the sample is sucked into a pipette. This can lead to spread of disease.

Summary of the Invention

In preferred embodiments the present invention overcomes at least some of the above deficiencies of conventional body fluid extraction devices.

According to one broad form of the invention, there is provided a device for extracting body fluid having a syringe-type construction. The device includes a tubular body having a proximal end, a distal end, and a bore.

A piston is disposed within the bore. The piston has a proximal face, a distal face, and an outer face which is in slidable contact with the bore.

A plunger, which has a shank, is mounted slidably at the proximal end of the tubular body and removably attached to the proximal face of the piston for pushing the piston from the proximal end of the tubular body

towards the distal end of the tubular body during a preparatory stroke in which external pressure is applied to the plunger.

A sealing means is used to seal the shank slidably to the proximal end of the tubular body so as to form a first chamber defined by the bore, the shaft, the proximal face of the piston and the distal face of the sealing means. A pressure reduction is formed in the first chamber during the preparatory stroke of the plunger.

Closure means are provided to close the distal end of the tubular body so as to form a second chamber defined by the bore, the distal face of the piston and the closure means. The closure means is adapted to cooperate with filling means which places the body fluid in communication with the second chamber.

After the preparatory stroke when external pressure is removed from the plunger, the pressure reduction in the first chamber causes the piston to move towards the proximal end of the tubular body and to draw the body fluid into the second chamber.

The rate of extraction of body fluid is preferably made controllable by providing a cam arrangement in which rotation of the sealing means causes a variation of a frictional force on the plunger. Non-circular cross sections are preferably provided on a lip at the proximal end of the tubular body and to a groove around an outer surface of the sealing means which engages with the lip. The sealing means can be rotated within the lip about an axis of rotation. The sealing means is constructed from a compressible elastic material such that, during rotation, its motion relative to the lip, combined with the non-circular cross sections, causes a variation in an internal pressure in the compressible elastic material. The magnitude of the internal pressure is determined by an angle of rotation of the sealing means relative to the

lip. The shaft of the plunger passes through a hole in the sealing means so that the internal pressure is communicated as a controllable pressure of the sealing means on the shaft. This results in a controllable frictional force between the sealing means and the shaft, and this retards the rate of movement of the plunger, the rate of movement of the piston, and the rate of body fluid extraction.

In a preferred embodiment of the invention a bung is situated within the bore between the piston and the distal end of the tubular body and constitutes the closure means. The bung has an outer wall which is in slidable contact with the bore, so as to form the second chamber defined by the bore, the distal face of the piston, and the bung. At the end of the preparatory stroke, an arresting means retains the bung at the distal end of the tubular body.

In the abovementioned preferred embodiment, the arresting means which retains the bung at the distal end of the tubular body preferably comprises a circumferential rib around the bore and a circumferential groove around the outer wall of the bung. The bung is constructed from an elastic material and has a distal surface with a generally convex shape so that, during the preparatory stroke, the distal surface passes the circumferential rib. At the end of the preparatory stroke, the circumferential rib is substantially aligned with the circumferential groove. The circumferential rib has a cross section with an acute edge proximate the distal end of the tubular body. The acute edge engages with the circumferential groove so as to impede the movement of the bung towards the proximal end of the tubular body, and thus acts to retain the bung at the distal end of the tubular body.

In this way, a body fluid extraction device is

provided in which the rate of body fluid extraction can be controlled easily and accurately. In addition, the body fluid extraction device can be constructed from a plastic-like material so that hazards due to shattering of evacuated vials are eliminated. Further, the pressure reduction in the first chamber need only be created immediately before the device is to be used; thus avoiding the problems due to loss of low pressure in the evacuated vial. The device can be pre-filled easily and accurately to predetermined levels with fluids such as anticoagulant agents. Finally, samples containing precise amounts of body fluid can be withdrawn from the body fluid extraction device because a cannula can be fitted to the distal end of the tubular body, and the fluid can be expelled from the device in the same way that fluids can be expelled from a hypodermic syringe.

Brief Description of the Drawings

The invention will now be further described with reference to the accompanying drawings in which:

Fig. 1 is a longitudinal section of a body fluid extraction device in accordance with a preferred embodiment of the invention in which the device is shown before use;

Fig. 2 is a longitudinal section of the body fluid extraction device of Fig. 1 in which the device is shown at the end of a preparatory stroke;

Fig. 3 is a longitudinal section of the body fluid extraction device of Fig. 1 in which the device is shown after body fluid has been extracted;

Fig. 4 is an end view of a sealing means adapted to fit into a proximal end of the body fluid extraction device of Fig. 1, viewed from the proximal end of the device;

Fig. 5 is an end view of the body fluid extraction device of Fig. 1, viewed from the proximal end of the

device;

Fig. 6 is a longitudinal sectional view of a needle like device which can be utilised in the withdrawal of body fluid from the body fluid extraction device; and

Fig. 7 is a longitudinal section of a body fluid extraction device according to a second embodiment of the invention in which the device is shown before use.

Detailed Description of the Preferred Embodiment

Figs. 1 to 3 show an illustrative embodiment of the body fluid extraction device 1 which comprises syringe-like tubular body 2, piston 3, plunger 4, sealing means 5, and bung 6. Bore 7 is situated inside tubular body 2 and extends from proximal end 8 to distal end 9. Bore 7, piston 3, plunger 4, and bung 6 all have longitudinal axes which are substantially coincident.

Piston 3 is disposed within tubular body 2 in slidable contact with bore 7 and is shaped so as to form a substantially air-tight seal against bore 7.

Plunger 4 is removably attached to proximal face 10 of piston 3 and extends out of proximal end 8 of tubular body 2 through hole 11 in sealing means 5.

Sealing means 5 forms substantially air-tight seals against bore 7 and plunger 4. In addition circular lip 23 surrounding the proximal end of body 2 is sealingly engaged by groove 22 in sealing means 5. Plunger 4 can slide through hole 11 while retaining a substantially air-tight seal with sealing means 5.

First chamber 12 is defined by proximal face 10 of piston 3, bore 7, plunger 4, and face 13 of sealing means 5. The position of piston 3 relative to proximal end 8 defines a volume of first chamber 12.

Bung 6 is disposed within tubular body 2 in slidable contact with bore 7 between distal face 14 of piston 3 and distal end 9 of tubular body 2. Bung 6 is shaped so as to form a substantially air-tight seal against bore 7.

Distal face 14 of piston 3, tubular body 2, and bung 6 define second chamber 15 in which body fluid is to be collected and temporarily stored and into which anti-coagulants and other reagents may be pre-filled.

Fig. 1 shows body fluid extraction device 1 in a state before use. In this state, proximal face 10 of piston 3 is close to sealing means 5 so that the volume of first chamber 12 is small.

Body fluid extraction device 1 is prepared for use by a preparatory stroke in which external pressure is applied to plunger 4 along longitudinal axis 16 of tubular body 2 to cause plunger 4, piston 3, and bung 6 to move away from proximal end 8 toward distal end 9.

During the preparatory stroke, the movement of piston 3 causes the volume of first chamber 12 to increase. Because sealing means 5 forms substantially air-tight seals with tubular body 2 and plunger 4, substantially no air enters first chamber 12, and so the increase of the volume of that chamber causes a pressure decrease there.

At, or close to, the end of the preparatory stroke, plunger 4, piston 3, and bung 6 reach the position shown in Fig. 2. At this position, an arresting means impedes the movement of bung 6 so that it cannot move freely back toward proximal end 8.

Preferably, the arresting means comprises circumferential rib 17 around bore 7 and circumferential groove 18 around the outer wall of bung 6. Bung 6 is constructed from an elastic material and has a distal surface 19 with a generally convex shape so that, during the preparatory stroke, distal surface 19 passes circumferential rib 17. At the end of the preparatory stroke, circumferential rib 17 is substantially aligned with circumferential groove 18. Circumferential rib 17 has a cross section with an acute edge 20 proximate distal

end 9 of tubular body 2. Acute edge 20 engages with circumferential groove 18 so as to impede the movement of bung 6 back towards proximal end 8 of tubular body 2, and thus acts to retain bung 6 at distal end 9.

With the device in the state illustrated in Fig. 2, a filling means allows body fluid such as blood to be brought into fluid contact with second chamber 15. Preferably, the filling means comprises cannula 21 as shown in Figs. 2 and 3. When distal end 9 is brought into contact with cannula 21, bung 6 is pierced; thus preparing a path for body fluid to flow into second chamber 15.

After the preparatory stroke, external pressure is removed from plunger 4. The pressure reduction in first chamber 12 exerts an attractive force on proximal face 10 of piston 3 to cause it to move toward proximal end 8 and away from distal end 9. This movement of piston 3, together with the arrested position of bung 6, creates a pressure reduction in second chamber 15 which causes body fluid to be drawn into that chamber.

As second chamber 15 fills with body fluid, piston 3 and plunger 4 move away from distal end 9 toward proximal end 8. When piston 3 reaches a position sufficiently close to proximal end 8, the body fluid extraction ceases. At this point, the cannula 21 may be removed, and plunger 4 may be removed from piston 3. In this way, second chamber 15 forms a substantially sealed container for holding body fluid.

The rate of extraction of body fluid can be controlled, for example, by governing the rate at which plunger 4 (and hence piston 3) are allowed to move back towards proximal end 8. In the preferred embodiment, this rate is governed by a cam arrangement which can be used to adjust a frictional force exerted on plunger 4 by sealing means 5.

As illustrated in Figs. 4 and 5, such a frictional

force can be rendered adjustable by providing on sealing means 5 a body portion 35 having a non-circular outer cross section, and a similar non-circular inner cross section to a portion 34 of the tubular body 2 proximal end 8 of tubular body 2. Body portion 35 has a large dimension 24 and a small dimension 25. Similarly, portion 34 of the tubular body has a large dimension 26 and a small dimension 30.

Sealing means 5 is constructed from a compressible elastic material such that any attempt to deform its outer surface results in a variation of an internal pressure within the compressible elastic material. Plunger 4 passes through hole 11 in sealing means 5 so that the internal pressure is communicated as a pressure of sealing means 5 on plunger 4. This results in a frictional force between sealing means 5 and plunger 4 which retards its rate of movement.

Sealing means 5 can be rotated within portion 34 of the tubular body 2 about longitudinal axis 16. When sealing means 5 is rotated relative to portion 34 of tubular body 2 such that large dimensions 26 and 24 are substantially collinear. The internal pressure in sealing means 5 is a minimum. However, when sealing means 5 is rotated relative to portion 34 of tubular body 2 such that large dimension 26 is substantially collinear with small dimension 30, the internal pressure in sealing means 5 is a maximum.

Thus, by varying an angle of rotation of sealing means 5 relative to tubular body 2, a user of the device can control the amount of pressure exerted by sealing means 5 on plunger 4. This results in a controllable frictional force between sealing means 5 and plunger 4 which controllably retards the rate of movement of plunger 4, the rate of movement of piston 3, and the rate of body fluid extraction.

After body fluid extraction device 1 is filled, as illustrated in Fig. 3, cannula 21 and plunger 4 can be removed to form a substantially sealed container in which body fluid can be stored.

Samples of body fluid can be withdrawn from body fluid collection device 1 using several methods. A first method comprises the steps of inserting a needle, cannula or similar device through bung 6 into second chamber 15 containing the body fluid, attaching a plunger to proximal face 10 of piston 3, and applying external pressure along longitudinal axis 16 so as to move piston 3 towards distal end 9 and to expel body fluid through the cannula. Circumferential rib 17 around bore 7 is provided with acute edge 20 to engage with circumferential groove 18 around the outer surface of bung 6 to ensure that the insertion of a cannula or the like through bung 6 does not cause the bung to move into bore 7 toward proximal end 8, but instead causes acute edge 20 to further engage with circumferential groove 18. Preferably, acute angle 20 is thirty degrees.

Fig 6 shows a preferred form of a needle-like device 27 for insertion through bung 6 to allow withdrawal of body fluid from second chamber 15. Device 27 is circular in cross-section and has a bore 28 extending axially through it. A first end portion 29 of device 27 is of narrow external diameter and is sharpened to point 31. Second end portion 32 is frustoconical in shape. An annular ridge 33 is formed between first and second end portions 29 and 32. In use first end portion is pushed through bung 6. The body fluid in second chamber 15 may be expressed through bore 28 by depressing plunger 4 and thus piston 13. This form of device has the advantage that after communication has been established with the contents of the second chamber 15 there are no sharp edges projecting from device 1 on which a user could be cut.

A second method of withdrawing a sample of body fluid from body fluid extraction device 1, for which method piston 3 is constructed from a penetrable material, comprises the steps of inserting a cannula attached to a suitable sampling device such as a hypodermic syringe through hole 11 in sealing means 5 and through piston 3 into second chamber 15, and to withdraw body fluid into the sampling device. Circumferential ledge 28 around bore 7 engages with circumferential slot 29 around the outer surface of piston 3 to ensure that the insertion of the cannula through piston 3 does not cause that piston to move into bore 7 toward distal end 9.

Before use, body fluid extraction device 1 can be operated as a hypodermic syringe to pre-fill tubular body 2 with fluids such as anticoagulants or agents for separating red and white blood cells.

Fig. 7 shows a fluid or blood extracting device quite similar to that of the device shown in Fig. 1 but includes a plug 114 which is screwed, by screw thread 116, into sealing engagement with end 93 of body 91 at the tapered matching surfaces 115. Plug 114 also provides an air seal about plunger 96 at cylindrical region 114.

Plug 114 frictionally grips plunger 96 at cylindrical portion 117, the frictional grip being adjustable by way of adjusting the screw pressure applied to plug 114. Tight screw pressure applied to plug 114 results in tapered surfaces 115 radially compressing the volume of plug 114 that surrounds portion 117, thus increasing the frictional grip between plug 114 and plunger 96. By reducing the screw force applied to plug 114, but not so much as to violate the seal at surfaces 115, the radial pressure applied to surface portion 117 is reduced and the frictional grip reduced.

In the arrangement of Fig. 7 engagement portion 98 of plunger 96 comprises a cylindrical boss separated from the

remainder of plunger 96 by a groove. Engagement portion 98 is resiliently gripped by piston head 95 which is made of rubber or some similar elastomeric material.

Immediately before use the device is in the configuration as illustrated in Fig. 7. Cap 112 is removed and a suitable cannular inserted into sleeve 111. Piston head 95 is then pressed fully down to end 94, by applying pressure to handle 97. By virtue of the seal applied by plug 114 at surface area 118 with plunger 96 and at surfaces 115 with body 91, a substantially evacuated volume is formed between piston head 95 and plug 114.

With piston head 95 fully depressed to end 94, the cannular is inserted into the appropriate vessel and by releasing the pressure applied to handle 97, the evacuated volume behind piston head 95 will retract piston head 5 back toward end 93 and thus allow the collection of the blood sample within the device. The speed of retraction of piston head 95 can be adjusted by adjusting the screw tensioning of plug 114. Thus the device will provide a smooth rate of retraction of piston head 95 at an adjustable speed.

Plug 114 will serve to prevent the complete removal of piston head 95, after removal of the cannular the cap 112 is replaced over sleeve 111, and the sample of blood or other fluid, is now ready for safe and convenient transportation or storage.

CLAIMS:-

1. A device for extracting body fluid comprising:
a tubular body having a proximal end, a distal end, and a bore;

a piston disposed within the bore, the piston having a proximal face, a distal face, and an outer face, the outer face being in slidable contact with the bore;

a plunger mounted slidably at the proximal end of the tubular body and removably attached to the proximal face of the piston for pushing the piston from the proximal end of the tubular body towards the distal end of the tubular body during a preparatory stroke in which an external pressure is applied to the plunger, the plunger having a shank;

sealing means for slidably sealing the proximal end of the tubular body to the shank of the plunger so as to form a first chamber defined by the bore, the shaft, the sealing means, and the proximal face of the piston, so that a pressure reduction is formed in the first chamber during the preparatory stroke of the plunger;

closure means to close the distal end of the tubular body so as to form a second chamber defined by the bore, the distal face of the piston and the closure means;

the closure means is adapted to cooperate with filling means for placing the body fluid in fluid communication with the second chamber so that, after the external pressure is removed from the plunger, the pressure reduction in the first chamber causes the piston to move towards the proximal end of the tubular body and to draw body fluid into the second chamber.

2. A device for extracting body fluid as claimed in claim 1 in which the closure means comprises

a bung situated within the bore between the piston and the distal end of the tubular body, the bung having an outer wall in slidable contact with the bore, so as to

form the second chamber defined by the bore, the distal face of the piston, and the bung and in which arresting means are provided for retaining the bung at the distal end of the tubular body after the preparatory stroke;

3. A device for extracting body fluid as claimed in claim 1 or claim 2 wherein the sealing means is constructed from a compressible elastic material, the shaft of the plunger passes through a hole in the sealing means, and the device for extracting body fluid includes a cam arrangement which comprises:

a first cam means for creating a controllable deformation of the sealing means; and

a second cam means for cooperating with the first cam means to create the controllable deformation of the sealing means, the second cam means being rotatably engaged with the first cam means such that relative rotation of the second cam means with respect to the first cam means causes the controllable deformation of the sealing means and a corresponding controllable internal pressure in the compressible elastic material, thereby creating a controllable frictional force to be applied to the shaft of the plunger to enable the body fluid to be extracted at a controllable rate.

4. A device for extracting body fluid as claimed in claim 3 in which the first cam means has a non-circular inner cross section and the second cam means has a non-circular outer cross section.

5. A device for extracting body fluid as claimed in claim 4 wherein the first cam means comprises a lip at the proximal end of the tubular body.

6. A device for extracting body fluid as recited in claim 4 wherein the second cam means comprises a groove around an outer surface of the sealing means.

7. A device for extracting body fluid as recited in claim 2 wherein the bung is constructed from an elastic

material and has a distal surface with a generally convex shape and the arresting means comprises:

a circumferential rib around the bore proximate the distal end of the tubular body; and

a circumferential groove around the outer wall of bung so that, at the end of the preparatory stroke, the circumferential rib is substantially aligned with the circumferential groove so as to impede a movement of the bung towards the proximal end of the tubular body.

8. A device for extracting body fluid as claimed in claim 5 wherein the circumferential rib has an acute edge proximate the distal end of the tubular body.

9. A device for extracting body fluid as claimed in claim 1 wherein the device includes filling means comprising a needle, cannula or similar device which is removably attached to the distal end of the tubular body.

10. A device for extracting body fluid as claimed in claim 1 wherein the piston is constructed from a penetrable material and samples of body fluid may be withdrawn by inserting a cannula through the piston.

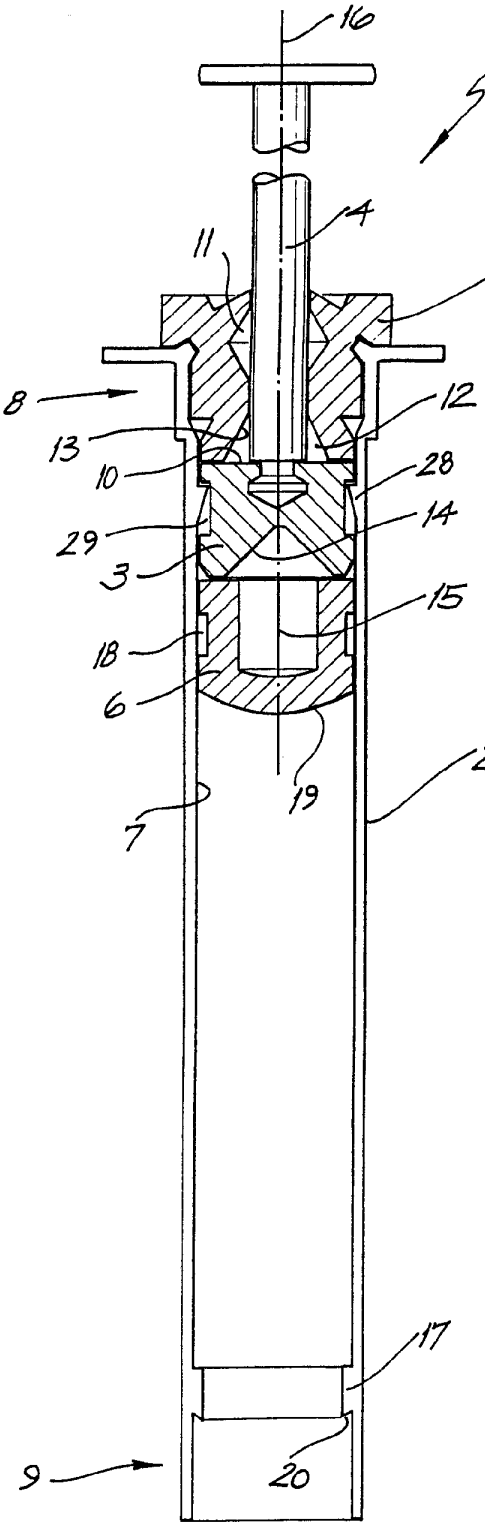

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FIG. 1

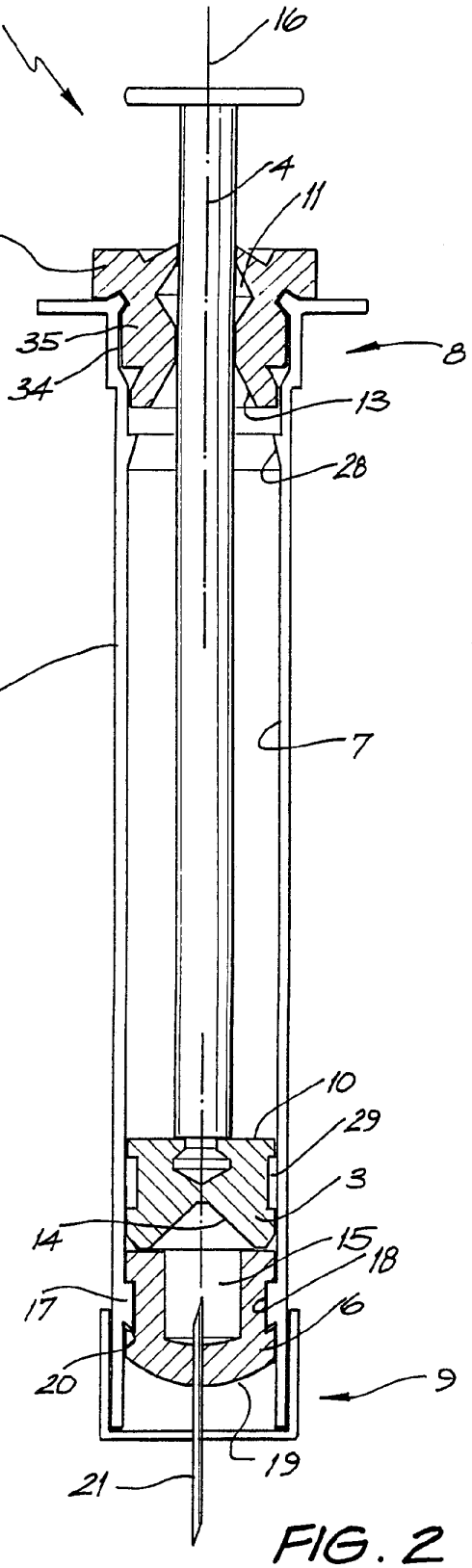

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FIG. 2

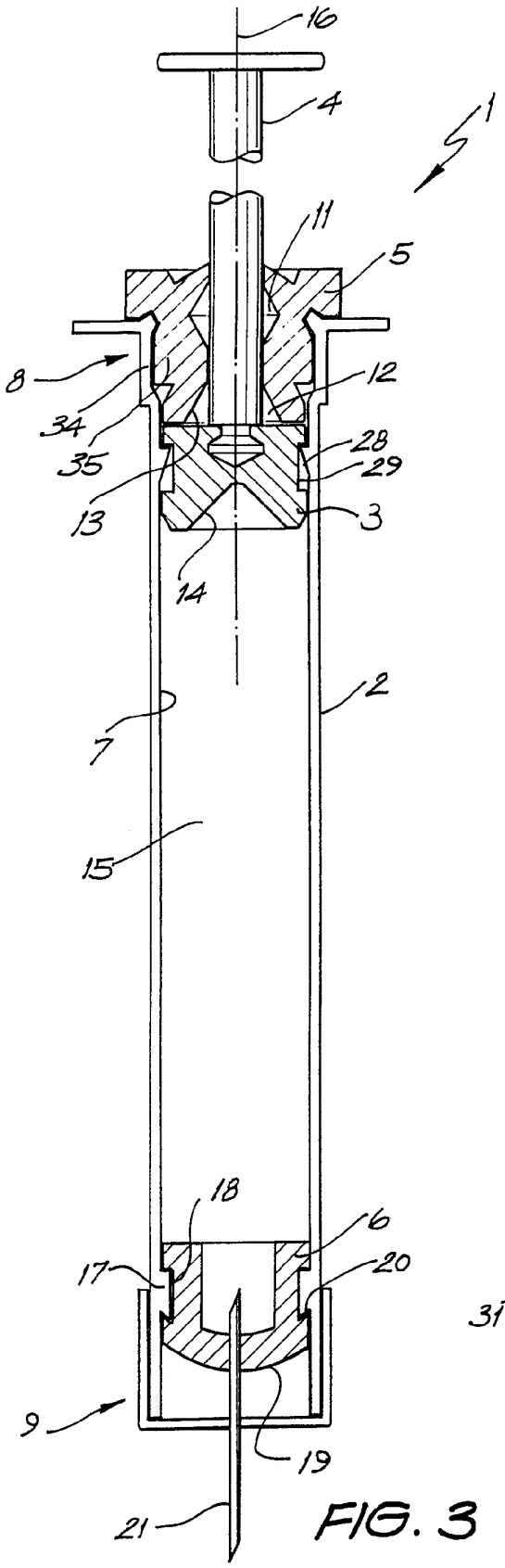


FIG. 3

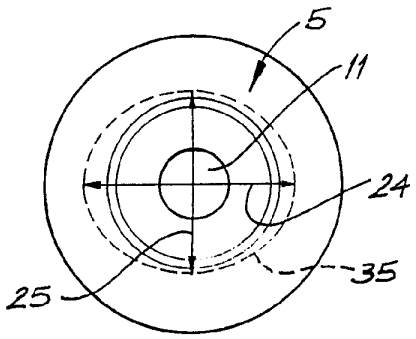


FIG. 4

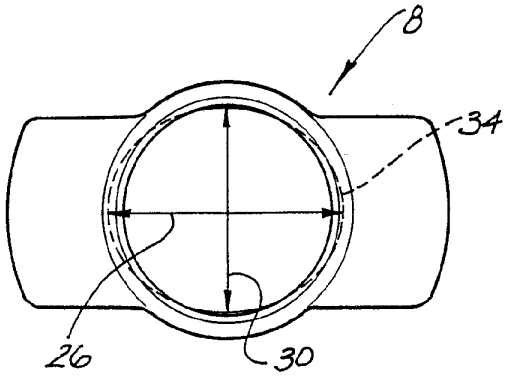


FIG. 5

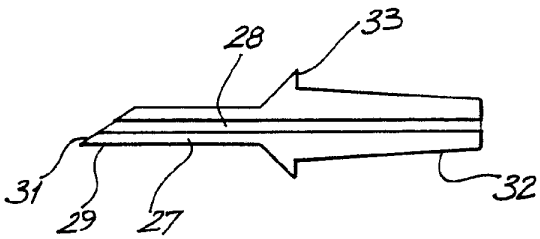


FIG. 6

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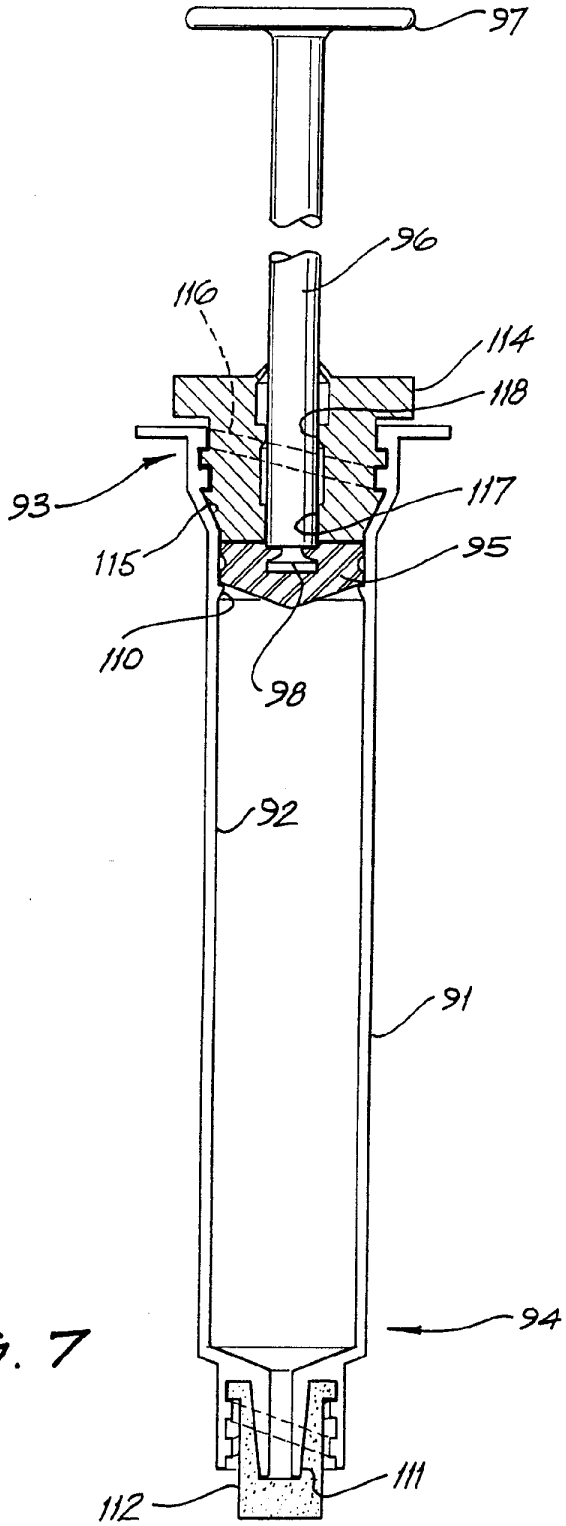


FIG. 7

INTERNATIONAL SEARCH REPORT

I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all)[6]

According to International Patent classification (IPC) or to both National Classification and IPC

Int. Cl.[5] A61B 5/14

II. FIELDS SEARCHED

Minimum Documentation Searched [7]

Classification System	Classification Symbols
IPC	A61B 5/14

Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in the Fields Searched [8]

AU:IPC as above

III. DOCUMENTS CONSIDERED TO BE RELEVANT [9]

Category*	Citation of Document, [11] with indication, where appropriate of the relevant passages [12]	Relevant to Claim No [13]
X,Y	EP,A,0279956 (VAN-TEC INCORPORATED) 31 August 1988 (31.08.88) See whole document, particularly claim 1.	(1,9-10)
Y	US,A,4361155 (ANASTASIO) 30 November 1982 (30.11.82) See column 3, lines 40-45.	(9)
Y	US,A,3930492 (HATSUNO et al) 6 January 1976 (06.01.76) See column 2.	(9-10)
A	US,A,4041934 (GENESE) 16 August 1977 (16.08.77)	

(continued)

* Special categories of cited documents : [10]

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"P" document published prior t 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 oonflict 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

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IV. CERTIFICATION

Date of the Actual Completion of the International Search	Date of Mailing of this International Search Report
22 May 1992 (22.05.92)	2 June 1992 (02.06.92)
International Searching Authority	**Signature of Authorized Officer**
AUSTRALIAN PATENT OFFICE	A HENDRICKSON

FURTHER INFORMATION CONTINUED FROM THE SECOND SHEET

A	US,A,4215702 (AYER) 5 August 1980 (05.08.80)	A US,A,4215702
A	US,A,4257426 (BAILEY) 24 March 1981 (24.03.81)	
A	GB,A,2218076 (BATES) 8 November 1989 (08.11,89)	

V. ☐ OBSERVATIONS WHERE CERTAIN CLAIMS WERE FOUND UNSEARCHABLE [1]

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claim numbers ..., because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claim numbers ..., 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. ☐ Claim numbers ..., because they are dependent claims and are not drafted in accordance with the second and third sentences of PCT Rule 6.4a

VI. ☐ OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING [2]

This International Searching Authority found multiple inventions in this international application as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims of the international application.
2. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims of the international application for which fees were paid, specifically claims:

3. ☐ No required additional search fees were timely paid by the applicant. Consaquently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claim numbers:

4. ☐ As all searchable claims could be searched without effort justifying an additional fee, the International Searching Authority did not invite payment of any additional fee.

Remark on Protest

☐ The additional search fees were accompanied by applicant's protest.

☐ No protest accompanied the payment of additional search fees.

ANNEX TO THE INTERNATIONAL SEARCH REPORT ON INTERNATIONAL APPLICATION NO. PCT/AU 92/00105

This Annex lists the known "A" publication level patent family members relating to the patent documents cited in the above-mentioned international search report. The Australian Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent Document Cited in Search Report	Patent Family Member	
US 4361155		
EP 279956	JP 63246145	US 4766908
US 3930492		

END OF ANNEX

JOURNAL OF CLINICAL MICROBIOLOGY, June 2003, p. 2275–2278 Vol. 41, No. 6
0095-1137/03/$08.00+0 DOI: 10.1128/JCM.41.6.2275–2278.2003
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MINIREVIEW

Blood Culture Contamination: Persisting Problems and Partial Progress

Melvin P. Weinstein*

Departments of Medicine and Pathology, University of Medicine and Dentistry of New Jersey—Robert Wood Johnson Medical School, and Microbiology Laboratory, Robert Wood Johnson University Hospital, New Brunswick, New Jersey 08903-0019

Although it has been widely appreciated for many years among physicians and microbiologists that blood cultures are among the most important laboratory tests performed in the diagnosis of serious infections (35), it has become equally apparent in more recent years that contaminated blood cultures are common (25, 42), enormously costly (3, 29), and frequently confusing for clinicians (1, 12, 14, 26). Clinical studies of bloodstream infections over 3 decades have provided guidelines for differentiating true pathogens from contaminants or organisms of unknown significance (14, 18, 41, 42); however, a true "gold standard" for differentiating pathogens from contaminants does not exist (4, 25). Moreover, the most common blood culture contaminants, coagulase-negative staphylococci (CoNS), which were almost always such several decades ago (18, 41), now are pathogens more frequently (19, 25, 26, 42), and judging the clinical significance of this group of microorganisms in blood has proven to be especially problematic (1, 11, 22, 24, 26, 42; S. J. Peacock, I. C. Bowler, and D. W. Crook., Letter, Lancet **346:**191-192, 1995). This review focuses on how pathogen-contaminant decisions are made, the phenomenon of increasing contamination of blood cultures, potential methods for addressing high contamination rates, and practical laboratory approaches to the workup of likely contaminants.

TOOLS FOR INTERPRETING THE CLINICAL SIGNIFICANCE OF POSITIVE BLOOD CULTURES

A number of clinical and laboratory tools have been proposed to aid microbiologists and physicians in deciding whether a blood isolate is a pathogen or a contaminant. These include the identity of the microorganism itself; clinical features such as fever, leukocytosis, and results of imaging studies (available to the clinician but usually not to the microbiologist); the proportion of blood culture sets positive as a function of the number of sets obtained; the time it takes for growth to be detected once a blood culture is received in the laboratory; and the number of culture vials within a culture set that show growth. Some of these tools have proven to be quite useful, whereas others have not.

The identity of the microorganism that grows from a positive blood culture provides important interpretative information. MacGregor and Beaty (18) documented this observation in the early 1970s, and studies by my colleagues and I confirmed and updated the earlier findings (41, 42). A predictive model that assessed multiple variables also documented microorganism identity as an independent predictor (4). Microorganisms that always or nearly always (>90%) represent true bacteremia or fungemia include *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Escherichia coli* and other members of the *Enterobacteriaceae*, *Pseudomonas aeruginosa*, and *Candida albicans* (42). Although published data from large studies with multiple isolates of the following organisms are lacking, it is my observation that *Streptococcus pyogenes*, *Streptococcus agalactiae*, *Listeria monocytogenes*, *Neisseria meningitidis*, *Neisseria gonorrhoeae*, *Haemophilus influenzae*, members of the *Bacteroides fragilis* group, *Candida* species other than *C. albicans*, and *Cryptococcus neoformans* always or virtually always represent true infection. In contrast, microorganisms such as *Corynebacterium* species, *Bacillus* species other than *B. anthracis*, and *Propionibacterium acnes* represent true bacteremia only rarely (42). Detection of CoNS, the most frequent of all blood culture isolates, can be especially vexing. These bacteria are most often contaminants, but they have taken on increased clinical importance as the etiologic agents of catheter-associated bacteremia and bacteremia in patients with vascular and other prostheses (19, 26, 42). Accordingly, one can no longer judge the clinical significance of a CoNS isolate solely on the basis of its identity. Similarly, the clinical significance of other microorganisms also cannot be judged based only their identity. For example, in a recent study, enterococci and viridans group streptococci were pathogens 78 and 38% of the time, respectively, and *Clostridium perfringens* most often (77%) was a contaminant, whereas other *Clostridium* species most often (80%) were pathogens (42).

The number of blood culture sets that grow microorganisms, especially when measured as a function of the total number obtained, has proved to be a useful aid in interpreting the clinical significance of positive blood cultures (18, 41, 42). In contrast to patients with endocarditis or other bloodstream infections, in whom all blood cultures or the majority thereof are positive, patients whose blood cultures grow contaminants usually have only a single blood culture (when two or more are obtained) that is positive (42). Although obvious, it bears emphasis that if only a single blood culture is obtained, the value

* Mailing address: Robert Wood Johnson Medical School, 1 Robert Wood Johnson Pl., New Brunswick, NJ 08903-0019. Phone: (732) 235-7713. Fax: (732) 235-7951. E-mail: weinstei@umdnj.edu.

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of this tool ceases to exist; and this is but one reason (another being increased blood volume) that at least two blood culture specimens are recommended as standard practice (2, 23, 37). The value of obtaining more than a single blood culture is that it also assists in interpreting the clinical significance of positive results by virtue of the following calculation. If an institution has a baseline blood culture contamination rate of 3%, the probability of recovering the same organism in two culture sets from a patient, and of that organism being a contaminant, is less than 1 in 1,000 ($0.03 \times 0.03 = 0.0009$)!

A laboratory tool that has been used as an aid to differentiating clinically significant isolates from contaminants is assessment of the time necessary for microbial growth to occur (4). The underlying premise is that growth of pathogens, which are likely to be present in larger inocula, will be detected earlier than that of contaminants, which are likely to be present in much smaller quantities (18). Whereas this concept likely has validity, the degree of overlap in the detection times of true pathogens versus contaminants is such that this variable cannot be relied upon as a predictor of a true-positive culture (8). Moreover, with the wide use of continuously monitoring blood culture systems and the concomitant decrease in the time to detection of growth, the time difference between the detection of true pathogens and contaminants has been narrowed even further.

Some microbiologists and clinicians have used the number of culture bottles positive within a blood culture set as a guide to determine whether isolates represent true pathogens or contaminants. However, there now are published data, at least for CoNS, that show that this technique is not clinically useful (22; Peacock et al., letter). Although clinically significant CoNS may grow more often in multiple bottles within a set as opposed to a single bottle, and contaminants may more often grow in only one bottle of a set, the degree of overlap is such that for a given culture this information cannot predict clinical significance reliably (22; Peacock et al., letter). Accordingly, this criterion should not be used.

THE PARADOX OF INCREASING NUMBERS OF CONTAMINANTS

Despite numerous advances in blood culture methodology and systems in recent decades, some hospitals and laboratories have noted that an increasing proportion of blood culture isolates represent contamination compared with those in years past (42). There are several possible explanations for this unexpected observation. The newer continuously monitoring blood culture systems have improved algorithms for detecting microbial growth and may be detecting microorganisms present in low numbers that previously were missed. Moreover, several broth medium formulations such as the BACTEC Plus Resin media (Becton Dickinson, Sparks, Md.) and BacT/ALERT FN media (bioMerieux, Durham, N.C.) have been shown to have improved detection of staphylococci, including CoNS which most often are contaminants (10, 20, 28, 38, 40, 43, 45). Thus, the ability of new systems and media to detect these organisms, even when present in small numbers, may be responsible in part for the observed increase in the proportion of blood cultures with contaminants.

The increased use of central venous access catheters and utilization of these devices for the purpose of obtaining blood specimens for culture may also be contributing to the increased numbers of contaminated blood cultures. Several studies have documented increased contamination when blood cultures are obtained in this fashion (5, 6, 7; R. B. Sivadas, B. Vazirani, S. Mirrett, and M. P. Weinstein, Abstr. 101st Gen. Meet. Am. Soc. Microbiol., abstr. C10, 2001), perhaps because it is more difficult to sterilize these devices than it is the skin before blood is obtained. Although physicians and nurses may believe they are saving patients the pain of an extra needle stick when blood cultures are obtained from catheters rather than by venipuncture, they may actually be doing their patients and the health care system a disservice if contaminants are grown from the culture resulting in the need for even more cultures, other diagnostic studies, unnecessary antibiotic therapy, and the associated incremental costs of care.

Prior to the human immunodeficiency virus (HIV) era, blood cultures traditionally were obtained by a two-needle technique, using a sterile needle and syringe to perform the venipuncture, then changing to a second sterile needle before inoculating the blood culture vial. The purpose of the two-needle technique was to reduce the chance that skin microorganisms that might be present on the needle used for the venipuncture would be inoculated into the blood culture vial, thereby resulting in a contaminated blood culture. As the knowledge of HIV as a bloodborne pathogen and the risks of needle stick transmission of HIV became evident, several studies were undertaken to determine whether contamination rates would be affected if only one needle was used for both venipuncture and inoculation of blood culture vials (9, 15, 16). The results of each of these studies showed no significant increase in contamination rates when the single-needle technique was used. Subsequently, however, a meta-analysis suggested that single-needle blood cultures were associated with contamination rates of 3.7% compared with 2.0% when a two-needle technique was used (30). Since the current standard of care continues to be the single-needle technique in order to reduce the risk of occupational needle stick injuries, slightly higher contamination rates may have to be tolerated.

REDUCING THE NUMBER OF CONTAMINATED BLOOD CULTURES

Although it is not possible to achieve contamination rates of zero or even close to zero (31), there are potential means by which contamination can be reduced. These include the use of collection methods that increase the chances for sterility, for example, obtaining blood via venipuncture rather than from an intravascular catheter or using a two-needle rather than a single-needle technique, as has already been mentioned. For the reasons already stated, the two-needle method is unlikely to return to widespread use; however, laboratories and institutions can and should actively promote blood cultures obtained from venipuncture rather than intravascular devices as a means of practicing evidence-based medicine.

There is also evidence that some antiseptic preparations may be more efficacious than others in reducing contamination rates. Povidone iodine preparations require 1.5 to 2 min of contact time to produce their maximum antiseptic effect, whereas iodine tincture requires approximately 30 s (13). Health care

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workers who obtain blood cultures are often in a hurry, do not understand the importance of antiseptic preparation contact time, and are less likely to wait 1.5 to 2 min as opposed to half a minute before obtaining blood. At least two studies have documented a significantly lower contamination rate using iodine tincture compared with an iodophor (17, 31). Another report compared the use of 0.2% chlorine peroxide and 10% povidone iodine and demonstrated lower contamination rates when chlorine peroxide was used (29). Lastly, an alcoholic solution of 0.5% chlorhexidine gluconate used as an antiseptic prior to blood culture was associated with significantly lower contamination rates compared with a standard povidone-iodine preparation (21).

Several published studies have shown that trained phlebotomists or blood culture teams can reduce contamination rates in individual institutions (27, 32, 36), and this has been confirmed in my own institution (Sivadas et al., 101st Gen. Meet. Am. Soc. Microbiol.). At a New York City, N.Y., community teaching hospital, the contamination rate for blood cultures drawn by a blood culture team using a commercially available blood culture prep kit was approximately 1% compared with rates of 4.8% for blood cultures drawn by resident physicians using the same method (36). The contamination rate when residents did not use the commercial prep kit was even higher (8.4%) (36). In a large survey of over 600 hospitals sponsored by the College of American Pathologists, median contamination rates for institutions in which more than half of all blood cultures were collected by resident physicians was 3.9%, compared with 2.2% in the remaining institutions (27). In a pilot study at my institution, contamination of blood cultures obtained by phlebotomists trained and monitored monthly by microbiology laboratory staff was 3%, compared with nearly 11% for blood cultures obtained by resident physicians, nondegree nursing assistants, and nurses (M. P. Weinstein, unpublished observation). Subsequently, my colleagues and I assessed contamination in a larger study and again found that samples collected by phlebotomists had lower contamination rates than those collected by nondegree nursing assistants, nurses, and resident physicians (the last of whose samples had the highest contamination rates) (Sivadas et al., 101st Gen. Meet. Am. Soc. Microbiol.).

Whether or not commercially marketed blood culture prep kits are associated with reduced blood culture contamination rates remains controversial. Some studies have shown reduced contamination (27, 36) with commercial prep kits, whereas others have shown no difference (44). The manufacturer of at least one commercial prep kit has offered ongoing in-service education for personnel obtaining blood cultures (M. P. Weinstein, personal observation), which itself may be associated with reduced contamination rates.

LABORATORY WORKUP OF LIKELY BLOOD CULTURE CONTAMINANTS

In the real world of clinical microbiology laboratories, nearly half of all positive blood cultures represent contamination (42). Complete laboratory workup of contaminant isolates is associated with increased technologist workload and institutional cost. Therefore, some laboratories have developed algorithms for dealing with this problem based, at least in part, on many of the studies reviewed in this article.

At the University of Iowa, for example, Richter et al. (25) tested, validated, and implemented an algorithm to minimize the workup of blood culture contaminants. CoNS, aerobic and anaerobic diphtheroids, *Micrococcus* spp., *Bacillus* spp., and viridans group streptococci are considered contaminants if certain criteria are met. If two or more blood cultures are obtained and only one is positive, the isolate is reported as a probable contaminant and susceptibility testing is not done unless the physician calls the laboratory. If only a single blood culture is obtained and grows one of the likely contaminants, a pathology resident reviews the patient's chart and judges the clinical significance of the isolate based on published data (42). Susceptibility testing is not done if the isolate is judged to be a contaminant. If two or more blood cultures are obtained and two cultures are positive within a 48-h period, one of two actions is taken. If the isolates are viridans group streptococci, they are presumed to be clinically significant and a full workup is done. If one of the other likely contaminants is present, the pathology resident reviews the patient's chart, and the laboratory workup proceeds according to the resident's judgment regarding clinical significance.

In my laboratory, a similar protocol is followed, but it is modified somewhat based on the fact that pathology residents are not always assigned to microbiology. The same microorganisms are considered likely contaminants. If two or more blood cultures are submitted and only one is positive, neither species identification nor susceptibility testing is done; the isolate is reported as a probable contaminant. If only one blood culture is submitted and it grows a likely contaminant, the workup is the same; the isolate is reported to be of indeterminate significance and the physician is advised to call the laboratory director if additional workup is needed. If two or more blood cultures grow a likely contaminant other than CoNS (see below) within a 48-h period, a full workup is done. If the isolates are the same, the identification and susceptibility results are reported. If the isolates are different, they are reported as probable contaminants without susceptibility results.

When two or more blood cultures grow CoNS, my laboratory undertakes species identification and reports susceptibility results. I find that the additional information assists in determining whether the isolates are clinically significant (12, 39). If the strains isolated have the same biochemical profile and antibiogram, it is probable that they are identical (although only molecular typing provides proof). This information increases the likelihood that the isolates represent clinically significant bacteremia, and identification and susceptibility results are reported to the clinician. However, if the biochemical profiles and antibiograms are not the same (i.e., two or more differences in biochemical results and susceptibilities [susceptible versus resistant]), the isolates are much more likely to represent contamination. In this instance, the laboratory reports that two different CoNS strains were identified, and susceptibility results are not provided. Although this technique has proven clinically useful in most circumstances, the algorithm is not foolproof. Two studies from the same center in Belgium have described polyclonal CoNS bacteremia (33, 34). Thus, in patients who have multiple positive blood cultures growing CoNS that appear to be different strains, the labora-

tory may need to perform additional testing if clinicians believe clinically significant infection is present.

As is apparent from the foregoing discussion, the current state of the art remains suboptimal. Although progress has been made, the interpretation of the clinical significance of microorganisms that are common blood culture contaminants and the technical effort and institutional costs associated with working up probable contaminants remain problematic. Gold standards for solving these problems still are elusive.

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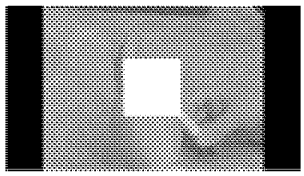
Closed system

Preattached extension tubing offers a closed system to minimize blood exposure during catheter insertion.

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The system is constructed with BD Vialon biomaterial, a proprietary catheter material that softens in the vein.

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	Filing Date	2023-10-25
	First Named Inventor	Bobby E. ROGERS
	Art Unit	
	Examiner Name	
	Attorney Docket Number	069366-0577657_KUR2C05US

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	14	6569117		2003-05-27	ZIV DAVID	
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	16	8603009		2013-12-10	TAN ALVIN CHEE LEONG	
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	29	20040073171		2004-04-15	ROGERS BOBBY E	
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	22	2019534792A	JP		2019-12-05	プライメタルズ・テクノロジーズ・オーストリア・ゲーエムベーハー		☒
	23	H09504726A	JP		1997-05-13	BAXTER INT		☒
	24	9605875A1	WO		1996-02-29	BAXTER INT		☐
	25	2013181352A1	WO		2013-12-05	MAGNOLIA MEDICAL TECHNOLOGIES INC		☐
	26	2014058945	WO		2014-04-17	BULLINGTON GREGORY J		☐
	27	2017019552A1	WO		2017-02-02	KURIN INC		☐
	28	2018125929A1	WO		2018-07-05	KURIN INC		☐
	29	S5825146A	JP		1983-02-15	BECTON DICKINSON CO		☒

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	18494622
	Filing Date	2023-10-25
	First Named Inventor	Bobby E. ROGERS
	Art Unit	
	Examiner Name	
	Attorney Docket Number	069366-0577657_KUR2C05US

	30	S5867238A	JP		1983-04-21	BECTON DICKINSON CO		☒
	31	5643474	JP		2014-12-17	ヴェロシス，インク．		☒
	32	5825146B2	JP		2015-12-02	JVC KENWOOD CORP,		☒
	33	2020000340A	JP		2020-01-09	TOSHO INC		☒
	34	2013240628	JP		2013-12-05	COVIDIEN LP		☒
	35	H02224742	JP		1990-09-06	SPACELABS INC		☒
	36	S5789869	JP		1982-06-04	BECTON DICKINSON CO		☒
	37	2005349196	JP		2005-12-22	BECTON DICKINSON CO		☒
	38	10243129	DE		2004-04-01	RITTER GMBH		☒
	39	7203008	DE		1972-05-10	IMMUNO AG FUER CHEM-MED PROD		☒
	40	10038026	DE		2001-02-22	ZIERDEN PETER		☒

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
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	41	29913417	DE		2000-12-28	ZIERDEN PETER		☒
	42	10134913	DE		2003-02-20	HIBERNA AG		☒
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	44	2541494	DE		1977-03-31	GUERRA LUIS A		☒
	45	2008101025	WO		2008-08-21	EDWARDS LIFESCIENCES CORP		☐
	46	0448795A2	EP		1991-10-02	BECTON DICKINSON CO		☐
	47	2007033319A1	WO		2007-03-22	EDWARDS LIFESCIENCES CORP		☐
	48	199216144	WO		1992-10-01	GOLDSPILL PTY. LTD.		☐

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	1	International Search Report and Written Opinion dated Nov. 5, 2015, for PCT application No. PCT/US2015/035870. 6 pages.	☐

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	Attorney Docket Number	069366-0577657_KUR2C05US

	2	International Search Report and Written Opinion dated 16 July 2020 for PCT application no. PCT/US2020/026276. 9 pages.	☐
	3	Bullington, et al., Systems and Methods for Sample Collection with Reduced Hemolysis, Exhibit H in U.S. Appl. No. 62/517,681, dated Jun. 9, 2017, 131 pages.	☐
	4	International Search Report and Written Opinion dated Jun. 19, 2020, for PCT application No. PCTUS2020/023617. 12 pages.	☐
	5	International Search Report/Written Opinion for PCT/US17/68569 dated Apr. 25, 2018. 9 pages.	☐
	6	International Search Report and Written Opinion for PCT/US16/43709, Dated October 19,2016. 13 pages.	☐
	7	Retractable Techs., Inc. v. Becton Dickinson & Co., CA No. 2:07-CV-250, Claim Construction Order (E.D. Tex., Jan. 20, 2009). 20 pages.	☐
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	24	De Korte, Dirk, et al. "Effects of skin disinfection method, deviation bag, and bacterial screening on clinical safety of platelet transfusions in the Netherlands." Transfusion 46.3 (2006): 476-485.	☐
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	41	BD Diagnostics, "Venous Blood Collection, BD Vacutainer Passive Shielding Blood Collection Needle " literature (2005) 2 pages.	☐
	42	Barnard, Dorothy R., et al. "Fibronectin (cold insoluble globulin) in the neonate," The Journal of Pediatrics, Vol. 102, Issue 3, March 1983, Pages 453-455.	☐
	43	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.	☐
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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
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	Art Unit	
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[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.

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	Examiner Name	
	Attorney Docket Number	069366-0577657_KUR2C05US

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)	2024-04-23
Name/Print	Benjamin F. Hudson	Registration Number	71,474

This collection of information is required by 37 CFR 1.97 and 1.98. 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 1 hour 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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Application Data Sheet 37 CFR 1.76	Attorney Docket Number	MGMD-012/01US 316052-MGMD
	Application Number	
Title of Invention	SYSTEMS AND METHODS FOR SAMPLE COLLECTION WITH REDUCED HEMOLYSIS	

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.

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☐ 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
	Gregory	J.	Bullington	

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

City	State/Province	Country of Residence
Bellevue	WA	US

Mailing Address of Inventor:

Address 1	5825 134th Place SE
Address 2	
City	Bellevue
State/Province	WA
Postal Code	98006
Country	US

Inventor 2 Remove

Legal Name

Prefix	Given Name	Middle Name	Family Name	Suffix
	Richard	G.	Patton	

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

City	State/Province	Country of Residence
Seattle	WA	US

Mailing Address of Inventor:

Address 1	2561 Magnolia Blvd. W
Address 2	
City	Seattle
State/Province	WA
Postal Code	98199
Country	US

Inventor 3 Remove

Legal Name

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	Shan	E.	Saw	

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Application Data Sheet 37 CFR 1.76	Attorney Docket Number	MGMD-012/01US 316052-MGMD
	Application Number	
Title of Invention	SYSTEMS AND METHODS FOR SAMPLE COLLECTION WITH REDUCED HEMOLYSIS	

City	Seattle	State/Province	WA	Country of Residence	US

Mailing Address of Inventor:

Address 1	4027 Sunnyside Ave. N		
Address 2			
City	Seattle	State/Province	WA
Postal Code	98103	Country	US

Inventor 4 — Remove

Legal Name

Prefix	Given Name	Middle Name	Family Name	Suffix
	Jay	M.	Miazga	

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

City	Seattle	State/Province	WA	Country of Residence	US

Mailing Address of Inventor:

Address 1	4025 McKinley Pl. N		
Address 2			
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	Jed		McCann	

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Mailing Address of Inventor:

Address 1	7321 22nd Ave. NW		
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Inventor 6 — Remove

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	Paul		Goldenbaum	

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Mailing Address of Inventor:

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Title of the Invention	SYSTEMS AND METHODS FOR SAMPLE COLLECTION WITH REDUCED HEMOLYSIS		
Attorney Docket Number	MGMD-012/01US 316052-MGMD	**Small Entity Status Claimed**	☒
Application Type	Provisional		
Subject Matter	Utility		
Total Number of Drawing Sheets (if any)	36	**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:

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☐ **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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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.
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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).

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

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Application Data Sheet 37 CFR 1.76	Attorney Docket Number	MGMD-012/01US 316052-MGMD
	Application Number	
Title of Invention	SYSTEMS AND METHODS FOR SAMPLE COLLECTION WITH REDUCED HEMOLYSIS	

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.

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Application Data Sheet 37 CFR 1.76	Attorney Docket Number	MGMD-012/01US 316052-MGMD
	Application Number	
Title of Invention	SYSTEMS AND METHODS FOR SAMPLE COLLECTION WITH REDUCED HEMOLYSIS	

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 Data Sheet 37 CFR 1.76	Attorney Docket Number	MGMD-012/01US 316052-MGMD
	Application Number	
Title of Invention	SYSTEMS AND METHODS FOR SAMPLE COLLECTION WITH REDUCED HEMOLYSIS	

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	Magnolia Medical Technologies, Inc.		
Mailing Address Information For Applicant:			
Address 1	2001 Sixth Avenue		
Address 2	Suite 1630		
City	Seattle	**State/Province**	WA
Country	US	Postal Code	98121
Phone Number		Fax Number	
Email Address			

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Assignee Information including Non-Applicant Assignee Information:

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Application Data Sheet 37 CFR 1.76	Attorney Docket Number	MGMD-012/01US 316052-MGMD
	Application Number	
Title of Invention	SYSTEMS AND METHODS FOR SAMPLE COLLECTION WITH REDUCED HEMOLYSIS	

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.

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

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Address 2			
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Signature:

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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	/Michael D. Wintemitz/			Date (YYYY-MM-DD)	2016-11-18
First Name	Michael	Last Name	Wintemitz	Registration Number	73102

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Application Data Sheet 37 CFR 1.76	Attorney Docket Number	MGMD-012/01US 316052-MGMD
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Title of Invention	SYSTEMS AND METHODS FOR SAMPLE COLLECTION WITH REDUCED HEMOLYSIS	

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.

SYSTEMS AND METHODS FOR SAMPLE COLLECTION WITH REDUCED HEMOLYSIS

Background

[1001] Embodiments described herein relate generally to the parenteral procurement of bodily-fluid samples, and more particularly to systems and methods for parenterally procuring bodily-fluid samples, such as blood, with reduced hemolysis.

[1002] Health care practitioners routinely draw bodily-fluids from a patient for various testing and/or donation purposes. In some instances, the process of obtaining the bodily-fluids, and in particular, blood, can result in a degradation and/or breakdown of portions and/or constituents contained in the bodily-fluid. Specifically, hemolysis of red blood cells (i.e., a rupturing of the red blood cells and the release of cytoplasm) during blood draw is a known problem in the field of phlebotomy and/or medical testing. Hemolysis of blood is the most common pre-analytical source of error in clinical testing, accounting for nearly 60% of all rejected samples (Bonini P, Plebani M, Ceriotti F, Rubboli F (2002). Errors in laboratory medicine. *Clinical Chemistry*, 48, 691-698; and Plebani M, Carraro P (1997). Mistakes in a stat laboratory: types and frequency. *Clinical Chemistry*, 43, 1348-1351). Moreover, hemolyzed sample rates from hospital emergency rooms can be as high as 30% (Grant M (2003). The effect of blood drawing techniques and equipment on the hemolysis of ED laboratory blood samples. *Journal of Emergency Nursing*, 29 (2), 116-121, and Soderberg J, Jonsson PA, Wallin O, Grankvist K, Hultdin J (2009). Hemolysis index—an estimate of pre-analytical quality in primary health care. *Clinical Chemistry and Laboratory Medicine*, 47, 940-944). In some know blood draw systems, the arrangement and/or coupling of multiple devices to form a fluid flow path from a patient to, for example, a sample reservoir or container, shear stress exerted on or within the red blood cells, exposure time, and/or the like can lead to an increased likelihood of hemolysis within a sample volume.

[1003] Thus, a need exists for systems and methods for sample collection with reduced hemolysis.

Summary

[1004] Systems and methods for parenterally procuring bodily-fluid samples, such as blood, with reduced hemolysis are described herein. In some embodiments, a collection system has a proximal end portion, a distal end portion, and an inner surface defining a fluid flow path therethrough. The distal end portion is configured to be placed in fluid communication with a patient. The proximal end portion is configured to be placed in fluid communication with a fluid reservoir. The fluid flow path defined by the inner surface is associated with at least one flow characteristic configured to limit a stress within the flow of the bodily-fluid between the distal end portion and the proximal end portion.

Brief Description of the Drawings

[1005] FIG. 1 is a schematic illustration of a bodily-fluid collection device according to an embodiment.

[1006] FIG. 2 is a perspective view of a needle included in a bodily-fluid collection device according to an embodiment.

[1007] FIG. 3 is an enlarged view of a portion of the needle of FIG. 2, identified by the region A_1.

[1008] FIGS. 4-6 are illustrations of a needle used to deliver a cannula to a portion of the body according to an embodiment.

[1009] FIG. 7 is a perspective view of a portion of a needle included in a bodily-fluid collection device according to another embodiment.

[1010] FIG. 8 is a perspective view of a portion of a bodily-fluid collection device according to an embodiment.

[1011] FIG. 9 is a cross-sectional view of the bodily-fluid collection device of FIG. 8, taken along the line 9-9.

[1012] FIG. 10 is an enlarged view of a portion of the bodily-fluid collection device of FIG. 9, identified by the region A_2.

[1013] FIG. 11 is a front view of a portion of a bodily-fluid collection device according to an embodiment.

[1014] FIG. 12 is a cross-sectional view of the portion of the bodily-fluid collection device of FIG. 11, taken along the line 12-12.

[1015] FIG. 13 is an enlarged view of a portion of the bodily-fluid collection device of FIG. 12, identified by the region A_3.

[1016] FIG. 14 is a cross-sectional view of a portion of a bodily-fluid collection device according to another embodiment.

[1017] FIG. 15 is an enlarged view of a portion of the bodily-fluid collection device of FIG. 14, identified by the region A_4.

[1018] FIG. 16 is a cross-sectional view of a portion of a bodily-fluid collection device according to another embodiment.

[1019] FIG. 17 is a cross-sectional view of a portion of a bodily-fluid collection device according to another embodiment.

[1020] FIG. 18 is a perspective view of a portion of a bodily-fluid collection device according to an embodiment.

[1021] FIG. 19 is an exploded view of the portion of the bodily-fluid collection device of FIG. 18.

[1022] FIG. 20 is a cross-sectional view of the portion of the bodily-fluid collection device of FIG. 18, taken along the line 20-20.

[1023] FIG. 21 is a perspective view of a restrictor included in a bodily-fluid collection device according to an embodiment.

[1024] FIG. 22 is a cross-sectional view of the restrictor of FIG. 21, taken along the line 22-22.

[1025] FIG. 23 is a top view of a baffle included in the restrictor of FIG. 21.

[1026] FIG. 24 is a cross-sectional view of the baffle of FIG. 23, taken along the line 24-24.

[1027] FIG. 25 is a perspective view of a restrictor included in a bodily-fluid collection device according to an embodiment.

[1028] FIG. 26 is a cross-sectional view of the restrictor of FIG. 25, taken along the line 26-26.

[1029] FIG. 27 is a perspective view of an adapter included in a bodily-fluid collection device according to an embodiment.

[1030] FIG. 28 is a cross-sectional view of the adapter of FIG. 27, taken along the line 28-28.

[1031] FIG. 29 is a front view of a portion of the adapter of FIG. 27.

[1032] FIG. 30 is a cross-sectional view of the portion of the adapter illustrated in FIG. 29, taken along the line 30-30.

[1033] FIG. 31 is a perspective view of the portion of the adapter illustrated in FIG. 29 coupled to a fluid reservoir according to an embodiment.

[1034] FIG. 32 is an exploded view of the fluid reservoir of FIG. 31.

[1035] FIG. 33 is a cross-sectional view of the portion of the adapter and the fluid reservoir illustrated in FIG. 31, taken along the line 33-33.

[1036] FIG. 34 is a cross-sectional view of an adapter coupled to a fluid reservoir according to another embodiment.

[1037] FIG. 35 is a cross-sectional view of an adapter coupled to a fluid reservoir according to another embodiment.

[1038] FIG. 36 is a cross-sectional view of an adapter coupled to a fluid reservoir according to another embodiment.

[1039] FIG. 37 is a perspective view of an adapter coupled to a fluid reservoir according to another embodiment.

[1040] FIG. 38 is a cross-sectional view of the adapter and the fluid reservoir of FIG. 37, taken along the line 38-38.

[1041] FIG. 39 is a perspective view of an adapter coupled to a fluid reservoir according to another embodiment.

[1042] FIG. 40 is a perspective view of an adapter coupled to a fluid reservoir according to another embodiment.

[1043] FIGS. 41 and 42 are cross-sectional views of the adapter and the fluid reservoir of FIG. 40, taken along the line 41-41, in a first configuration and a second configuration, respectively.

[1044] FIG. 43 is a perspective view of an adapter and a fluid reservoir according to another embodiment.

[1045] FIG. 44 is a cross-sectional view of the adapter and the fluid reservoir of FIG. 43, taken along the line 44-44.

[1046] FIGS. 45-47 are cross-sectional views of an adapter and a fluid reservoir each according to a different embodiment.

[1047] FIG. 48 is a perspective of an adapter included in a bodily-fluid collection device according to another embodiment.

[1048] FIG. 49 is a cross-sectional view of the adapter of FIG. 48, taken along the line 49-49.

[1049] FIG. 50 is a perspective view of a fluid reservoir included in a bodily-fluid collection device according to an embodiment.

[1050] FIG. 51 is a cross-sectional view of the adapter illustrated in FIG. 49 coupled to the fluid reservoir illustrated in FIG. 50, taken along the line 51-51 in FIG. 50.

[1051] FIG. 52 is a perspective view of a fluid reservoir included in a bodily-fluid collection device according to another embodiment.

[1052] FIG. 53 is a cross-sectional view of the fluid reservoir of FIG. 52, taken along the line 53-53.

[1053] FIG. 54 is a perspective view of a fluid reservoir included in a bodily-fluid collection device according to another embodiment.

[1054] FIG. 55 is an exploded view of a plunger included in the fluid reservoir of FIG. 54.

[1055] FIG. 56 is a cross-sectional view of the fluid reservoir of FIG. 54, taken along the line 56-56.

[1056] FIG. 57 is a perspective view of a fluid reservoir included in a bodily-fluid collection device according to another embodiment.

[1057] FIG. 58 is a cross-sectional view of the fluid reservoir of FIG. 57, taken along the line 58-58.

[1058] FIG. 59 is a front view of a fluid reservoir included in a bodily-fluid collection device according to another embodiment.

[1059] FIG. 60 is a cross-sectional view of a fluid reservoir included in a bodily-fluid collection device according to another embodiment.

[1060] FIG. 61 is a perspective view of an adapter included in a bodily-fluid collection device according to another embodiment.

[1061] FIG. 62 is an exploded view of the adapter of FIG. 61.

[1062] FIG. 63 is a cross-sectional view of the adapter of FIG. 61, taken along the line 63-63.

[1063] FIG. 64 is a perspective view of an adapter included in a bodily-fluid collection device according to another embodiment.

[1064] FIG. 65 is an exploded view of the adapter of FIG. 64.

[1065] FIG. 66 is a cross-sectional view of the adapter of FIG. 65, taken along the line 66-66.

[1066] FIG. 67 is a perspective view of an adapter included in a bodily-fluid collection device according to another embodiment.

[1067] FIG. 68 is a cross-sectional view of the adapter of FIG. 67, taken along the line 68-68.

[1068] FIG. 69 is a perspective view of an adapter included in a bodily-fluid collection device according to another embodiment.

[1069] FIG. 70 is an exploded view of the adapter of FIG. 69.

[1070] FIG. 71 is a cross-sectional view of the adapter of FIG. 69, taken along the line 71-71.

Detailed Description

[1071] Systems and methods for parenterally procuring bodily-fluid samples, such as blood, with reduced hemolysis are described herein. In some embodiments, a collection system has a proximal end portion, a distal end portion, and an inner surface defining a fluid flow path therethrough. The distal end portion is configured to be placed in fluid communication with a patient. The proximal end portion is configured to be placed in fluid communication with a fluid reservoir. The fluid flow path defined by the inner surface is associated with at least one flow characteristic configured to limit a stress within the flow of the bodily-fluid between the distal end portion and the proximal end portion.

[1072] As used in this specification and the appended 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.

[1073] As used herein, "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. Moreover, while the embodiments and/or devices herein are specifically described as reducing, limiting, inhibiting, and/or substantially preventing hemolysis of blood withdrawn therethrough, any of the embodiments and/or devices can be used for controlling a flow of any suitable bodily-fluid (e.g., such as those listed above) when withdrawn from the body of a patient through that device.

[1074] 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 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).

[1075] As used herein, the terms "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.

[1076] As used herein, the terms "about," "approximately," and "substantially" when used in connection with a numerical value is intended to convey that the value so defined is nominally the value stated. Said another way, the terms about, approximately, and substantially when used in connection with a numerical value generally include the value stated plus or minus a given tolerance. For example, in some instances, a suitable tolerance can be plus or minus 10% of the value stated; thus, about 0.5 would include 0.45 and 0.55, about 10 would include 9 to 11, about 1000 would include 900 to 1100. In other instances, a suitable tolerance can be plus or minus an acceptable percentage of the last significant figure in the value stated. For example, a suitable tolerance can be plus or minus 10% of the last significant figure; thus, about 10.1 would include 10.09 and 10.11, approximately 25 would include 24.5 and 25.5. Such variance can result from manufacturing tolerances or other practical considerations (such as, for example, tolerances associated with a measuring instrument, acceptable human error, or the like).

[1077] As used herein, the term "laminar" refers to an organized and/or orderly fluid flow in parallel layers without lateral mixing, crosscurrents, eddy currents, and/or the like. More generally, the term "laminar" is intended to convey a flow of fluid that is smooth and/or free of turbulence. Moreover, the term "substantially" when used in connection with "laminar" is intended to convey that a fluid flow so defined is nominally a laminar fluid flow. As one example, a portion of a fluid transfer device defining a lumen that is described as facilitating and/or otherwise causing a "substantially laminar" fluid flow therethrough is intended to

convey that, although laminar fluid flow is desirable, some non-laminar flow can occur. Such variances (e.g., turbulence or the like) can result from manufacturing tolerances, or other practical considerations. Thus, a fluid having a "substantially laminar" flow includes such non-laminar flow characteristics within an industry-accepted tolerance. For example, while it may be desirable that a bodily-fluid transfer device transfer a laminar flow of blood therethrough a "substantially laminar flow" of blood can be 99% laminar, 95% laminar, 90% laminar, or any other acceptable tolerance thereof.

[1078] The embodiments described herein can be formed or constructed of one or more biocompatible materials. 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.

[1079] In some current phlebotomy procedures, blood is drawn from a patient using multiple components that are physically and fluidically coupled to define a fluid flow path between the patient and a collection device and/or fluid reservoir used to capture the bodily-fluid sample. In some such systems, however, the physical and/or fluidic interfaces formed between the components can result in turbulent regions and/or eddy currents within the flow of the blood, which in turn, can result in a stress within the flow that is sufficient to sheer, rupture, and/or otherwise damage the red blood cells. In addition, the process of drawing blood from a patient often involves exposing the blood to a negative pressure differential produced, for example, by placing an evacuated container (e.g., a Vacutainer ™) in fluid communication with a portion of the body. In some instances, the pressure differential can increase an internal stress within a flow of blood to an extent that results in hemolysis of the red blood cells. In other instances, the pressure differential can be attributed to the physical

exertion associated with a clinician actuating, for example, a syringe with a force sufficient to rupture the red blood cells during the collection process. A number of factors (for example, small veins, dehydration, veins with scar tissue, presence of sclerosis, and/or the like) can make vascular access a challenge. In such cases, excess negative pressure exerted during the collection process can result in hemolysis.

[1080] While such a negative pressure differential often facilitates withdraw of the blood, it also can produce a relatively high shear stresses within the red blood cells and/or a relatively high flow velocity of the blood through a flow path defined between the patient and the fluid reservoir (e.g., evacuated container). As a result, the red blood cells contained within the flow of blood can be damaged as the cells pass through the physical and/or fluidic interfaces formed between different components of a transfer device. In some instances, the relatively high velocity of the blood flow as the blood enters the containers can result in the blood impacting an inner surface of the container with a force sufficient to damage the red blood cells and/or other components of the blood. In addition, exposure time of a needle and/or catheter within the vein can result in hemolysis of the red blood cells.

[1081] Thus, to mitigate the risk of hemolysis of a sample volume of blood, various portions of a fluid flow path between the patient and the sample reservoir can be optimized. Such optimization can be done holistically (i.e., a system wide optimization) or done piecemeal (i.e., optimization of at least one potential source of hemolysis). By way of example, in some instances, any of the embodiments described herein, can be used independently to mitigate the risk of hemolysis at a specific point along a fluid flow path between a patient and a sample reservoir. That is to say, the embodiments described herein can be characterized by the potential source of hemolysis that the embodiments, so characterized, mitigate. For example, the embodiments described herein generally address six potential categories, portions, and/or sources of hemolysis along a fluid flow path between a patient and a fluid reservoir. Namely, the embodiments described herein can be used to mitigate the risk of hemolysis otherwise associated with (1) blood flow from, for example, a vein into a puncture member, needle, cannula, and/or the like, (2) blood flow through changing geometries and/or physical and fluidic interfaces; (3) blood flow rates and/or velocity within the fluid flow path; (4) blood flow from an adapter, puncture member, needle, cannula, and/or the like into a fluid reservoir; (5) blood flow exposure to a negative

pressure differential within a fluid reservoir, and (6) blood flow through a multi-lumen adapter and/or the like.

[1082] FIG. 1 is a schematic illustration of a portion of a bodily-fluid collection device 100, according to an embodiment. Generally, the bodily-fluid collection device 100 (also referred to herein as "fluid collection device," "collection device," or "device") can be used to percutaneously withdraw bodily-fluid from a patient. In some instances, the device 100 can be used to withdraw a volume of blood from a patient that is to be used as a biological sample for testing and/or assays associated with medical diagnosis and/or treatment. In other instances, the device 100 can be used to withdraw a volume of blood for collection purposes such as, for example, blood donation or the like. More particularly, the device 100 is configured to limit, inhibit, and/or substantially prevent hemolysis of at least a portion of the blood drawn therethrough, as described in further detail herein.

[1083] The device 100 has a proximal end portion 101 and a distal end portion 102 and defines a lumen 104 therethrough. More specifically, the device 100 includes an inner surface 103 that defines the lumen 104. The device 100 can be any suitable device or group of devices (e.g., a system including multiple devices). In some embodiments, for example, the device 100 can be a needle, a cannula, a trocar, a catheter, and/or the like. In such embodiments, the distal end portion 102 of the device 100 can include a sharpened, angled, or beveled edge configured to puncture the cutaneous layer of the body to place the lumen 104 in fluid communication with, for example, a vascular structure and/or the like. The proximal end portion 101 of the device 100 can be physically and/or fluidically coupled to any other suitable device such as, for example, a collection reservoir (not shown in FIG. 1). As such, the lumen 104 defined by the device 100 defines fluid pathway through which blood can flow from the patient to an intermediary collection device and/or directly to the collection reservoir.

[1084] As described above, in some embodiments, the device 100 is configured to reduce, limit, inhibit, and/or substantially prevent hemolysis of blood withdrawn from the body and through the device. For example, in embodiments in which the device 100 is a needle, cannula, catheter, and/or the like, the distal end portion 102 of the device 100 can include rounded edges and/or a substantially smooth contour. As such, the constituents of the blood (e.g., the red blood cells or "erythrocytes") can flow relatively smoothly into the lumen

104 (e.g., in response to a negative pressure differential produced, for example, by a syringe and/or an evacuated container coupled thereto) substantially without being damaged.

[1085] Moreover, in some embodiments, the shape, size, and/or contour of the inner surface 103 can selectively control the flow of blood through the device 100. By way of example, in some embodiments, the inner surface 103 can form a substantially smooth contour, which can facilitate a laminar flow of the blood therethrough. In addition, the inner surface 103 can have a contour that can selectively control an amount of negative pressure within a region of the lumen 104. For example, in some embodiments, the inner surface 103 can have a diameter that is varied along the length of the device 100. That is to say, a first portion of the inner surface 103 can have a diameter that is different from a diameter of a second portion of the inner surface 103 and thus, can reduce, constrict, limit, and/or otherwise control a flow of blood therethrough. In some such embodiments, the first portion of the inner surface 103 can be disposed between the second portion of the inner surface 103 and a third portion of the inner surface 103 having a diameter greater than or equal to the diameter of the second portion of the inner surface 103. In such embodiments, a region of the lumen 104 having a relatively larger diameter can be associated with a larger pressure than a region of the lumen 104 having a relatively smaller diameter, while conversely, a velocity associated with the region of the lumen 104 having the relatively larger diameter is less than a velocity associated with the region of the lumen having the relatively smaller diameter based on the simplified Bernoulli's Equation mathematically represented by equation 1 below:

$$P_1 + {}^1/_2\,\rho V_1^2 = P_2 + {}^1/_2\,\rho V_2^2 \qquad \text{Equation 1}$$

wherein P is pressure within the lumen, ρ is density of the fluid, and V is velocity of the fluid.

[1086] While described above as being a needle, catheter, cannula, trocar, and/or the like, in other embodiments, the device 100 can be any suitable component included in a fluid transfer system. For example, the device 100 can be an adapter, a locking mechanism, a cannula, a coupling mechanism, a port, an inlet, and outlet, and/or the like. By way of example, in some embodiments, the device 100 can be an adapter configured to be physically and fluidically coupled to at least one other device such as, for example, a needle. Thus, the adapter (i.e., the device 100) can have an inner surface with a contour that can control a flow of bodily-fluid therethrough. Moreover, an interface between the device 100 and the needle

(and/or any other suitable device) can be arranged to reduce turbulence of a flow of bodily-fluid therebetween, as described in further detail herein.

[1087] In some embodiments, the device 100 can be coupled to a fluid reservoir or container (e.g., at the proximal end portion 101). As such, the contour of the inner surface 103 of the device 100 can control a flow of bodily-fluid therethrough (as described above), while the orientation of the device 100 relative to the fluid reservoir or container can control and/or direct the flow of bodily-fluid through the proximal end portion 101 toward an inner surface of the fluid reservoir to, for example, reduce a force associated with a portion of the flow of bodily-fluid impacting the inner surface. In some embodiments, the device 100 can be an insert or the like at least partially disposed within the fluid reservoir or container.

[1088] Although not shown in FIG. 1, in some embodiments, the device 100 can be used with (e.g., physically and fluidically coupled to) a device or mechanism configured to modulate a negative pressure within a fluid reservoir or container. For example, in some embodiments, the device 100 can be coupled to a syringe or the like configured to transition between a first configuration and a second configuration to produce a negative pressure within an inner volume. As such, a rate at which the syringe can be transitioned from the first configuration (e.g., associated with a plunger in a distal position) to the second configuration (e.g., associated with the plunger in a proximal position) can be constrained (e.g., limited, inhibited, slowed, governed, controlled, etc.), thereby reducing a negative pressure exerted through the lumen 104 of the device, as described in further detail herein.

[1089] While the device 100 is described above as including a surface, mechanism, portion, etc. configured to reduce hemolysis of a volume of blood in a mechanical manner (e.g., reducing pressure and/or turbulence within a flow path via a contour, restrictor, or the like; reducing forces associated with a portion of the volume of blood impacting a surface of a fluid reservoir via a coupling mechanism, interface, etc.; reducing damage to constituents in the volume of blood by limiting or eliminating sharp edges, corners, etc.; and/or the like), in other embodiments, the device can be configured to chemically modify one or more characteristics associated with the volume of blood. For example, in some embodiments, the inner surface 103 of the device 100 can be coated with a chemical configured to limit lysis of erythrocytes (red blood cells) by strengthening or weakening a cell wall of the erythrocytes. More specifically, in some embodiments, the device 100 can be configured to introduce a chemical into a flow of blood that can, for example, increase a rigidity of the cell wall of

erythrocytes (e.g., decrease flexibility), which in turn, can reduce a likelihood of lysis of the erythrocytes (e.g., hemolysis of the blood) as the blood flows through the device 100. In other embodiments, the device 100 can be configured to introduce a chemical into a flow of blood that can, for example, decrease a rigidity of the cell wall of erythrocytes (e.g., increase flexibility), which in turn, can reduce a likelihood of lysis of the erythrocytes as the blood flows through the device 100.

[1090] While described above as coating the inner surface 103 with the chemical configured to modify a characteristic of the cell wall of the erythrocytes, in other embodiments, the device 100 can include any suitable device, mechanism, and/or method for introducing such a chemical to the volume of blood flowing therethrough. For example, the device 100 can include a chamber containing such a chemical, a baffle impregnated with such a chemical, a dispensing or dispersing device (e.g., sprayer or the like) configured to dispense a volume of such a chemical, impregnation of the chemical directly into the material used to produce the device 100 and/or any other suitable means for introducing such a chemical.

[1091] FIGS. 2-7 illustrate embodiments configured to mitigate the risk of hemolysis as a volume of blood flows from the patient (e.g., a vein of a patient) and into a lumen-defining device such as a needle or the like. Specifically, FIGS. 2 and 3 illustrate a puncture member 210 coupled to an adapter 220 according to an embodiment. The puncture member 210 has a proximal end portion 211 and a distal end portion 212 and defines a lumen 213 therebetween. The proximal end portion 211 of the puncture member 210 is physically and fluidically coupled to a distal end portion 222 of the adapter 220, as described above with reference to FIG. 1. More specifically, the proximal end portion 211 of the puncture member 210 is coupled to the adapter 220 such that an interface therebetween forms a substantially smooth and/or continuous surface. Said another way, the interface between the puncture member 210 and the adapter 220 can be such that a transition between the lumen 213 of the puncture member 210 and a lumen (not shown in FIGS. 2-6) defined by the adapter is substantially smooth and/or continuous (i.e., does not introduce a discontinuity such as a change in alignment and/or diameter), as described in further detail herein.

[1092] The distal end portion 212 of the puncture member 210 is configured to be inserted through the cutaneous layer of the patient to transfer fluid to and/or from the patient. For example, the distal end portion 212 can be inserted into a vein of a patient and the adapter 220 can be coupled to a fluid reservoir and/or intermediary collection device configured to

receive a volume of blood from the patient via the lumen 213. More specifically, as shown in FIGS. 2 and 3, the distal end portion 212 of the puncture member 210 is sharpened, angled, and/or beveled, which facilitates the insertion of the puncture member 210 into the body. The lumen 213 of the puncture member 210 extends through the distal end portion 212, thereby defining an opening 214 that places the lumen 213 in fluid communication with, for example, a vascular structure (e.g., a vein) within which the distal end portion 212 is disposed. Furthermore, as shown in FIG. 3, a distal edge 215 of the puncture member 210 defining the opening 214 is substantially rounded, smoothed, contoured, blunted, and/or the like. In other words, the distal edge 215 defining the opening 214 forms a substantially round corner. Thus, blood drawn through the opening 214 and into the lumen 213 can flow past the distal edge 214 with reduced damage to, for example, the constituents of the blood (e.g., the erythrocytes) that would otherwise result from contact with a sharper, more abrupt, substantially orthogonal, and/or otherwise non-rounded distal edge 215.

[1093] In some instances, a puncture member can be used to deliver and/or place a portion of a catheter in a desired lumen within the body of a patient. For example, as shown in FIGS. 4-6, a puncture member 310 can be used to place a stented catheter and/or the like within a vein V. The puncture member 310 can be substantially similar to the puncture members 210 and/or 310 described above and thus, the puncture member is not described in further detail herein. As shown in FIG. 4, a user (e.g., a phlebotomist, nurse, technician, physician, doctor, etc.) can manipulate a portion of the puncture member 310 (e.g., either directly or indirectly) to place at least a distal end portion 312 of the puncture member 310 within a lumen defined by the vein V. Once disposed in the vein V, a guidewire 316 can be advanced through the lumen defined by the puncture member 310, as shown in FIG. 4. With the guidewire 316 positioned within the vein V, the user can advance an introducer catheter 317 and, for example, a stented catheter 318 along the guide wire 316 to dispose a distal end portion of at least the introducer catheter 317 within the lumen of the vein V, as indicated by the arrow AA in FIG. 5. In some instances, the stented catheter 318 can be inserted into the vein V concurrently with the introducer catheter 317. In other instances, the stented catheter 318 can be advanced within the introducer catheter 317 after the distal end portion of the introducer catheter 317 is disposed in the vein 317.

[1094] With the distal end portion of the stented catheter 318 disposed in the vein V, the guidewire 316 and the introducer catheter 317 can be moved in the proximal direction (i.e.,

withdrawn from the vein V), as indicated by the arrow BB in FIG. 6. In some embodiments, as the introducer catheter 317 is withdrawn from the vein V, the distal end portion of the stented catheter 318 can transition from a first configuration to a second configuration. For example, the stented catheter 318 can be in a collapsed configuration (e.g., the first configuration) when disposed in the introducer catheter 317 (FIG. 5) such that a diameter of the stented catheter 318 is substantially uniform. When the introducer catheter 318 is withdrawn from the vein (FIG. 6), the distal end portion of the stented catheter 318 can expand and/or otherwise reconfigure such that a diameter of the distal end portion of the stented catheter 318 is greater than a diameter of a portion of the stented catheter 318 still disposed in the introducer catheter 317.

[1095] In some embodiments, the distal end portion of the stented catheter 318 can expand to an extent that places an outer surface of the stented catheter 318 in close proximity to or directly in temporary contact with an inner surface of the vein V defining the lumen. As such, blood can be withdrawn from the vein V into a fluid reservoir (not shown in FIGS. 4-6) via a lumen defined by the stented catheter 318. Moreover, with the distal end portion of the stented catheter 318 in close proximity to or directly in contact with the inner surface of the vein, the stented catheter 318 can inhibit, limit, and/or substantially prevent a collapse of at least a portion of the vein V (e.g., in response to a negative pressure differential between the vein V and the fluid reservoir (not shown). In some embodiments, the arrangement of at least the distal end portion of the stented catheter 318, when in the second configuration, can allow a flow of blood to enter the stented catheter 318 substantially without damaging the constituents of the blood, as described above with reference to FIGS. 2 and 3. While the puncture member 310 is described above as being retracted once the stented catheter 318 is placed in a desired position with the vein, in other embodiments, the puncture member 310 need not be retracted. As such, the stented catheter 318 can be, for example, a sleeve or the like disposed about the distal end portion 312 of the puncture member 310 to control a flow of blood entering the lumen of the puncture member 310. Moreover, as described above with reference to the puncture member 210, a surface of the puncture member 310 and/or the stented catheter 318 defining a distal opening can be substantially rounded, smoothed, contoured, blunted, and/or the like. In other words, a distal edge of the puncture member 310 and/or stented catheter 318 defining the distal opening forms a substantially round corner. Thus, blood drawn through the opening can flow past the distal edge with reduced damage to

the erythrocytes that would otherwise result from contact with a sharper, more abrupt, substantially orthogonal, and/or otherwise non-rounded distal edge 215.

[1096] While described above as placing a stented catheter, in other embodiments, a puncture member can be used to place any suitable catheter and/or cannula. For example, FIG. 7 illustrates a puncture member 410 and a catheter 418 according to another embodiment. The puncture member 410 can be used, for example, to place at least a portion of the catheter 418 within a lumen defined by the body (e.g., a vein). As shown in FIG. 7, a distal end portion 412 of the puncture member 410 can include a substantially rounded distal edge 415, as described above with reference to the puncture member 210. In this manner, a flow of blood can flow past the distal edge 415 to enter a lumen 413 defined by the puncture member 410. Similarly, the catheter 418 can include a distal edge 418A that is substantially rounded. As shown in FIG. 7, the distal end portion 412 of the puncture member 410 extends beyond the distal edge 418A of the catheter 418. In some embodiments, the distal end portion 412 of the puncture member 410 can form and/or can define a recessed portion 419 or the like that corresponds with a position at or near the distal edge 418A of the catheter 418. In this manner, when the puncture member 410 is inserted into, for example, a vein of a patient, an opening in the vein defined by the puncturing can be a diameter that is substantially the same as an outer diameter of the catheter 418. As such, the catheter 418 can be positioned within the vein without rupturing and/or otherwise dilating the opening in the vein. In some instances, once the catheter 418 is disposed in the lumen defined by the vein, the puncture member 410 can be retracted through the catheter 418 while at least a distal end portion of the catheter 418 remains within the vein. In such instances, the substantially rounded distal edge 418A can reduce and/or can substantially prevent hemolysis of a volume of blood flowing to the catheter 418, as described above with reference to the puncture member 310 in FIGS. 2 and 3.

[1097] While the puncture members 210, 310, and 410 are particularly shown and described above, in other embodiments, any suitable puncture member can be coupled to any compatible adapter, which in turn, can place the puncture member in fluid communication with a fluid collection device. For example, FIGS. 8-17 illustrate embodiments configured to mitigate the risk of hemolysis as a volume of blood flows through changing geometries and/or physical and fluidic interfaces of one or more adapters. Specifically, FIGS. 8-10 illustrate a puncture member 510 coupled to an adapter 520, according to another

embodiment. In some embodiments, the puncture member 510 and the adapter 520 can be and/or can form, for example, a butterfly needle or the like. More specifically, the puncture member 510 has a proximal end portion 511 and a distal end portion 512 and defines a lumen 513 therethrough. The proximal end portion 511 is coupled to the adapter 520, as described in further detail herein. The distal end portion 512 of the puncture member 510 can be any suitable configuration. For example, the distal end portion 512 of the catheter 510 can be substantially similar to or the same as the distal end portion 212 of the catheter 210 described above with reference to FIGS. 2 and 3. That is to say, the arrangement of the distal end portion 512 of the catheter 510 can limit and/or substantially prevent damage (e.g., hemolysis) to blood as blood flow past the distal end portion 512 and into the lumen 513.

[1098] The adapter 520 has a proximal end portion 521, a distal end portion 522, and an inner surface 523. As described above, the adapter 520 can have an overall shape substantially similar to known butterfly needles. While shown in FIG. 8 as being substantially cylindrical with varying diameters, the adapter 520 can be any suitable shape, size, or configuration such as square, rectangular, polygonal, and/or any other non-cylindrical shape. In this manner, the overall shape of the adapter 520 can facilitate the handling of the transfer device 520 by including similar geometric features as known butterfly needles. The distal end portion 522 of the adapter 520 is physically and fluidically coupled to the proximal end portion 511 of the puncture member 510, as described in further detail herein. The proximal end portion 521 of the adapter 520 can be any suitable configuration. In some embodiments, the proximal end portion 521 can be a port and/or a portion of a locking mechanism. For example, in this embodiment, the proximal end portion 521 of the adapter 520 is a locking mechanism configured as a male portion of a Luer Lok ®. Moreover, in this embodiment, such a locking mechanism is disposed at a proximal end portion of a cannula configured to extend between the proximal end portion 521 and the distal end portion 522 of the adapter 520. In other embodiments, the adapter 520 is monolithically formed without a cannula between the proximal end portion 521 and the distal end portion 522. Although the proximal end portion 521 is described as including a locking mechanism, in other embodiments, the proximal end portion 521 can be any suitable configuration configured to interface with any suitable device such that blood flows in a substantially laminar, smooth, and/or non-turbulent flow between the adapter 520 and the device.

[1099] As shown in FIGS. 9 and 10, the inner surface 523 of the adapter 520 defines a lumen 524 extending through the proximal end portion 521 and the distal end portion 522. In some embodiments, the arrangement of the inner surface 523 can reduce, inhibit, and/or substantially prevent, for example, hemolysis of a volume of blood flowing within the lumen 524. More specifically, as shown in FIG. 10, the distal end portion 522 of the adapter 520 is coupled to the proximal end portion 511 of the puncture member 510 such that the lumen 513 of the puncture member 510 is substantially aligned with and substantially the same diameter as the lumen 524 of the adapter 520. That is to say, the proximal end portion 511 of the puncture member 510 is coupled to the distal end portion 522 of the adapter 520 such that a substantially smooth and/or continuous transition is defined between the lumen 513 of the puncture member 510 and the lumen 524 of the adapter 520. Similarly, in embodiments including the cannula extending between the end portions, a distal end portion of the cannula can be coupled to the distal end portion 522 of the adapter 520 in such a manner as to define a substantially smooth transition therebetween.

[1100] In addition, the inner surface 523 of the adapter 520 defines a tapered portion that extends between the puncture member 510 and the cannula. Expanding further, a first portion of the inner surface 523 (e.g., a more proximal portion) defines a first diameter that is substantially the same as an inner diameter defined by the cannula, while a second portion of the inner surface (e.g., a more distal portion) defines a second diameter, smaller than the first diameter, that is substantially the same as an inner diameter defined by the lumen 513 of the puncture member 510. As shown in FIG. 10, the tapered portion can form a substantially smooth transition between, for example, the first diameter and the second diameter. In some instances, such a smooth transition, for example, from the first diameter to the second diameter can facilitate, produce, encourage, and/or force a substantially laminar flow (e.g., consistent, uniform, non-turbulent, uninterrupted, smooth, etc.) of a volume of bodily-fluid (e.g., blood) through the lumen 524. Moreover, the smooth or substantially uniform transitions between the puncture member 510 and the adapter 520 and/or the smooth or substantially uniform transitions between the various components of the adapter 520 can reduce eddy currents (i.e., circulating currents often resulting from a discontinuity) or the like within the flow of blood. Thus, when the distal end portion 512 of the puncture member 510 is disposed in a vein or the like and the proximal end portion 521 (e.g., a locking mechanism) is physically and fluidically coupled to a fluid reservoir, a volume of blood can flow within the lumens 513 and 524 from the patient to the fluid reservoir with reduced damage to the

constituents of the blood (e.g., hemolysis of the erythrocytes) that might otherwise occur as a result of misaligned interfaces and/or discontinuities; abrupt changes in diameter; turbulence and/or eddy currents within a flow of blood therethrough; and/or the like.

[1101] While the adapter 520 is particularly shown and described above with reference to FIGS. 8-10, in other embodiments, an adapter can be any suitable configuration and can be arranged within a system of components to form a physical and/or fluidic interface therebetween. For example, FIGS. 11-13 illustrate a first adapter 620 coupled to a second adapter 630 according to an embodiment. The first adapter 620 has a proximal end portion 621, a distal end portion 622 and an inner surface 623. The inner surface 623 of the first adapter 620 defines a lumen 624 extending through its proximal end portion 621 and its distal end portion 622.

[1102] As shown in FIGS. 12 and 13, the inner surface 623 of the first adapter 620 includes and/or otherwise forms a shoulder 625. More specifically, the shoulder 625 formed by the inner surface 623 is associated with a change in diameter of the inner surface 623. As shown in FIG. 13, the shoulder 625 forms a substantially annular discontinuity that has substantially rounded corners or edges. In this manner, the transition from a diameter of the inner surface 623 proximal to the shoulder 625 to a diameter of the inner surface distal to the shoulder 625 can be relatively smooth rather than forming a relatively sharp, abrupt, and/or orthogonal corner (e.g., shoulder). As such, the arrangement of the shoulder 625 can limit, inhibit, and/or substantially prevent hemolysis of blood as the blood flows within the lumen 624 past the shoulder 625.

[1103] The second adapter 630 has a proximal end portion 631, a distal end portion 632, and an inner surface 633. The inner surface 633 of the second adapter 630 defines a lumen 624 extending through its proximal end portion 631 and its distal end portion 632. As shown in FIGS. 11-13, a portion of the second adapter 630 can be inserted into a portion of the lumen 624 defined by the first adapter 620 to couple the second adapter 630 to the first adapter 620. In some embodiments, the first adapter 620 and the second adapter 630 can form a friction fit and/or the like, which in turn, can define a substantially fluid tight seal therebetween. Thus, the second adapter 630 can be inserted into the first adapter 620 to couple the second adapter 630 thereto.

[1104] Similarly, the distal end portion 632 of the second adapter 630 is configured to reduce, limit, and/or substantially prevent hemolysis of blood as the blood flow therethrough. Specifically, as shown in FIG. 13, a distal most surface of the second adapter 630 and the inner surface 633 of the second adapter 630 form a rounded corner 635 and/or smooth transition therebetween. The rounded corner 635 formed by the second adapter 630 defines a relatively smooth transition from an outer diameter of the second adapter 630 (e.g., at the distal end) to an inner diameter of the second adapter 630 (e.g., at the distal end) rather than forming a relatively sharp, abrupt, and/or orthogonal corner. In some embodiments, a radius of curvature associated with the rounded corner 635 of the second adapter 630 can be substantially similar to a radius of curvature associated with the shoulder 625 of the first adapter 620. Thus, when the second adapter 630 is disposed within the first adapter 620, a volume of bodily-fluid (e.g., blood) can flow through the lumen 624 of the first adapter 620 and the lumen 634 of the second adapter 630 to be disposed within a fluid reservoir or the like. Moreover, the arrangement of the shoulder 625 of the first adapter 620 and the rounded corner 635 of the second adapter 630 can, for example, reduce, limit, and/or substantially prevent hemolysis of blood flowing therethrough that might otherwise result from contact substantially abrupt, sharp, and/or orthogonal corners or the like. In addition, the arrangement of the shoulder 625 of the first adapter 620 and the rounded corner 635 of the second adapter 630 can facilitate, produce, encourage, and/or otherwise result in a substantially laminar flow through the lumens 624 and 634, respectively (e.g., with little turbulence, eddy currents, etc.).

[1105] Although the first adapter 620 and the second adapter 630 are shown in FIGS. 11-13 as each forming substantially rounded corners and/or shoulders, in other embodiments, a first adapter and a second adapter can be coupled together to form an interface therebetween having any suitable arrangement and/or configuration. For example, FIGS. 14 and 15 illustrate a first adapter 720 coupled to a second adapter 730 according to another embodiment. The first adapter 720 has a proximal end portion 721, a distal end portion 722 and an inner surface 723. The inner surface 723 of the first adapter 720 defines a lumen 724 extending through its proximal end portion 721 and its distal end portion 722. Furthermore, the inner surface 723 includes and/or otherwise forms a shoulder 725. In this embodiment, the shoulder 725 is associated with a change in diameter of the inner surface 723. As shown in FIG. 15, the shoulder 725 forms a substantially annular discontinuity with a substantially orthogonal corner. Said another way, the shoulder 725 has a substantially non-rounded

corner (e.g., has no radius of curvature of a nominal radius of curvature) that defines an edge or the like.

[1106] The second adapter 730 has a proximal end portion 731, a distal end portion 732, and an inner surface 733. The inner surface 733 of the second adapter 730 defines a lumen 724 extending through its proximal end portion 731 and its distal end portion 732. As shown in FIGS. 14 and 15, a portion of the second adapter 730 can be inserted into a portion of the lumen 724 defined by the first adapter 720 to couple the second adapter 730 to the first adapter 720. As shown in FIG. 14, the distal most surface of the second adapter 730 and the inner surface 733 of the second adapter 730 form a substantially orthogonal corner 735 (e.g., a substantially non-rounded corner, as described above). In some embodiments, the first adapter 720 and the second adapter 730 can be substantially similar to known adapters (e.g., each adapter forms relatively abrupt and/or substantially orthogonal corners and/or edges).

[1107] While such corners, discontinuities, and/or edges are described above as a potential source of blood hemolyzation, in this embodiment, a gasket 726 is disposed between and in contact with the shoulder 725 of the first adapter 720 and the distal surface of the second adapter 730, as shown in FIG. 15. The gasket 726 can be, for example, an elastomeric gasket and/or the like that is in contact with the distal surface of the second adapter 730 and the shoulder 725 of the first adapter 720 to define a substantially fluid tight seal therebetween. Moreover, the gasket 726 defines an opening and/or lumen therethrough that can have a size and/or diameter substantially similar to the size and/or diameter of the lumens 724 and 734. Thus, the arrangement of the gasket 726 can reduce a magnitude of the discontinuities formed by the shoulder 725 of the first adapter 720 and the distal end of the second adapter 730. As a result, the gasket 726 disposed between the shoulder 725 of the first adapter 720 and the distal surface of the second adapter 730 can, for example, reduce, limit, and/or substantially prevent hemolysis of blood flowing therethrough that might otherwise result from relatively large changes and/or discontinuities in the diameters of the inner surfaces 723 and 733, respectively. In addition, the gasket 726 can facilitate, produce, encourage, and/or otherwise result in a substantially laminar flow of fluid through the lumens 724 and 734, respectively (i.e., with little to no turbulence, eddy currents, etc.).

[1108] In some embodiments, the gasket 726 can be configured to restrict, limit, reduce, and/or otherwise control a flow of blood and/or a pressure exerted therethrough. For example, while the gasket 726 is described above as having substantially the same size and/or

diameter as the lumens 724 and 734, in other embodiments, the gasket 726 can have a size and/or diameter that is greater than or less than the diameter of the lumens 724 and 734. Specifically, in some embodiments, the size and/or diameter of the gasket 726 can be less than the diameter of the lumens 724 and 734 and, as such, the gasket 726 can restrict, constrict, reduce, limit, and/or otherwise control a flow of blood therethrough. In some embodiments, such a reduction and/or restriction of the blood flowing through the gasket 726 can reduce a likelihood of hemolysis of the blood resulting from, for example, a flow rate and/or a large pressure differential between a volume having a relatively high pressure disposed on a first side of the gasket 726 and a volume having a relatively low pressure disposed on a second side of the gasket 726.

[1109] FIG. 16 illustrates a portion of a first adapter 820 coupled to a portion of a second adapter 830 according to another embodiment. The first adapter 820 has a proximal end portion 821 configured to be coupled to a distal end portion 832 of the second adapter 830, as described in further detail herein. Although only the proximal end portion 821 of the first adapter 820 is shown in FIG. 16, the first adapter 820 can be similar in size and/or shape as the first adapters 620 and/or 720, unless otherwise expressed. The first adapter 820 includes an inner surface 823 that defines a lumen 824 extending through at least its proximal end portion 821. As shown in FIG. 16, the inner surface 823 of the first adapter 820 includes and/or otherwise forms a shoulder 825. The shoulder 825 formed by the inner surface 823 is associated with a change in diameter of the inner surface 823. More specifically, the shoulder 825 is associated with and/or forms a tapered or chamfered portion of the inner surface 823, as described in further detail herein.

[1110] Although only the distal end portion 832 of the second adapter 830 is shown in FIG. 16, the second adapter 830 can be any suitable shape, size, or configuration. For example, the distal end portion 832 of the second adapter 830 can form and/or can include a locking mechanism or the like while a proximal end portion (not shown in FIG. 16) can be coupled to and/or can form any suitable portion of a fluid collection device such as, for example, a fluid reservoir, a conduit, a flow control mechanism, and/or the like. In this embodiment, the distal end portion 832 of the second adapter 830 includes and/or forms a locking mechanism configured to form a threaded coupling with, for example, the proximal end portion 821 of the first adapter 820. In other embodiments, the distal end portion 832 of the second adapter 830 can be any suitable configuration.

[1111] As shown in FIG. 16, the second adapter 830 includes an inner surface 833 that defines a lumen 834 extending through at least its distal end portion 832. Moreover, the distal end portion 832 of the second adapter 830 includes and/or forms a distal surface 835 that is substantially tapered or chamfered. In some embodiments, the distal surface 835 of the second adapter 830 can have a size, shape, angle, etc. that substantially corresponds with the shoulder 825 defined by the first adapter 820. Thus, when the first adapter 820 is coupled to the second adapter 830 (e.g., via a threaded coupling or the like), the distal surface 835 of the second adapter 830 can be brought into contact with the shoulder 825 of the first adapter 820. Moreover, the arrangement of the first adapter 820 and the second adapter 830 is such that when the distal surface 835 of the second adapter 830 is placed in contact with the shoulder 825 of the first adapter 820, the inner surfaces 833 and 823, respectively, are brought into alignment, as shown in FIG. 16. In this manner, the inner surfaces 823 and 833 can form a substantially continuous surface having, for example, a substantially constant diameter. Thus, by reducing and/or substantially eliminating a discontinuity otherwise associated with the physical and fluidic coupling of the first adapter 820 and the second adapter 830, blood can flow within the lumens 824 and 834 of the adapters 820 and 830, respectively, with little or substantially no hemolysis of the blood flowing therethrough.

[1112] Although the inner surfaces 823 and 833 of the first adapter 820 and the second adapter 830, respectively, are described above as having a substantially constant diameter, in other embodiments, a diameter of each inner surface 823 and 833 can be varied. Such arrangement, however, is such that the inner surfaces 823 and 833 form a substantially smooth transition between, for example, a smaller diameter and a larger diameter. Thus, the substantially smooth transition in the diameters of the inner surfaces 823 and 833 can still facilitate a substantially laminar flow therethrough, which in some instances, can limit and/or substantially prevent hemolysis of blood flowing from the first adapter 820 and through the second adapter 830.

[1113] While the flow of bodily-fluid (i.e., blood) is described above as first flowing through the first adapter 820 and then flowing through the second adapter 930, in other embodiments, the flow through a set of adapters can be reversed. For example, FIG. 17 illustrates a first adapter 920 and a second adapter 930 according to another embodiment. The first adapter 920 has a distal end portion 922 configured to be coupled to a proximal end portion 931 of the second adapter 930, as described in further detail herein. Although only

the distal end portion 922 of the first adapter 920 is shown in FIG. 17, the first adapter 920 can be similar in size and/or shape as the first adapters 620 and/or 720, unless otherwise expressed. The first adapter 920 includes an inner surface 923 that defines a lumen 924 extending through at least its distal end portion 922. As shown in FIG. 17, a portion of the second adapter 930 is inserted into the lumen 924, as described in further detail herein.

[1114] Although only the proximal end portion 931 of the second adapter 930 is shown in FIG. 17, the second adapter 930 can be any suitable shape, size, or configuration. For example, the proximal end portion 931 of the second adapter 930 can form and/or can include a locking mechanism or the like while a proximal end portion (not shown in FIG. 17) can be coupled to and/or can form any suitable portion of a fluid collection device such as, for example, a puncture member, a needle, a conduit, a flow control mechanism, and/or the like. In this embodiment, the proximal end portion 931 of the second adapter 930 includes and/or forms a locking mechanism configured to form a threaded coupling with, for example, the distal end portion 922 of the first adapter 920. In other embodiments, the proximal end portion 931 of the second adapter 930 can be any suitable configuration.

[1115] As shown in FIG. 17, the second adapter 930 includes an inner surface 933 that defines a lumen 934 extending through at least its proximal end portion 931. Moreover, a region of the proximal end portion 931 of the second adapter 930 is disposed within the lumen 924 of the first adapter 920. For example, the inner surface 923 of the first adapter 920 has a diameter that corresponds to an outer diameter associated with the region of the proximal end portion 931 of the second adapter 930. Thus, as shown in FIG. 17, the diameter defined by the inner surface 923 of the first adapter 920 is greater than a diameter defined by the inner surface 933 of the second adapter 930, as described in further detail herein.

[1116] The proximal end portion 931 of the second adapter 930 includes and/or forms a proximal surface 935 with a substantially rounded corner and/or smooth transition. For example, the proximal surface 935 formed by the second adapter 930 defines a relatively smooth transition from an inner diameter of the second adapter 930 (e.g., defined by the inner surface 933) to an outer diameter of the second adapter 930 (e.g., at the distal end) rather than forming a relatively sharp, abrupt, and/or orthogonal corner. When a portion of the second adapter 930 is disposed within the lumen 923 of the first adapter 920, a volume of bodily-fluid (e.g., blood) can flow through the lumen 934 of the second adapter 930 and into the lumen 924 of the first adapter 920. Thus, the arrangement of the proximal surface 935 of the

second adapter 930 can, for example, facilitate, produce, encourage, and/or otherwise result in a substantially laminar flow of a volume of bodily-fluid (i.e., blood) as the volume flows from the lumen 934 of the second adapter 930 into the lumen 924 of the first adapter 920. Specifically, the proximal surface 935 of the second adapter 930 allows for a gradual transition from the diameter associated with the lumen 934 of the second adapter 930 (i.e., the smaller diameter) to the diameter associated with the lumen 924 of the first adapter 920 (i.e., the larger diameter). Such a smooth transition can, for example, reduce eddy currents and/or other forms of turbulence that can otherwise result from a substantially abrupt change in diameter or the like. Thus, the arrangement of the first adapter 920 and the second adapter 930 can allow a volume of blood to expand as the flow of blood exits the lumen 934 of the second adapter 930, which in some instances, can reduce, limit, and/or substantially prevent hemolysis of blood flowing therethrough.

[1117] While the first adapters 620, 720, 820, and 920 are shown and described above as receiving and/or otherwise being directly coupled to the second adapters 630, 730, 830, and 930, respectively, in other embodiments, a first adapter can be indirectly coupled to a second adapter via an intervening structure. In such embodiments, the intervening structure can define a lumen that can place the first adapter in fluid communication with the second adapter. Moreover, the intervening structure can limit, modulate, and/or control a flow rate of a volume of fluid (i.e., blood) therethrough. For example, FIGS. 18-26 illustrate embodiments configured to mitigate the risk of hemolysis otherwise associated with a relatively high flow rate and/or velocity along a fluid flow path that exceeds known shear force and exposure time limits that can rupture red blood cells. Specifically, FIGS. 18-20 illustrate a first adapter 1020 indirectly coupled to a second adapter 1030 via a restrictor 1050, according to an embodiment. The first adapter 1020 includes a proximal end portion 1021, a distal end portion 1022, and an inner surface 1023. The inner surface 1023 defines a lumen 1024 extending through the proximal end portion 1021 and the distal end portion 1022 (see e.g., FIG. 20). In some embodiments, the first adapter 1020 can be substantially similar to and/or the same as the first adapter 720 described above with reference to FIGS. 14 and 15. Thus, aspects of the first adapter 1020 are not described in further detail herein.

[1118] The second adapter 1030 has a proximal end portion 1031, a distal end portion 1032, and an inner surface 1033. The inner surface 1033 of the second adapter 1030 defines a lumen 1024 extending through its proximal end portion 1031 and its distal end portion 1032

(see e.g., FIG. 20). In some embodiments, the second adapter 1030 can be substantially similar to and/or the same as the second adapter 730 described above with reference to FIGS. 14 and 15. Thus, aspects of the second adapter 1030 are not described in further detail herein.

[1119] The restrictor 1050 has a proximal end portion 1051, a distal end portion 1052, and an inner surface 1053. The inner surface 1053 of the restrictor 1050 defines a lumen 1054 extending through its proximal end portion 1051 and its distal end portion 1052 (see e.g., FIG. 20). In this embodiment, the restrictor 1050 is coupled between the first adapter 1020 and the second adapter 1030 to define a fluid pathway therebetween (e.g., via the lumen 1054). More specifically, the restrictor 1050 can include any suitable interface, locking mechanism, surface, etc. at or near the proximal end portion 1051 and the distal end portion 1052 configured to couple the restrictor 1050 to the first adapter 1020 or the second adapter 1030. As shown in FIGS. 18-20, the restrictor 1050 includes a locking mechanism or the like at its distal end portion 1052 that is configured to couple the distal end portion 1052 of the restrictor 1050 to the proximal end portion 1021 of the first adapter 1020. For example, in some embodiments, the distal end portion 1052 of the restrictor 1050 can include a threaded female Luer Lok ® configured to form a threaded coupling with a corresponding threaded male Luer Lok ® of the first adapter 1020, as shown in FIG. 20.

[1120] As shown in FIGS. 19 and 20, the proximal end portion 1051 of the restrictor 1050 receives the second adapter 1030. For example, as described above with reference to the first adapter 620 and the second adapter 630 in FIGS. 11-13, a portion of the second adapter 1030 is inserted through the proximal end portion 1051 of the restrictor 1050 to be disposed in the lumen 1054. In some embodiments, the restrictor 1050 and the second adapter 1030 can form a friction fit and/or the like, which in turn, can define a substantially fluid tight seal therebetween. In other embodiments, the proximal end portion 1051 of the restrictor 1050 and the distal end portion 1032 of the second adapter 1030 can include any suitable coupling and/or locking mechanism configured to couple the second adapter 1030 to the restrictor 1050 (e.g., as described above with reference to the coupling between the first adapter 1020 and the restrictor 1050).

[1121] As shown in FIGS. 19 and 20, the restrictor 1050 or the first adapter 1020 includes a gasket 1026 configured to minimize a discontinuity between the lumen 1024 of the first adapter 1020 and the lumen 1054 of the restrictor 1050 when coupled. Similarly, the

second adapter 1030 or the restrictor 1050 includes a gasket 1036. The gaskets 1026 and 1036 can be substantially similar in form and function to the gasket 726 shown and described above with reference to FIGS. 14 and 15. Thus, the gaskets 1026 and 1036 are disposed within the lumen 1024 of the first adapter 1020 and the lumen 1054 of the restrictor 1050, respectively. The arrangement of the gaskets 1026 and 1036 can reduce a magnitude of the discontinuities formed between the inner surfaces 1023, 1033, and 1053 of the first adapter 1020, the second adapter 1030, and the restrictor 1050, respectively, which in turn, can reduce, limit, and/or substantially prevent hemolysis of blood flowing therethrough, as described in detail above. In some embodiments, the gaskets 1026 and 1036 can be configured to restrict and/or reduce a pressure and/or a flow rate associated with the first adapter 1020, the second adapter 1030, and/or the restrictor 1050, as described above with reference to the gasket 726. In some instances, restricting and/or reducing the pressure and/or flow rate associated with the first adapter 1020, the second adapter 1030, and/or the restrictor 1050 (e.g., via the gaskets 1026 and 1036) can, for example, limit shear forces and/or exposure time experienced by red blood cells as the red blood cells flow through the first adapter 1020, the second adapter 1030, and the restrictor 1050, and/or the interfaces therebetween.

[1122] The inner surface 1053 of the restrictor 1050 is configured to control a flow of fluid through the lumen 1053. For example, as shown in FIG. 20, the inner surface 1053 of the restrictor 1050 includes a choke portion 1055 or the like. In some embodiments, the choke portion 1055 corresponds to a portion of the inner surface 1053 having a reduced diameter relative to the other portions of the inner surface 1053. More specifically, the choke portion 1055 forms a relatively smooth transition (e.g., a gradual change) from a region of the inner diameter 1053 associated with a first diameter to a region (i.e., the choke portion 1055) associated with a second diameter, smaller than the first diameter. Thus, the choke portion 1055 restricts, controls, and/or reduces a flow of fluid therethrough.

[1123] Expanding further, the reduction in the diameter of the inner surface 1053 at or along the choke portion 1055 selectively controls a pressure within the lumen 1054. For example, in some embodiments, the second adapter 1030 can be fluidically coupled (e.g., either directly or indirectly) to an evacuated container or the like, resulting in a negative pressure within the lumens 1034, 1054, and 1024. Thus, the reduced diameter associated with the choke portion 1055 results in a reduced pressure differential between the lumen 1024

of the first adapter 1020 (i.e., at a time directly before the exposure to the negative pressure) and a portion of the lumen 1054 of the restrictor 1050 that is distal to the choke portion 1055. As such, when the first adapter 1020 is in fluid communication with, for example, a vascular structure (e.g., via a needle, catheter, cannula, etc.), a magnitude of the negative pressure exerted on or in the vascular structure is reduced, thereby limiting, reducing, and/or substantially preventing hemolysis of blood as it flows into the lumen 1024 defined by the first adapter 1020. Moreover, the smooth transition in the diameter of the inner surface 1053 from the first diameter to the second diameter (associated with the choke portion 1055), facilitates, encourages, and/or otherwise results in a substantially laminar flow through the lumen 1054 of the restrictor 1050.

[1124] While the restrictor 1050 is particularly shown and described above with reference to FIGS. 18-20, in other embodiments, a restrictor, configured to control a flow of fluid therethrough, can be any suitable configuration. For example, FIGS. 21-24 illustrate a restrictor 1150 according to another embodiment. The restrictor 1150 has a proximal end portion 1151, a distal end portion 1152, and an inner surface 1153. The inner surface 1153 of the restrictor 1150 defines a inner volume 1154 extending through its proximal end portion 1151 and its distal end portion 1152 (see e.g., FIG. 22). Although not shown in FIGS. 21-24, the restrictor 1150 can be disposed between two components of a fluid transfer device to define a fluid flow path therethrough. For example, in some embodiments, the proximal end portion 1151 can be coupled to an adapter such as, for example, the second adapter 1030, described above with reference to FIGS. 18-20. Similarly, the distal end portion 1152 can be coupled to an adapter such as, for example, the first adapter 1020, described above. As such, the proximal end portion 1151 and the distal end portion 1152 can be substantially similar to or the same as the proximal end portion 1051 and the distal end portion 1052, respectively, of the restrictor 1050 and thus, are not described in further detail herein.

[1125] As shown in FIGS. 22-24, the restrictor 1150 includes a baffle 1156 disposed in the inner volume 1154. The baffle 1156 can be any suitable shape, size, or configuration. For example, in this embodiment, the baffle 1156 is substantially rectangular (see e.g., FIG. 20) with a size that substantially corresponds to the inner volume 1154 of the restrictor 1150, as described in further detail herein. The baffle 1156 includes an inner surface 1157 that defines an inner volume 1158. As shown in FIG. 24, the inner surface 1157 of the baffle 1156 defines a gradual bow toward the center of the baffle 1156. More specifically, the

arrangement of the inner surface 1157 is such that a distance between opposite sides of the baffle 1156 gradually varies as the inner surface 1157 extends outward from a longitudinal centerline CL (shown in FIG. 22) of the baffle 1156. For example, in this embodiment, a distance between opposite portions of the inner surface 1157 gradually increases from a first distance, at a first position associated with a perimeter of the inner surface 1157, to second distance, at a second position disposed between the perimeter of the inner surface 1157 and the longitudinal centerline CL, and then gradually decreases from the second distance to a third distance, at a position associated with and/or near the longitudinal center CL. In this manner, the baffle 1156 can selectively control a flow of fluid through the inner volume 1158, as described in further detail herein.

[1126] Referring back to FIG. 22, in this embodiment, an outer surface of the baffle 1156 is in contact with the inner surface 1153 of the restrictor 1150 when disposed in the inner volume 1154. In some embodiments, the outer surface of the baffle 1156 and the inner surface 1153 of the restrictor 1150 define a friction fit or the like that forms a substantially fluid tight seal. As such, the arrangement of the baffle 1156 and the inner surface 1153 of the restrictor 1150 can limit, inhibit, and/or substantially prevent a flow of fluid between the outer surface of the baffle 1156 and the inner surface 1153 of the restrictor 1150. More specifically, the inner volume 1158 of the baffle 1156 defines a fluid flow path that places a first portion of the inner volume 1154, which is distal to the baffle 1156, in fluid communication with a second portion of the inner volume 1154, which is proximal to the baffle 1156. In this manner, the arrangement of the inner surface 1157 of the baffle 1156 can restrict, inhibit, guide, limit, choke, and/or otherwise control a flow of fluid through the restrictor 1150. Moreover, the smooth or gradual change in distance between opposite portions of the inner surface 1157 of the baffle (as described above) facilitates, encourages, and/or otherwise results in a substantially laminar flow through the inner volume 1154 of the restrictor 1150.

[1127] Although not shown in FIGS. 21-24, in some embodiments, the inner volume 1158 of the baffle 1156 can include a medium disposed therein. For example, in some embodiment, the baffle 1156 can include a substantially porous material or the like that can slow and/or filter a flow of fluid (e.g., blood) therethrough. In other embodiments, the user can manipulate the restrictor 1150 to modify and/or control a flow of fluid through the restrictor 1150. For example, in some instances, the user can exert a force on a portion of the

restrictor 1150 sufficient to deform that portion. As such, a portion of the force can correspondingly deform the baffle 1156, which in turn, can change a contour of the inner surface 1157. Thus, the user can exert a force on the restrictor 1150 to, for example, increase, decrease, or otherwise control a flow of fluid through the baffle 1156. By way of example, a user can exert a force of the restrictor 1150 to reduce a distance between opposite portions of the inner surface 1157, which in turn, can reduce a negative pressure differential produced by an evacuated container being placed in fluid communication with the restrictor 1150.

[1128] FIGS. 25 and 26 illustrate a restrictor 1250 according to another embodiment. The restrictor 1250 has a proximal end portion 1251, a distal end portion 1252, and an inner surface 1253. The inner surface 1253 of the restrictor 1250 defines a inner volume 1254 extending through its proximal end portion 1251 and its distal end portion 1252 (see e.g., FIG. 26). As described above, the restrictor 1250 can be physically and fluidically coupled between, for example, a pair of components of a fluid transfer device to restrict and/or otherwise control a flow of fluid therebetween. For example, although not shown in FIGS. 25-26, the proximal end portion 1251 can be coupled to an adapter such as, for example, the second adapter 1030, described above with reference to FIGS. 18-20. Similarly, the distal end portion 1252 can be coupled to an adapter such as, for example, the first adapter 1020, as described above. In this manner, the proximal end portion 1251 and the distal end portion 1252 can be substantially similar to or the same as the proximal end portion 1051 and the distal end portion 1052, respectively, of the restrictor 1050 and thus, are not described in further detail herein.

[1129] The restrictor 1250 includes and/or defines a set of chambers 1259, as shown in FIG. 26. More specifically, the restrictor 1250 includes a set of walls that can form, for example, a set of semi-spherical portions, which in turn, result in the inner surface 1253 defining the set of chambers 1259. Thus, the chambers 1259 are, for example, a set of semi-spherical portions of the inner volume 1254. As shown in FIG. 26, the chambers 1259 are serially arranged along a longitudinal centerline CL of the restrictor 1250. In some embodiments, the size and/or shape of each chamber 1259 can vary. For example, as shown in FIG. 26, the chamber 1259 disposed at or near the proximal end portion 1251 of the restrictor 1250 is smaller than the adjacent chamber 1259. In other embodiments, the size and/or shape of each chamber 1259 can be substantially uniform. With the inner surface 1253 defining the semi-spherical chambers 1259, a diameter of the inner volume 1254 (e.g.,

associated with a cross-sectional shape of the inner surface 1253) is varied along a length of the longitudinal centerline CL. For example, a diameter of the inner volume 1254 gradually increases or decreases in an alternating manner between a relatively smaller diameter, associated with a position along the longitudinal centerline substantially between adjacent chambers 1259 and a relatively larger diameter, associated with a position along the longitudinal centerline substantially in the center of a given chamber 1259.

[1130] In some embodiments, the arrangement of the chambers 1259 selectively controls a pressure within the inner volume 1254. For example, in some embodiments, the proximal end portion 1251 of the restrictor 1250 can be fluidically coupled (e.g., either directly or indirectly) to an evacuated container or the like, resulting in a negative pressure within the inner volume 1254. Thus, the alternating increase and decrease corresponding to each chamber 1259 results in a changing pressure differential along the longitudinal centerline CL. In some embodiments, such an alternating arrangement can, for example, act as a peristaltic pump or the like. Thus, the restrictor 1250 can draw a fluid through the inner volume 1254 via a pressure differential that is at least partially controlled by the arrangement of the inner surface 1253. That is to say, while an evacuated container is the source of a negative pressure, the arrangement of the chambers 1259 at least partially controls a pressure differential between the proximal end portion 1251 and the distal end portion 1252. In this manner, hemolysis of blood can be reduced and/or substantially prevented, which might otherwise occur in response to a shear force produced by a relatively rapid and/or relatively large pressure drop associated with placing an evacuated container in fluid communication with a vascular structure. Moreover, the smooth and/or gradual transitions in the diameter of the inner surface 1253 associated with the chambers 1259, facilitates, encourages, and/or otherwise results in a substantially laminar flow through the inner volume 1254 of the restrictor 1250.

[1131] Although not shown, any of the restrictors 1050, 1150, and/or 1250 can be fluidically coupled (either directly or indirectly) to and/or monolithically formed with an adapter configured to engage a fluid reservoir such as an evacuated container. In some embodiments, such adapters can include an inner surface configured to reduce discontinuities or the like within a portion of a fluid flow path and/or otherwise configured to facilitate a substantially laminar fluid flow therethrough, as described in detail above. Moreover, the adapters can engage any suitable fluid reservoir or container. For example, FIGS. 27-44

illustrate embodiments (i.e., adapters and fluid reservoirs) configured to mitigate the risk of hemolysis as blood flow from an adapter, a puncture member, a needle, a cannula, and/or the like into a fluid reservoir. Specifically, FIGS. 27-33 illustrate an adapter 1330 configured to engage a fluid reservoir 1360 (FIGS. 29-33) according to an embodiment. The adapter 1330 has a proximal end portion 1331, a distal end portion 1332, and an inner surface 1333. The inner surface 1333 defines a lumen 1334 extending through the proximal end portion 1331 and the distal end portion 1332 (see e.g., FIG. 27). As shown in FIGS. 27 and 28, in some embodiments, the adapter 1330 can include and/or can be coupled to a shroud 1343. In such embodiments, the shroud 1343 can define an inner volume 1344 within which a portion of a fluid reservoir can be disposed. In other embodiments, the adapter 1330 need not include and/or need not be coupled to the shroud 1343.

[1132] The adapter 1330 can be any suitable shape, size, or configuration. For example, as shown in FIGS. 29 and 30, the distal end portion 1332 of the adapter 1330 includes and/or is coupled to a lock mechanism or the like. In this embodiment, the distal end portion 1332 includes and/or forms a female portion of a Luer Lok ® or the like. Thus, the distal end portion 1332 of the adapter 1330 can be coupled to a corresponding male portion of a Luer Lok ® or the like, as described above with reference to the distal end portion 1052 of the restrictor 1050 shown in FIG. 20. The proximal end portion of the adapter 1330 includes and/or is coupled to a puncture member 1338 defining a lumen 1339 in fluid communication with the lumen 1334 of the adapter 1330. The puncture member 1338 can be any suitable configuration. For example, in some embodiments, the puncture member 1338 is a needle. As shown in FIG. 30, the puncture member 1325 is disposed within a sheath 1341. More specifically, the sheath 1341 is at least temporarily disposed about the puncture member 1338 and is configured to limit and/or substantially prevent an accidental contact with the puncture member 1338. Furthermore, the sheath 1341 can maintain the puncture member 1338 in a substantially sterile environment prior to use and can selectively control a flow of bodily-fluid through the puncture member 1338, as described in further detail herein.

[1133] As shown in FIG. 30, a diameter of the inner surface 1333 at or near the distal end portion 1332 is larger than a diameter of the puncture member 1338. In this manner, the inner surface 1333 forms and/or defines a smooth transition from a larger diameter at or near the distal end portion 1332 to a smaller diameter at or near the puncture member 1338. In some instances, such a smooth transition from the larger diameter to the smaller diameter can

facilitate, produce, encourage, and/or force a substantially laminar flow of a volume of bodily-fluid (e.g., blood) through the lumen 1334. Moreover, the smooth transition can reduce eddy currents or the like within the flow of blood that can otherwise result from a relatively abrupt change in diameter or the like. Thus, a volume of blood can flow within the lumens 1334 and 1339 with reduced damage to the constituents of the blood (e.g., hemolysis of the erythrocytes) that might otherwise occur as a result of misaligned interfaces and/or discontinuities; abrupt changes in diameter; turbulence and/or eddy currents within a flow of blood therethrough; and/or the like.

[1134] As described above, the adapter 1330 is configured to couple to and/or otherwise engage a fluid reservoir 1360. The fluid reservoir 1360 can be any suitable shape, size, or configuration. For example, in this embodiment, the fluid reservoir 1360 is an evacuated container such as a Vacutainer™, a BacT/ALERT® SN, a BacT/ALERT® FA, and/or any other type of container, vial, bottle, reservoir, etc. As shown in FIGS. 31-33, the fluid reservoir 1360 includes a proximal end portion 1361 and a distal end portion 1362, and defines an inner volume 1364. The distal end portion 1362 includes a port 1363 through which the puncture member 1338 can be inserted to place the inner volume 1364 of the fluid reservoir 1360 in fluid communication with the lumen 1334 of the adapter 1330. For example, in some embodiments, the port 1363 can be a self-healing septum or the like. Thus, the port 1363 can be substantially in a sealed configuration prior to insertion of, for example, the puncture member 1338 and subsequently, can transition from an open configuration to the sealed configuration when, for example, the puncture member 1338 is removed from the port 1363.

[1135] In some embodiments, a fluid reservoir can include a flow control member or the like disposed in its inner volume. For example, as shown in FIGS. 32 and 33, the fluid reservoir 1360 includes a flow control member 1367 disposed within the inner volume 1364. In this embodiment, the flow control member 1367 can be, for example, an insert or funnel that defines a channel 1368 configured to receive a flow of fluid from the lumen 1339 of the puncture member 1338. More specifically, as shown in FIG. 33, a first end of the flow control member 1367 can be disposed adjacent to and/or can be coupled to the port 1363 and a second end, opposite the first end, can extend toward an inner surface of the fluid reservoir 1360. In this manner, the second end of the flow control member 1367 can be adjacent to the inner surface of the fluid reservoir 1360 such that an axis associated with a portion of the

channel 1368 at or near the second end is substantially parallel to and/or otherwise directed toward the inner surface of the fluid reservoir 1360.

[1136] In use, the adapter 1330 and/or the fluid reservoir 1360 can be manipulated to insert the puncture member 1338 through the port 1363 of the fluid reservoir 1360. As such, the sheath 1341 disposed about the puncture member 1338 can deform to allow the puncture member 1338 to be inserted through the port 1363. With the fluid reservoir 1360 being an evacuated container, the insertion of the puncture member 1338 is such that a negative pressure within the fluid reservoir 1360 is exerted through the lumen 1334 of the adapter 1330 (e.g., via the lumen 1339 of the puncture member 1338). Thus, when the distal end portion 1332 is fluidically coupled (either directly or indirectly) to a device or member in fluid communication with the body of a patient, the negative pressure draws a volume of bodily-fluid (e.g., blood) from the patient and into the fluid reservoir 1360. More specifically, the distal end portion 1332 of the adapter 1330 can be coupled (either directly or indirectly) to any suitable adapter, restrictor, and/or needle described herein to receive a flow of, for example, blood from the patient with reduced or substantially no hemolyzation of the blood. Furthermore, by disposing the flow control member 1367 in the inner volume 1364, a flow of blood can be directed within the channel 1338 toward the inner surface, which in turn, can decrease a force otherwise associated with an impact of the volume of blood contacting the inner surface. Thus, hemolysis of the blood associated with such a contact is reduced or substantially prevented.

[1137] While the adapter 1330 is shown in FIGS. 31-33 as not including and/or not be coupled to the shroud 1343, in other embodiments, the adapter 1330 can be coupled to the shroud 1343 when engaging the fluid reservoir 1360. Furthermore, while the flow control member 1367 is particularly shown in FIG. 33, in some embodiments, a second end of a flow control member can extend within the inner volume 1364 to a position adjacent to and/or substantially abutting a bottom or proximal surface (i.e., a surface opposite the port 1363). In other embodiments, a flow control member can extend in a spiral or helical manner from the port 1363. As such, a second end of the flow control member can be substantially tangential to the inner surface of the fluid reservoir and thus, fluid exiting a channel defined by the flow control member can flow along a circumference of the inner surface (e.g., tangent to the inner surface).

[1138] In other embodiments, a fluid reservoir can include any suitable flow control member. For example, FIG. 34 illustrates a fluid reservoir 1460 according to another embodiment. The fluid reservoir 1460 includes a proximal end portion 1461 and a distal end portion 1462, and defines an inner volume 1464. The distal end portion 1462 includes a port 1463 configured to receive, for example, a puncture member 1438 of an adapter 1430, as described in detail above with reference to FIGS. 31-33. The inner volume 1464 of the fluid reservoir 1460 includes and/or houses a flow control member 1467 operable to control a flow of fluid from, for example, the adapter 1430 into the inner volume 1464, as described in further detail herein. The fluid reservoir 1460 can be any suitable shape, size, or configuration. For example, in this embodiment, the fluid reservoir 1460 is an evacuated container such as a Vacutainer™, a BacT/ALERT® SN, a BacT/ALERT® FA, and/or any other type of container, vial, bottle, reservoir, etc. In some embodiments, the fluid reservoir 1460 can be substantially similar to or the same as the fluid reservoir 1360 described above with reference to FIGS. 31-33. Thus, such similar aspects of the fluid reservoir 1460 are not described in further detail herein.

[1139] The fluid reservoir 1460 can differ from the fluid reservoir 1360, however, in the arrangement of the flow control member 1467. More specifically, while the flow control member 1367 is shown in FIG. 33 as tapering to a substantially uniform diameter as the flow control member 1367 extends away from the port 1363, in this embodiment, the flow control member 1467 has a varying diameter as the flow control member 1467 extends away from the port 1463. In this manner, a channel 1468 defined by the flow control member 1467 has a cross-sectional area and/or diameter that is dependent on, for example, a position along a longitudinal centerline CL defined by the flow control member 1467. For example, the channel 1468 can have a first diameter at a first end portion nearest to the port 1463, a second diameter at an end portion opposite the first end portion, and a third diameter at a portion disposed therebetween. As shown in FIG. 34, the end portions of the flow control member 1467 can be flared or the like such that the first diameter and the second diameter are each greater than the third diameter. Said another way, the diameter of the channel 1468 can taper along the longitudinal centerline CL from a larger diameter associated with the end portions of the flow control member 1467 to a smaller diameter at or near a center portion of the flow control member 1467.

[1140] With the fluid reservoir 1460 being an evacuated container or the like, a pressure (i.e., a negative pressure) within the channel 1468 is dependent on a position along the longitudinal centerline CL. That is to say, the pressure within the channel 1468 is dependent on the diameter of the channel 1468, in which a larger diameter is associated with a larger pressure. In a similar manner, the velocity of a flow of bodily-fluid (e.g., blood) within the channel 1468 is also dependent on the diameter of the channel 1468, however, such dependency is inverse to that associated with the pressure (i.e., a larger diameter is associated with less velocity). Thus, as blood (or other bodily-fluid) flows through the channel 1468, the increase in diameter at the end portion of the flow control member 1467 opposite the port 1463 results in a decrease in velocity associated with the flow of bodily-fluid therethrough. As such, a force otherwise associated with a volume of blood contacting an inner surface of the fluid reservoir 1460 is reduced, which in turn, can reduce and/or substantially prevent hemolysis of the volume of blood. Moreover, the diameter of the channel 1468 can be such that a pressure within the channel 1468 is maintained below a threshold that can otherwise result in hemolysis of blood flowing therethrough.

[1141] While the flow control members 1367 and 1467 are shown and described above as controlling a flow of, for example, blood through the channels 1368 and 1468, respectively, in other embodiments, a fluid reservoir can include a flow control member having any suitable configuration. For example, FIG. 35 illustrates a fluid reservoir 1560 according to another embodiment. The fluid reservoir 1560 includes a proximal end portion 1561 and a distal end portion 1562, and defines an inner volume 1564. The distal end portion 1562 includes a port 1563 configured to receive, for example, a puncture member 1538 of an adapter 1530, as described in detail above with reference to FIGS. 31-33. The inner volume 1564 of the fluid reservoir 1560 includes and/or houses a flow control member 1565 operable to control a flow of fluid from, for example, the adapter 1530 into the inner volume 1564, as described in further detail herein. The fluid reservoir 1560 can be any suitable shape, size, or configuration. For example, in this embodiment, the fluid reservoir 1560 is an evacuated container such as a Vacutainer™, a BacT/ALERT® SN, a BacT/ALERT® FA, and/or any other type of container, vial, bottle, reservoir, etc. In some embodiments, the fluid reservoir 1560 can be substantially similar to or the same as the fluid reservoir 1360 described above with reference to FIGS. 31-33. Thus, such similar aspects of the fluid reservoir 1560 are not described in further detail herein.

[1142] As shown in FIG. 35, the flow control member 1565 is disposed within the inner volume 1564 at or near the port 1563. In this embodiment, the flow control member 1565 is a baffle insert or the like. Specifically, the flow control member 1565 forms and/or includes an angled baffle having a set of substantially parallel angled surfaces configured to direct a flow of blood or other bodily-fluid. For example, the puncture member 1538 of the adapter 1530 can be inserted through the port 1563 to place a distal end portion of the puncture member 1538 within the flow control member 1565. As such, when a flow of blood is expelled and/or drawn through a lumen defined by the puncture member 1538 (e.g., via a negative pressure differential produced by the evacuated container), the flow of blood contacts at least one angled surface of the flow control member 1565. Thus, the blood can flow along the angled surface toward an inner surface of the fluid reservoir 1560. By diverting, guiding, and/or otherwise directing the flow of blood to the inner surface, a force is reduced, which can otherwise result from an impact of the volume of blood contacting the inner surface. Thus, hemolysis of the blood associated with such a contact is reduced or substantially prevented.

[1143] While the flow control member 1565 is shown and described as forming and/or including a set of parallel angled surfaces configured to direct a flow of bodily-fluid toward the inner surface of the fluid reservoir 1560, in other embodiments, a flow control member can be any suitable baffle or the like. For example, in some embodiments, a flow control member can be an angled baffle or the like having a set of angled surfaces with an alternating orientation or the like. By way of example, a flow control member can include a first set of angled surfaces with a cross-sectional orientation (as shown in FIG. 35) that forms a 30° with a given plane and a second set of angled surfaces with a cross-sectional orientation that forms a 150° orientation with the given plane (i.e., a mirrored orientation), with each angled surface of the first set being disposed between two angled surfaces of the second set (or vice versa). In some embodiments, a baffle can include a set of surfaces that are each substantially V-shaped or U-shaped.

[1144] In other embodiments, a flow control member can be an absorbent or porous baffle or the like that can fill at least a portion of an inner volume of a fluid reservoir. In this manner, a flow of blood can be expelled or drawn from a lumen of an adapter (e.g., a lumen of a puncture member or the like) and absorbed by the absorbent baffle. In such embodiments, a volume of blood can be subsequently released or expelled from the absorbent

baffle via a centripetal or centrifugal action and/or the like. In some embodiments, a flow control member can be a baffle including a set of angled surfaces with an absorbent material disposed therebetween.

[1145] While the flow control members 1367, 1467, and 1565 are shown as independent components disposed within the fluid reservoirs 1360, 1460, and 1560, respectively, in other embodiment, a fluid reservoir can include a flow control member that is integral with another portion of the fluid reservoir such as, for example, a port. For example, FIG. 36 illustrates a fluid reservoir 1660 according to another embodiment. The fluid reservoir 1660 can be any suitable shape, size, or configuration. For example, in this embodiment, the fluid reservoir 1660 is an evacuated container such as a Vacutainer™, a BacT/ALERT® SN, a BacT/ALERT® FA, and/or any of type of container, vial, bottle, reservoir, etc. In some embodiments, the fluid reservoir 1660 can be substantially similar to or the same as the fluid reservoir 1360 described above with reference to FIGS. 31-33. Thus, such similar aspects of the fluid reservoir 1660 are not described in further detail herein.

[1146] The fluid reservoir 1660 includes a proximal end portion 1661 and a distal end portion 1662, and defines an inner volume 1664. The distal end portion 1662 includes a port 1663 configured to receive, for example, a puncture member 1638 of an adapter 1630, as described in detail above with reference to FIGS. 31-33. The port 1663 in this embodiment, however, includes an inner surface 1665 configured to control a flow of fluid into the inner volume 1664 of the fluid reservoir 1660. As shown in FIG. 36, the inner surface 1665 of the port 1663 has a varied diameter that forms a constriction disposed between a proximal end portion and a distal end portion of the port 1663. For example, in some embodiments, the inner surface 1665 can form a constriction or otherwise can have a reduced diameter at or near a center of the port 1663 (i.e., at or near a midpoint between the proximal end portion and the distal end portion of the port).

[1147] In some embodiments, the inner surface 1665 can have a reduced diameter at a position that is proximal to the puncture member 1638 when the adapter 1630 is engaged with the fluid reservoir 1660. Similarly stated, the arrangement of the fluid reservoir 1660 and the adapter 1630 is such that when the adapter 1630 engages the fluid reservoir 1660, the puncture member 1638 is disposed in a distal position relative to a portion of the inner surface 1665 associated with the smallest diameter. Thus, the arrangement of the inner surface 1665 of the port 1663 can, for example, result in a venturi effect within a volume of

bodily-fluid as the volume of bodily-fluid flows from the puncture member 1638 into the port 1663. In other words, with the inner surface 1665 forming a constriction and/or reduction in diameter, a pressure associated with a volume on opposite sides of the constriction and/or reduction in diameter can be controlled. For example, the fluid reservoir 1660, being an evacuated container, defines a negative pressure within a portion of the inner volume 1664 proximal to the portion of the inner surface 1665 having the reduced diameter. In some embodiments, the constriction and/or reduced diameter formed by the inner surface 1665 results in a corresponding decrease in pressure associated with the reduced diameter. Thus, by selectively controlling a portion of the inner surface 1665 that is distal to the reduced diameter (i.e., selectively increasing the diameter of the inner surface 1665) a pressure within a volume distal to the reduced diameter can be less than, for example, the pressure within the volume proximal to the reduced diameter. Thus, hemolysis within a flow of blood is reduced or substantially prevented that might otherwise result from a rapid exposure to the negative pressure differential produced by the fluid reservoir 1660.

[1148] While the flow control members 1367, 1467, 1565, and the port 1663 are shown and described above as receiving and/or otherwise guiding a flow of bodily-fluid (e.g., blood) into the inner volumes 1364, 1464, 1564, 1664, respectively, in some embodiments, an adapter can be arranged to selectively direct a flow of bodily-fluid into a fluid reservoir. For example, FIGS. 37 and 38 illustrate an adapter 1760, according to another embodiment. The adapter 1760 is configured for selective engagement with a fluid reservoir 1760 to deliver a flow of bodily-fluid into an inner volume 1764. The adapter 1760 includes at least a shroud 1743 and a puncture member 1768. Although not shown in FIGS. 37 and 38, an inner surface of the adapter 1760 can be substantially similar to or the same as the inner surface 1363 of the adapter 1360 described above with reference to FIG. 30. That is to say, the adapter 1760 can include an inner surface that defines a substantially smooth transition between, for example, a lumen associated with an inlet of the adapter 1760 (e.g., a catheter, cannula, and/or locking mechanism) and a lumen of the puncture member 1768, thereby reducing and/or substantially preventing hemolysis of blood flowing therethrough.

[1149] As shown in FIG. 38, the arrangement of the adapter 1760 is such that the puncture member 1768 is disposed at non-orthogonal orientation relative to the shroud 1743. More specifically, at least a portion of the puncture member 1768 extends within an inner volume 1744 of the shroud 1743 and toward an inner surface. Thus, when the fluid reservoir

1760 is inserted into the inner volume 1744 of the shroud 1743, the puncture member 1768 punctures a port 1763 of the fluid reservoir 1760 (e.g., substantially similar to the port 1363 of the fluid reservoir 1360 described above with reference to FIGS. 31-33) at a substantially non-orthogonal angle. For example, the fluid reservoir 1760 can be inserted into the inner volume 1743 of the shroud 1744 with a substantially parallel or orthogonal orientation relative thereto. As the fluid reservoir 1760 is moved in the distal direction, the port 1763 is brought into contact with the puncture member 1768 and with the fluid reservoir 1760 parallel or orthogonal to the shroud 1743, the puncture member 1768 punctures the port 1763 at an angle associated with the orientation of the puncture member 1768 relative to the shroud (e.g., non-orthogonal). Therefore, as shown in FIG. 38, an end portion of the puncture member 1768 can be adjacent to, in contact with, and/or otherwise near an inner surface of the reservoir 1760 defining the inner volume 1764. In this manner, directing the flow of blood to the inner surface reduces a force, which can otherwise result from an impact of the volume of blood contacting the inner surface. Thus, hemolysis of the blood associated with such a contact is reduced or substantially prevented.

[1150] In some embodiments, the adapter 1730 can be configured to engage, for example, a standard fluid reservoir such as, for example, a Vacutainer ™ or the like. That is to say, in some embodiments, the adapter 1730 is configured to be compatible with existing fluid reservoirs without modifications being made thereto. In other embodiments, a fluid reservoir can have any suitable configuration. For example, FIG. 39 illustrates an adapter 1830 physically and fluidically coupled to a fluid reservoir 1860 according to another embodiment. The adapter 1830 can be any suitable adapter such as, for example, the adapter 1330 described above with reference to FIGS. 29 and 30. In this manner, the adapter 1830 includes a puncture member 1838 configured to puncture a port or the like of the fluid reservoir 1860, as described in further detail herein.

[1151] The fluid reservoir 1860 includes a proximal end portion 1861 and a distal end portion 1862, and defines an inner volume (not shown in FIG. 39). The distal end portion 1862 includes a port 1863 configured to receive, for example, the puncture member 1838 of the adapter 1830, as described in detail above with reference to FIGS. 31-33. The port 1863 in this embodiment, however, is disposed in a substantially horizontal position. More specifically, in some embodiments, the port 1863 can be disposed in a substantially tangential arrangement relative to, for example, an inner surface of the fluid reservoir 1860. Thus,

when the puncture member 1838 is inserted through the port 1863, an end portion of the puncture member 1838 can be placed adjacent to, at, or substantially near a portion of the inner surface of the fluid reservoir 1860, as described above with reference to the adapter 1730 and fluid reservoir 1760. Similarly stated, the arrangement of the port 1863 can be such that when the puncture member 1838 is inserted therethrough, at least the end portion of the puncture member 1838 (not shown in FIG. 39) is in a tangential orientation relative to the inner surface of the fluid reservoir 1860. In this manner, directing a flow of blood to the inner surface reduces a force, which can otherwise result from an impact of the volume of blood contacting the inner surface. Thus, hemolysis of the blood associated with such a contact is reduced or substantially prevented.

[1152] While a flow of bodily-fluid (e.g., blood) into the fluid reservoirs 1360, 1460, 1560, 1660, 1760, and 1860 is described above as being passively controlled by, for example, the flow control members 1367, 1467, 1565, the port 1663, the adapter 1730, and/or the port 1863, respectively, in other embodiments, a flow of bodily-fluid into a fluid reservoir can be actively controlled. That is to say, while the flow of bodily-fluid into the fluid reservoirs 1360, 1460, 1560, 1660, 1760, 1860 is controlled without user intervention (i.e., beyond the intervention of coupling the adapters 1330, 1430, 1530, 1660, 1760, and 1860 to the fluid reservoirs 1360, 1460, 1560, 1660, 1760, and 1860 respectively), in other embodiments, a user can manipulate an adapter and/or fluid reservoir to actively control a flow of fluid into the fluid reservoir. For example, FIGS. 40-42 illustrate an adapter 1930 and a fluid reservoir 1960, according to another embodiment. The fluid reservoir 1960 can be any suitable reservoir that defines an inner volume 1964 configured to receive a flow of bodily-fluid such as, for example, an evacuated container or the like. More specifically, as described above with reference to the fluid reservoir 1360 in FIGS. 31-33, the fluid reservoir 1960 includes a port 1963 through which a portion of the adapter 1930 can be inserted to gain access to the inner volume 1964, as described in further detail herein.

[1153] As shown in FIGS. 40-42, the adapter 1930 includes a proximal end portion 1931 and a distal end portion 1932, and defines an inner volume 1934. Although not shown, the distal end portion 1932 of the adapter 1930 can be coupled to any suitable lumen-defining device such as a needle, cannula, catheter, and/or sterile flexible tubing. In some embodiments, the distal end portion 1932 can include a locking mechanism or the like that can physically and fluidically couple the adapter 1930 to any suitable corresponding device

and/or component. The proximal end portion 1931 of the adapter 1930 receives a portion of the fluid reservoir 1960. For example, as shown in FIGS. 41 and 42, at least a portion of the port 1963 is inserted through the proximal end portion 1931 of the adapter 1930 to be disposed within a portion of the inner volume 1934.

[1154] As shown in FIGS. 41 and 42, the adapter 1930 further includes a cannula 1935 and an actuator 1945. Specifically, the cannula 1935 extends through the proximal end portion 1931 and the distal end portion 1932 of the adapter 1930, thereby defining a fluid pathway through the adapter 1930. The cannula 1935 can be any suitable shape, size, or configuration. For example, in some embodiments, the cannula 1935 is a substantially flexible tube formed of a biocompatible plastic or the like. In this manner, at least a portion of the cannula 1935 can be manipulated (e.g., by the actuator 1945) to bend, flex, kink, and/or otherwise reconfigure the cannula 1935, as described in further detail herein. The arrangement of the cannula 1935 can be such that when the fluid reservoir 1960 is inserted into the inner volume 1934 of the adapter 1930, an end portion of the cannula 1935 punctures the port 1963 of the fluid reservoir 1960 and thus, places the inner volume 1964 of the fluid reservoir 1960 in fluid communication with a lumen defined by the cannula 1935. Thus, a negative pressure within the fluid reservoir 1960 (e.g., the fluid reservoir 1960 is an evacuated container) exerts or draws suction through the lumen defined by the cannula 1935, as described in further detail herein.

[1155] The actuator 1945 of the adapter 1930 can be any suitable configuration. For example, as shown in FIGS. 41 and 42, the actuator 1945 can be a trigger or the like coupled to the adapter 1930 via a pivot point, pin, axle, etc. More specifically, a first portion of the actuator 1945 extends from and/or beyond an outer surface of the adapter 1930 and a second portion is disposed within the inner volume 1934 defined by the actuator 1930. Thus, a user (e.g., a phlebotomist, doctor, technician, nurse, etc.) can actuate the actuator 1945 by pivoting the actuator 1945 relative to the adapter 1930. In this manner, a portion of the actuator 1945 disposed in the inner volume 1934 of the adapter 1930 can be increased or decreased, for example, by exerting a force or removing a force, respectively, on the actuator 1945 (i.e., pivoting the actuator 1945 relative to the adapter 1930).

[1156] As shown, the portion of the actuator 1945 disposed within the inner volume 1934 of the adapter 1930 defines an opening 1946 through which the cannula 1935 can extend. Therefore, actuating the actuator 1945 (e.g., pivoting the actuator 1945 relative to the adapter

1930) results in a corresponding manipulation of a portion of the cannula 1935. For example, in some instances, while the actuator 1945 is in a first configuration, the position of the opening 1946 relative to the adapter 1930 can be such that the cannula 1935 (disposed therein) is pulled, bent, bowed, deformed, kinked, etc. Such deformation of the cannula 1935 can result in, for example, a constriction and/or pinching of the cannula 1935, which in turn, can constrict and/or at least partially obstruct the lumen defined by the cannula 1935, as shown in FIG. 41.

[1157] Conversely, a force can be exerted to actuate the actuator 1945, thereby pivoting the actuator 1945 relative to the adapter 1930. As described above, such pivoting motion can, for example, increase a portion of the actuator 1945 disposed in the inner volume 1934, which in turn, can change the position and/or orientation of the opening 1946 relative to the adapter 1930. Thus, the repositioning and/or reorienting of the opening 1946 actively (e.g., by exerting a force) or passively (e.g., by removing or reducing an existing force) reconfigures at least the portion of the cannula 1935 disposed therein. For example, as shown in FIG. 42, when the actuator 1945 is placed in the second configuration, the cannula 1935 can be substantially straight or substantially undeformed. Thus, the lumen defined by the cannula 1935 is substantially unobstructed and/or otherwise not constricted by the actuator 1945.

[1158] In use, when the fluid reservoir 1960 is placed in fluid communication with the lumen defined by the cannula 1935 (see e.g., FIGS. 41 and 42), the negative pressure and/or suction (described above) within the lumen of the catheter 1935 can be modulated by actuating the actuator 1945 between its first configuration, associated with a smaller amount of suction, and its second configuration, associated with a larger amount of suction. Moreover, when the distal end portion 1932 of the adapter 1930 is placed in fluid communication with the body of a patient (e.g., either directly or indirectly via a lumen-defining device, a needle, etc.), the negative pressure within the fluid reservoir 1960 draws blood, or other bodily-fluids, through the lumen defined by the cannula 1935 and into the inner volume 1964. In this manner, actuating the actuator 1945 to control or modulate the amount of suction or negative pressure within the lumen of the cannula 1935 can reduce a magnitude of negative pressure that would otherwise be exerted on the flow of blood. Thus, hemolysis of the blood is reduced or substantially prevented that might otherwise result from a rapid exposure to a negative pressure differential produced by the fluid reservoir 1960.

[1159] Although the lumen of the cannula 1935 is shown in FIG. 41 as being partially constricted when the actuator 1945 is in its first configuration, in other embodiments, the actuator 1945 can deform the cannula 1935 a sufficient amount to result in a substantially complete constriction of the lumen. Moreover, while not shown in FIGS. 40-42, in some embodiments, the actuator 1945 can include and/or can be operably coupled to a bias member such as a spring or the like. As such, the bias member can exert a force that at least temporarily maintains the actuator 1945 in, for example, the first configuration until an actuating force is exerted on the actuator 1945, which is sufficient to overcome the force of the bias member.

[1160] While the adapter 1930 is shown and described above as controlling a flow of bodily-fluid into the fluid reservoir 1960 by manipulating the cannula 1935, in other embodiments, an adapter can control a flow of bodily-fluid into a fluid reservoir in any suitable manner. For example, FIGS. 43 and 44 illustrate an adapter 2030 and a fluid reservoir 2060, according to another embodiment. The fluid reservoir 2060 can be any suitable reservoir that defines an inner volume 2064 configured to receive a flow of bodily-fluid such as, for example, an evacuated container or the like. More specifically, as described above with reference to the fluid reservoir 1360 in FIGS. 31-33, the fluid reservoir 2060 includes a port 2063 through which a portion of the adapter 2030 can be inserted to gain access to the inner volume 2064, as described in further detail herein.

[1161] As shown in FIGS. 43 and 44, the adapter 2030 includes a proximal end portion 2031 and a distal end portion 2032. The proximal end portion 2031 of the adapter 2030 is open and/or defines an opening configured to receive at least a portion of the port 2063 of the fluid reservoir 2060. The distal end portion 2032 of the adapter 2030 includes a port 2033 or the like that can be coupled to any suitable lumen-defining device such as a cannula, catheter, and/or sterile flexible tubing (not shown in FIGS. 43 and 44). In some embodiments, the distal end portion 2032 can include a locking mechanism or the like fluidically coupled to the port 2033 and configured to physically and fluidically couple the adapter 2030 to any suitable corresponding device and/or component.

[1162] As shown in FIG. 44, the adapter 2030 includes a puncture member 2038 that extends from a surface of the adapter 2030 to, for example, puncture the port 2063 of the fluid reservoir 2060. Furthermore, the adapter 2030 defines a lumen 2036 that extends through a portion of the adapter 2030 to fluidically couple the port 2033 to the puncture

member 2038. Thus, the puncture member 2038 can puncture the port 2063 of the fluid reservoir 2060 to place the inner volume 2064 of the fluid reservoir 2060 in fluid communication with, for example, the port 2033 of the adapter 2030, which in turn, can be in fluid communication (e.g., either directly or indirectly via an intervening structure) a portion of the body of a patient. Moreover, a negative pressure within the fluid reservoir 2060 (e.g., the fluid reservoir 2060 is an evacuated container) exerts or draws suction through the lumen 2036 and the port 2033 of the adapter 2030 to, for example, draw a flow of bodily-fluid from the patient through the adapter 2030 and into the inner volume 2064 of the fluid reservoir 2060.

[1163] As shown in FIGS. 43 and 44, the arrangement of the adapter 2030 is such that the fluid reservoir 2060 is in a substantially vertical orientation when coupled to the adapter 2030. Thus, when a volume of bodily-fluid (e.g., blood) is expelled from the puncture member 2038, in response to the negative pressure within the fluid reservoir 2060, the bodily-fluid flows in a substantially vertical direction from a lower position to an upper position. While the fluid reservoir 2060 defines a negative pressure that produces a suction force operable in drawing a flow of bodily-fluid from the puncture member 2038, the bodily-fluid expelled therefrom is also exposed to a substantially opposing force associated with gravitational acceleration (i.e., approximately 9.81 meters-per-second-squared ($^{m}/_{s^2}$)). Thus, when a volume of blood is drawn through the adapter 2030 and into the inner volume 2064 of the fluid reservoir 2060, the force associated with gravity acts to slow a velocity of the flow of blood within the inner volume 2064. As such, hemolysis of blood is reduced and/or substantially prevented that can otherwise result from a force associated with a volume of blood impacting an inner surface of the fluid reservoir 2060 defining the inner volume 2064.

[1164] While the adapters and fluid reservoirs described above with reference to FIGS. 27-44 control and/or direct a flow of fluid (i.e., blood) into a fluid reservoir to, for example, reduce hemolysis, in some embodiments, the arrangement of a fluid reservoir and/or an adapter can be such that a negative pressure operable in drawing a volume of blood into the fluid reservoir can be configured modulated and/or controlled. For example, FIGS. 45-60 illustrate embodiments configured to mitigate the risk of hemolysis associated with blood flow to a negative pressure differential within a fluid reservoir. Specifically, FIG. 45 illustrates an adapter 2130 and a fluid reservoir 2160 according to another embodiment. The adapter 2130 can be any suitable adapter such as, for example, the adapter 1330 described

above with reference to FIGS. 29 and 30. In this manner, the adapter 2130 includes a puncture member 2138 configured to puncture a port or the like of the fluid reservoir 2160, as described in further detail herein. The fluid reservoir 2160 includes a proximal end portion 2161 and a distal end portion 2162, and defines an inner volume 2164. The proximal end portion 2161 includes a port 2163A configured to receive, for example, an output member (e.g., a needle, puncture member, cannula, etc.) from, for example, a vacuum source or the like, as described in further detail herein. Similarly, the distal end portion 2162 includes a port 2163 configured to receive, for example, the puncture member 2138 of the adapter 2130, as described in detail above with reference to FIGS. 31-33. In some embodiments, the ports 2163A and 2163 can be substantially similar in form and/or function. In some embodiments, the port 2163A disposed at or near the proximal end portion 2161, for example, can include a frangible seal, a self-healing port, a one-way valve, and/or the like.

[1165] As shown in FIG. 45, the fluid reservoir 2160 includes an elastomeric member 2178 (and/or any other suitable member or material) disposed within the inner volume 2164. The elastomeric member 2178 is in contact with an inner surface of the fluid reservoir 2160 (defining at least a portion of the inner volume 2164) to form a substantially fluid tight seal therebetween. Thus, a portion of the inner volume 2164 that is proximal to the elastomeric member 2178 is substantially fluidically isolated from a portion of the inner volume 2164 that is distal to the elastomeric member 2178. In some embodiments, the portion of the inner volume 2164 disposed between the elastomeric member 2178 and the port 2163 (i.e., disposed at the distal end portion 2162 of the fluid reservoir 2160) can define, for example, a negative pressure, prior to the insertion of the puncture member 2138 through the port 2163. In other embodiments, both portions of the inner volume 2164 (e.g., on either side of the elastomeric member 2178) define a negative pressure, prior to the insertion of the puncture member 2138 through the port 2163. In still other embodiments, the inner volume 2164, in its entirety, need not define a negative pressure, prior to the insertion of the puncture member 2138 through the port 2163.

[1166] As shown in FIG. 45, the plunger 2145 can "float" and/or otherwise be disposed in a substantially fixed position within the inner volume 2164 prior to the port 2163A being fluidically coupled to a vacuum source (not shown in FIG. 45). Moreover, the arrangement of the fluid reservoir 2160 is such that when the actuator 2130 engages the fluid reservoir 2160, the puncture member 2138 is in a distal position relative to the elastomeric member

2178 and thus, substantially fluidically isolated from the portion of the inner volume 2164 that is proximal to the elastomeric member 2178. In a similar manner, the fluid reservoir 2160 can be manipulated such that an outlet of a vacuum source (not shown in FIG. 45) punctures and/or is otherwise inserted through the port 2163A to be placed in fluid communication with the portion of the inner volume 2164 proximal to the elastomeric member 2178. Thus, a user can actuate the vacuum source (e.g., via an electric switch, a pre-charged negative pressure created in a manufacturing process, mechanical actuation, and/or the like), such that the vacuum source draws a vacuum (e.g., a suction force) through its output and into the portion of the inner volume 2164 proximal to the elastomeric member 2178.

[1167] In some instances, the suction force and/or negative pressure can be sufficient to overcome a friction force between the elastomeric member 2178 and the inner surface, thereby resulting in a movement of the elastomeric member 2178 within the inner volume 2164 towards the port 2163A. The movement of the elastomeric member 2178 results in a change in volume associated with the portions of the inner volume 2164 disposed on either side of the elastomeric member 2178. In some instances, the increase in volume of the portion of the inner volume 2164 distal to the elastomeric member 2178 results in a negative pressure that is sufficient to draw a flow of bodily-fluid through the puncture member 2138 and into the inner volume 2164. As such, in some instances, a rate and/or magnitude of the vacuum drawn by the vacuum source can be controlled to, for example, change a characteristic associated with a pressure difference within the inner volume 2164 of the fluid reservoir 2160 and, for example, the adapter 2130. Thus, hemolysis of the blood is reduced or substantially prevented that might otherwise result from a rapid exposure to a negative pressure differential produced by the fluid reservoir 2160.

[1168] While the elastomeric member 2178 is shown and described above as "floating" within the inner volume 2164, in other embodiments, a fluid reservoir can include an elastomeric member and/or the like that is coupled to a plunger. For example, FIG. 46 illustrates an adapter 2230 and a fluid reservoir 2260 according to another embodiment. The adapter 2230 can be any suitable adapter such as, for example, the adapter 1330 described above with reference to FIGS. 29 and 30. In this manner, the adapter 2230 includes a puncture member 2238 configured to puncture a port or the like of the fluid reservoir 2260, as described in further detail herein.

[1169] The fluid reservoir 2260 includes a proximal end portion 2261 and a distal end portion 2262, and defines an inner volume 2264. The proximal end portion 2261 includes a port 2263A configured to be coupled to, for example, a vacuum source or the like, as described in further detail herein. Similarly, the distal end portion 2262 includes a port 2263 configured to receive the puncture member 2238 of the adapter 2230, as described in detail above with reference to FIGS. 31-33. In some embodiments, the ports 2263A and 2263 can be substantially similar in form and/or function. In some embodiments, the port 2263A disposed at or near the proximal end portion 2261, for example, can include a frangible seal, a self-healing port, a one-way valve, a locking mechanism, and/or the like. Thus, the port 2263A can physically and fluidically couple to a corresponding outlet port of a vacuum source (not shown in FIG. 46). For example, in some embodiments, an outlet port of a vacuum source and the port 2263A can form a threaded coupling or the like. In such embodiments, when the vacuum source is actuated, the port 2263A can be transitioned from a first, substantially sealed configuration to a second, substantially open configuration.

[1170] As shown in FIG. 46, the fluid reservoir 2260 includes a plunger 2275 disposed within the inner volume 2264. The plunger 2275 includes and/or is coupled to an elastomeric member 2278 disposed within the inner volume 2264. The elastomeric member 2278 is in contact with an inner surface of the fluid reservoir 2260 (defining at least a portion of the inner volume 2264) to form a substantially fluid tight seal therebetween. Thus, a portion of the inner volume 2264 that is proximal to the elastomeric member 2278 is substantially fluidically isolated from a portion of the inner volume 2264 that is distal to the elastomeric member 2278, as described above with reference to the elastomeric member 2178 in FIG. 46. In this embodiment, at least a portion of the plunger 2275 is movably disposed within a support member 2264A extending from a surface of the fluid reservoir 2260. As shown, the support member 2264A can, for example, divide the inner volume into a first portion and a second portion. Moreover, the support member 2264A can include a seal or the like that is in contact with an outer surface of the plunger to form a substantially fluid tight seal therebetween. Thus, the first portion of the inner volume 2264 can be substantially isolated from the second portion of the inner volume 2264.

[1171] The arrangement of the fluid reservoir 2260 is such that when the actuator 2230 engages the fluid reservoir 2260, the puncture member 2238 is in a distal position relative to the elastomeric member 2278 and thus, substantially fluidically isolated from the portion of

the inner volume 2264 that is proximal to the elastomeric member 2278. A user can similarly manipulate the fluid reservoir to couple the port 2263A to an outlet of a vacuum source (not shown in FIG. 46). In this manner, the portion of the inner volume 2264 that is proximal to the support member 2264A is placed in fluid communication with the vacuum source. Thus, a user can actuate the vacuum source (e.g., via an electric switch, a pre-charged negative pressure created in a manufacturing process, mechanical actuation, and/or the like) such that the vacuum source draws a vacuum (e.g., a suction force) through its output and into the portion of the inner volume 2264 proximal to the support member 2264A.

[1172] In some instances, the suction force and/or negative pressure can be sufficient to move the plunger 2275 within the inner volume 2264 towards the port 2263A. The movement of the plunger 2275 results in a corresponding movement of the elastomeric member 2278 and thus, changes a volume associated with the portions of the inner volume 2264 disposed on either side of the elastomeric member 2278. In some instances, the increase in volume of the portion of the inner volume 2264 distal to the elastomeric member 2278 results in a negative pressure that is sufficient to draw a flow of bodily-fluid through the puncture member 2238 an into the inner volume 2264. As such, in some instances, a rate and/or magnitude of the vacuum drawn by the vacuum source can be controlled to, for example, change a characteristic associated with a pressure difference within the inner volume 2264 of the fluid reservoir 2260 and, for example, the adapter 2230. Thus, hemolysis of the blood is reduced or substantially prevented that might otherwise result from a rapid exposure to a negative pressure differential produced by the movement of the plunger 2375 within the fluid reservoir 2260.

[1173] In some embodiments, the arrangement of the plunger 2275 and the support member 2264A can, for example, maintain a sterility of a portion of the inner volume 2264 distal to the support member 2264A. Specifically, as described above, the support member 2264A can include the seal that engages the outer surface of the plunger 2275 to fluidically isolate a portion of the inner volume 2264 proximal to the support member 2264A from a different portion of the inner volume 2264 distal to the support member 2264A. As such, when the port 2263A is placed in fluid communication with the vacuum source (not shown in FIG. 46), the portion of the inner volume 2264 proximal to the support member 2264A can be exposed, for example, to a non-sterile environment (e.g., associated with the vacuum source), while the sterility of the portion of the inner volume 2264 is maintained.

[1174] FIG. 47 illustrates an adapter 2330 and a fluid reservoir 2360 according to another embodiment. The adapter 2330 can be any suitable adapter such as, for example, the adapter 1330 described above with reference to FIGS. 29 and 30. In this manner, the adapter 2330 includes a puncture member 2338 configured to puncture a port or the like of the fluid reservoir 2360, as described in further detail herein.

[1175] The fluid reservoir 2360 includes a proximal end portion 2361 and a distal end portion 2362, and defines an inner volume 2364. The proximal end portion 2361 includes a port 2363A configured to be coupled to, for example, a vacuum source or the like, as described in further detail herein. Similarly, the distal end portion 2362 includes a port 2363 configured to receive the puncture member 2338 of the adapter 2330, as described in detail above with reference to FIGS. 31-33. As shown in FIG. 47, the fluid reservoir 2360 includes a plunger 2375 disposed within the inner volume 2364. The plunger 2375 includes and/or is coupled to an elastomeric member 2378 disposed within the inner volume 2364. The elastomeric member 2378 is in contact with an inner surface of the fluid reservoir 2360 (defining at least a portion of the inner volume 2364) to form a substantially fluid tight seal therebetween. As such, the fluid reservoir 2360 can be substantially similar to the fluid reservoir 2260 described above with reference to FIG. 46.

[1176] The fluid reservoir 2360 can differ from the fluid reservoir 2260, however, by including a bias member 2377 (e.g., a linear spring, a torsion spring, a leaf spring, a compression member, and/or the like) disposed about and in contact with a portion of the plunger 2375. In this manner, when the port 2363A is physically and fluidically coupled to an outlet of a vacuum source (not shown in FIG. 47) and the vacuum source is actuated, the vacuum source draws a vacuum (e.g., a suction force) through its output and into the portion of the inner volume 2364. Thus, the vacuum source can exert a suction force within a portion of the inner volume 2364 that results in a proximal movement of the plunger 2375. The arrangement of the bias member 2377, however, is such that the bias member 2377 exerts a reaction force in response to the movement of the plunger 2375. As such, the bias member 2377 can at least partially control a movement of the plunger 2375 within the inner volume 2364, for example, to reduce speed at which the plunger 2375 is moved. Thus, hemolysis of the blood is reduced or substantially prevented that might otherwise result from a rapid exposure to a negative pressure differential produced by the movement of the plunger 2375 within the fluid reservoir 2360.

[1177] While the adapters in the embodiments above have been shown and described as being physically and/or fluidically coupled to a corresponding fluid reservoir configured as an evacuated container, in other embodiments, an adapter can be configured to physically and/or fluidically couple to any suitable fluid reservoir and/or any suitable intervening structure. For example, FIGS. 49 and 50 illustrate an adapter 2430 according to another embodiment. The adapter 2430 can be any suitable shape or size and can be configured to be placed in fluid communication with any suitable fluid reservoir. For example, as described in further detail herein with reference to FIGS. 51 and 52, in some instances, the adapter 2430 can be physically and fluidically coupled to a fluid reservoir 2460 configured as, for example, a syringe or the like.

[1178] As shown in FIGS. 49 and 50, the adapter 2430 has a proximal end portion 2431 and a distal end portion 2432. In this embodiment, the distal end portion 2432 of the adapter 2430 includes, for example, a locking mechanism (e.g., a Luer Lok® or the like) that can physically and fluidically couple the adapter 2430 to a corresponding locking mechanism of any other suitable device such as, for example, an extension set or the like. In other embodiments, the distal end portion 2432 can be any suitable configuration such as, for example, a port, a septum, and/or the like. In a similar manner, the proximal end portion 2431 of the adapter 2430 includes, for example, a locking mechanism (e.g., a Luer Lok® or the like) that can physically and/to fluidically couple the adapter 2430 to, for example, the fluid reservoir 2460, as described in further detail herein.

[1179] The adapter 2430 includes a delivery member 2438 that extends from a portion of adapter 2430 toward the proximal end portion 2431. The delivery member 2438 defines a lumen 2439 extending at least partially through the delivery member 2438. More specifically, in this embodiment, the lumen 2439 extends through the distal end portion 2432 of the adapter 2430 but does not extend through the proximal end portion 2431. Similarly stated, the lumen 2439 does not extend through a proximal surface of the delivery member 2438. For example, as shown in FIGS. 49 and 50, the delivery member 2438 can have a substantially rounded or hemispherical proximal surface that is substantially closed and/or continuous. Alternatively, the delivery member 2438 defines at least one opening 2440 disposed along a circumference of the delivery member 2438 at a position distal to, for example, the proximal surface. Thus, while the delivery member 2438 does not define an

opening though a proximal most surface, opening(s) 2440 place a proximal end portion of the lumen 2439 in fluid communication with a volume outside of the delivery member 2438.

[1180] As described above, the adapter 2430 can be physically and fluidically coupled to the fluid reservoir 2460 (see e.g., FIG. 52). The fluid reservoir 2460 can be any suitable shape, size, or configuration. For example, in this embodiment, the fluid reservoir 2460 is a syringe or the like, as shown in FIG. 51. The fluid reservoir 2460 has a proximal end portion 2461 and a distal end portion 2462 and defines an inner volume 2464. The distal end portion 2462 is configured to be physically and fluidically coupled to an adapter such as, for example, the adapter 2430. For example, the distal end portion 2462 can include a locking mechanism (e.g., a Luer Lok® or the like) configured to be physically and fluidically coupled to the proximal end portion 2431 (e.g., the corresponding locking member included therein) of the adapter 2430. Moreover, when the adapter 2430 is coupled to the fluid reservoir 2460, the delivery member 2438 is at least partially disposed in the inner volume 2464 of the fluid reservoir 2460 and as such, the opening(s) 2440 defined by the delivery member 2438 place the lumen 2439 of the adapter 2430 in fluid communication with the inner volume 2464 of the fluid reservoir 2460, as described in further detail herein.

[1181] As shown in FIGS. 51 and 52, the proximal end portion 2461 movably receives a plunger 2475 that is at least partially disposed in the inner volume 2464, as described in further detail herein. As shown in FIG. 52, the fluid reservoir 2460 includes a seal member 2479 disposed within the inner volume 2464. More specifically, the seal member 2479 is disposed within a proximal portion of the inner volume 2464 and about a portion of the plunger 2475. As such, the seal member 2479 forms a substantially fluid tight seal between an inner surface of the fluid reservoir 2460 and an outer surface of the seal member 2479 and an outer surface of the plunger 2475 and an inner surface of the seal member 2479. Furthermore, the seal member 2479 defines an opening 2479A extending therethrough that can place a portion of the inner volume 2464 proximal to the seal member 2479 in fluid communication with a portion of the inner volume 2464 distal to the seal member 2479. The arrangement of the fluid reservoir 2460 is such that the seal member 2479 is maintained in a substantially fixed position when the plunger 2475 is moved within the inner volume 2464, as described in further detail herein.

[1182] As shown in FIG. 52, the plunger 2475 has a proximal end portion 2476 and a distal end portion 2477. The distal end portion 2477 of the plunger 2475 includes and/or is

coupled to an elastomeric member 2478 or the like. For example, in some embodiments, the elastomeric member 2478 can form a substantially fluid tight seal with an inner surface of the fluid reservoir 2460. As described above, the plunger 2475 is movably disposed within the inner volume 2464 of the fluid reservoir 2460. More specifically, the plunger 2475 can be moved within the inner volume 2464 in an axial direction between a first position (e.g., a distal position) and a second position (e.g., a proximal position) relative to the fluid reservoir 2460. For example, in some embodiments, the plunger 2475 can be disposed in a distal position relative to the fluid reservoir 2460 prior to use. A user can then manipulate the fluid reservoir 2460 and/or the plunger 2475 to move the plunger 2474 in a proximal direction within the inner volume 2464. With the elastomeric member 2478 in contact with the inner surface of the fluid reservoir 2460, the proximal movement of the plunger 2475 relative to the fluid reservoir 2460 produces a negative pressure within a portion of the inner volume 2464 that is distal to the elastomeric member 2478.

[1183] When the adapter 2430 is coupled to the fluid reservoir 2460 (as shown in FIG. 52), the negative pressure within the portion of the inner volume 2464 results in a suction through the lumen 2439 of the delivery member 2438. Thus, when the distal end portion 2431 of the adapter 2430 is coupled to a device or other intervening structure, which in turn, is in fluid communication with a portion of the body and/or intervening device (e.g. catheter, fluid reservoir, etc.), the suction force within the lumen 2439 can draw a bodily-fluid (e.g., blood) through the lumen 2439 and into the inner volume 2464 of the fluid reservoir 2460. Moreover, the arrangement of the seal member 2479 within the inner volume 2464 can reduce, limit, modulate, and/or otherwise at least partially control a rate at which the plunger 2479 can be moved within the inner volume 2464. For example, with the elastomeric member 2478 forming a substantially fluid tight seal with the inner surface of the fluid reservoir 2460, the proximal movement of the plunger 2464 reduces and/or compresses a volume defined between the elastomeric member 2478 and the seal member 2479, which in turn, increases a pressure within that volume. Therefore, with the seal member 2479 similarly forming a substantially fluid tight seal with the inner surface of the fluid reservoir 2460 and with an outer surface of the plunger 2475, air within the volume between the seal member 2479 and the elastomeric member 2478 is forced through the opening 2479A defined by the seal member 2479, thereby limiting the rate at which the plunger 2479 is moved within the inner volume 2464. As such, a negative pressure and/or a suction force drawn through the lumen 2439 of the adapter 2430 is correspondingly controlled and/or modulated.

[1184] As described above, in some embodiments, the arrangement of the delivery member 2438 can also limit and/or otherwise modulate a pressure and/or a suction force within the lumen 2439. In this manner, when withdrawing a volume of blood, hemolysis of the blood flowing through the lumen 2439 and into the inner volume 2464 of the fluid reservoir 2460 is reduced or substantially prevented. Specifically, the arrangement opening(s) 2440 and the lumen 2439 of the delivery member 2438 can, for example, reduce a negative pressure within the lumen 2439 and/or can slow a flow of blood delivered to the inner volume 2464 of the fluid reservoir 2460 to an extent that can reduce and/or substantially prevent hemolysis of the blood that can otherwise result from, inter alia, a volume of blood being exposed to a rapid pressure drop or the like. In addition, the arrangement of an inner surface defining the lumen 2439 can, for example, reduce turbulence, eddy currents, and/or any other disturbance that can otherwise result from a discontinuity or the like.

[1185] While the fluid reservoir 2460 is particularly shown and described above with reference to FIGS. 51 and 52, in other embodiments, any suitable fluid reservoir can be coupled to, for example, the adapter 2430 to receive a volume of blood with reduced hemolysis of its constituents. For example, FIGS. 53 and 54 illustrate a fluid reservoir 2560 according to another embodiment. In this embodiment, the fluid reservoir 2560 is, for example, a syringe or the like having a proximal end portion 2561 and a distal end portion 2562 and defining an inner volume 2564. The distal end portion 2562 is configured to be physically and fluidically coupled to an adapter such as, for example, the adapter 1530, as described in detail above.

[1186] The proximal end portion 2561 of the fluid reservoir 2560 is substantially open and receives at least a portion of a plunger 2575. Moreover, the proximal end portion 2561 of the fluid reservoir 2560 includes an actuator 2570 that is operable in moving the plunger 2575 within the inner volume 2564. For example, as shown in FIGS. 53 and 54, the fluid reservoir 2560 includes a protrusion 2569 to which the actuator 2570 is pivotally coupled. More specifically, the actuator 2570 includes a first end portion 2571, a second end portion 2572, and a pivot portion 2573 disposed therebetween. The second end portion 2572 of the actuator 2570 is coupled to a portion of the plunger 2575, as described in further detail herein. The pivot portion 2573 is coupled to the protrusion 2569 via, for example, a pin, an axle, a rod, and/or the like configured to allow the actuator 2570 to pivot about the protrusion

2569 (e.g., about an axis defined by the protrusion 2569) in response to a force exerted on the first end portion 2571. In this manner, the actuator 2570 can be arranged, for example, as a trigger or the like which when actuated, is operable in moving the plunger 2575 relative to the fluid reservoir 2560, as described in further detail herein.

[1187] As shown in FIG. 54, the plunger 2575 has a proximal end portion 2576 and a distal end portion 2577. The distal end portion 2577 of the plunger 2575 includes and/or is coupled to an elastomeric member 2578 or the like. For example, in some embodiments, the elastomeric member 2578 can form a substantially fluid tight seal with an inner surface of the fluid reservoir 2560. As described above, the plunger 2575 is movably disposed within the inner volume 2564 of the fluid reservoir 2560. More specifically, the proximal end portion 2576 of the plunger 2575 is coupled to the second end portion 2572 of the actuator 2570 such that an actuation of the actuator 2570 results in a movement of the plunger 2570 within the inner volume 2564.

[1188] For example, a user can exert a force on the first end portion 2571 (e.g., with his or her thumb or finger) of the actuator 2570, which in turn, results in a pivoting motion about the protrusion 2569 that places the first end portion 2571 in a position closer to an outer surface of the fluid reservoir 2560 and places the second end portion 2572 in a corresponding position farther away from the fluid reservoir 2560. In other words, the pivoting of the actuator 2570 about the protrusion 2569 moves the second end portion 2572 in a proximal direction. Moreover, the trigger arrangement of the actuator 2570 (as described above) defines a range of motion through which the actuator 2570 can pivot and thus, defines a range of motion through which the plunger 2575 is moved in the proximal direction (i.e., a stroke length). As such, the user can serially actuate the actuator 2570 to move the plunger 2575 a desired distance in the proximal direction.

[1189] With the elastomeric member 2578 of the plunger 2575 forming a substantially fluid tight seal with the inner surface of the fluid reservoir 2560, the proximal movement of the plunger 2575 relative to the fluid reservoir 2560 produces a negative pressure within a portion of the inner volume 2564 that is distal to the elastomeric member 2578. Thus, when the fluid reservoir is coupled to an adapter and/or any other suitable lumen-defining device in fluid communication with the body of a patient, the negative pressure results in a suction force within that lumen that can draw a bodily-fluid (e.g., blood) through the lumen and into the inner volume 2564 of the fluid reservoir 2560. Moreover, by limiting the stroke length

(as described above) of the plunger 2575, a rate at which the plunger 2575 can be moved within the inner volume 2564 is reduced, limited, modulated, and/or otherwise at least partially controlled. As a result, a negative pressure and/or a suction force drawn through, for example, the lumen of the lumen-defining device is correspondingly controlled and/or modulated. Therefore, by limiting the stroke of the plunger 2575, a negative pressure within the inner volume 2564 of the fluid reservoir 2560 and/or a rate at which blood (or other bodily-fluid) flows into the inner volume 2564 can be controlled to an extent that can reduce and/or substantially prevent hemolysis of the blood that can otherwise result from, inter alia, a volume of blood being exposed to a rapid pressure drop or the like.

[1190] While the actuator 2570 is particularly shown in FIGS. 52 and 53, in other embodiments, the actuator 2570 can be any suitable device, mechanism, and/or member that is operative in moving the plunger 2575 within the fluid reservoir 2560. For example, while actuator 2570 is described above as being actuated by a user's thumb or finger, in other embodiments, and actuator can include a first end portion that extends a given length of the fluid reservoir as to be engaged by a user's palm or more than one finger (e.g., each finger excluding the thumb of the user). In other embodiments, a fluid reservoir can include an actuator that is a switch, a push button, a toggle, and/or the like configured to close an electric circuit or the like when actuated. Thus, when the electric circuit is closed, a current can flow through the electric circuit, for example, to a mechanism (e.g., including an electric motor) configured to move a plunger within the fluid reservoir.

[1191] FIGS. 54-56 illustrate a fluid reservoir 2660 according to another embodiment. The fluid reservoir 2660 can be any suitable shape, size, or configuration. For example, in this embodiment, the fluid reservoir 2660 is a syringe or the like, as shown in FIG. 54. The fluid reservoir 2660 has a proximal end portion 2661 and a distal end portion 2662 and defines an inner volume 2664 (see e.g., 56). The distal end portion 2662 is configured to be physically and fluidically coupled to an adapter (not shown in FIGS. 54-56) such as, for example, the adapter 2430 described above with reference to FIGS. 48-51.

[1192] The proximal end portion 2661 of the fluid reservoir 2660 movably receives a plunger 2675 that is at least partially disposed in the inner volume 2664. As shown in FIGS. 55 and 56, the plunger 2675 has a proximal end portion 2676 and a distal end portion 2677. The distal end portion 2677 of the plunger 2675 includes and/or is coupled to an elastomeric member 2678 or the like. For example, in some embodiments, the elastomeric member 2678

can form a substantially fluid tight seal with an inner surface of the fluid reservoir 2660, as described in detail above. The proximal end portion 2676 of the plunger 2675 is coupled to an actuator 2670. For example, in some embodiments, at least a portion of the actuator 2670 can be hollow and configured to be movably disposed (e.g., in an axial direction) about the proximal end portion 2676 of the plunger 2675. Expanding further, the proximal end portion 2676 of the plunger 2675 includes a set of protrusions 2676A or the like (e.g., tabs, pins, bumps, etc.) configured to engage and/or otherwise disposed in a corresponding set of openings 2670A when the actuator 2670 is disposed about the proximal end portion 2676. In some embodiments, each protrusion 2676A can include an indicator or the like that can be viewable when disposed in a corresponding opening 2670A of the actuator 2670, as described in further detail herein.

[1193] As shown in FIGS. 55 and 56, the plunger 2675 includes a bias member 2674 (e.g., a linear spring, a torsion spring, and/or the like) disposed between the proximal end portion 2676 and the actuator 2670. In this manner, the bias member 2674 can, for example, maintain the actuator 2670 is a substantially fixed position relative to the proximal end portion 2676 until a force is exerted on the actuator 2670 or the plunger 2675 that is sufficient to overcome a force exerted by the bias member 2674. For example, in some embodiments, a user can manipulate the fluid reservoir 2660 to fluidically couple the distal end portion 2662, for example, to an adapter (e.g., the adapter 2430), which in turn can be directly or indirectly coupled to a device in fluid communication with a portion of the body. Thus, the inner volume 2664 of the fluid reservoir 2660 is placed in fluid communication with the portion of the body. With the fluid reservoir 2660 in fluid communication with the portion of the body, the user can manipulate the actuator 2670, for example, to move the plunger 2675 within the inner volume 2664. For example, a user can exert a force on the actuator 2670 to move the actuator 2670 and the plunger 2675 in the proximal direction relative to the fluid reservoir 2660. The arrangement of the bias member 2674 can be such that at least a portion of the force exerted by the user on the actuator 2670 transitions the bias member 2674 from a first configuration (e.g., a compressed configuration) to a second configuration (e.g., an extended configuration). Thus, the bias member 2674 can absorb at least a portion of the force (e.g., an excess portion of force above a predetermined threshold), exerted by the user, that would otherwise be exerted on the plunger 2675. In this manner, a rate at which the plunger 2675 is moved within the inner volume 2664 can be at least partially controlled and/or otherwise limited, which in turn, can reduce and/or substantially prevent hemolysis of the blood drawn

into the inner volume 2664 that can otherwise result from, inter alia, a volume of blood being exposed to a rapid pressure drop or the like.

[1194] In some embodiments, the arrangement of the protrusions 2676A of the proximal end portion 2676 within the openings 2670A of the actuator 2670, for example, can define a range of motion of the actuator 2670 relative to the plunger 2675 (e.g., can prevent a movement of the actuator 2675 beyond a predetermined threshold relative to the plunger 2675. In some embodiments, the protrusions 2676A can each include an indicator or the like that are viewable through the openings 2670A and therefore, can provide an indication to the user associated with the movement of the actuator 2670 relative to the plunger 2675. For example, in some embodiments, when a force is exerted on the actuator 2670 that is greater than a predetermined threshold, the actuator 2670 can be moved relative to the plunger 2675 and at least a portion of the force can transition the bias member 2674 from its first configuration to its second configuration. Thus, when the bias member 2674 is in its second configuration (e.g., an extended configuration), the actuator 2670 can be in a position relative to the plunger 2675 that is associated with at least a portion of the indicator of the protrusions 2676A being viewable through the openings 2670A. As such, the indicators can provide a visual indication of when a force exerted by the user exceeds a predetermined threshold. In some embodiments, the arrangement of the protrusions 2676A and the openings 2670A can be such that when a force exerted on the actuator 2670 exceeds the predetermined threshold, the plunger 2675 and/or the actuator 2670 also provide an auditory (e.g., a clicking sound) or a haptic indication.

[1195] While the actuators 2570 and 2670 are particularly shown and described above, in other embodiments, a fluid reservoir can include any suitable actuator operable in moving a plunger within an inner volume of the fluid reservoir. For example, FIGS. 57 and 58 illustrate a fluid reservoir 2760 according to another embodiment. The fluid reservoir 2760 can be any suitable shape, size, or configuration. For example, in this embodiment, the fluid reservoir 2760 is a syringe or the like, as shown in FIG. 57. The fluid reservoir 2760 has a proximal end portion 2761 and a distal end portion 2762 and defines an inner volume 2764 (see e.g., 56). The distal end portion 2762 is configured to be physically and fluidically coupled to an adapter (not shown in FIGS. 57 and 58) such as, for example, the adapter 2430 described above with reference to FIGS. 48-51. The proximal end portion 2761 of the fluid reservoir 2760 movably receives a plunger 2775 that is at least partially disposed in the inner

volume 2764. As shown in FIG. 58, the plunger 2775 has a proximal end portion 2776 and a distal end portion 2777. The distal end portion 2777 of the plunger 2775 includes and/or is coupled to an elastomeric member 2778 or the like, as described in detail herein. The proximal end portion 2776 of the plunger 2775 is coupled to an actuator 2770 operable in moving the plunger 2775 relative to the fluid reservoir 2760.

[1196] The actuator 2770 can be any suitable shape, size, or configuration. For example, as shown in FIGS. 57 and 58, the actuator 2770, in this embodiment, is a dial rotatably coupled to the fluid reservoir 2760 and the plunger 2775. More specifically, the actuator 2770 can be disposed about the proximal end portion 2761 of the fluid reservoir 2760 such that the actuator 2770 can rotate relative thereto without, for example, unthreading or removing the actuator 2770 from the fluid reservoir 2760. In other words, the actuator 2770 can be coupled to the proximal end portion 2761 of the fluid reservoir 2760 for rotational motion while substantially preventing a linear motion of the actuator 2770 relative to the fluid reservoir 2760. As shown in FIG. 58, an outer surface of the plunger 2775 includes and/or otherwise forms a set of continuous threads 2775A arranged in a helical manner along a length of the plunger 2775 (e.g., substantially the entire length). Moreover, a portion of the plunger 2775 is configured to extend through, for example, a threaded opening defined by the actuator 2770. Thus, the set of threads 2775A engage a surface of the actuator 2770 to define a threaded coupling therebetween, which can allow the plunger 2775 to be moved in an axial direction within the inner volume 2764 of the fluid reservoir 2760.

[1197] Specifically, in use, the fluid reservoir 2760 can be manipulated to couple the distal end portion 2762 to an adapter or other device in fluid communication with a portion of the body, thereby placing the inner volume 2764 of the fluid reservoir 2760 in fluid communication with the portion of the body and/or intervening device (e.g. catheter, etc.). With the inner volume 2764 in fluid communication with the portion of the body, the actuator 2770 can be rotated relative to the fluid reservoir 2760, which in turn, results in the threads 2775A being advanced along a surface of the actuator 2770. Thus, the plunger 2775 is moved in an axial direction (e.g., a proximal direction) within the inner volume 2764, which in turn, increases a portion of the inner volume 2764 that is distal to the elastomeric member 2778. Such an increase results in, for example, a negative pressure within the portion of the inner volume 2764 distal to the elastomeric member 2778 and therefore, a suction force is exerted that is operable in drawing a bodily-fluid (i.e., blood) into the inner volume 2764 of

the fluid reservoir 2760. In some embodiments, the arrangement of the actuator 2770 and the plunger 2775 (i.e., the threaded coupling) limits a rate at which the plunger 2775 is moved within the inner volume 2764. In this manner, limiting the rate at which the plunger 2775 is moved within the inner volume 2764 can reduce and/or substantially prevent hemolysis of the blood drawn into the inner volume 2764 that can otherwise result from, inter alia, a volume of blood being exposed to a rapid pressure drop or the like.

[1198] While the actuator 2770 is shown and described above as forming a threading coupling with the plunger 2775, in other embodiments, a fluid reservoir can include an actuator that is monolithically formed with a plunger. For example, FIG. 59 illustrates a fluid reservoir according to another embodiment. The fluid reservoir 2860 has a proximal end portion 2861 and a distal end portion 2862 and defines an inner volume 2864. The distal end portion 2862 is configured to be physically and fluidically coupled to an adapter (not shown in FIG. 59) such as, for example, the adapter 2430 described above with reference to FIGS. 48-51. In this embodiment, the fluid reservoir 2860 includes an outer surface that defines a set of continuous threads arranged in a helical manner along a length of the fluid reservoir 2860, as described above with reference to the plunger 2775 in FIG. 58.

[1199] The fluid reservoir 2860 is rotatably coupled to an actuator 2870. The actuator 2870 includes a proximal end portion 2871, a distal end portion 2872, and a plunger 2875. The actuator 2870 further includes an inner surface that defines a set of continuous threads 2899 (e.g., female threads or grooves) arranged in a helical manner along a length of the inner surface. In this manner, the actuator 2870 can be disposed about the fluid reservoir 2860 such that the set of threads 2860A of the fluid reservoir 2860 are disposed within the corresponding set of threads 2899 of the actuator 2870, while the plunger 2875 extends from the proximal end portion 2871 of the actuator 2870 within the inner volume 2864 of the fluid reservoir 2860. Moreover, as shown in FIG. 59, a distal end portion 2877 of the plunger 2875 includes and/or is coupled to an elastomeric member 2878 configured to form a substantially fluid tight seal with an inner surface of the fluid reservoir 2860, as described in detail herein.

[1200] Thus, in use, the fluid reservoir 2860 can be manipulated to couple the distal end portion 2862 to an adapter or other device in fluid communication with a portion of the body, thereby placing the inner volume 2864 of the fluid reservoir 2860 in fluid communication with the portion of the body. With the inner volume 2864 in fluid communication with the

portion of the body, the actuator 2870 can be rotated relative to the fluid reservoir 2860, which in turn, results in the threads 2899 of the actuator 2870 being advanced along the corresponding threads 2860A of the fluid reservoir 2860. Thus, the actuator 2870 can be moved in the proximal direction relative to the fluid reservoir 2860, which results in the plunger 2875 being moved in an axial direction (e.g., a proximal direction) within the inner volume 2864. As such, a portion of the inner volume 2864 that is distal to the elastomeric member 2878 is increased. Such an increase results in, for example, a negative pressure within the portion of the inner volume 2864 distal to the elastomeric member 2878 and therefore, a suction force is exerted that is operable in drawing a bodily-fluid (i.e., blood) into the inner volume 2864 of the fluid reservoir 2860. In some embodiments, the arrangement of the actuator 2870 and the fluid reservoir 2860 (i.e., the threaded coupling) limits a rate at which the plunger 2875 is moved within the inner volume 2864. In this manner, limiting the rate at which the plunger 2875 is moved within the inner volume 2864 can reduce and/or substantially prevent hemolysis of the blood drawn into the inner volume 2864 that can otherwise result from, inter alia, a volume of blood being exposed to a rapid pressure drop or the like.

[1201] FIG. 60 illustrates a fluid reservoir 2960 according to another embodiment. The fluid reservoir 2960 can be any suitable shape, size, or configuration. For example, in this embodiment, the fluid reservoir 2960 can be configured to receive a portion of an actuator 2970 (e.g., arranged as a syringe or the like), as described in further detail herein. The fluid reservoir 2960 has a first chamber 2990 and a second chamber 2991, which are formed unitarily (e.g., joined at a proximal end portion of the fluid reservoir 2960. The first chamber 2990 includes a proximal end portion 2961 and a distal end portion 2962 and defines an inner volume 2964. The distal end portion 2962 is configured to be physically and fluidically coupled to an adapter such as, for example, the adapter 2430 described above with reference to FIGS. 48-51. The proximal end portion 2961 movably receives a first plunger 2975 of the actuator 2970, which is at least partially disposed in the inner volume 2964, as described in further detail herein. In this manner, the first chamber 2990 is configured to receive and at least temporarily store a volume of bodily-fluid, as described in further detail herein.

[1202] Similarly, the second chamber 2991 includes a proximal end portion 2992 and a distal end portion 2993 and defines an inner volume 2994. The distal end portion 2993 of the second chamber 2991 is closed (i.e., does not define a port or other opening). The proximal

end portion 2992 movably receives a second plunger 2995 of the actuator 2970, which is at least partially disposed in the inner volume 2994, as described in further detail herein. As shown in FIG. 60, the second chamber 2991 has a size and/or shape that are/is smaller than the first chamber 2990. Thus, in some embodiments, the second chamber 2991 can be an auxiliary chamber or the like. For example, with the distal end portion 2993 of the second chamber 2991 being closed and/or sealed, in this embodiment, the second chamber 2991 can act as a dampener or the like configured to dampen a movement of the actuator 2970 relative to the fluid reservoir 2960.

[1203] As described above, the actuator 2970 includes the first plunger 2975 movably disposed in the inner volume 2964 of the first chamber 2990 and the second plunger 2995 movably disposed in the inner volume 294 of the second chamber 2991. As shown in FIG. 60, the first plunger 2975 has a proximal end portion 2976 and a distal end portion 2977. The proximal end portion 2976 of the first plunger 2975 is coupled to and/or otherwise unitarily formed a proximal end portion 2996 of the second plunger 2995. The distal end portion 2977 of the first plunger 2975 includes and/or is coupled to an elastomeric member 2978 or the like. In some embodiments, the elastomeric member 2978 can form a substantially fluid tight seal with an inner surface of the first chamber 2990, as described in detail above. Similarly, the second plunger 2995 has the proximal end portion 2996 and a distal end portion 2997. The proximal end portion 2996 of the second plunger 2995 is coupled to and/or otherwise unitarily formed with the proximal end portion 2976 of the first plunger 2975. The distal end portion 2997 of the second plunger 2995 includes and/or is coupled to an elastomeric member 2998. As described above with reference to the elastomeric member 2978, the elastomeric member 2998 of the second plunger 2995 can form a substantially fluid tight seal with an inner surface of the second chamber 2991. In this manner, the actuator 2970 can be moved relative to the fluid reservoir 2960 to move the first plunger 2975 within the inner volume 2964 of the first chamber 2990 and the second plunger 2995 within the inner volume 2994 of the second chamber 2991 in a substantially concurrent movement, as described in further detail herein.

[1204] In use, for example, the fluid reservoir 2960 can be manipulated to couple the distal end portion 2962 to an adapter or other device in fluid communication with a portion of the body, thereby placing the inner volume 2964 of the fluid reservoir 2960 in fluid communication with the portion of the body and/or intervening device (e.g. catheter, etc.).

Once the inner volume 2964 is placed in fluid communication with the portion of the body, the actuator 2970 can be moved in the proximal direction relative to the fluid reservoir 2960, which in turn, moves the first plunger 2975 within the inner volume 2964. More specifically, with the elastomeric member 2978 of the plunger 2975 forming a substantially fluid tight seal with the inner surface of the fluid reservoir 2960, the proximal movement of the first plunger 2975 relative to the fluid reservoir 2960 produces a negative pressure within a portion of the inner volume 2964 that is distal to the elastomeric member 2978. Thus, when the fluid reservoir is coupled to an adapter and/or any other suitable lumen-defining device in fluid communication with the body of a patient, the negative pressure results in a suction force within that lumen that can draw a bodily-fluid (e.g., blood) through the lumen and into the inner volume 2964 of the fluid reservoir 2960.

[1205] In a similar manner, the proximal movement of the actuator 2970 moves the second plunger 2995 within the inner volume 2994 of the second chamber 2991 substantially concurrently with the first plunger 2975, thereby increasing a portion of the inner volume 2994 that is distal to the elastomeric member 2998. With the elastomeric member 2998 of the second plunger 2995 forming a substantially fluid tight seal with the inner surface of the second chamber 2991, such an increase in the portion of the inner volume 2994 that is distal to the elastomeric results in a negative pressure within that portion of the inner volume 2994. Moreover, with the distal end portion 2993 of the second chamber 2991 being closed and/or sealed, the movement of the second plunger 2995 within the second chamber 2991, for example, can act to dampen the movement of the actuator 2970 relative to the fluid reservoir 2960. Specifically, the increase of the portion of the inner volume 2994 distal to the elastomeric member 2998 produces, for example, a suction force therein that resists the proximal movement of the second plunger 2995. Thus, an effective force exerted on the actuator 2970 to move the first plunger 2975 within the first chamber 2990 and the second plunger 2995 within the second chamber 2991 can be modulated, reduced, limited, and/or otherwise controlled, which in turn, can limit a rate at which the actuator 2970 is moved relative to the fluid reservoir 2960. In other words, the arrangement of the second chamber 2991 and the second plunger 2995 dampen the force exerted on the actuator 2970 and thus, the movement of the actuator 2970 relative to the fluid reservoir 2960. Therefore, by limiting the rate at which the actuator 2970 is moved relative to the fluid reservoir 2960, a negative pressure within the inner volume 2964 of the first chamber 2991 and/or a rate at which blood (or other bodily-fluid) flows into the inner volume 2964 can be controlled to an extent that

can reduce and/or substantially prevent hemolysis of the blood that can otherwise result from, inter alia, a volume of blood being exposed to a rapid pressure drop or the like.

[1206] While the embodiments are shown and described above as defining a single flow path from the patient to a fluid reservoir, in some embodiments, a fluid transfer device and/or system can include, for example, any suitable extension set, Y-adapter, T-adapter, junction, split, and/or the like configured to define more than one fluid flow path. Moreover, in such embodiments, a fluid transfer device and/or system can include any suitable coupling mechanism, lock mechanism, hub, and/or the like configured to couple, for example, a first lumen-defining device to a second lumen-defining device such that hemolysis of a flow of blood therethrough is limited and/or substantially prevented. For example, FIGS. 61-71 illustrate embodiments configured to mitigate the risk of hemolysis as blood flows through a multi-lumen adapter and/or the like. Specifically, FIGS. 61-63 illustrate a hub 3020 configured to receive a lumen-defining device 3080 according to an embodiment.

[1207] The hub 3020 has a proximal end portion 3021, a distal end portion 3022 and an inner surface 3023 defining a lumen 3024 therethrough (see e.g., FIG. 63). The distal end portion 3022 of the hub 3020 includes and/or is coupled to a cannula 3022A and/or other suitable lumen-defining device. Although not shown in FIGS. 61-63, in some embodiments, the cannula 3022A can be coupled to an adapter, a restrictor, locking mechanism, and/or the like. In some embodiments, the cannula 3022A can be, for example, an indwelling cannula with a distal end portion disposed within the body of a patient. In other embodiments, the distal end portion 3022 of the hub 3020 can include and/or can form a locking mechanism configured to physically and fluidically couple the hub 3020 to any suitable device. The proximal end portion 3021 of the hub 3020 includes and/or is coupled to a proximal cap 3027 and an actuator 3045. For example, in some embodiments, the proximal cap 3027 can be coupled to the proximal end portion 3021 via a press fit, a snap fit, a friction fit, a threaded coupling, an adhesive, ultrasonic welding and/or the like. Moreover, the proximal cap 3027 defines an opening 3028 that is, for example, substantially aligned with the lumen 3024 defined by the inner surface 3023. In this manner, a portion of the lumen-defining device 3080 can be inserted through the opening 3028 of the proximal cap 3027 to be disposed within the hub 3020, as described in further detail herein.

[1208] As shown in FIGS. 62 and 63, the actuator 3045 is disposed between the proximal end portion 3021 and the proximal cap 3027. More specifically, the actuator 3045 forms a

substantially annular ring or the like that is movably disposed within a space defined between a proximal surface of the hub 3020 and a distal surface of the proximal cap 3027. In this manner, the actuator 3045 defines an opening 3046 that can be selectively aligned with the opening 3028 of the proximal cap 3027 and the inner surface 3023 of the hub 3020. Moreover, the actuator 3045 includes and/or is coupled to a bias member 3047 (see e.g., FIG. 62), which can exert a force to temporarily maintain the actuator 3045 in a predetermined position relative to the hub 3020, for example, until a force is exerted on the actuator 3045 sufficient to overcome the force exerted by the bias member 3047, as described in further detail herein.

[1209] As shown in FIG. 63, the inner surface 3023 of the hub 3020 defines the lumen 3024 extending through its proximal end portion 3021 and its distal end portion 3022, which is configured to receive a portion of the lumen-defining device 3080. Furthermore, the inner surface 3023 includes and/or otherwise forms a shoulder 3025. In this embodiment, the shoulder 3025 is associated with a change in diameter of the inner surface 3023. For example, a first portion of the inner surface 3023 (e.g., a proximal portion) can have a first diameter that is larger than a diameter of a second portion of the inner surface (e.g., a distal portion). In this manner, the shoulder 3025 can be placed in contact with a surface of the lumen-defining device 3080 when inserted therein, as described in further detail herein.

[1210] The hub 3020 further includes a valve 3026 disposed within the lumen 3024. The valve 3026 can be, for example, a one-valve, a port, and/or the like, which can be transitioned between a first, substantially closed configuration and a second, substantially opened configuration. Thus, when in the first configuration, the valve 3026 can fluidically isolate a portion of the lumen 3024 that is proximal to the valve 3026 from a portion of the lumen 3024 that is distal to the valve 3026. Conversely, when the valve 3026 is in the second configuration, the lumen 3024 can define a fluid flow path substantially through the hub 3020. In some embodiments, the insertion of the portion of the lumen-defining device 3080 can be operable in transitioning the valve 3026 from the first configuration to the second configuration, as described in further detail herein.

[1211] The lumen-defining device 3080 has a proximal end portion 3031, a distal end portion 3032, and a flange 3086. The lumen-defining device 3080 also defines a notch 3085 and a lumen 3083 extending through the proximal end portion 3081 and the distal end portion 3082, as described in further detail herein. As shown in FIGS. 62 and 63, the distal end

portion 3082 of the lumen-defining device 3080 is configured to be inserted through the proximal cap 3027 and the actuator 3045 to be disposed within the hub 3020, as described in further detail herein. Moreover, the lumen-defining device 3080 includes a seal member 3087 disposed about an outer surface of the distal end portion 3082, which is placed in contact with the inner surface 3023 of the hub 3020 which the lumen-defining device 3080 is disposed therein.

[1212] As shown, for example, in FIGS. 61 and 63, the proximal end portion 3081 of the lumen-defining device 3080 is physically and fluidically coupled to a cannula 3088. The cannula 3088 can be any suitable configuration. For example, in this embodiment, the cannula 3088 is a bifurcated cannula having a first portion 3088A and a second portion 3088B (also referred to herein as a "first cannula" and a "second cannula," respectively). The first portion 3088A and second portion 3088B can be physically and fluidically coupled to any suitable device (e.g., at a proximal end). For example, as shown in FIG. 61, the second portion 3088B includes a port or locking mechanism that can physically and fluidically couple the second portion 3088B to, for example, a fluid source and/or the like. Although not shown, the first portion 3088A can include a port or the like substantially similar to that of the second portion 3088B that can physically and fluidically couple the first portion 3088A to, for example, a fluid reservoir and/or the like. In other embodiments, the first portion 3088A and the second portion 3088B can be arranged in any suitable manner and can each be physically and fluidically coupled to any suitable device, mechanism, and/or member included in a fluid transfer system.

[1213] In use, a portion of the lumen-defining device 3080 can be inserted into the hub 3020 to define a fluid flow path between the cannula 3022A, coupled to the distal end portion 3022 of the hub 3020, and the cannula 3088 coupled to the proximal end portion 3081 of the lumen-defining device 3080. More specifically, in some instances, a user can manipulate the hub 3020 by exerting a force on the actuator 3045, thereby moving the actuator 3045 from a first position, in which the opening 3046 of the actuator 3045 is substantially unaligned with the opening 3028 of the proximal cap 3027, to a second position, in which the opening 3046 is aligned with the opening 3028. Thus, with the actuator 3045 in the second position, the opening 3028 of the proximal cap 3027, the opening 3046 of the actuator 3046, and the lumen 3024 of the hub 3020 are sufficiently aligned to allow the distal end portion 3082 of the lumen-defining device 3080 to be inserted through the proximal cap 3027, the actuator

3045, and into the lumen 3024. As shown in FIG. 63, the lumen-defining device 3080 can be inserted into the hub 3020 by a predetermined amount that places the distal end portion 3082 extends through the valve 3026, thereby transitioning the valve 3026 from its first, substantially closed configuration to its second, substantially open configuration. Moreover, a distal surface of the lumen-defining device 3080 in contact with the shoulder 3025, as shown in FIG. 63.

[1214] With the distal surface of the lumen-defining device 3080 in contact with the shoulder 3025, the flange 3086 of the lumen-defining device 3080 is disposed within a recessed surface defined by the proximal cap 3027. In some embodiments, the shape and/or size of the recessed surface and the flange 3086 can be such that the lumen-defining device 3080 is placed into a predetermined radial position such that the lumen 3024 of the hub 3020 and the lumen 3083 of the lumen-defining device 3080 are substantially aligned, as shown in FIG. 63. Moreover, the seal member 3087 disposed about the outer surface at or near the distal end portion 3082 of the lumen-defining device 3080 is placed in contact with the inner surface 3023 of the hub 3020. In this manner, the arrangement of the flange 3086 disposed within the recessed surface of the proximal cap 3027 and the seal member 3087 in contact with the inner surface 3023 of the hub 3020, the lumen-defining device 3080 is placed in a predetermined radial position relative to the hub 3020. For example, in this embodiment, the lumen 3083 of the lumen-defining device 3080 and the lumen 3024 of the hub 3020 form a substantially continuous transition therebetween. That is to say, the lumens 3083 and 3024 are substantially aligned and/or a discontinuity defined therebetween is sufficiently minimized or obviated so as to not produce turbulence within a flow of bodily-fluid therethrough.

[1215] In addition, once the lumen-defining device 3080 is disposed in the desired and/or predetermined position within the hub 3020, the user can remove the force exerted on the actuator 3045. As such, the bias member 3047 can exert a force to move the actuator 3045 from its second position to its first position (e.g., a biased position). Thus, as shown in FIG. 63, the actuator 3045 is moved out of alignment with the hub 3020, resulting in a portion of the actuator 3045 being disposed in the notch 3085 defined by the lumen-defining device 3080, which in turn, can maintain the lumen-defining device 3080 in a substantially fixed position within the hub 3020. In this manner, a user can couple the first portion 3088A or the second portion 3088B of the cannula 3088 to, for example, a fluid reservoir such as those

described herein, which in turn, can exert a suction force (e.g., in response to a negative pressure differential) through the lumen-defining device 3080 and the hub 3020. Therefore, when the cannula 3022A is in fluid communication with the body of a patient (e.g., either directly or indirectly via an intervening structure), a volume of, for example, blood can be withdrawn with a reduced amount of hemolysis. Specifically, the alignment of the lumen 3024 defined by the hub 3020 and the lumen 3083 of the lumen-defining device 3080, for example, can reduce turbulence, eddy currents, and/or any other disturbance that can otherwise result from a discontinuity or the like. Thus, the flow of blood therethrough can be substantially laminar and substantially free of hemolysis.

[1216] Although the valve 3026 is particularly shown and described above with reference to FIGS. 62 and 63, in other embodiments, a hub can include any suitable valve. For example, FIGS. 64-66 illustrate a hub 3120 configured to receive a lumen-defining device 3180 according to another embodiment. The hub 3120 and the lumen-defining device 3080 can be substantially similar in form and/or function as the hub 3020 and the lumen-defining device 3080 described above with reference to FIGS. 61-63. Thus, such similar aspects are not described in further detail herein.

[1217] As shown in FIGS. 64-66, the hub 3120 has a proximal end portion 3121, a distal end portion 3122, and an inner surface 3123 defining a lumen 3124 therethrough (see e.g., FIG. 66). The distal end portion 3122 of the hub 3120 includes and/or is coupled to a cannula 3122A and/or other suitable lumen-defining device. While the hub 3020 is shown and described as being coupled to a single cannula and/or a cannula defining a single lumen, in this embodiment, the hub 3120 is coupled to a bifurcated cannula having a first portion (also referred to herein as "first cannula" or "cannula 3122A") and a second portion 3122B. In other embodiments, the hub 3120 can be coupled to a single cannula and/or a cannula defining a single lumen. The proximal end portion 3121 of the hub 3120 includes and/or is coupled to a proximal cap 3127 and an actuator 3145, as described in detail above. The proximal cap 3127 defines an opening 3128 that is, for example, substantially aligned with the lumen 3124 defined by the inner surface 3123. In this manner, a portion of the lumen-defining device 3180 can be inserted through the opening 3128 of the proximal cap 3127 to be disposed within the hub 3120, as described in further detail herein.

[1218] As shown in FIGS. 65 and 66, the actuator 3145 is disposed between the proximal end portion 3121 and the proximal cap 3128. The actuator 3145 forms a substantially annular

ring or the like that is movably disposed within a space defined between a proximal surface of the hub 3120 and a distal surface of the proximal cap 3127. In addition, the actuator 3145 includes and/or is coupled to a bias member 3147, which can exert a force to temporarily maintain the actuator 3145 in a predetermined position relative to the hub 3120, for example, until a force is exerted on the actuator 3145 sufficient to overcome the force exerted by the bias member 3147. In this manner, the arrangement of the proximal end portion 3121 of the hub 3120, the proximal cap 3127, and the actuator 3145 can be substantially similar to the proximal end portion 3021 of the hub 3020, the proximal cap 3027, and the actuator 3045 described above with reference to FIGS. 62 and 63.

[1219] As shown in FIG. 66, the inner surface 3123 of the hub 3120 defines the lumen 3124 extending through its proximal end portion 3121 and its distal end portion 3122, which is configured to receive a portion of the lumen-defining device 3180. Furthermore, the inner surface 3123 includes a valve and a sealing surface 3125. As shown in FIG. 66, in this embodiment, the valve is a ball valve 3126, which can be transitioned between a first, substantially closed configuration and a second, substantially opened configuration. More specifically, the hub 3120 includes a bias member 3148 in contact with the ball valve 3126. In this manner, the bias member 3148 can exert a force on the ball valve 3126 that places the ball valve 3126 in contact with the sealing surface 3125. Thus, a contact sufficient to maintain a substantially fluid tight seal can be maintained when the ball valve 3126 is in contact with the sealing surface 3125 (e.g., in the first configuration) via a force exerted by the bias member 3148. Conversely, when a force exerted on the ball valve 3126, opposite the force exerted by the bias member 3148, is sufficient to overcome the force exerted by the bias member 3148, the ball valve 3126 can be removed from contact with the sealing surface 3125 and thus, a fluid flow path can be defined therethrough. In some embodiments, the insertion of the portion of the lumen-defining device 3180 can be operable in transitioning the ball valve 3126 from the first configuration to the second configuration, as described in further detail herein.

[1220] The lumen-defining device 3180 has a proximal end portion 3181, a distal end portion 3182, and a flange 3186. The lumen-defining device 3180 also defines a notch 3185 and a lumen 3183 extending through the proximal end portion 3181 and the distal end portion 3182, as described in further detail herein. As shown, for example, in FIGS. 64-66, the proximal end portion 3181 of the lumen-defining device 3180 is physically and fluidically

coupled to a cannula 3188. The cannula 3188 can be any suitable configuration. For example, in this embodiment, the cannula 3188 is a single cannula and/or a cannula that defines a single lumen. In other embodiments, the cannula 3188 can be a bifurcated cannula, as described in detail above with reference to the cannula 3088 in FIG. 61. Moreover, although not shown in FIGS. 64-66, the cannula 3188 can include any suitable port, locking mechanism, and/or the like, as described above.

[1221] As shown in FIGS. 65 and 66, the distal end portion 3182 of the lumen-defining device 3180 is configured to be inserted through the proximal cap 3127 and the actuator 3145 to be disposed within the hub 3120, as described in further detail herein. Moreover, the lumen-defining device 3180 includes a seal member 3187 disposed about an outer surface of the distal end portion 3182, which is placed in contact with the inner surface 3123 of the hub 3120 which the lumen-defining device 3180 is disposed therein. As shown in FIG. 66, the lumen 3183 of defined by the lumen-defining device 3080 at or near the distal end portion 3182 is diverted, for example, into one or more channels and defining a substantially smooth transition therebetween. In some embodiments, the one or more channels, for example, can be offset from the lumen 3183 (e.g., non-coaxial). In other words, each channel is radially offset from a longitudinal centerline CL, as shown in FIG. 66. Thus, when a distal surface of the lumen-defining device 3180 is placed in contact with, for example, the ball valve 3126, the channels and/or the lumen 3183 are/is substantially unobstructed, as described in further detail herein.

[1222] In use, a portion of the lumen-defining device 3180 can be inserted into the hub 3120 to define a fluid flow path between the cannula 3122A, coupled to the distal end portion 3122 of the hub 3120, and the cannula 3188 coupled to the proximal end portion 3181 of the lumen-defining device 3180. More specifically, in some instances, a user can manipulate the hub 3120 by exerting a force on the actuator 3145, thereby moving the actuator 3145 from a first position, in which the opening 3146 of the actuator 3145 is substantially unaligned with the opening 3128 of the proximal cap 3127, to a second position, in which the opening 3146 is aligned with the opening 3128, as described in detail above. As shown in FIG. 66, the lumen-defining device 3180 can be inserted into the hub 3120 by a predetermined amount that places a distal surface of the lumen-defining device 3180 in contact with the ball valve 3126. In this manner, the lumen-defining device 3180 can be inserted into the hub 3180 until the flange 3186 of the lumen-defining device 3180 is disposed within a recessed surface

defined by the proximal cap 3127, thereby aligning the lumen-defining device 3180, as described in detail above. Moreover, the seal member 3187 disposed about the outer surface at or near the distal end portion 3182 of the lumen-defining device 3180 is placed in contact with the inner surface 3123 of the hub 3120. In this manner, the lumen-defining device 3180 can be inserted into a position that removes the ball valve 3126 from the sealing surface 3125, thereby defining a fluid flow path between the lumen 3124 of the hub 3120 and the lumen 3183 (and/or channels) of the lumen-defining device 3180.

[1223] Once the lumen-defining device 3180 is disposed in the desired and/or predetermined position within the hub 3120, the user can remove the force exerted on the actuator 3145. As such, the bias member 3147 can exert a force to move the actuator 3145 from its second position to its first position (e.g., a biased position), resulting in a portion of the actuator 3145 being disposed in the notch 3185 defined by the lumen-defining device 3180. Thus, the actuator 3145 can maintain the lumen-defining device 3180 in a substantially fixed position within the hub 3120, as described in detail above. In this manner, a user can couple the cannula 3188, for example, to a fluid reservoir such as those described herein. Therefore, when the cannula 3122A is in fluid communication with the body of a patient (e.g., either directly or indirectly via an intervening structure), a volume of, for example, blood can be withdrawn with a reduced amount of hemolysis, as described in detail above. Specifically, the alignment of the lumen 3124 defined by the hub 3120 and the channels and/or lumen 3183 of the lumen-defining device 3180, for example, can reduce turbulence, eddy currents, and/or any other disturbance that can otherwise result from a discontinuity or the like. Thus, the flow of blood therethrough can be substantially laminar and substantially free of hemolysis.

[1224] Although the hubs 3020 and 3120 have a proximal end portion including an actuator, in other embodiments, a hub can have any suitable configuration and need not include an actuator. For example, FIGS. 67 and 68 illustrate a hub 3320 configured to receive a lumen-defining device 3280 according to another embodiment. The hub 3220 and the lumen-defining device 3280 can be substantially similar in form and/or function as the hub 3020 and the lumen-defining device 3080 and/or the hub 3120 and the lumen-defining device 3180, described in detail above. Thus, such similar aspects are not described in further detail herein. As shown in FIGS. 67 and 68, the hub 3220 has a proximal end portion 3221, a distal end portion 3222, a secondary port 3289, and an inner surface 3223 defining a

lumen 3224 therethrough (see e.g., FIG. 68). The hub 3220 further includes a valve 3226 disposed within the lumen 3224, as described in further detail herein.

[1225] The distal end portion 3222 of the hub 3220 includes and/or is coupled to a cannula 3222A and/or other suitable lumen-defining device, as described above with reference to the hub 3020 in FIGS. 61-63. The proximal end portion 3221 of the hub 3220 includes and/or is coupled to a proximal cap 3227. As shown in FIGS. 67 and 68, in this embodiment, the proximal cap 3237 can be, for example, a locking mechanism or the like configured to form a treaded coupling with a portion of the lumen-defining device 3280, as described in further detail herein.

[1226] As shown in FIG. 68, the inner surface 3223 of the hub 3220 defines the lumen 3224 extending through its proximal end portion 3221 and its distal end portion 3222, which is configured to receive a portion of the lumen-defining device 3280. Furthermore, the inner surface 3223 includes and/or otherwise forms a shoulder 3225. In this embodiment, the shoulder 3225 is associated with a change in diameter of the inner surface 3223. For example, a first portion of the inner surface 3223 (e.g., a proximal portion) can have a first diameter that is larger than a diameter of a second portion of the inner surface (e.g., a distal portion). In this manner, the shoulder 3225 can be placed in contact with a surface of the lumen-defining device 3280 when inserted therein, as described in detail above with reference to the hub 3020. In some embodiments, the shoulder 3225 can form, for example, a seat or a recessed portion configured to receive a portion of the lumen-defining device 3280.

[1227] The valve 3226 of the hub 3220 can be, for example, a one-valve, a port, and/or the like, which can be transitioned between a first, substantially closed configuration and a second, substantially opened configuration. Thus, when in the first configuration, the valve 3226 can fluidically isolate a portion of the lumen 3224 that is proximal to the valve 3226 from a portion of the lumen 3224 that is distal to the valve 3226. Conversely, when the valve 3226 is in the second configuration, the lumen 3224 can define a fluid flow path substantially through the hub 3220. In some embodiments, the insertion of the distal end portion 3282 of the lumen-defining device 3280 can be operable in transitioning the valve 3226 from the first configuration to the second configuration, as described in further detail herein.

[1228] The secondary port 3289 of the hub 3280 can be any suitable port or the like. For example, in some embodiments, the hub 3220 can be arranged as a T-adapter or the like, in

which the proximal end portion 3221 defines a first port and the secondary port 3289 extends in a substantially perpendicular direction from the first port. In this manner, the secondary port 3289 is in fluid communication with the lumen 3224 defined by the hub 3220 and can be configured to receive and/or deliver a fluid from and/or to the lumen 3224 of the hub 3220. Moreover, the arrangement of the secondary port 3289 is such that when the valve 3226 is in its closed configuration, the secondary port 3289 is fluidically isolated from a portion of the lumen 3224 proximal to the valve 3226.

[1229] The lumen-defining device 3080 has a proximal end portion 3031, a distal end portion 3032, and a flange 3086. The lumen-defining device 3080 also defines a notch 3085 and a lumen 3083 extending through the proximal end portion 3081 and the distal end portion 3082, as described in further detail herein. As shown in FIGS. 62 and 63, the distal end portion 3082 of the lumen-defining device 3080 is configured to be inserted through the proximal cap 3027 and the actuator 3045 to be disposed within the hub 3020, as described in further detail herein. Moreover, the lumen-defining device 3080 includes a seal member 3087 disposed about an outer surface of the distal end portion 3082, which is placed in contact with the inner surface 3023 of the hub 3020 which the lumen-defining device 3080 is disposed therein.

[1230] The lumen-defining device 3280 has a proximal end portion 3281 and a distal end portion 3282, and defines a lumen 3283 therethrough. As shown, for example, in FIG. 68, the proximal end portion 3281 of the lumen-defining device 3280 is physically and fluidically coupled to a cannula 3288. The cannula 3288 can be any suitable configuration. For example, in this embodiment, the cannula 3288 is a single cannula and/or a cannula that defines a single lumen. In some embodiments, the cannula 3288 can be substantially similar to the cannula 3188 described above wither reference to FIGS. 64-66.

[1231] As shown in FIG. 68, the distal end portion 3282 of the lumen-defining device 3280 is configured to be inserted through the proximal cap 3227 to be disposed within the hub 3220. More specifically, a portion of the lumen-defining device 3280 can be inserted into the proximal cap 3227 and configured to form, for example, a threaded coupling or the like. For example, in some embodiments, a portion of an outer surface of the lumen-defining device 3280 can include a set of treads or the like configured to engage a corresponding set of threads included in and/or defined by the proximal cap 3227. Thus, in use, as the lumen-defining device 3280 is inserted through the proximal cap 3227, the proximal cap 3227

and/or the lumen-defining device 3280 can be rotated to form the threaded coupling therebetween. Moreover, the arrangement of the lumen-defining device 3280 can be such that when coupled to the proximal cap 3227, the distal end portion 3282 of the lumen-defining device 3280 extends through the valve 3226. Thus, the valve 3226 is transitioned from its first, substantially closed configuration to its second, substantially open configuration. In some embodiments, the valve 3226 can be configured to form a substantially fluid tight seal about a portion of the lumen-defining device 3280, which in turn, can maintain the secondary port 3289 in fluid isolation from, for example, the lumen 3283 of the lumen-defining device 3280. Moreover, the lumen-defining device 3280 is advanced such that a distal surface of the lumen-defining device 3280 is in contact with the shoulder 3225, as shown in FIG. 68.

[1232] In this embodiment, the arrangement of the lumen-defining device 3280 and the proximal cap 3227 (i.e., the coupling therebetween) is such that the lumen 3283 of the lumen-defining device 3280 and the lumen 3224 of the hub 3220 form a substantially continuous transition therebetween. That is to say, the lumens 3283 and 3224 are substantially aligned and/or a discontinuity defined therebetween is sufficiently minimized or obviated so as to not produce turbulence within a flow of bodily-fluid therethrough. Therefore, when the cannula 3222A is in fluid communication with the body of a patient (e.g., either directly or indirectly via an intervening structure), a volume of, for example, blood can be withdrawn with a reduced amount of hemolysis. Specifically, the alignment of the lumen 3224 defined by the hub 3220 and the lumen 3283 of the lumen-defining device 3280, for example, can reduce turbulence, eddy currents, and/or any other disturbance that can otherwise result from a discontinuity or the like. Thus, the flow of blood therethrough can be substantially laminar and substantially free of hemolysis.

[1233] While the hubs 3020, 3120, and 3220 are shown and described above as receiving the lumen-defining devices 3080, 3180, and 3280 (e.g., a connector), respectively, in other embodiments, a hub can be configured to receive a terminated end of a cannula or the like (e.g., without a connector or other lumen-defining device). For example, FIGS. 69-71 illustrate a hub 3320 configured to receive a cannula 3388 according to another embodiment. The hub 3320 and the lumen-defining device 3080 can be substantially similar in form and/or function as the hub 3020 and the lumen-defining device 3080 and/or the hub 3120 and the

lumen-defining device 3180, described in detail above. Thus, such similar aspects are not described in further detail herein.

[1234] As shown in FIGS. 69-71, the hub 3320 has a proximal end portion 3321, a distal end portion 3322, and an inner surface 3323 defining a lumen 3324 therethrough (see e.g., FIG. 71). The distal end portion 3322 of the hub 3320 includes and/or is coupled to a cannula 3322A and/or other suitable lumen-defining device. In some embodiments, the distal end portion 3322 of the hub 3320 can be substantially similar to the distal end portion 3322 of the hub 3020 described above with reference to FIGS. 61-63. The proximal end portion 3321 of the hub 3320 includes and/or is coupled to a proximal cap 3327, as described in detail above. The proximal cap 3327 defines an opening 3328 that is, for example, substantially aligned with the lumen 3324 defined by the inner surface 3323. In this manner, a portion of the cannula 3388 can be inserted through the opening 3328 of the proximal cap 3327 to be disposed within the hub 3320, as described in further detail herein.

[1235] As shown in FIGS. 70 and 71, the proximal end portion 3321 of the hub 3320 further includes and or is coupled to a first coupling member 3345 and a second coupling member 3349. As described above with reference to the actuator 3145, the first coupling member 3345 is disposed between the proximal end portion 3321 and the proximal cap 3327. The first coupling member 3345 is configured to selective receive a portion of the second coupling member 3349. The second coupling member 3349 is configured to be disposed about a portion of the cannula 3388. Thus, the second coupling member 3349 can be inserted substantially concurrently with the cannula 3388. Moreover, the second coupling member 3349 is configured to engage the first coupling member 3345 disposed within the hub 3320, for example, to at least temporarily maintain the cannula 3388 in a fixed position. For example, in some embodiments, the second coupling portion 3349 can form a snap fit, a press fit, a friction fit, and/or the like when placed in contact with the first coupling member 3345, as described in further detail herein.

[1236] As shown in FIG. 71, the inner surface 3323 of the hub 3320 defines the lumen 3324 extending through its proximal end portion 3321 and its distal end portion 3322, which is configured to receive a portion of the cannula 3388. Furthermore, the inner surface 3323 includes and/or otherwise forms a shoulder 3325. In this embodiment, the shoulder 3325 is associated with a change in diameter of the inner surface 3323. For example, a first portion of the inner surface 3323 (e.g., a proximal portion) can have a first diameter that is larger than

a diameter of a second portion of the inner surface (e.g., a distal portion). In this manner, the shoulder 3325 can be placed in contact with a surface of the cannula 3388 when inserted therein, as described in detail above with reference to the hub 3020.

[1237] The hub 3320 further includes a valve 3326 disposed within the lumen 3324. The valve 3326 can be, for example, a one-valve, a port, and/or the like, which can be transitioned between a first, substantially closed configuration and a second, substantially opened configuration. Thus, when in the first configuration, the valve 3326 can fluidically isolate a portion of the lumen 3324 that is proximal to the valve 3326 from a portion of the lumen 3324 that is distal to the valve 3326. Conversely, when the valve 3326 is in the second configuration, the lumen 3324 can define a fluid flow path substantially through the hub 3320. In some embodiments, the insertion of the portion of the cannula 3388 can be operable in transitioning the valve 3326 from the first configuration to the second configuration, as described in further detail herein.

[1238] In use, a portion of the cannula 3388 can be inserted into the hub 3320 to define a fluid flow path between the cannula 3322A, coupled to the distal end portion 3322 of the hub 3320, and the cannula 3388 coupled to the proximal end portion 3381 of the cannula 3388. More specifically, in some instances, a user can insert an end portion of the cannula 3388 through the second coupling member 3349. Once the second coupling member 3349 is disposed about the cannula 3380, the cannula 3388 can be inserted into the hub 3320 by a predetermined amount that extends, for example, a distal end portion of the cannula 3388 through the valve 3326, thereby transitioning the valve 3326 from its first, substantially closed configuration to its second, substantially open configuration. Moreover, a distal surface of the cannula 3388 in contact with the shoulder 3325, as shown in FIG. 71. As the cannula 3388 is moved into its desired position within the hub 3320, the second coupling member 3349 is inserted through the opening 3328 defined by the proximal cap 3327 and into contact with the first coupling member 3345. Thus, the second coupling member 3349 can engage the first coupling member 3345 to define, for example, a snap fit or the like. In some embodiments, the arrangement of the second coupling member 3349 can be such that when it engages the first coupling member 3349, a space through which the cannula 3388 extends is reduced. As such, the second coupling member 3349 can clamp the cannula 3388 and with the second coupling member 3349 being coupled to the first coupling member 3345, the first coupling member 3345 and the second coupling member 3349 can act to at least

temporarily maintain the cannula 3388 in a substantially fixed position relative to the hub 3320. Although described above as being moved substantially concurrently with the cannula 3388, in other embodiments, the second coupling member 3349 can be moved after the distal surface of the cannula 3388 is placed in contact with the shoulder 3325.

[1239] In some embodiments, the arrangement of the hub 3320 and the cannula 3388 is such that when the cannula 3388 is maintained in the substantially fixed position, the lumen 3324 of the hub 3320 is substantially aligned with a lumen defined by the cannula 3388. For example, in this embodiment, the lumen of the cannula 3388 and the lumen 3324 of the hub 3320 form a substantially continuous transition therebetween. That is to say, the lumens are substantially aligned and/or a discontinuity defined therebetween is sufficiently minimized or obviated so as to not produce turbulence within a flow of bodily-fluid therethrough. In this manner, a user can couple the cannula 3388 to, for example, a fluid reservoir such as those described herein, which in turn, can exert a suction force (e.g., in response to a negative pressure differential) through the cannula 3388 and the hub 3320. Therefore, when the cannula 3322A is in fluid communication with the body of a patient (e.g., either directly or indirectly via an intervening structure), a volume of, for example, blood can be withdrawn with a reduced amount of hemolysis. Specifically, the alignment of the lumen 3324 defined by the hub 3320 and the lumen of the cannula 3388, for example, can reduce turbulence, eddy currents, and/or any other disturbance that can otherwise result from a discontinuity or the like. Thus, the flow of blood therethrough can be substantially laminar and substantially free of hemolysis.

[1240] Although the embodiments are shown and described above as mitigating the risk of hemolysis of a volume of blood at a given point along a fluid flow path between a patient and a fluid reservoir, any embodiment configured to mitigate the risk of hemolysis at a given point along the fluid flow path can be used in conjunction with any suitable embodiment(s) configured to mitigate the risk of hemolysis at a different point along the fluid flow path. In some instances, a fluid transfer device can include any combination of the embodiments described herein, for example, to mitigate the risk of hemolysis otherwise associated with (1) blood flow from, for example, a vein into a puncture member, needle, cannula, and/or the like; (2) blood flow through changing geometries and/or physical and fluidic interfaces; (3) blood flow rates, pressures, and/or velocities within the fluid flow path; (4) blood flow from an adapter, puncture member, needle, cannula, and/or the like into a fluid reservoir; (5) blood

flow exposure to a negative pressure differential within a fluid reservoir; and/or (6) blood flow through a multi-lumen adapter and/or the like.

[1241] While the embodiments are shown and described above as mitigating the risk of hemolysis of a volume of blood during, for example, aspiration, blood draw, and/or any other procedure in which blood is withdrawn from the body, in other instances, any embodiment configured to mitigate the risk of hemolysis described herein, and/or any combination thereof, can be used in any suitable medical device and/or procedure in which it is desirable to reduce hemolysis. For example, any of the embodiments or combinations of the embodiments described herein such as the adapters, puncture members, restrictors, fluid reservoirs, gaskets, etc., and/or characteristics, geometries, and/or features thereof can be used to mitigate the risk of hemolysis in any suitable device and/or during any suitable medical procedure. Such devices and/or procedures can include but are not limited to, mechanical hearts and/or other organs, perfusion machines used, for example, during open-heart surgery, dialysis machines, and/or the like. In some instances, the embodiments and/or combination of embodiments described herein can be used to modulate pressure within such devices, produce a laminar flow through at least a portion of such devices, reduce and/or limit shear stress and/or exposure time experienced by red blood cells, and/or the like.

[1242] Although not shown or described herein, any of the embodiments can be used in a fluid transfer device configured to, for example, divert a predetermined pre-sample volume of bodily-fluid that can contain, for example, externally residing microbes prior to collection of a sample volume of bodily. For example, in some embodiments, the predetermined pre-sample volume can be about a drop or a few drops of blood, about 0.1 mL, about 0.3 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 11.0 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 other embodiments, 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 about 3 mL. In some instances, a venipuncture event can result in trauma to the blood flowing within the punctured vein that can at least temporarily hemolyze a portion of the blood. Thus, in some embodiments, the diverted pre-sample volume of blood can include, for example, the hemolyzed portion of the blood. Furthermore, by collecting the

predetermined pre-sample volume, the predetermined sample volume disposed in one or more sample reservoirs can be substantially free-from externally residing microbes.

[1243] Fluid transfer devices configured to divert a predetermined pre-sample volume of bodily-fluid can be any suitable configuration. For example, in some embodiments, such a fluid transfer device can be substantially similar to or the same as the fluid transfer 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; and/or U.S. Patent Publication No. 2014/0155782 entitled, "Sterile Bodily-Fluid Collection Device and Methods," filed December 4, 2012, the disclosures of which are incorporated herein by reference in their entireties and attached hereto as Exhibit A, Exhibit B, Exhibit C, and Exhibit D, respectively. Moreover, in some embodiments, such transfer devices can be configured to selectively obstruct a needle to prevent hemolyzed blood from entering a lumen defined by the needle during a venipuncture event. Such devices can be substantially similar to and/or the same as those described in U.S. Patent Publication No. 2014/0276578, entitled, "Methods and Apparatus for Selectively Occluding the Lumen of a Needle," filed September 18, 2014, the disclosure of which is incorporated herein by reference in its entirety and attached hereto as Exhibit E.

[1244] In some embodiments, the bodily-fluid transfer devices described herein can include and/or can be partially formed from antisepsis-saturated materials. For example, any of the valves, gaskets, seals, ports, and/or the like can be saturated with, for example, isopropyl alcohol. As such, when various components of a fluid transfer device are coupled and/or otherwise collectively form an interface, the components can be contemporaneously sterilized. In some embodiments, such a device can be substantially similar to or the same as those described in U.S. Patent Publication No. 2015/0246352 entitled, "Apparatus and Methods for Disinfection of a Specimen Container," filed March 3, 2015, the disclosure of which is incorporated herein by reference in its entirety and attached as Exhibit F.

[1245] While the device 100 is described above as including a surface, mechanism, portion, etc. configured to reduce hemolysis of a volume of blood in a mechanical manner (e.g., by mechanically changing one or more characteristics of a flow of blood within a fluid flow path), in other embodiments, any of the devices can be configured to chemically modify

one or more characteristics associated with the volume of blood. For example, in some embodiments, an inner surface of any of the embodiments described herein can be coated with a chemical configured to limit lysis of erythrocytes (red blood cells) by strengthening or weakening a cell wall of the erythrocytes. More specifically, in some embodiments, a can be configured to introduce a chemical into a flow of blood that can, for example, increase a rigidity of the cell wall of erythrocytes (e.g., decrease flexibility), which in turn, can reduce a likelihood of lysis of the erythrocytes (e.g., hemolysis of the blood) as the blood flows through the device. In other embodiments, a device can be configured to introduce a chemical into a flow of blood that can, for example, decrease a rigidity of the cell wall of erythrocytes (e.g., increase flexibility), which in turn, can reduce a likelihood of lysis of the erythrocytes as the blood flows through the device.

[1246] While described above as coating an inner surface of a device with the chemical configured to modify a characteristic of the cell wall of the erythrocytes, in other embodiments, any of the embodiments described herein can include any suitable device, mechanism, and/or method for introducing such a chemical to the volume of blood flowing therethrough. For example, a device can include a chamber containing such a chemical (e.g., a chamber within a Luer lock or the like), a baffle, wipe, valve, porous material (e.g., sintered glass or plastic), etc. impregnated with such a chemical, a dispensing or dispersing device (e.g., sprayer or the like) configured to dispense a volume of such a chemical, and/or any other suitable means for introducing such a chemical. Moreover, a device can include any suitable combination of devices, interfaces, members, mechanisms, etc. included in the embodiments described herein as well as any suitable means for introducing a chemical into a volume of blood flowing through such a device.

[1247] As described above, in some instances, introducing a chemical into a volume of blood (e.g., whole blood) can result in a strengthening of an erythrocyte membrane or outer structure, or in other words, can modify a magnitude of stability associated with the erythrocyte membrane. In some instances, such stabilization can result in an increased resistance to hemolysis caused by mechanical stress, osmotic stress, peroxyl radicals attack, heat, and/or the like. Examples of chemicals that can modify a characteristic associated with an erythrocyte membrane include phloridzin, cremophore (glycerol polyethylene glycol ricinoleate, lidocaine, antioxidants such as reduced glutathione (GSH), N-acetylcysteine, ebselen (2-phenyl-1, 2-benzoselenazol-3-one) and/or albumin, papaya leaf and/or other plant

extracts, tranquilizers and/or antihistamines such as phenothiazine, reserpine, and/or haloperidol, saponins and/or sapogenins, polyamines, anti-inflammatory drugs such as phenylbutazone, methylsergide, and/or indomethacin, and/or any other suitable chemical.

[1248] While various embodiments have been particularly shown and described, various changes in form and details may be made. While embodiments have been described above, it should be understood that they have been presented by way of example only, and not limitation. 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, in some embodiments, a restrictor such as, for example, the restrictor 650 can be used when collecting a bodily-fluid using any of the fluid reservoirs described herein. Similarly, the hub 3020 and lumen-defining device 3080 described above with reference to FIGS. 61-63 can be used with any of the adapters described herein. Moreover, any suitable combination of components described herein can be physically and/or fluidically coupled together to form a bodily-fluid collection device configured, for example, to reduce hemolysis in a withdrawn volume of blood.

[1249] 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 of bodily-fluid flow into a fluid reservoir. While various components have been described above a being physically and fluidically coupled, in other embodiments, any of the devices and/or embodiments can be, for example, monolithically formed with and/or otherwise joined to any other suitable device and/or embodiment. For example, while the first adapter 1020, the second adapter 1030, and the restrictor 1050 are described above with reference to FIGS. 18-20 as being formed separately and subsequently coupled, in other embodiments, the first adapter 1020 and/or the second adapter 1030 can be monolithically formed with the restrictor 1050. In some instances, such a monolithically formed component can be included in, for example, a pre-assembled and sterile blood collection device and/or the like.

[1250] Where methods and/or events described above indicate certain events and/or procedures occurring in certain order, the ordering of certain events and/or procedures may

be modified. Additionally, certain events and/or procedures may be performed concurrently in a parallel process when possible, as well as performed sequentially as described above.

Abstract

A collection system has a proximal end portion, a distal end portion, and an inner surface defining a fluid flow path therethrough. The distal end portion is configured to be placed in fluid communication with a patient. The proximal end portion is configured to be placed in fluid communication with a fluid reservoir. The fluid flow path defined by the inner surface is associated with at least one flow characteristic configured to limit a stress within the flow of the bodily-fluid between the distal end portion and the proximal end portion.

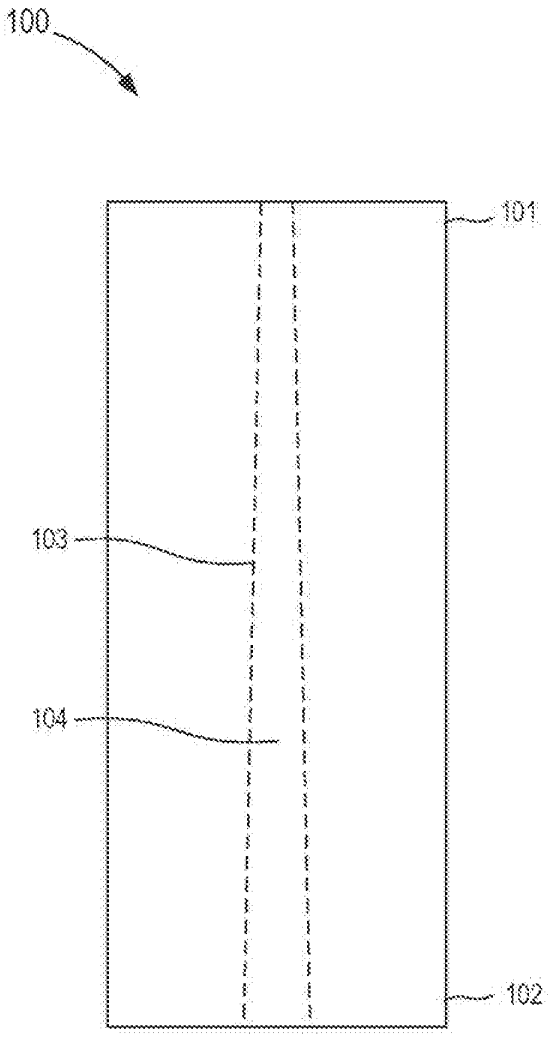


FIG. 1

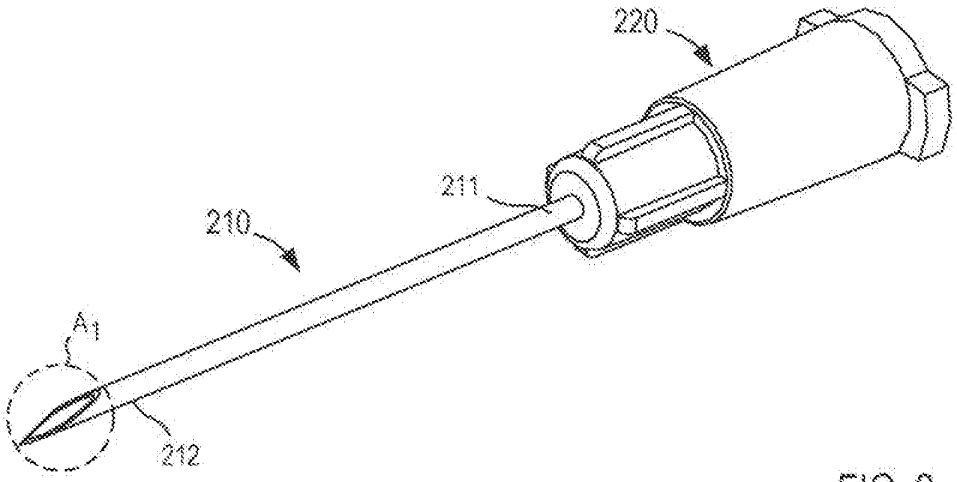


FIG. 2

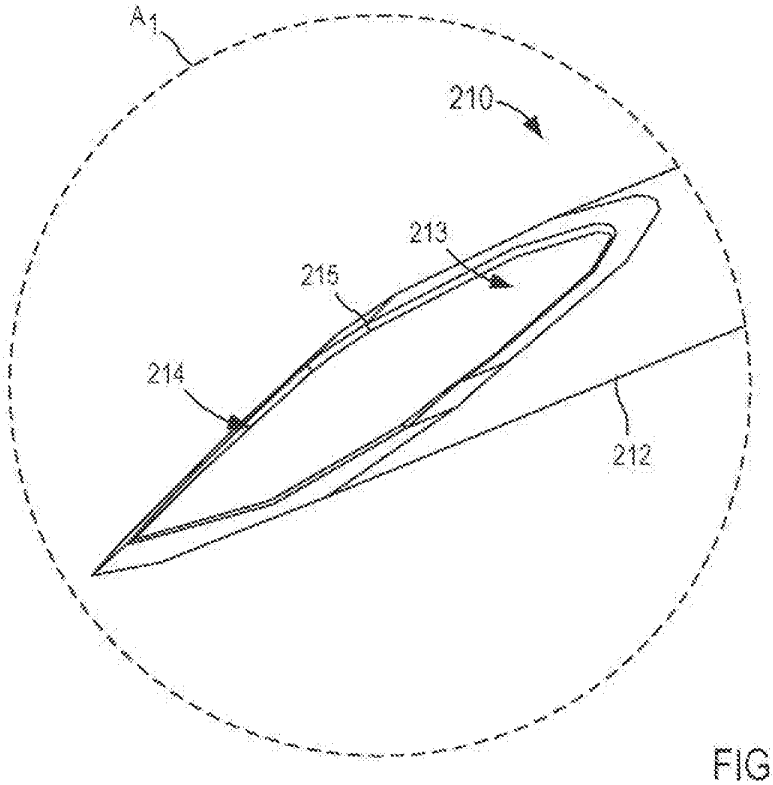


FIG. 3

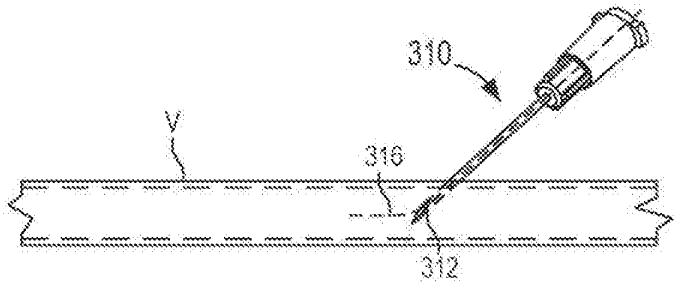


FIG. 4

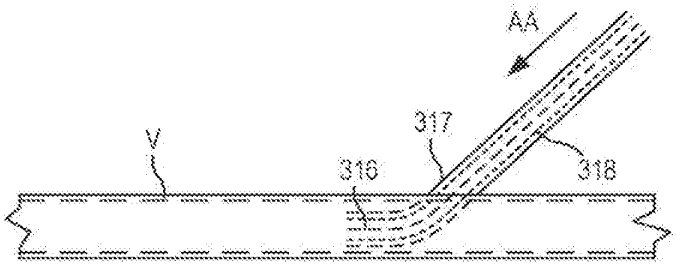


FIG. 5

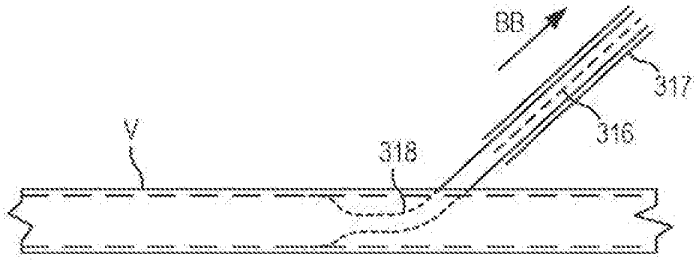


FIG. 6

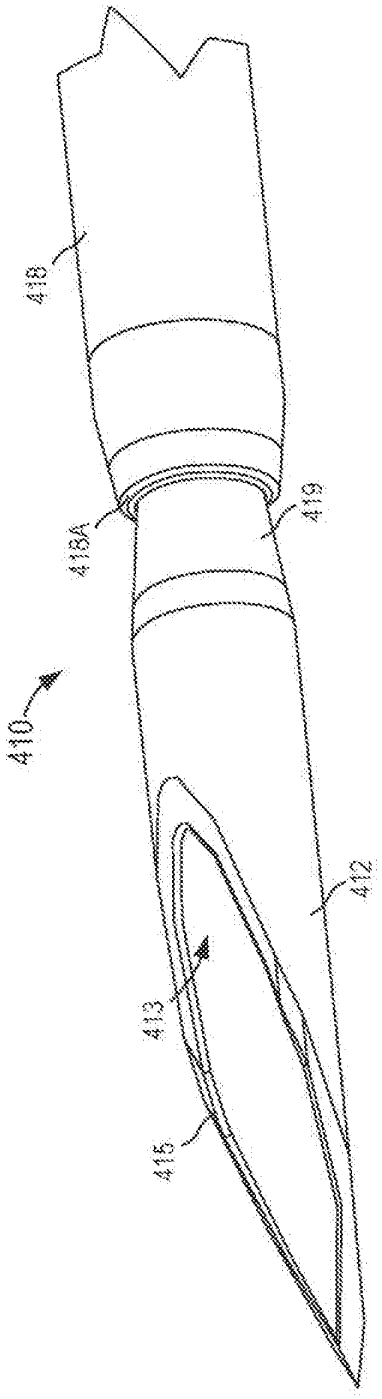


FIG. 7

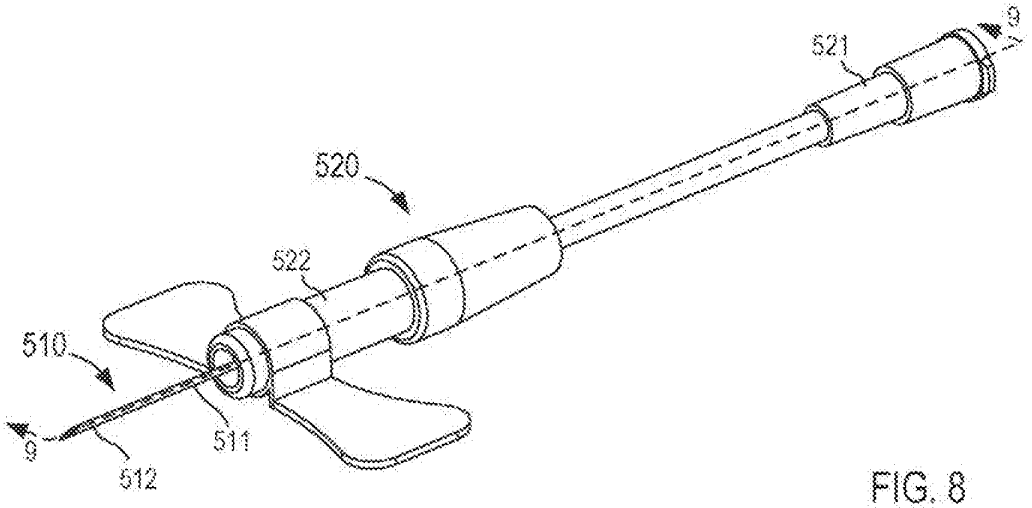


FIG. 8

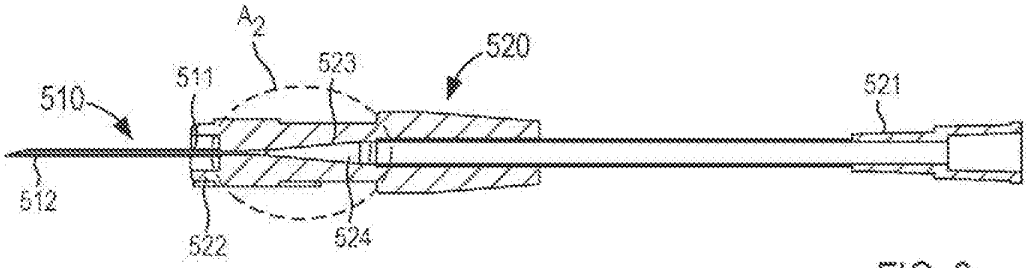


FIG. 9

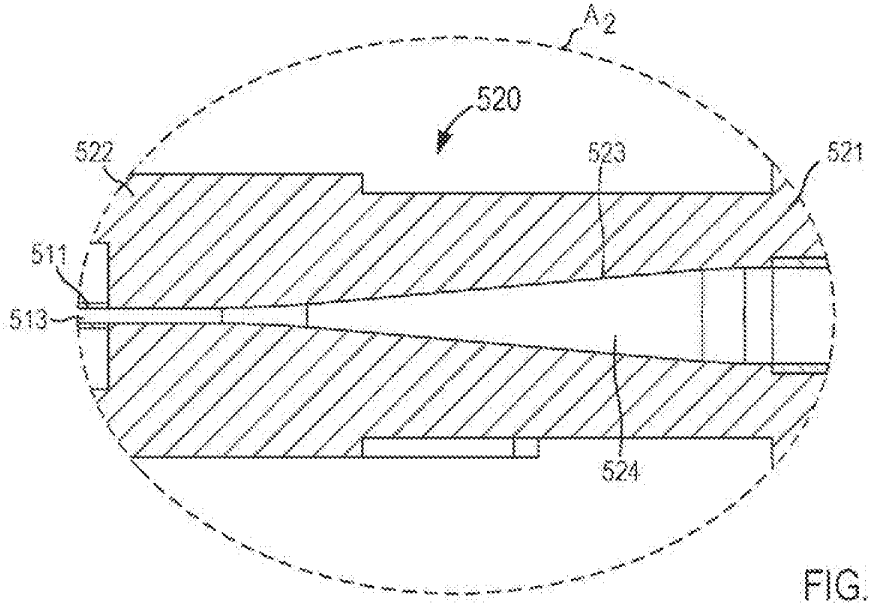


FIG. 10

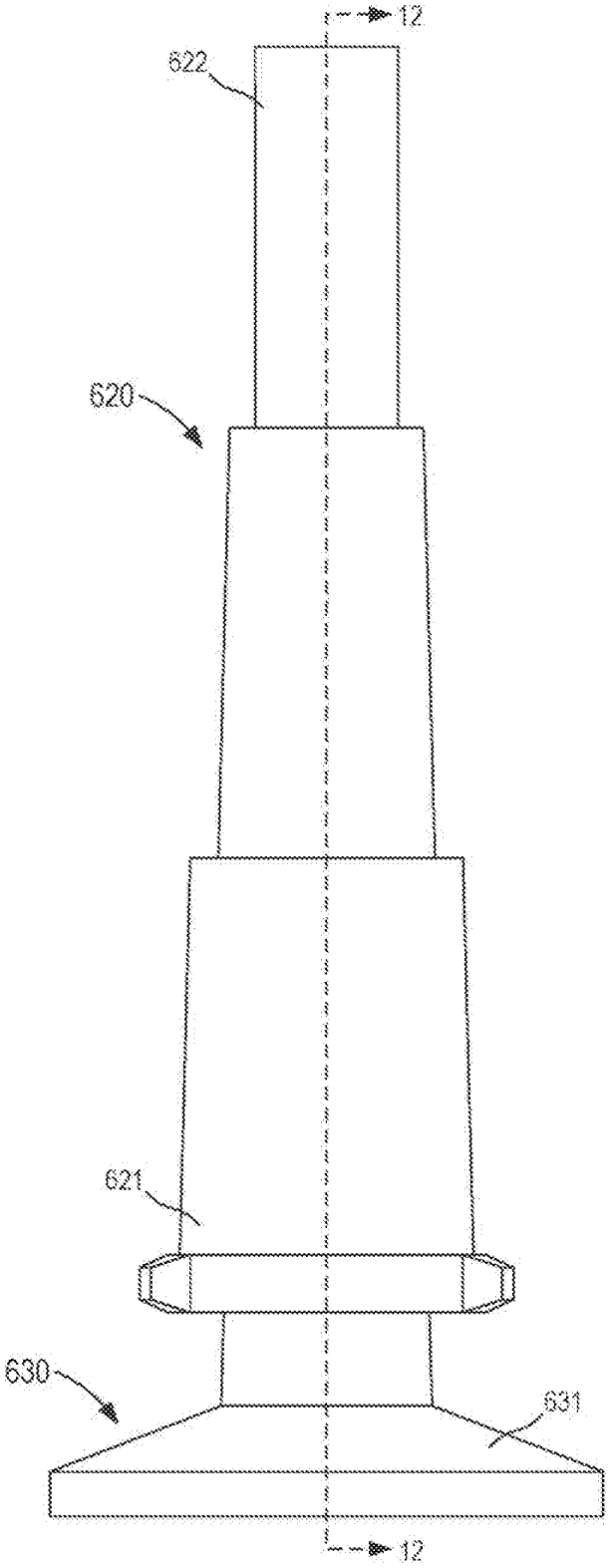


FIG. 11

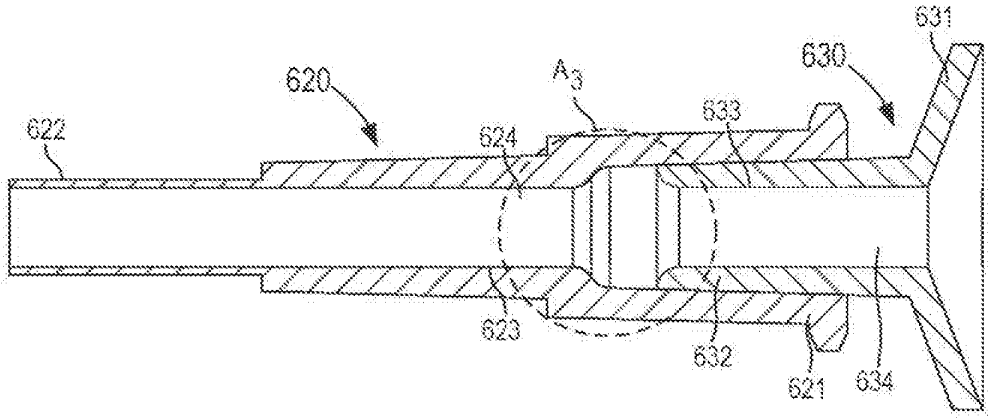

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FIG. 12

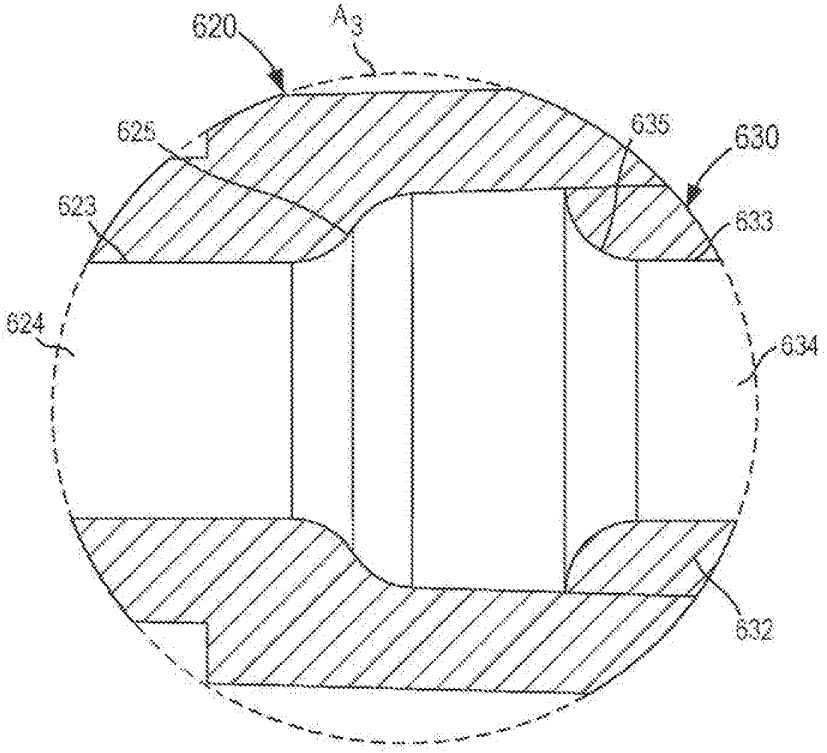

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FIG. 13

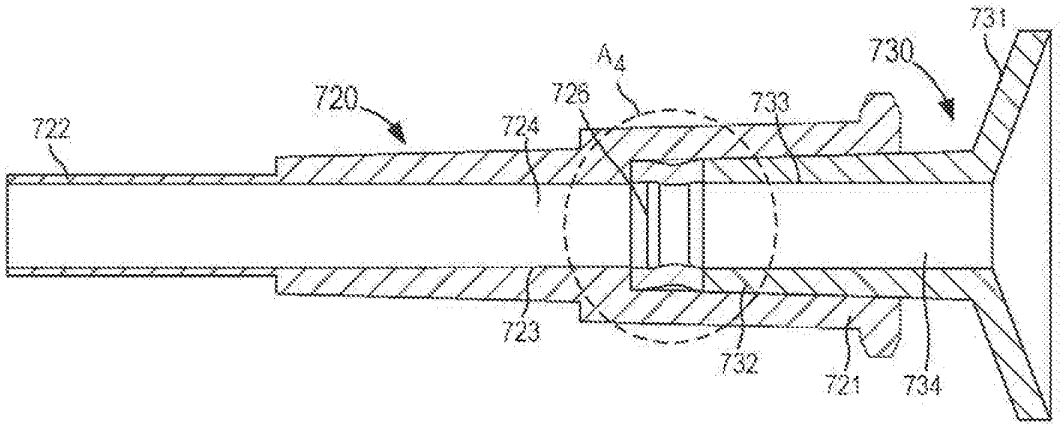

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FIG. 14

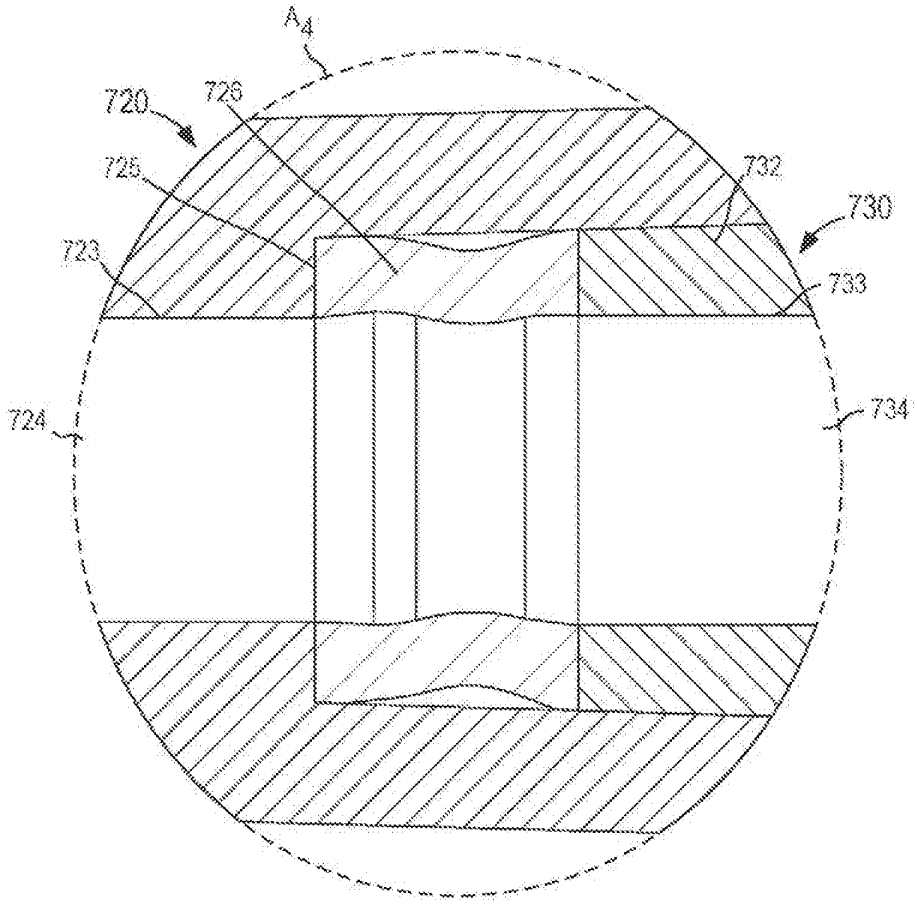

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FIG. 15

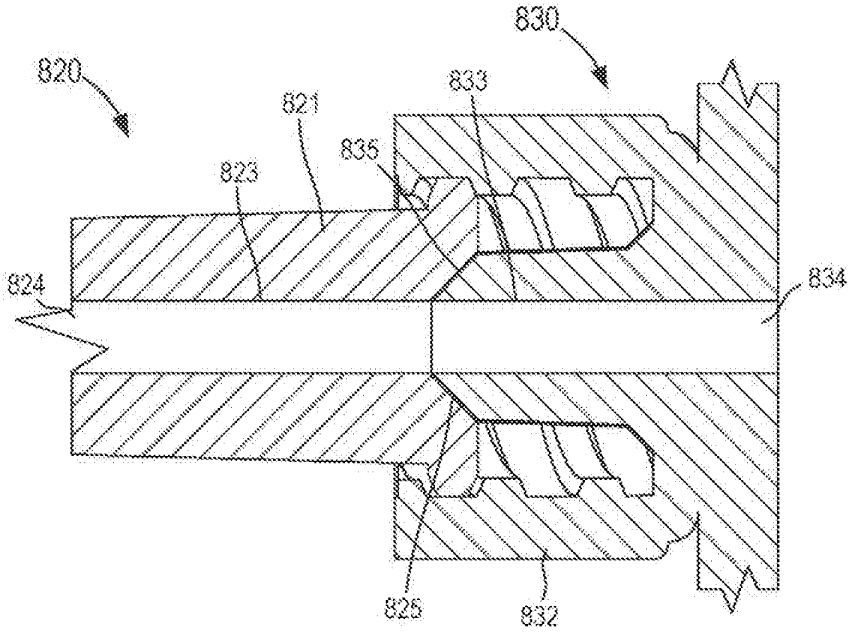

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FIG. 16

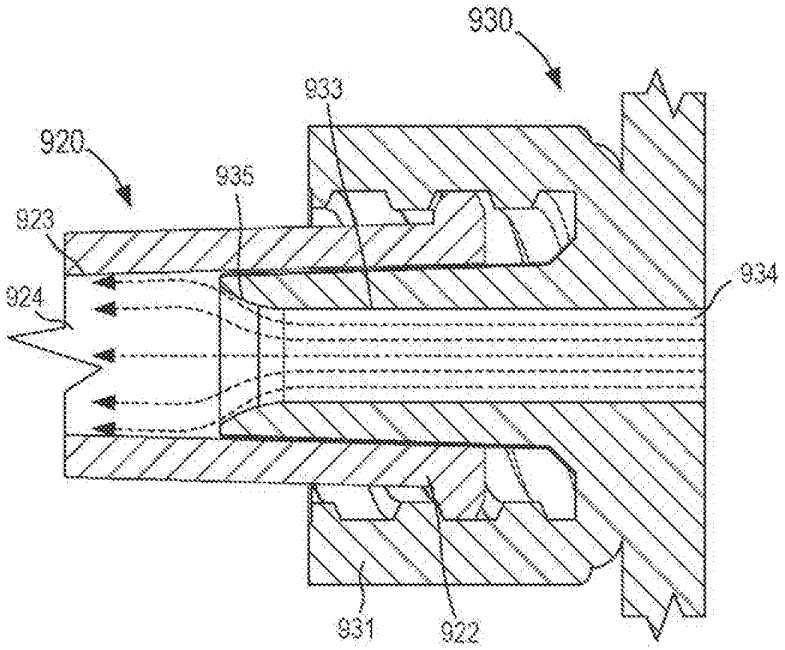

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FIG. 17

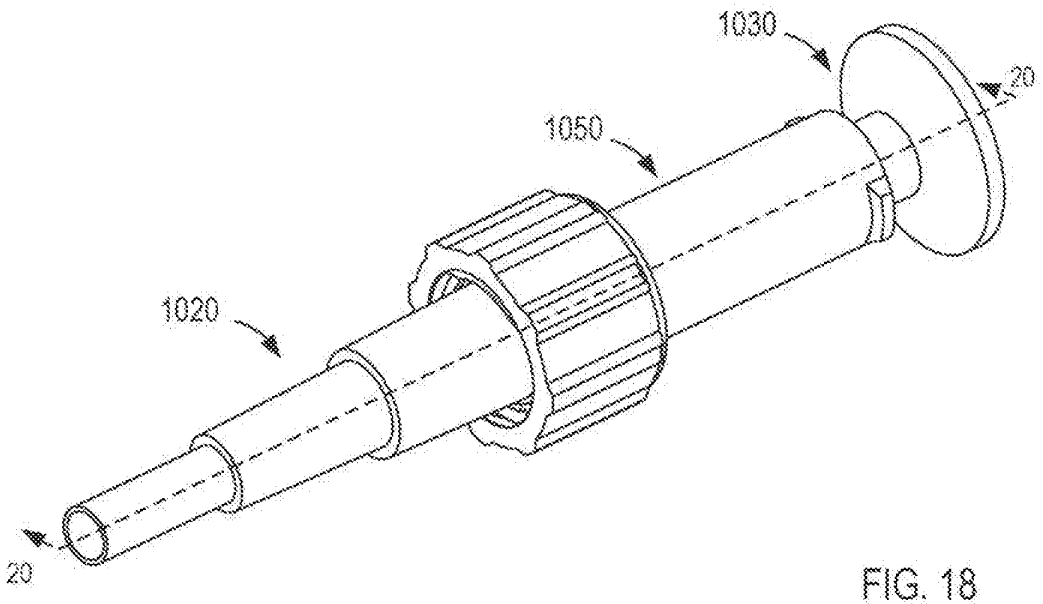

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FIG. 18

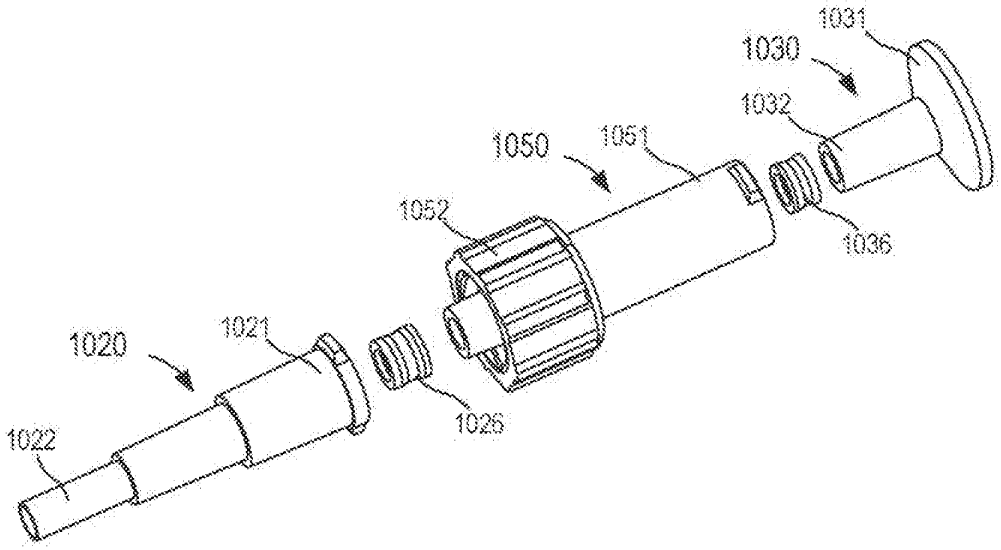

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FIG. 19

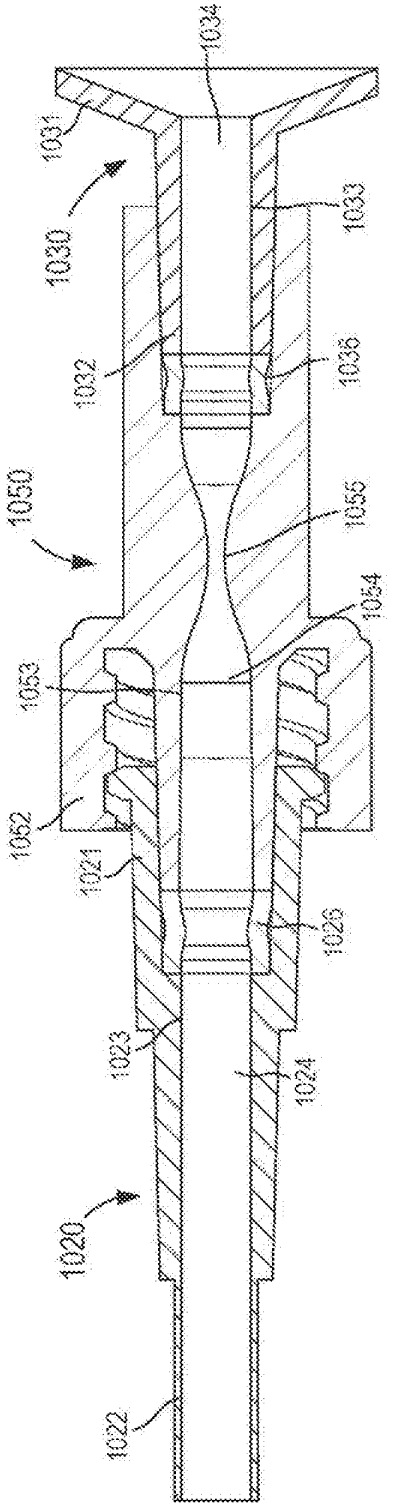

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FIG. 20

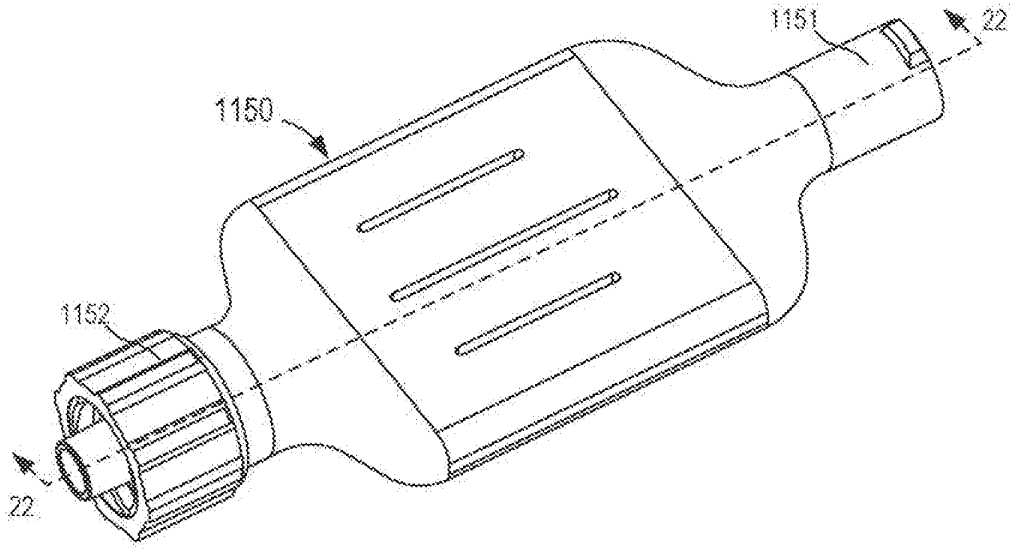


FIG. 21

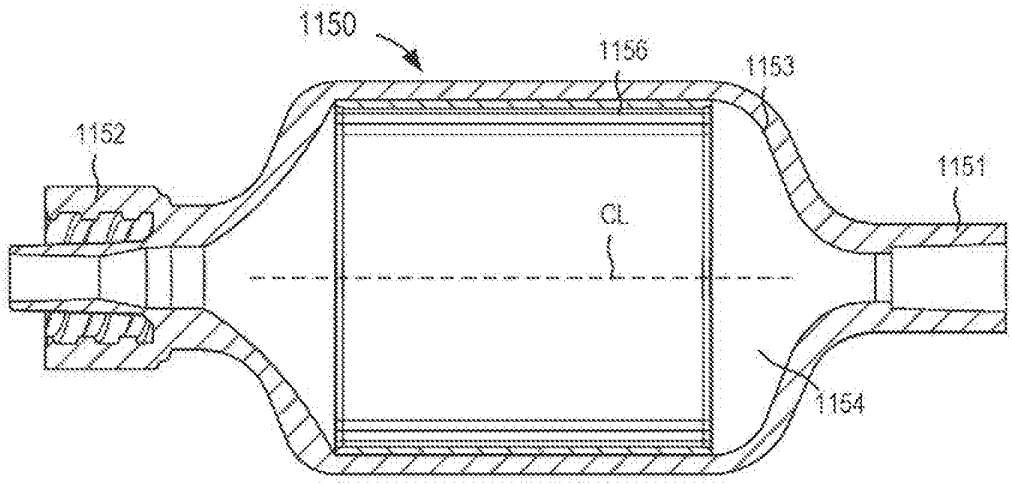


FIG. 22

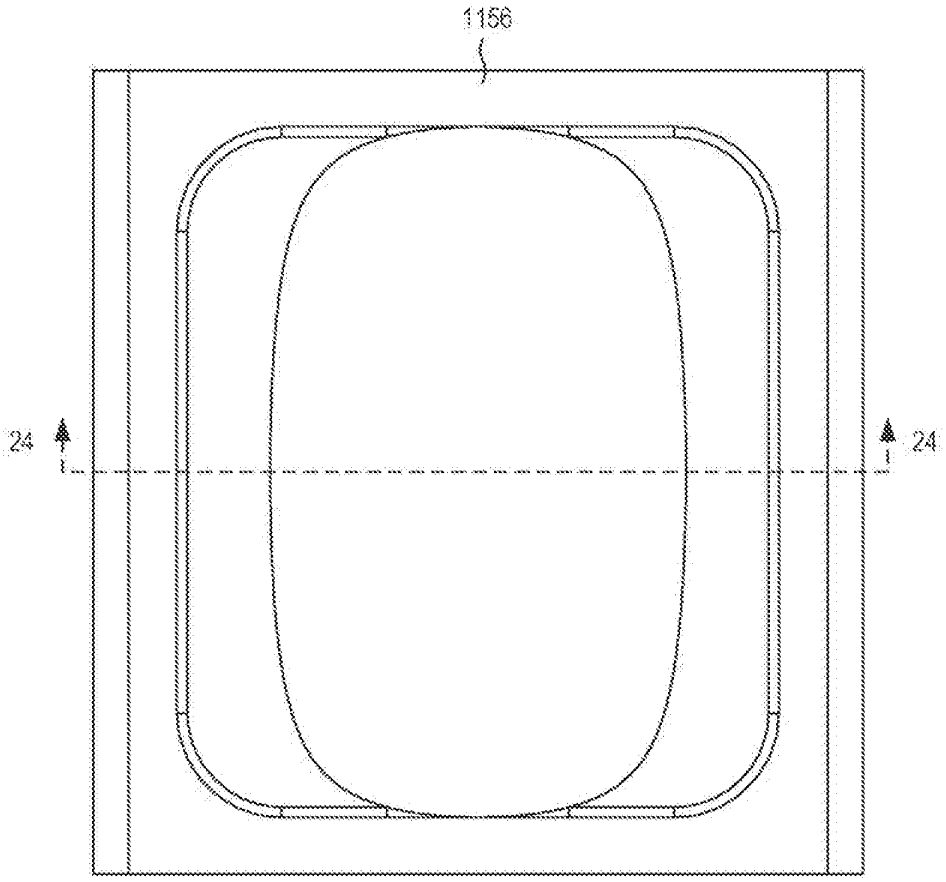


FIG. 23

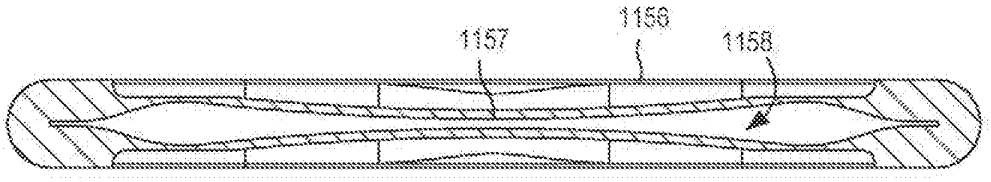


FIG. 24

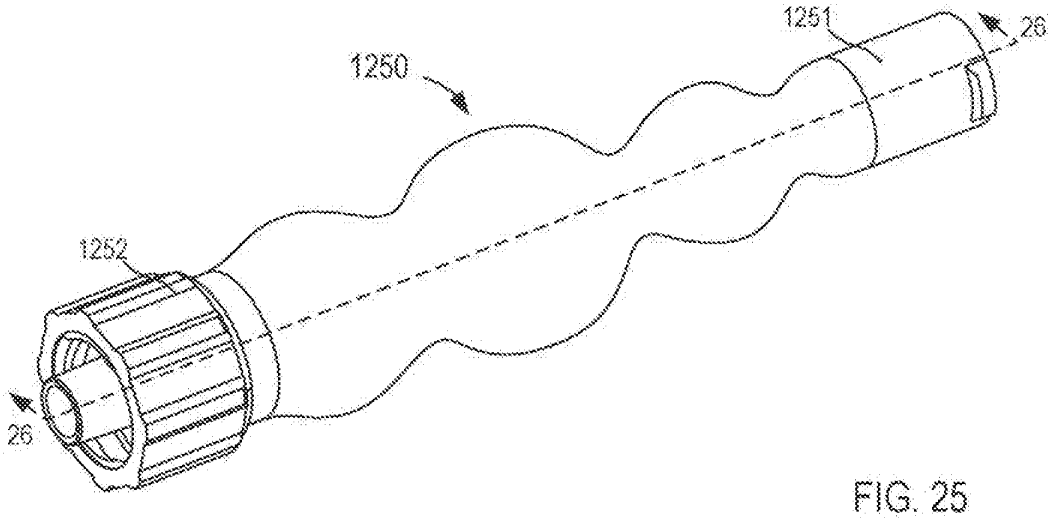

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FIG. 25

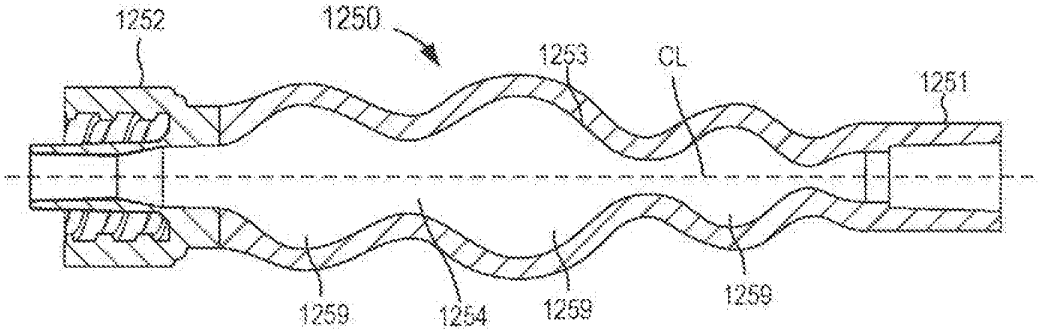

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FIG. 26

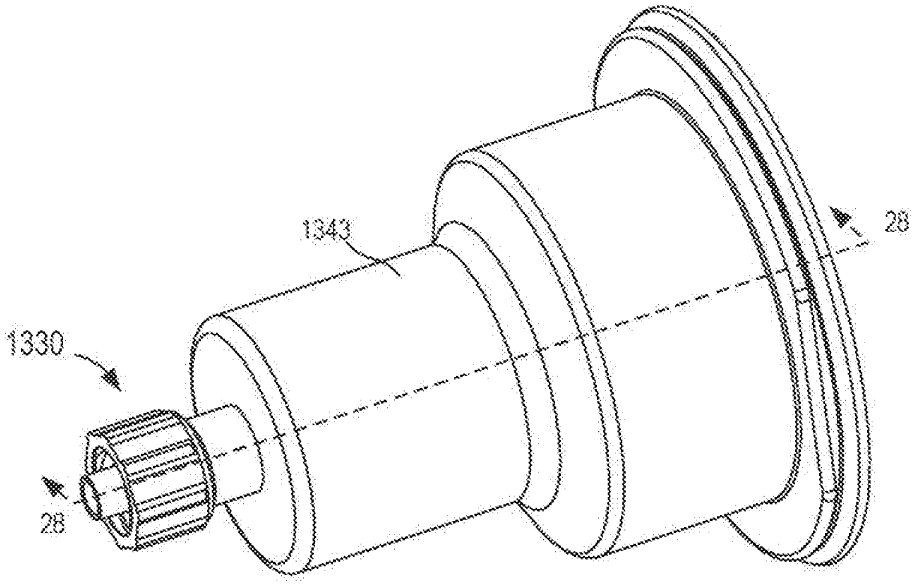


FIG. 27

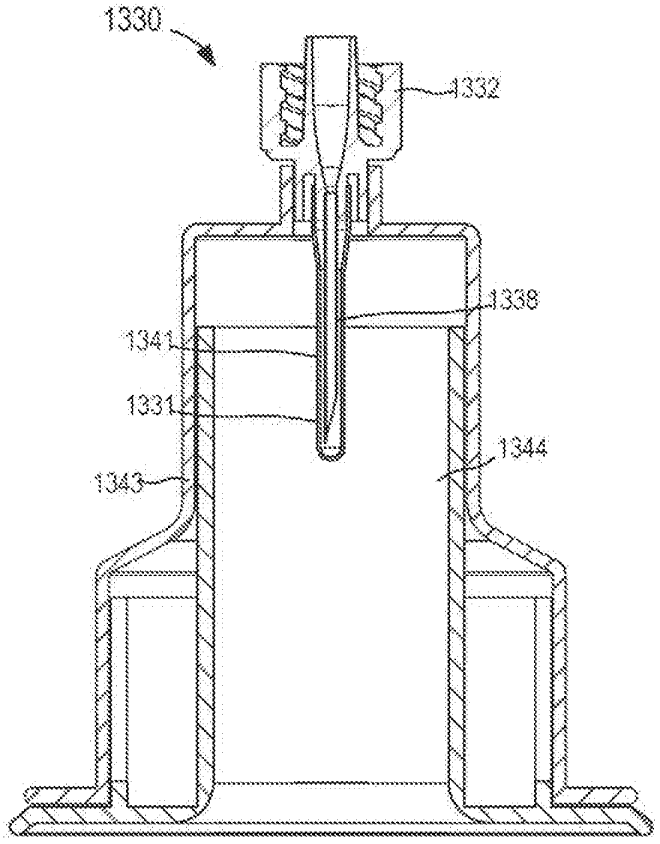


FIG. 28

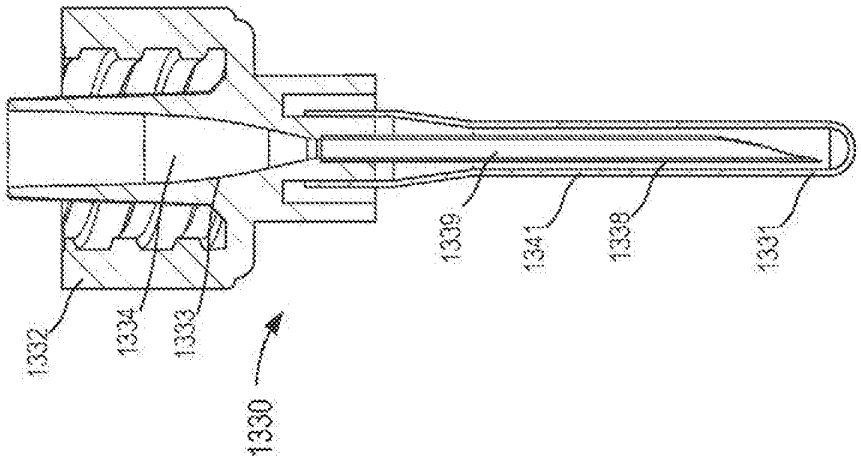


FIG. 30

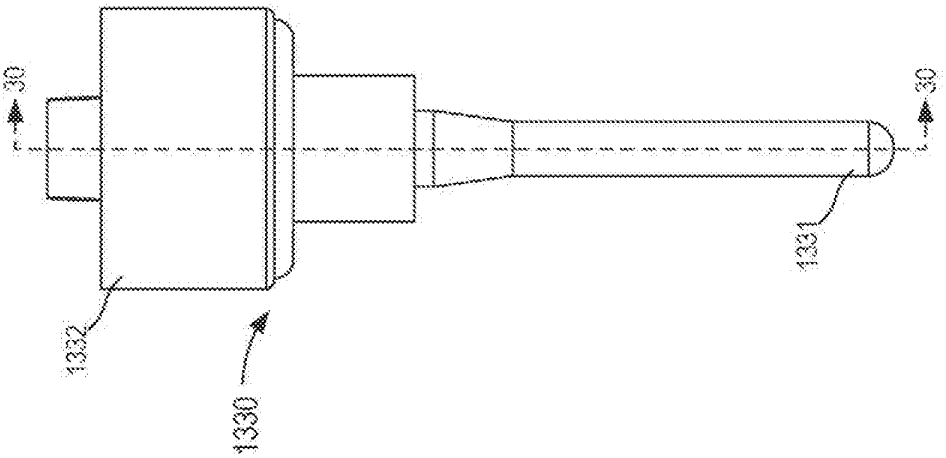


FIG. 29

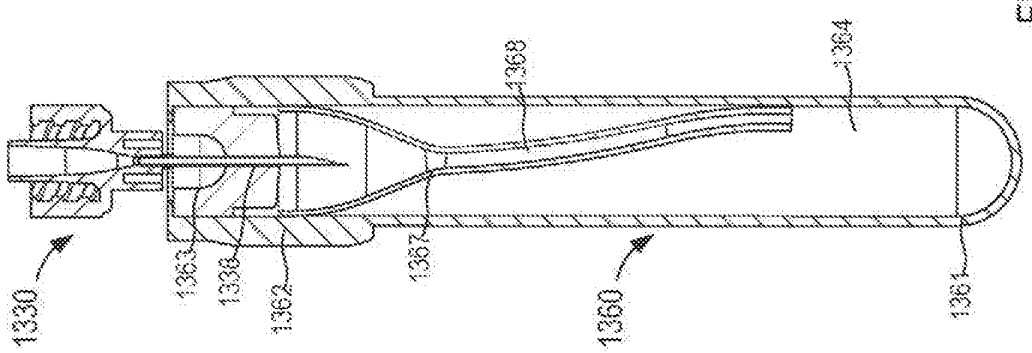


FIG. 33

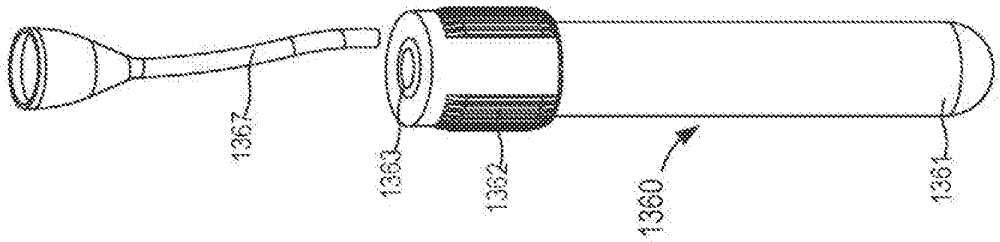


FIG. 32

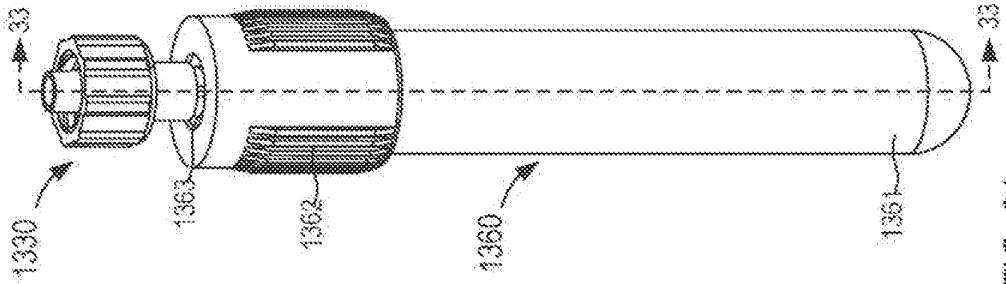


FIG. 31

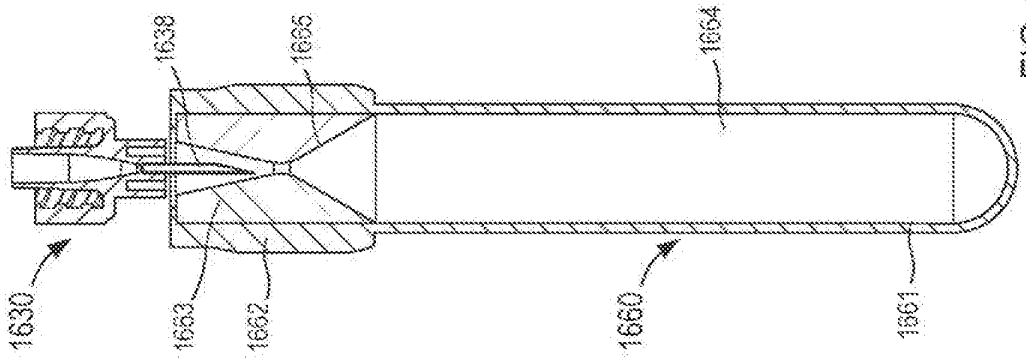


FIG. 36

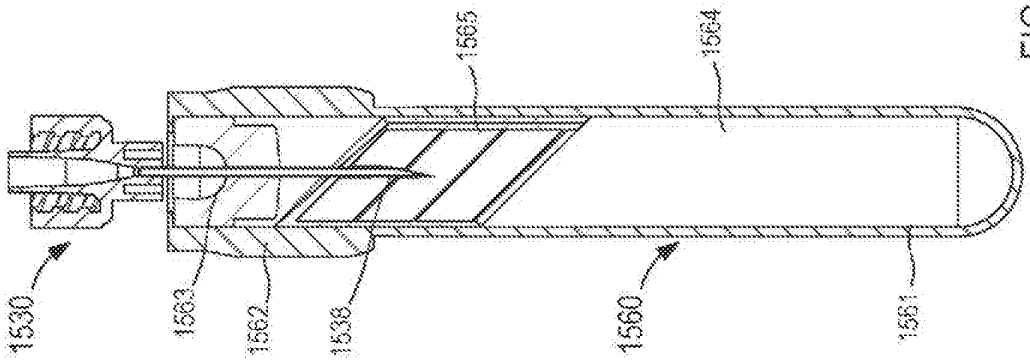


FIG. 35

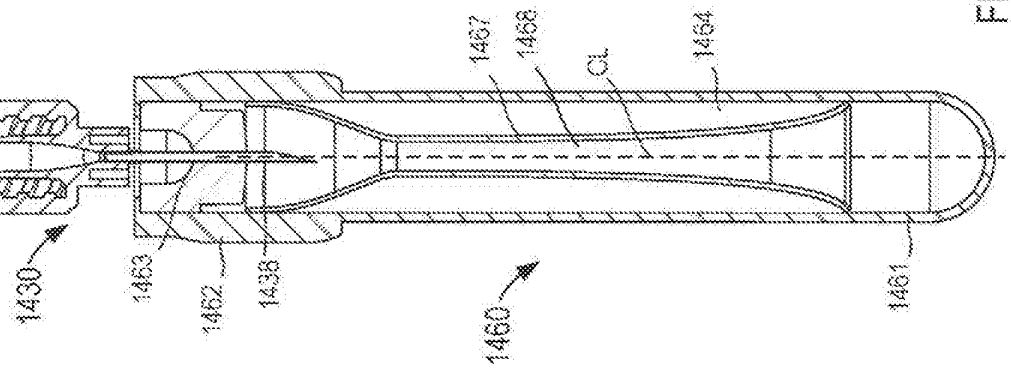


FIG. 34

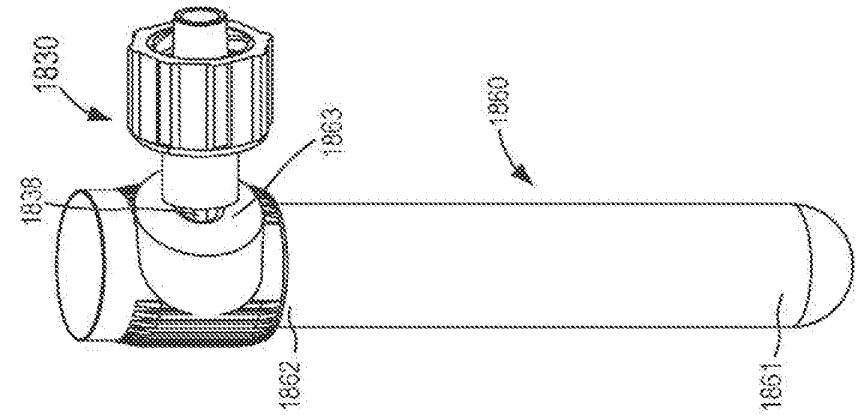


FIG. 39

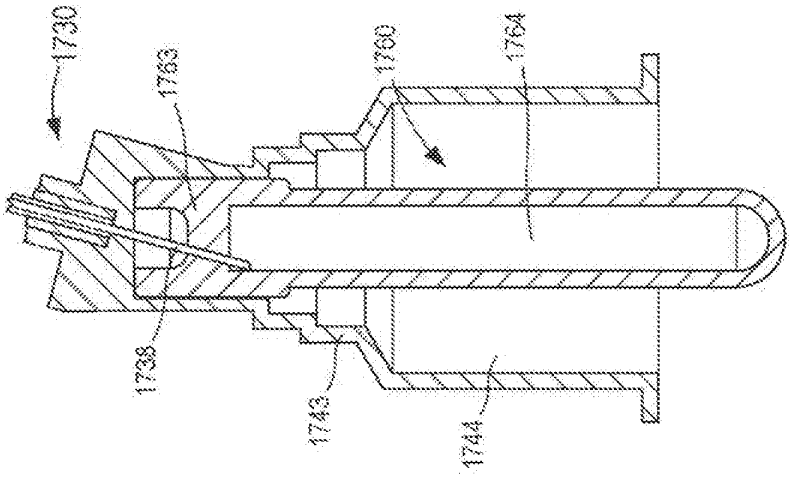


FIG. 38

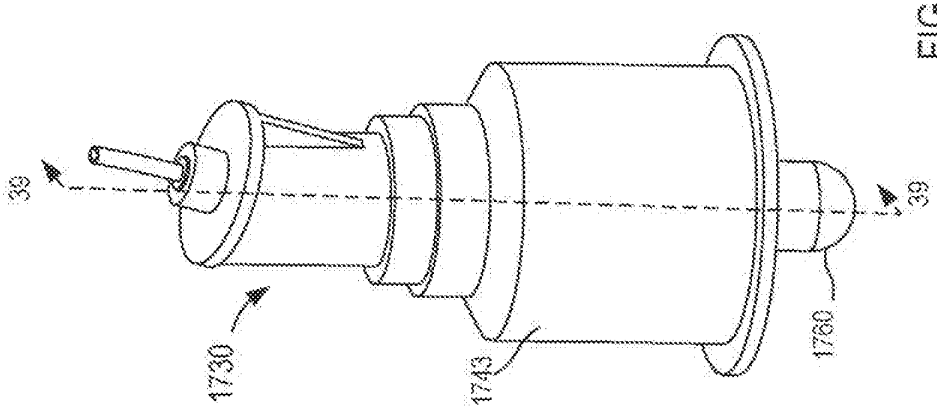


FIG. 37

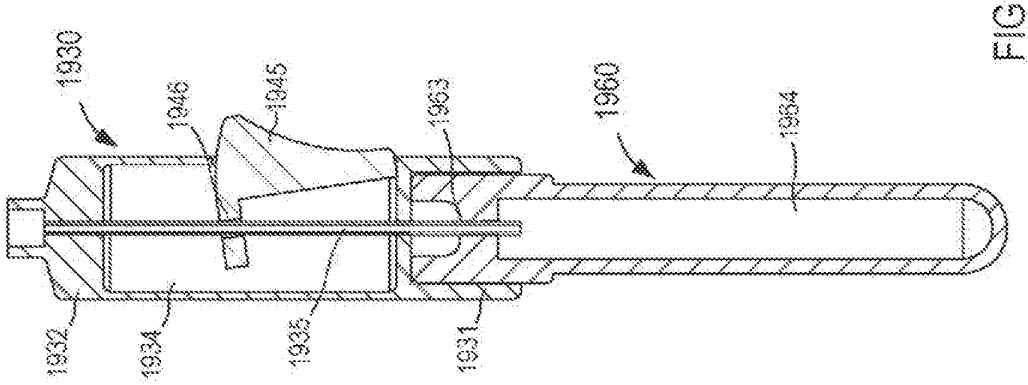


FIG. 42

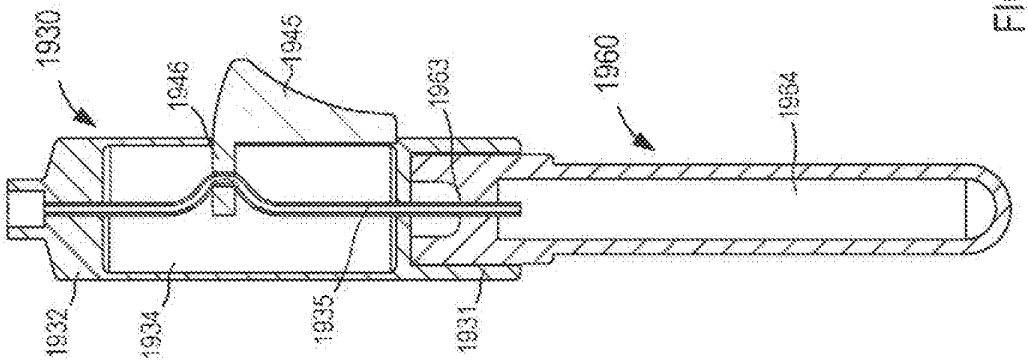


FIG. 41

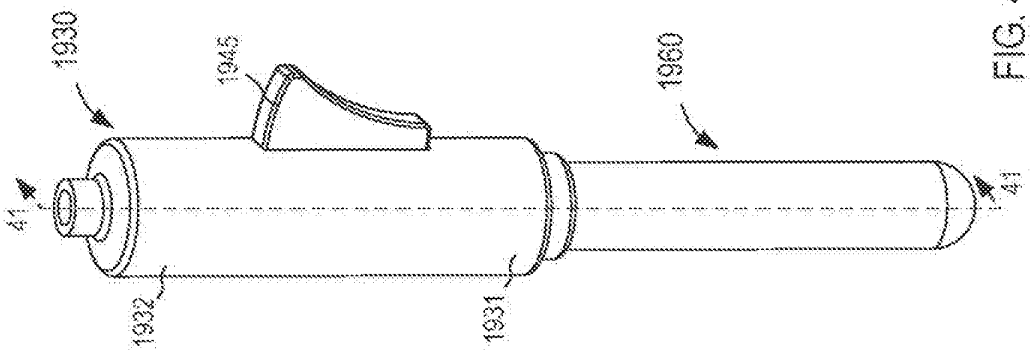


FIG. 40

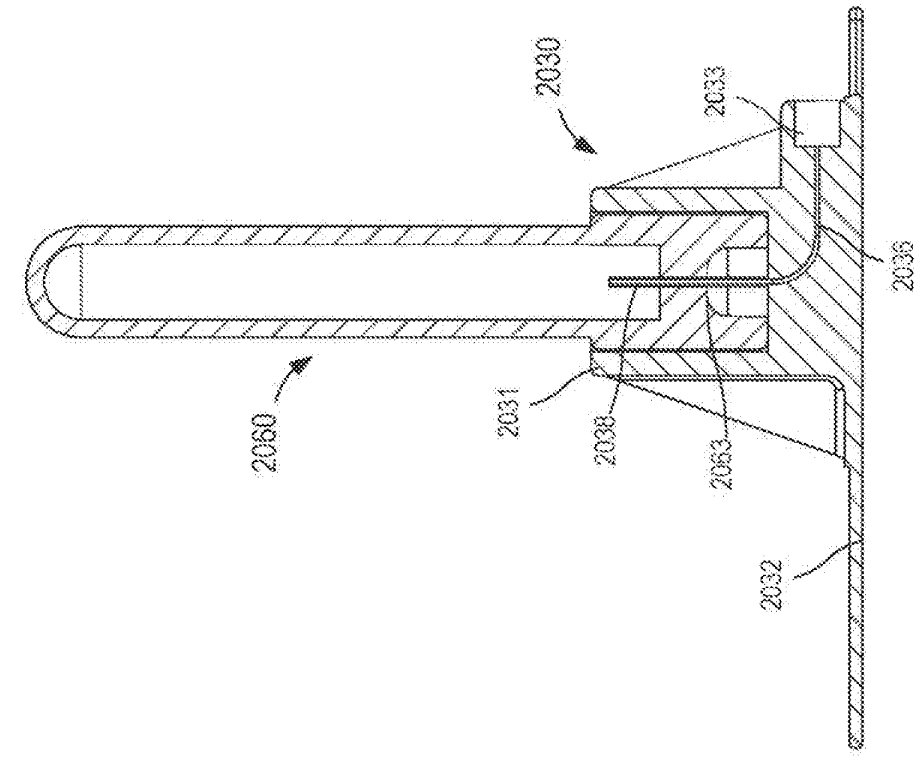

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FIG. 44

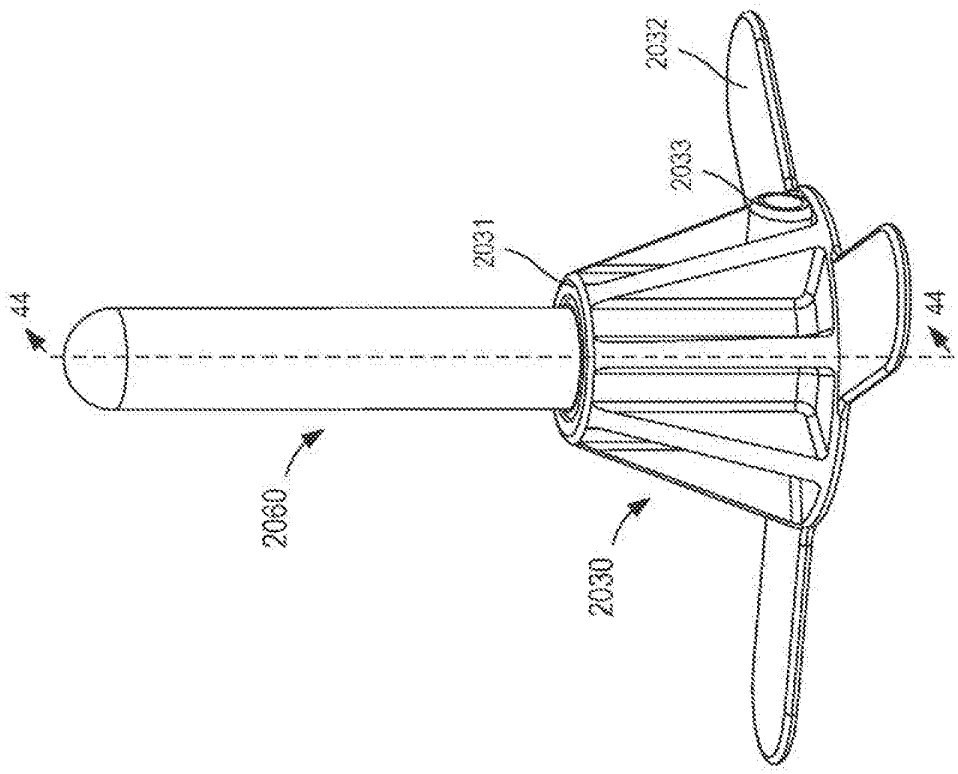

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FIG. 43

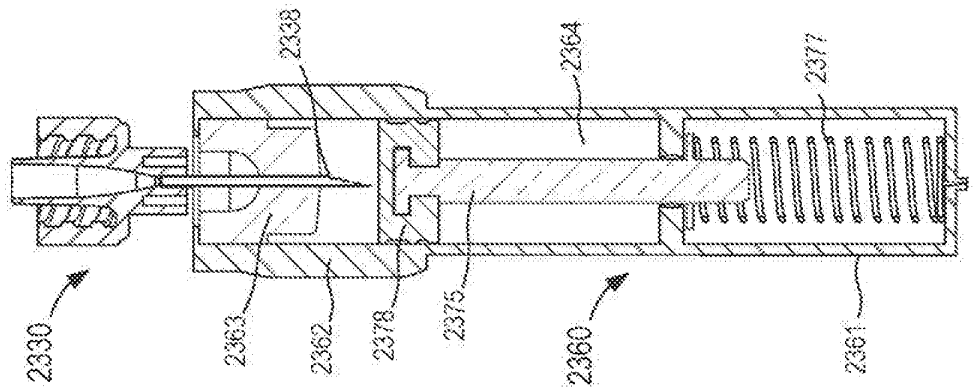


FIG. 47

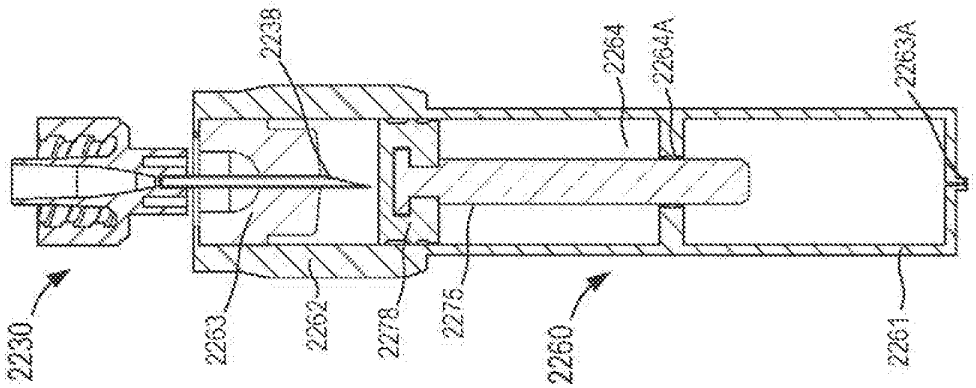


FIG. 46

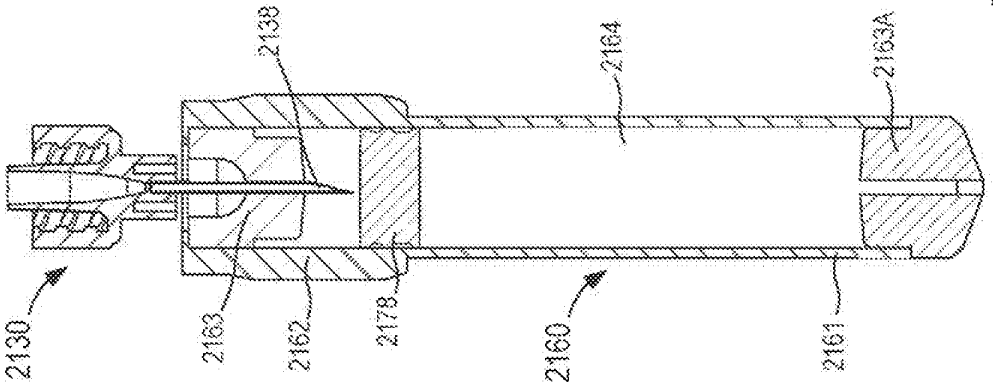


FIG. 45

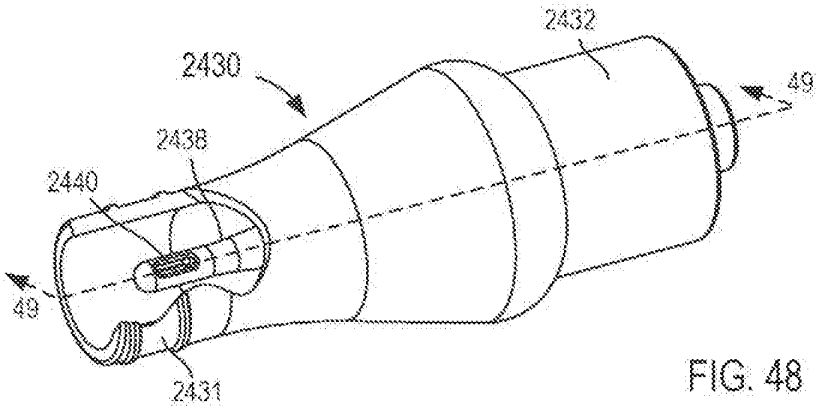


FIG. 48

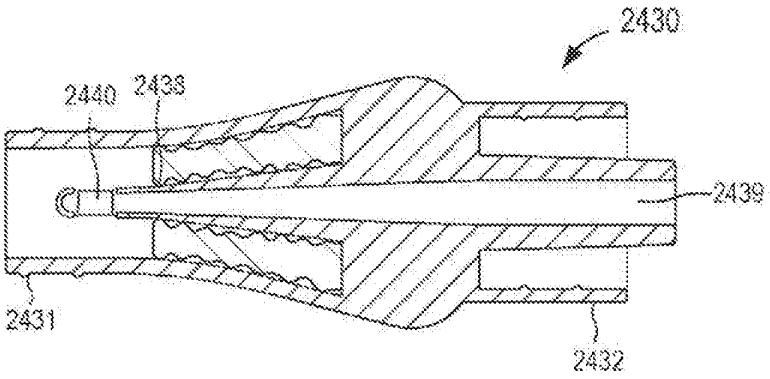


FIG. 49

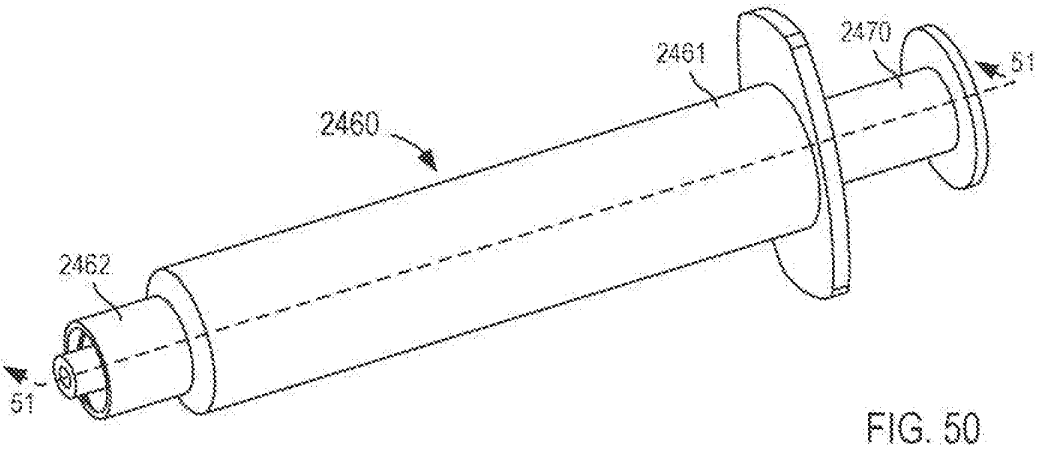


FIG. 50

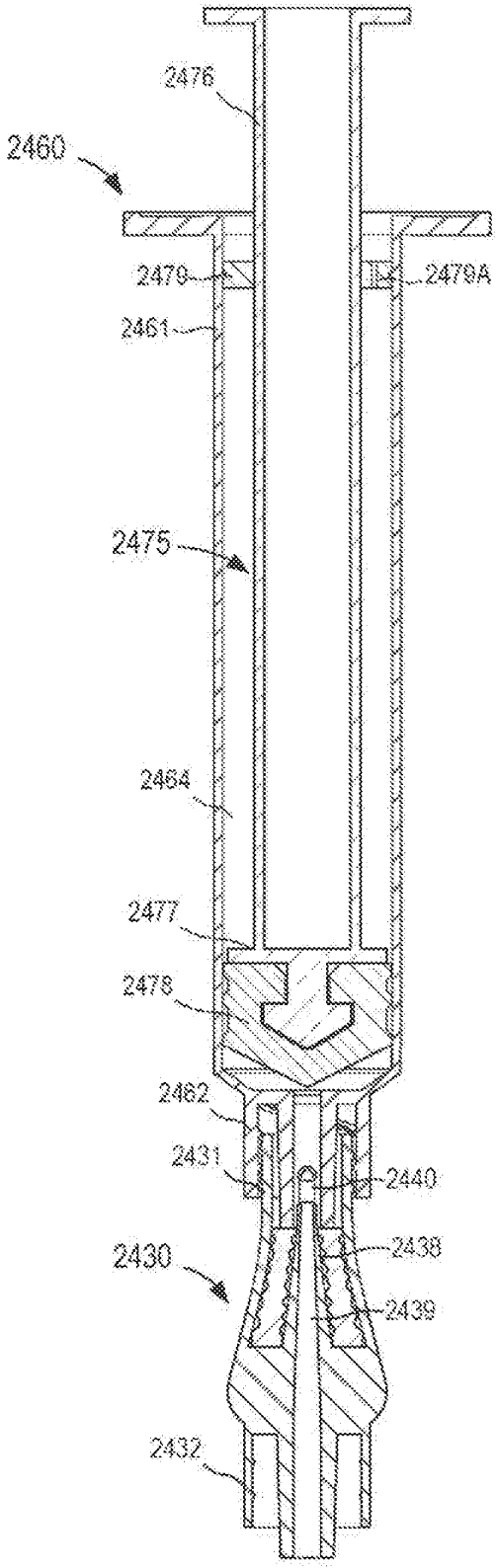

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FIG. 51

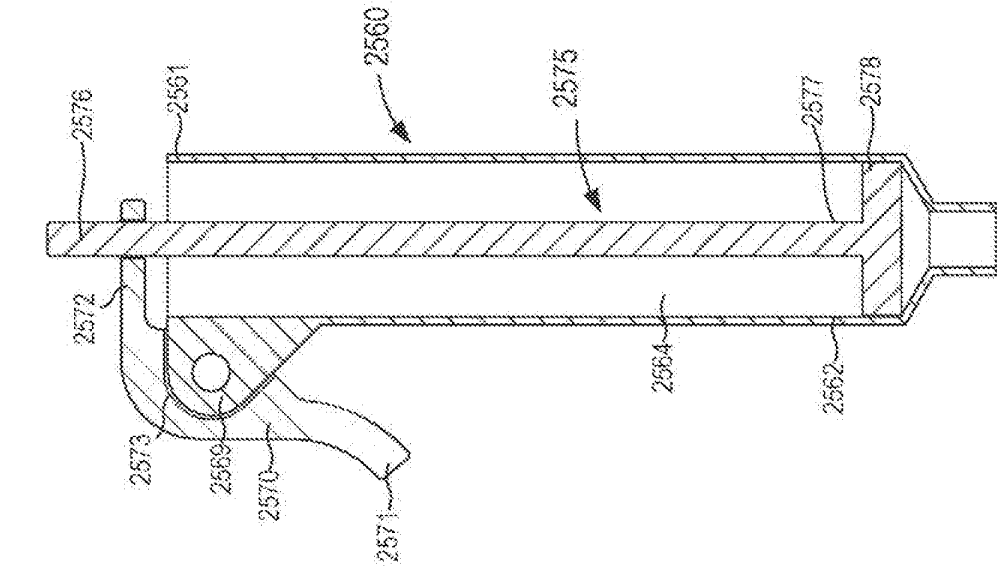

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FIG. 53

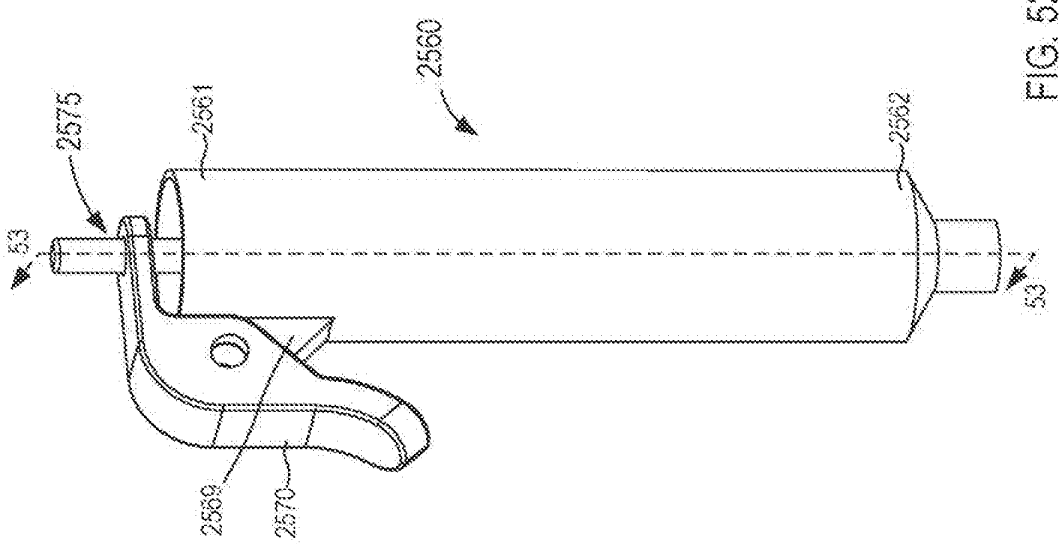

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FIG. 52

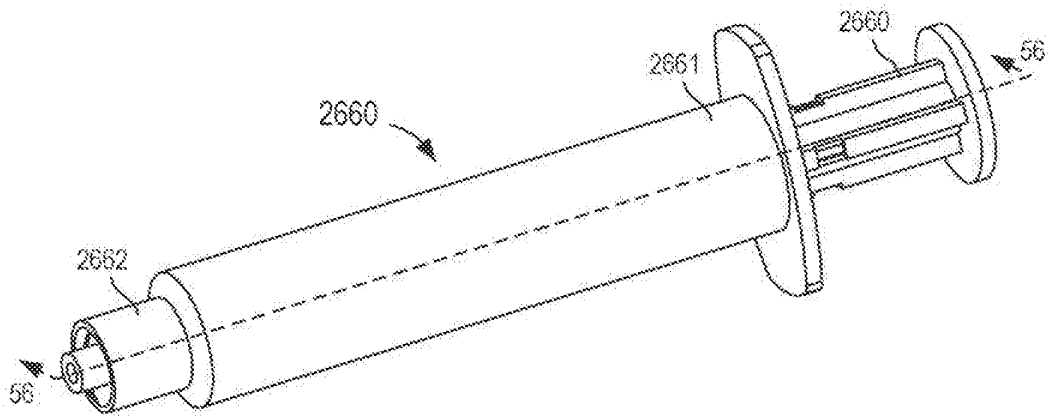

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FIG. 54

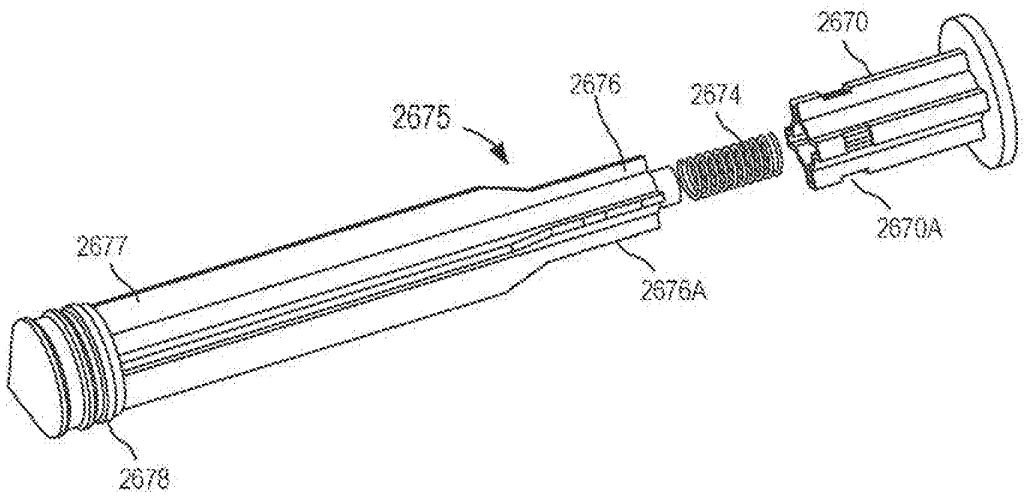

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FIG. 55

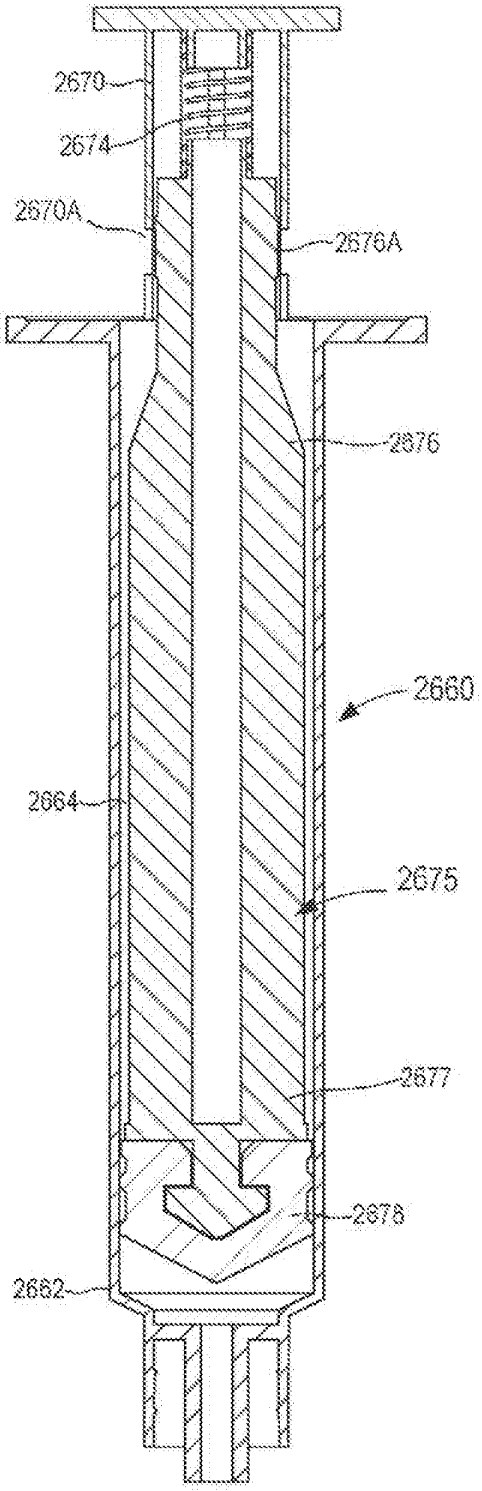


FIG. 56

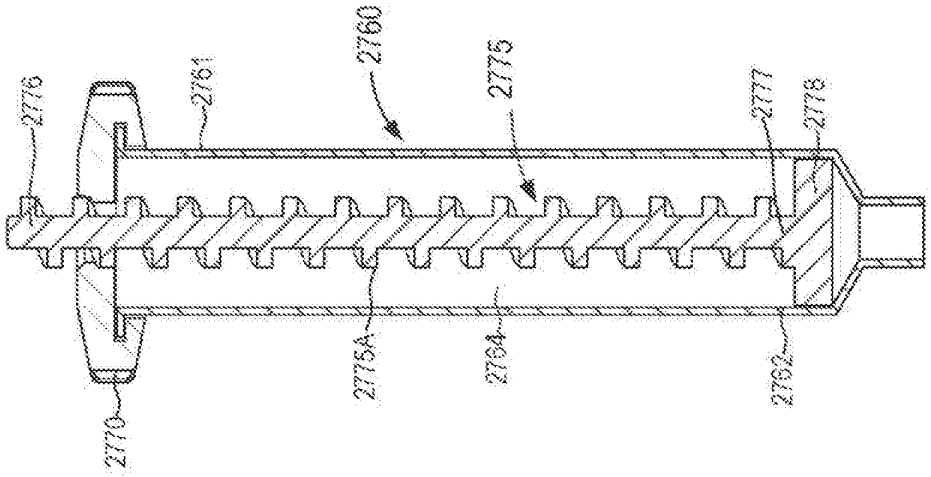

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FIG. 58

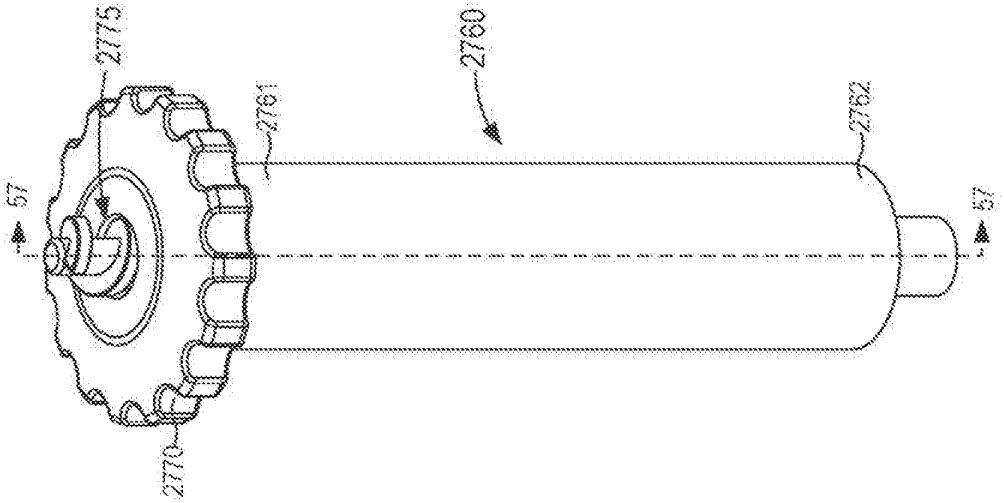

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FIG. 57

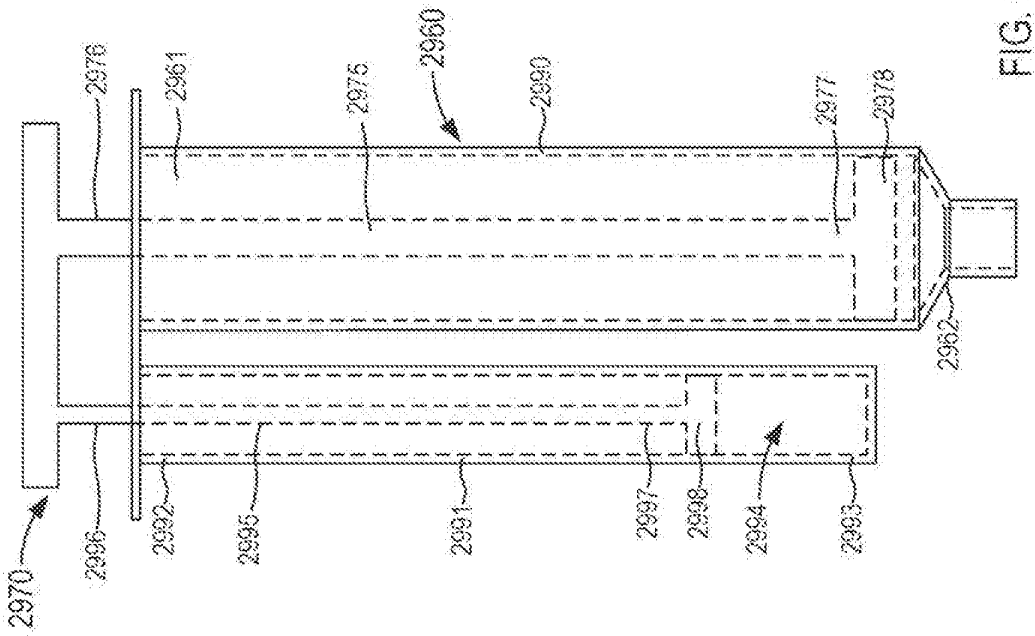

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FIG. 60

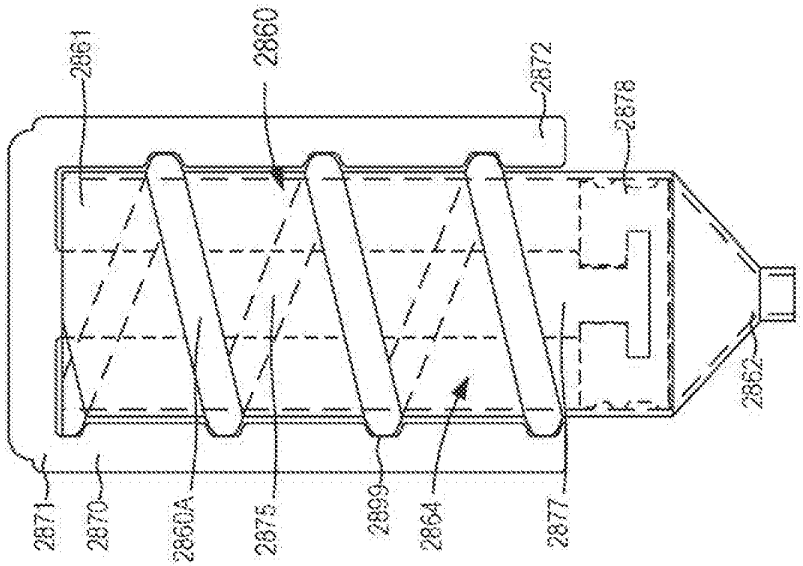

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FIG. 59

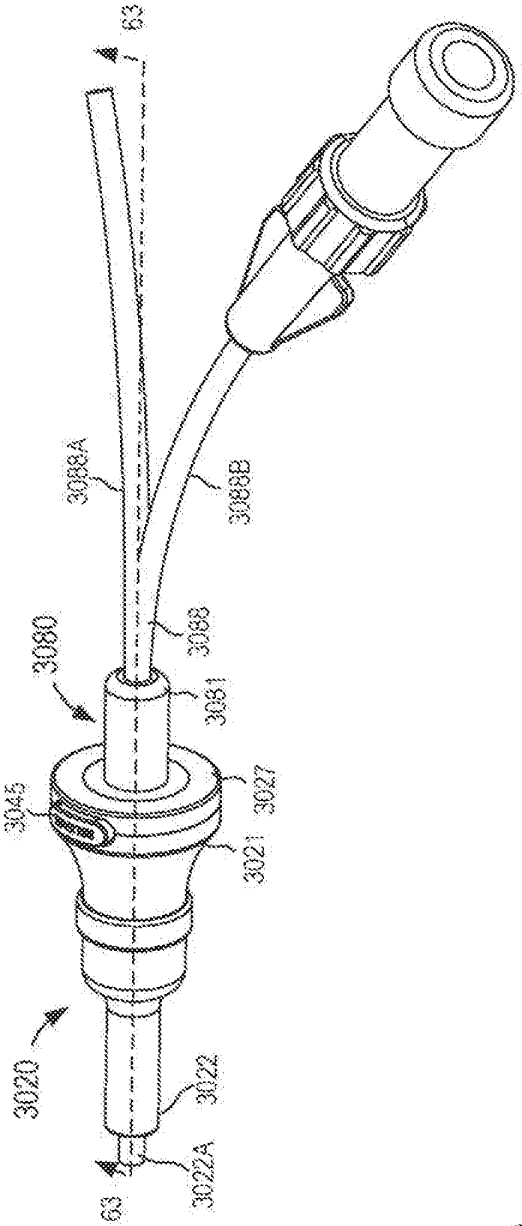

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FIG. 61

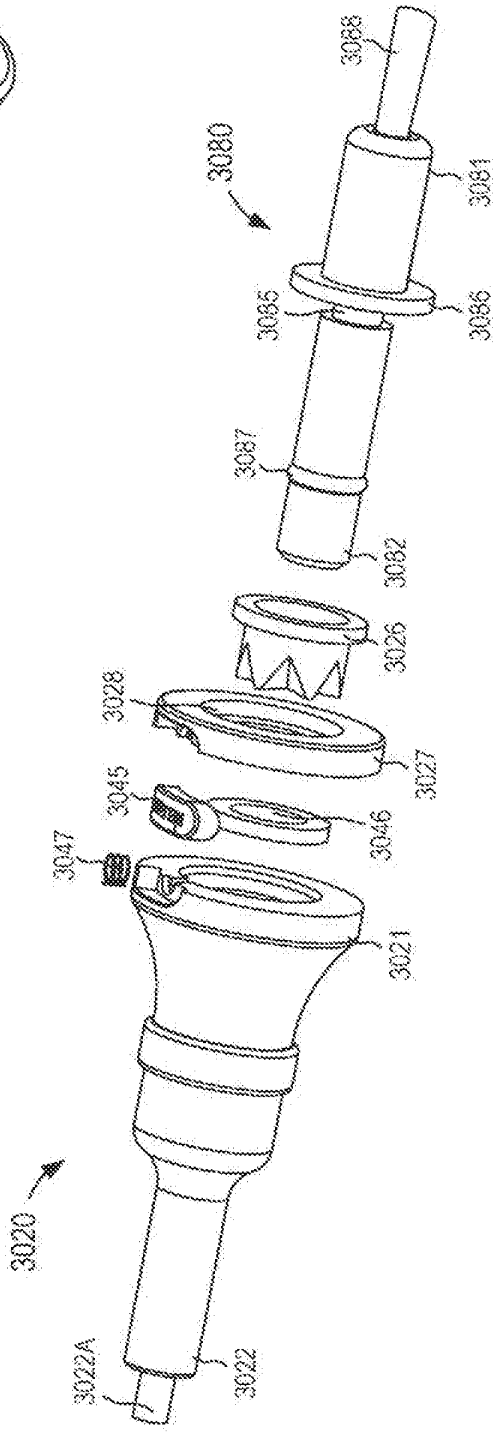

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FIG. 62

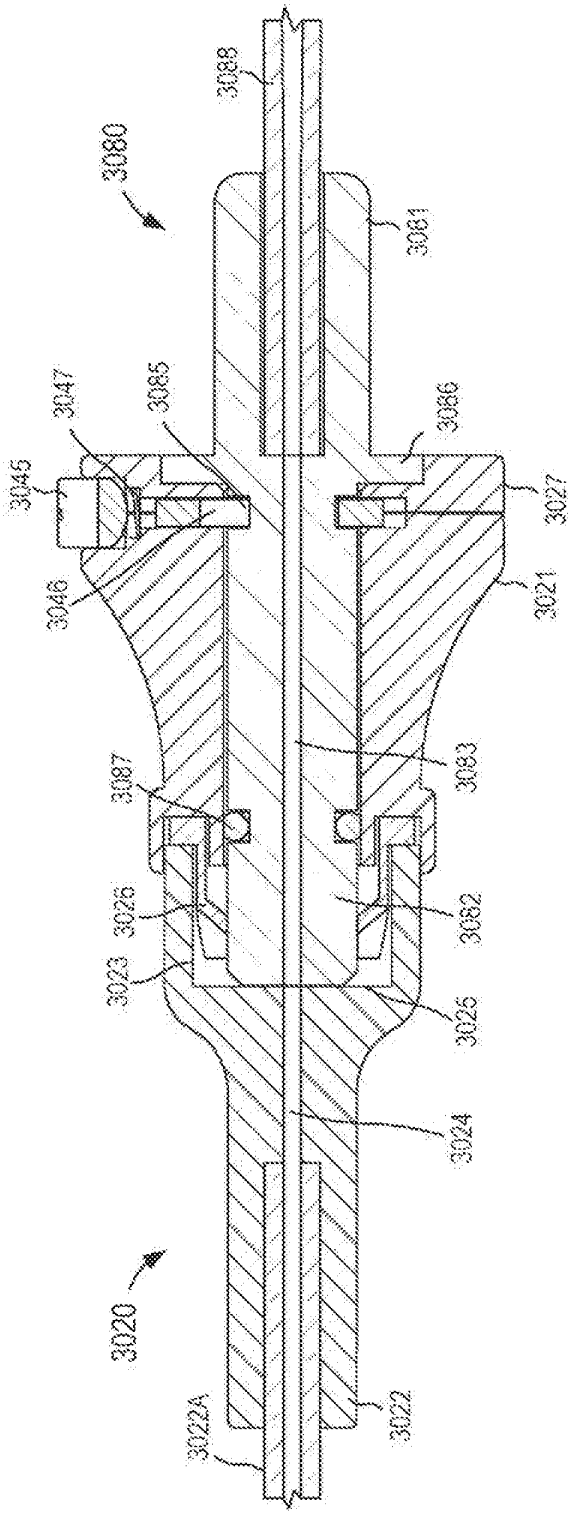

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FIG. 63

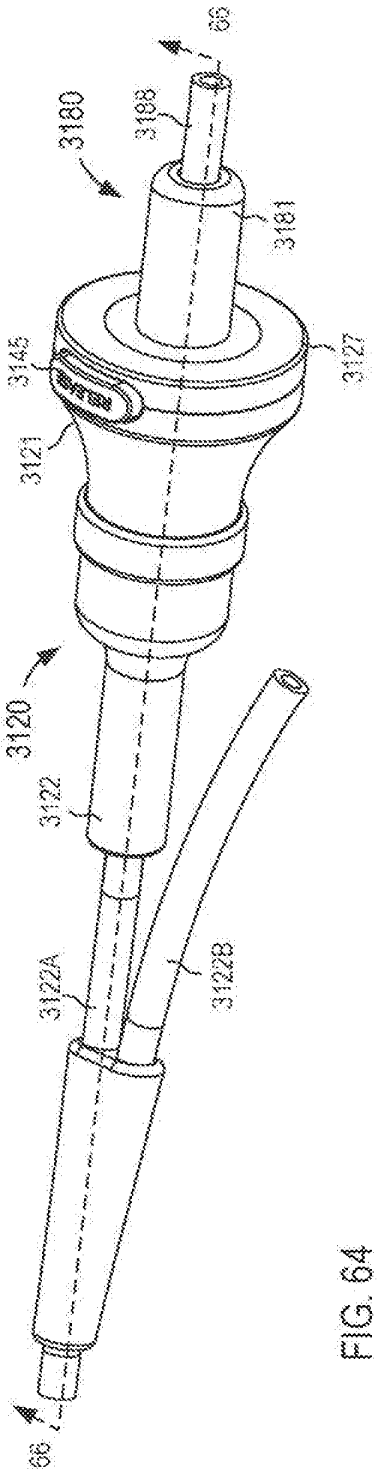

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FIG. 64

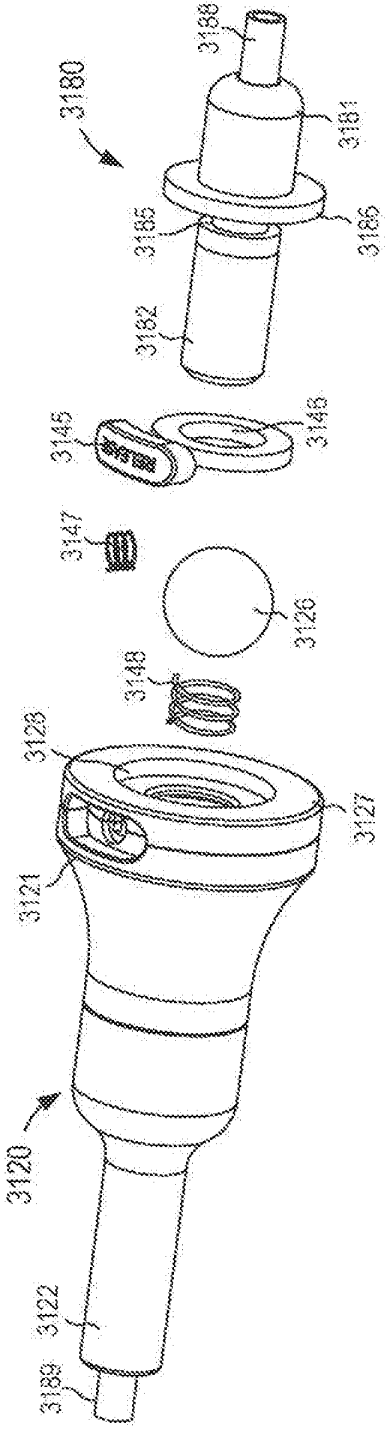

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FIG. 65

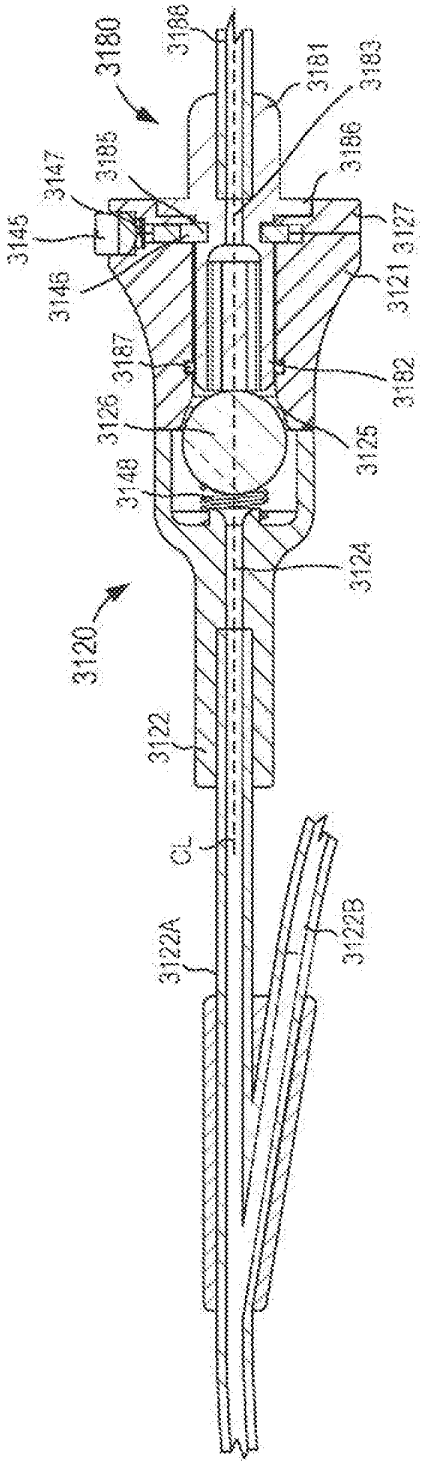

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FIG. 66

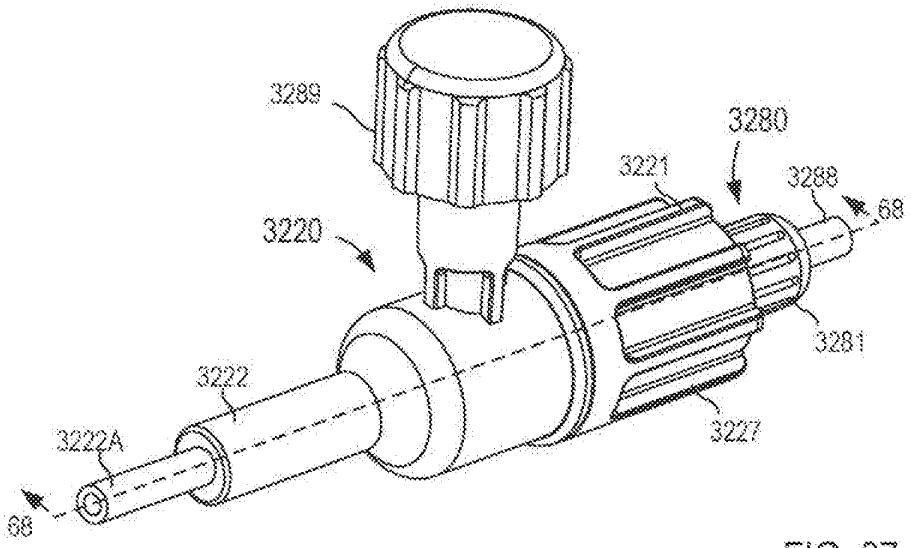

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FIG. 67

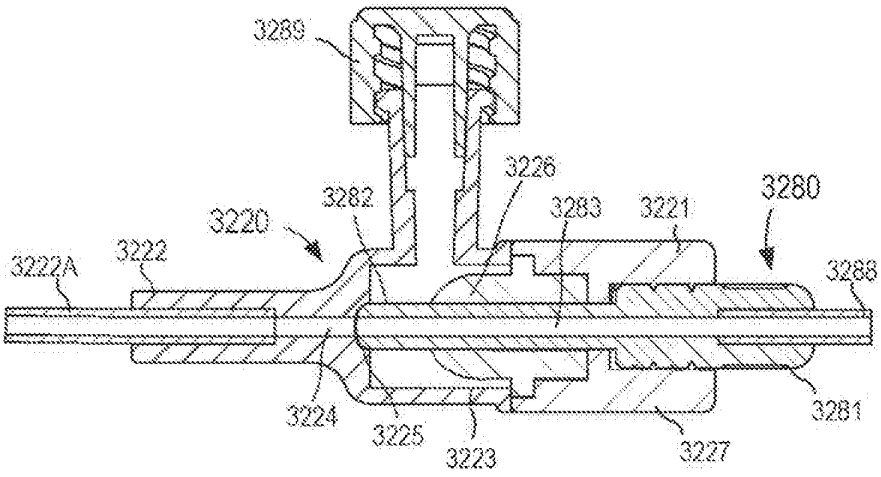

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FIG. 68

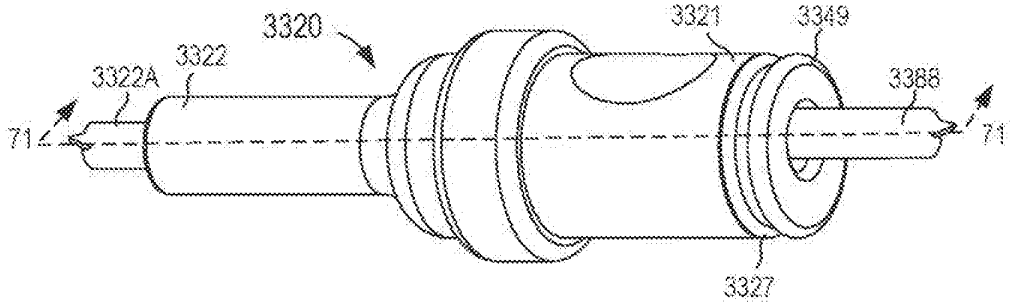

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FIG. 69

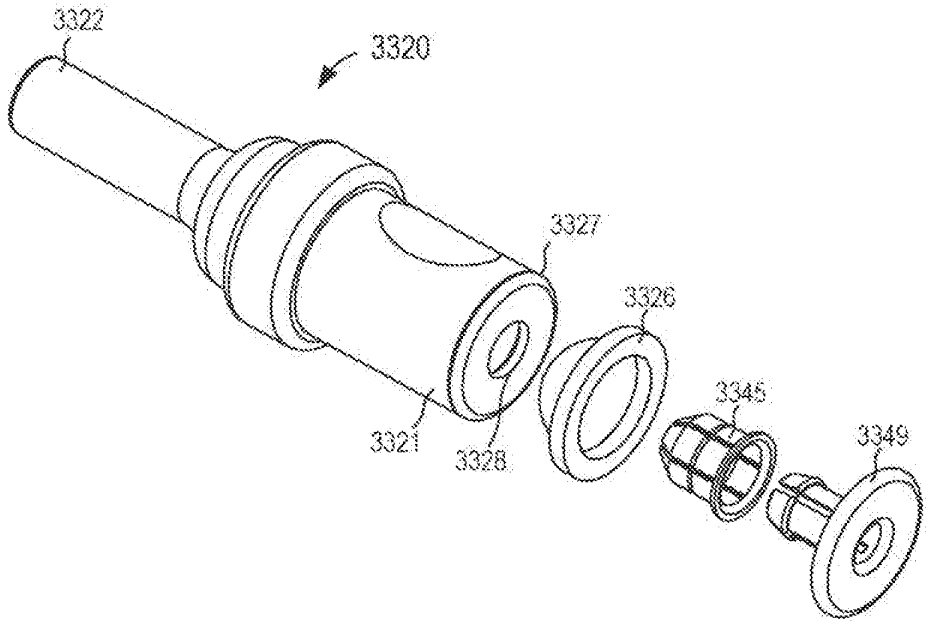

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FIG. 70

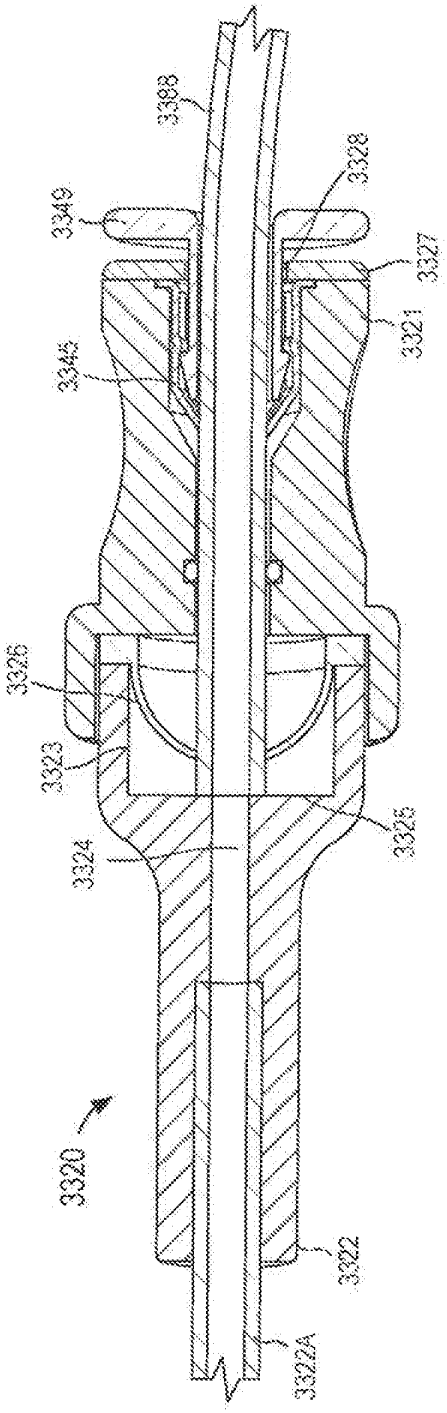

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FIG. 71

Effects of skin disinfection method, deviation bag, and bacterial screening on clinical safety of platelet transfusions in the Netherlands

Dirk de Korte, Joyce Curvers, Wim L.A.M. de Kort, Tiny Hoekstra, Cees L. van der Poel, Erik A.M. Beckers, and Jan H. Marcelis

BACKGROUND: Bacterial contamination of blood products is a great hazard for development of fatal transfusion reactions. Bacterial screening of platelet concentrates (PC) by aerobic and anaerobic culturing (BacT/ALERT, bioMérieux) was introduced in the Netherlands in October 2001.

STUDY DESIGN AND METHODS: In November 2002, a nationwide, uniform skin cleansing method was introduced with a double-swab disinfection with 70 percent isopropyl alcohol. One location routinely used an integrated diversion bag to collect the first 20 to 30 mL.

RESULTS: Over the calendar years 2002 and 2003, in total 113,093 PCs derived from pooled buffy coats were screened. After introduction of the new disinfection method, 0.85 percent were initially positive. This was a small reduction compared to the previous disinfection methods under which 0.95 percent were initially positive. The location with use of the diversion bag showed a significantly lower frequency of bacterial contamination, with 0.50 percent before and 0.37 percent after introduction of 70 percent isopropyl alcohol. In addition 8000 apheresis PCs were also screened, showing 24 initially positive samples (0.30%).

CONCLUSION: The use of the diversion bag and, to a lesser extent, the use of double swabs with 70 percent isopropyl alcohol, led to a reduction of contamination. As expected, predominant contamination with resident skin bacteria was reduced. The combination of diversion bag and new disinfection led to a frequency of initial positive results for pooled five-donor PCs, which is similar to that of single-donor apheresis PCs. Furthermore, the bacterial detection system and associated product recall procedures have been shown to be effective in preventing transfusion of contaminated PCs and/or related red cells, especially for rapidly growing bacteria.

Since the dramatic reduction of transfusion-transmitted viral infections though screening for various blood-borne viruses, transfusion-related bacterial infections have become one of the major risks of transfusion. Bacterial contamination is considered to be, after clerical errors, the second most common cause of death from transfusion, with mortality rates for platelet (PLT)-related sepsis ranging from 1 in 20,000 to 1 in 100,000 donor exposures.[1-3] In contrast, the current frequencies of virus transmission via blood components are estimated as 1 in 1,800,000 for hepatitis C virus, 1 in 220,000 for hepatitis B virus, and 1 in 2,300,000 for human immunodeficiency virus.[4,5] Therefore, additional screening of blood products for bacterial contamination is under consideration or has already been implemented in many countries, both in Europe and in North America.[6]

Because of their storage at room temperature, PLT products are most sensitive for bacterial contamination and thus a logical choice to start screening. In the Neth-

ABBREVIATIONS: CNS = coagulase-negative staphylococci; IPA = isopropyl alcohol; PC(s) = platelet concentrate(s); T5 = PCs prepared from pools of five buffy coats; TTBI = transfusion-transmitted bacterial infection.

From Sanquin Research, Amsterdam; Sanquin Blood Bank Region Southeast, Nijmegen; Sanquin Blood Supply Foundation, Amsterdam; Sanquin Blood Bank Region Southwest, Rotterdam; and Elisabeth Hospital, Tilburg, the Netherlands.

Address correspondence to: D. de Korte, PhD, Sanquin Research, Department of Blood Cell Research, Plesmanlaan 125, 1066 CX Amsterdam, the Netherlands; e-mail: D.deKorte@Sanquin.nl.

Received for publication May 26, 2005; revision received July 15, 2005, and accepted July 17, 2005.

doi: 10.1111/j.1537-2995.2006.00746.x

TRANSFUSION 2006;46:476-485.

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erlands, nationwide screening for bacterial contamination in 100 percent of PLT products was introduced at the end of 2001. All Dutch blood banks use the BacT/ALERT culturing system (bioMérieux [formerly Organon Teknika], Boxtel, the Netherlands), with a standardized protocol.

It has previously been shown that in the majority of positive cultures, bacterial contamination is a result of resident skin flora[7] most likely originating from the venipuncture plug.[8,9] Although hygienic precautions are taken to prevent contamination during collection, a further reduction of the number of products with bacterial contamination is desirable. To reduce the risk of contamination by skin flora two strategies can be used: 1) diversion of the first aliquot of the donation and 2) improvement of skin disinfection.

Regarding the first method we, as well as others, have previously shown that diversion of the first 10 mL of a whole-blood donation reduces the incidence of bacteria in the remaining whole-blood unit.[8,10,11] The effect of this diversion, however, on bacterial contamination of the final product, PLT concentrates (PCs) prepared from pooled buffy coats, has not yet been reported.

Considering skin disinfection, iodine is the most effective disinfectant. Because it is considered to be a donor-unfriendly agent, however, isopropyl alcohol (IPA) is the next best choice. McDonald and coworkers[12] have shown that improved skin disinfection methods drastically reduced the number of remaining bacteria on the phlebotomy puncture site—especially those methods with a double-swab method, with the best results for the combination of IPA and iodine. For this approach too, the final effect on bacterial contamination of buffy coat–derived PCs has not yet been reported.

From January 2002, at collection centers of the Sanquin Blood Bank Region Southeast (Nijmegen, the Netherlands), a collection system with an integrated diversion bag was used to divert the first 20 to 30 mL of the whole-blood donation. This volume was subsequently used for infection disease and immunohematology testing. All other collection centers of the Sanquin Blood Banks used standard whole-blood collection systems without a diversion bag. In October 2002, a standardized skin disinfection method, with 70 percent IPA in a double-swab method, was introduced in all the collection centers of the Sanquin Blood Banks (including Nijmegen). During the whole period all apheresis PCs were collected with a diversion pouch included in the system.

In this report we evaluate data on bacterial contamination in the Netherlands for all apheresis PCs and PCs prepared from pools of five buffy coats (T5), collected in 2002 and 2003. The large numbers enable us to make a reliable judgment of the effect of diversion and/or changed disinfection method on the final degree of bacterial contamination of PC.

MATERIALS AND METHODS

Blood collection with or without diversion

Whole blood was collected under standard blood banking conditions with either a four-bag top and bottom citrate phosphate dextrose (CPD)-saline adenine glucose mannitol (SAGM) red cell (RBC) inline filter system (Compoflex, Fresenius Hemocare, NPBI International, Emmer-Compascuum, the Netherlands) or a comparable system (Baxter PL146-CPD-70 mL 3-Optipure, Baxter, Utrecht, the Netherlands).

Sanquin Blood Bank Region Southeast (Nijmegen, the Netherlands) used a five-bag top and bottom CPD-SAGM RBC inline filter system (Compoflex, Fresenius Hemocare, NPBI International) including an integrated sample bag (T3941, Fresenius Hemocare), in which diversion of the first 20 to 30 mL of the donation was performed. After collection of the first volume, a clamp was set and the sample bag was sealed. Donation proceeded normally in the collection bag with CPD. All other collection centers collected blood for infectious diseases and immunohematology testing after donation was completed via a sampling site attached to the collection system.

Processing to PCs

Whole blood is processed similarly at all collection centers after collection, with rapid cooling to 20°C and overnight storage at this temperature.[13] Briefly, after a hard centrifugation of the whole blood, the buffy coats are collected. Five buffy coats (same blood group) are pooled and mixed with either 300 mL of plasma or additive solution (AS; PAS I, Baxter). The pooled buffy coats are centrifuged again (soft centrifugation) to produce T5 products. Preparation procedures for T5 varied slightly between regions, but these differences (type of leukodepletion filter and storage container) are not likely to cause variations in the degree of bacterial contamination.

The blood bank locations of Rotterdam (Region Southwest), Utrecht (Region Northwest), and Nijmegen (Region Southeast) used PAS II as AS in the T5 products; all other blood bank locations used plasma for pooling.

Skin disinfection

Before October 2002 skin disinfection was performed with various methods in the Sanquin collection centers, referred to as the "old skin disinfection method." Most centers (>95% of total collections) used a single swab method with 70 percent alcohol–0.5 percent chlorhexidine or 70 percent IPA, but some small centers used single swabs with iodine tincture, whereas one small center used a double-swab method with 70 percent alcohol–0.5 percent chlorhexidine. Because no differences were found between the various centers for the old methods,

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the data for the old methods have been pooled (with and without exclusion of the center with the diversion bag). Starting from October 2002, a uniform disinfection method was introduced nationwide with a 30-second spaced double-swab method with 70 percent IPA. Sanquin Blood Bank Region Southwest introduced this new disinfection method in October 2002, the Regions Northeast and Southeast did so in November 2002, and Region Northwest introduced it in January 2003.

Screening on bacterial contamination

For the screening on bacterial contamination, within 2 hours after preparation of a T5 (this is 16-22 hr after collection) or within 12 hours after collection of the apheresis product, both aerobic and anaerobic culture bottles were inoculated (approx. 7.5 mL per bottle; range, 5-10 mL). Inoculation was performed under aseptic conditions with a laminar airflow cabinet, as reported previously.[7]

Culture bottles were incubated at 35°C in the BacT/ALERT system until flagged positive or up to 7 days if negative (also in those cases were the corresponding bottle became positive). Positively flagged bottles were sent to regional reference laboratories for determination by plating the sample. PCs and RBCs related to an initially positive bottle were taken out of inventory or recalled. Corresponding RBCs, if available from stock or recall, were cultured in the BacT/ALERT (for 7 days; both aerobic and anaerobic bottle), and positively flagged bottles were also sent to the reference laboratories for determination.

Study design and statistical analysis

Both initial culture test results and data on the microbiologic determination have been included in analyses of the results over the complete calendar years 2002 and 2003. The results were used to test the effects of the new disinfection method and/or the diversion on the degree of contamination. The results of the center with the diversion bag were compared to the pooled results of all other centers not with the diversion bag.

Data showing a positive initial test, but without determination results, have been labeled as missing. If the determination test could not detect microorganisms, the initial test result has been labeled as negative determination culture.

Because the hypothesis was that the contamination degree would be decreased after introduction of diversion and/or new disinfection, differences in frequency of bacterial contamination between the (sub)groups were tested with a one-sided chi-square test unless indicated otherwise. Logistic regression was used to calculate the odds ratios (OR) for risk of bacterial contamination with the different methods (diversion and disinfection). Multivariate logistic regression was performed to correct for possible confounding effects, such as seasonal effects and AS.

All statistical analyses were performed with computer software (SPSS, version 11.0, SPSS Inc., Chicago, IL).

RESULTS

Number of contaminated products

In 2002 and 2003, a total of 122,907 PCs were tested in the BacT/ALERT system, with an aerobic and an anaerobic bottle per product, each inoculated with 7.5 mL of PC. The majority of these PCs were T5, but 1814 products were made by pooling three buffy coats, with an initially positive signal rate of 0.39 percent (n = 7). A total of 8000 apheresis PCs were tested, with 0.30 percent (n = 24) initially positive in the BacT/ALERT system. Because of their small numbers, the products made by pooling three buffy coats are left out of further analysis, and the apheresis products are presented as separate group, with limited data analyses, leaving 113,093 T5 products.

In approximately 10 percent of initially positive results, with some variation per region, no microorganism could be cultured from the positive bottle. Infrequently, however, a microorganism could be isolated from one of the associated RBCs (9 of 106). For a limited number of initially positive samples no information was reported regarding determination culture (these are labeled as missing), but for the large majority (98%) data on determination were available.

Effects of diversion and disinfection methods

In Table 1 the frequency of bacterial contamination for the different collection methods is shown. Diversion was associated with a significant reduction of bacterial contamination from 0.95 to 0.50 percent (chi-square test, $p = 0.002$) with the old skin disinfection method and from 0.85 to 0.37 percent (chi-square test, $p = 0.001$) when the new disinfection method was applied. For collections without diversion, the new skin disinfection method compared to the old methods resulted in a mild reduction in initially positive samples from 0.95 to 0.85 percent (chi-square test, $p = 0.049$). For collections with diversion, the new skin disinfection method compared to the old method also resulted in a reduction in initially positive samples from 0.50 to 0.37 percent (chi-square test, $p = 0.18$).

Calculated on initially positive samples, diversion resulted in an OR of 0.47 (95% CI, 0.35-0.63; $p < 0.001$) with univariate logistic regression. Multivariate logistic regression, with correction for disinfection method, time of screening (season), and AS resulted in an OR of 0.49 (95% CI, 0.36-0.67; $p = 0.003$).

For the new disinfection, the OR was 0.88 (95% CI, 0.77-1.00; $p = 0.05$) in univariate analysis and 0.87 (95% CI,

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TABLE 1. Degree of contamination in subsets of T5 products*

Collection method	No diversion	Diversion	Total
Old skin disinfections			
Total tested	42,582	4,362	46,944
Initially positive (%)	405 (0.95)	22 (0.50)	427 (0.91)
Positive determination culture (%)	373 (0.88)	18 (0.41)	391 (0.84)
Negative determination culture (%)	26 (0.06)	4 (0.09)	30 (0.06)
Missing subculture data	6	0	6
70 percent IPA skin disinfection			
Total tested	59,400	6,749	66,149
Initially positive (%)	505 (0.85)	25 (0.37)	530 (0.80)
Positive determination culture (%)	427 (0.72)	17 (0.25)	444 (0.67)
Negative determination culture (%)	68 (0.11)	8 (0.12)	76 (0.11)
Missing subculture data	10	0	10
Total test period			
Total tested	101,982	11,111	113,093
Initially positive (%)	910 (0.89)	47 (0.43)	957 (0.85)
Positive determination culture (%)	800 (0.78)	35 (0.32)	835 (0.74)
Negative determination culture (%)	94 (0.09)	12 (0.11)	106 (0.09)
Missing subculture data	16	0	16

* Absolute numbers, within parentheses: percentages of total tested.

0.76-0.99; p = 0.03) with multivariate analysis corrected for time of screening (season), AS, and diversion. Because of the study design, correction for the region was not possible, but no significant differences between the regions were found. Removing individual centers from the analysis did not alter any of the conclusions and only marginally affected estimated effect sizes and CIs.

The effects of the various interventions have been evaluated, either with the percentages of initially positive samples or with the percentage of positive samples resulting in a positive determination culture. The percentage of initially positive samples determines the effect of the interventions on the numbers of PCs and related RBCs blocked by the screening and thus the consequences for blood banking logistics. The positive determination cultures reflect the effect of the interventions on the final degree of bacterially contaminated PCs. The ORs were slightly lower (with lower p values) when calculated on the number of positive determination cultures, owing to the increase in negative determination cultures after introduction of diversion and/or the new disinfection method.

Plasma compared to AS

At three collection centers (Rotterdam in Region Southwest, Utrecht in Region Northwest, and Nijmegen in Region Southeast), T5 products were prepared in a mixture of PLT AS (PAS II, Baxter) and plasma (65:35 ratio, vol/vol; n = 35 812). We have compared the contamination in PAS II products without diversion with plasma products without diversion to evaluate the effect of AS on the degree of contamination.

The frequency of bacterial contamination was slightly reduced in PAS II PLT products (0.86%) compared to plasma products (0.91%; chi-square test, p = 0.44, not significant). This difference did not change after the introduction of the 70 percent IPA.

Determination results

Table 2 summarizes the different species found in the contaminated T5 products, with classification in some origin-related groups. The majority of detected microorganisms were skin bacteria, mainly diphtheroids or coagulase-negative staphylococci (CNS; and other Gram-positive cocci). The other bacteria belong either to the transient skin bacteria or to the gastrointestinal tract.

After diversion, contamination with skin flora (Table 2; both diphtheroids [chi-square test, p < 0.001] and the CNS plus group [chi-square test, p = 0.001]) was significantly reduced, whereas the other groups were not significantly reduced. The fact that no bacteria belonging to the gastrointestinal tract were found after diversion is probably due to their low frequency in combination with the relatively small numbers tested. The fraction of initially positive bottles with a negative determination culture was higher with diversion, although not significantly so (chi-square test, p = 0.36).

When comparing the old disinfection method with the new disinfection method (without diversion), a significant reduction of the CNS plus group was found (Table 2; chi-square test, p < 0.001), but no reduction of diphtheroids. Contamination with other bacteria was slightly reduced; however, this difference was significant only for *Staphylococcus aureus* (chi-square test, p = 0.02). As for diversion, an increase in the fraction with a negative determination culture was observed (chi-square test, p = 0.002).

Some significant differences in the type of microorganisms were detected between plasma and PAS II PLT

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TABLE 2. Determination of initially positive samples*

Variable	Old disinfection, no diversion	New disinfection, no diversion	Diversion (both disinfections)	Totals
Number of PCs tested	42,582	59,400	11,111	113,093
Initially positive bottles	405	505	47	957
Missing determination	6	10	0	16
Skin flora				
Diphtheroids†	160 (0.38)	230 (0.39)	18 (0.16)	408
CNS plus‡	153 (0.36)	119 (0.20)	12 (0.11)	284
S. aureus§	9 (0.02)	3 (0.005)	1 (0.01)	13
Transient skin flora				
Bacillus spp.‖	25 (0.06)	35 (0.06)	4 (0.04)	64
Gastrointestinal tract flora				
Gram-negative rods¶	8 (0.02)	9 (0.02)	0	17
Streptococci	5 (0.01)	1 (0.002)	0	6
Peptostreptococci	9 (0.02)	15 (0.03)	0	24
Residual group				
Others	4 (0.01)	15 (0.03)	0	19
No microorganism	26 (0.06)	68 (0.11)	12 (0.11)	106

* Values given as absolute numbers (percentage of total tested samples), with an additional column adding up absolute numbers.
† Diphtheroids include: *Propionibacterium* spp. (mainly acnes), *Corynebacterium* spp., and unspecified diphtheroid rods or Gram-positive rods (not spore forming).
‡ CNS plus include all coagulase-negative *Staphylococcus* subspecies (mainly epidermidis) and Gram-positive cocci (less than 10% of the total; aerococci [2]; micrococci [5], and unspecified [16]).
§ Although there are limited reports on *S. aureus* contamination originating from endogenous bacteremia in the donor.
‖ *Bacillus* spp. (roughly 50% *B. cereus*), including some unspecified spore formers (12).
¶ Various species, i.e., pseudomonas (1), brevundimonas (1), flavomonas (2), bacterioides spp. (4), salmonella (1), proteus vulgaris (1), and some unspecified (6 aerobic, 1 anaerobic).

products. Both *S. aureus* and Gram-negative rods had a significantly lower frequency in PAS II products (chi-square test, $p = 0.01$, two-sided). Moreover, the frequency of initially positive bottles with a negative determination culture was lower in PAS II (chi-square test, $p = 0.01$, two-sided). These differences might be explained by a lower initial load with bacteria, because less potentially contaminated whole blood–derived material is used.

Aerobic and anaerobic bottles

Table 3 shows the mean time until the aerobic and anaerobic bottles became positive, in relation to the determination result. In general, aerobic bottles became positive sooner than anaerobic bottles. From the positive aerobic bottles only 35 (11%) turned positive after 5 days, whereas from the positive anaerobic bottles 221 (35%) turned positive after 5 days. Except for diphtheroid (more particularly the *Propionibacterium* spp.) and peptostreptococci species, most bacteria did not show a preference for either the aerobic or the anaerobic bottles (Table 3). This is in agreement with the results of spiking studies by Brecher and colleagues[14] showing for most bacteria growth in both the aerobic and the anaerobic bottle. During the test period, only 46 positively flagged units were reported to become positive in both the aerobic and the anaerobic bottle. It must be kept in mind that every negative bottle (also in case the corresponding bottle became positive) was cultured for 7 days.

Apheresis products

Table 4 shows some details for the 8000 apheresis PCs, all collected with an apheresis set including a diversion pouch. Owing to small numbers, the 95 percent CIs overlap, and no significant differences were found between the old and new disinfection methods. As for the T5, the percentage of positively flagged bottles without microorganism in the determination culture was higher after introduction of the new disinfection method (chi-square test, $p = 0.26$). In the apheresis PCs in two cases a Gram-negative rod was detected (0.03%; an *Escherichia coli* and a *Bacteroides* spp.), in one case a *Bacillus* spp. (0.01%), and in two cases a *Streptococcus* (0.03%). In eight cases the bacteria belonged to the CNS plus group (0.1%), in three cases the bacteria belonged to the diphtheroids group (0.04%), and in seven cases a negative determination culture was obtained (0.09%). These frequencies were comparable to those found in the T5 products after diversion (Table 2), except for diphtheroids (0.04% vs. 0.16% in T5).

Follow-up procedures after positive flagging

PCs. For 790 (83% of total) positively flagged T5, data on recall procedures were available (Table 5). From these units, 386 (49%) units had to be recalled and 404 units were still at the blood bank. The majority (88%) of the recalled products had already been transfused and only 45 of the recalled products could be prevented from being transfused (Table 5). Positively flagged units, which were

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TABLE 3. Growth characteristics for different bacteria species

Variable	Total number of bottles	No data on time until positive	Both bottles positive	Aerobic bottle		Anaerobic bottle	
				Time until positive*	Number	Time until positive*	Number
Total	957	38	46	1.8	330	4.0	635
Skin flora							
Diphtheroids†	408	5	4	3.7	45	5.0	362
CNS plus‡	284	2	26	1.1	165	2.6	143
S. aureus§	13	0	0	0.9	6	1.3	7
Transient skin flora							
Bacillus spp.‖	64	1	7	1.7	41	2.1	29
Gastrointestinal tract flora							
Gram-negative rods¶	17	0	0	1.9	10	2.9	7
Streptococci	6	0	3	2.8	4	3.0	5
Peptostreptococci	24	1	0		0	3.9	23
Residual group							
Others	19		3	1.3	9	4.0	13
No microorganism	106	13	3	2.3	50	2.4	46
Missing determination	16	16					

* Mean time in days until positive signal with BacT/ALERT.
† Diphtheroids include: *Propionibacterium* spp. (mainly acnes), *Corynebacterium* spp., and unspecified diphtheroid rods or Gram-positive rods (not spore forming).
‡ CNS plus include all coagulase-negative *Staphylococcus* subspecies (mainly epidermidis) and Gram-positive cocci (less than 10% of the total; aerococci [2]; micrococci [5], and unspecified [16]).
§ Although there are limited reports on *S. aureus* contamination originating from endogenous bacteremia in the donor.
‖ *Bacillus* spp. (roughly 50% *B. cereus*), including some unspecified spore formers (12).
¶ Various species, i.e., pseudomonas (1), brevundimonas (1), flavomonas (2), bactericides spp. (4), salmonella (1), proteus vulgaris (1), and some unspecified (6 aerobic, 1 anaerobic).

TABLE 4. Degree of contamination in subsets of apheresis products*

Variable	Old skin disinfections	70% IPA skin disinfection	Total test period
Total number tested	3037	4963	8000
Initially positive (%)	7 (0.23)	17 (0.34)	24 (0.30)
Positive determination culture (%)	6 (0.20)	12 (0.24)	18 (0.23)
Negative determination culture (%)	1 (0.03)	5 (0.10)	6 (0.08)
Missing subculture	0	1	1

* Absolute numbers, within parentheses: percentages of total tested. All apheresis products were collected with a set with diversion pouch.

already transfused at the moment of detection, had a mean time until detection of 4.7 days, whereas for the units still in the blood bank the mean time until detection was 2.2 days. Of 345 units with a positive signal in the first 48 hours of culture, only 27 units had already been transfused.

Table 5 also shows the recall information in relation to the various microorganisms. For the rapidly growing bacteria, most of the PCs were still in the blood bank inventory or could successfully be recalled. The majority of already transfused PCs were contaminated with diphtheroids, mainly flagging positive between Day 4 and Day 7 of culture.

During this surveillance period, no severe clinical effects of units flagged positive after transfusion were reported to Sanquin or the Dutch hemovigilance system (Transfusion Reactions in Patients; TRIP). Over the entire period, there were 165 follow-up reports (for every case a report was asked, but only in 40% a response was received) of transfused products corresponding to cultures flagged positive after release. In two cases mild clinical symptoms (fever) were reported, but no direct relation with the PLT transfusion was established. During the same period, two cases of sepsis were reported after transfusion of PCs with a negative signal in the screening[15] (also after 7 days of culturing). In both cases *Bacillus cereus* was identified as the causative microorganism, but it remains unclear whether this microorganism could have entered the PC during preparation or storage, due to pinholes in the bag, or whether it was definitely a false-negative result of the screening system (present in the sample, but not resulting in a positive flagging of the culture).

Related RBCs. In case of a positive signal in the bacterial screening of a pooled PLT product, corresponding RBCs were cultured. Data on RBC recall and cultures were available for 94 percent (901/957) of the initially positive flagged T5 units. In 40 percent of these cases there was a positive signal from the BacT/ALERT for one of the RBC units. In 85 percent of positive RBC units, the same microorganism as in the corresponding PC was found (majority diphtheroids). In the majority of cases where the microorganism was of different species, it belonged to the same group. Only in 27 cases was the microorganism found in

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TABLE 5. Recall and transfusion details with respect to corresponding PCs and RBC units

	Corresponding PC units				Related RBC units			
Variable	Total number of PCs	Unknown*	Recall†	Transfused‡	Total number of RBC units	Unknown*	Recall†	Transfused‡
Total	957	167	386	341	4785	375	741	138
Skin flora								
Diphtheroids§	408	57	256	234	2040	76	553	113
CNS plus‖	284	54	57	42	1420	85	92	12
S. aureus¶	13	0	0	0	65	2	0	0
Transient skin flora								
Bacillus spp.**	64	10	16	12	320	15	28	2
Gastrointestinal tract flora								
Gram-negative rods††	17	0	3	3	85	25	2	1
Streptococci	6	1	1	1	30	0	1	0
Peptostreptococci	24	3	14	12	120	2	16	3
Residual group								
Others	19	3	11	9	95	0	6	1
No microorganism	106	23	28	28	530	90	43	6
Missing determination	16	16			80	80		

* No data on recall available.
† Recall of products already released to hospitals.
‡ Already transfused at time of recall.
§ Diphtheroids include: *Propionibacterium* spp. (mainly acnes), *Corynebacterium* spp., and unspecified diphtheroid rods or Gram-positive rods (not spore forming).
‖ CNS plus include all coagulase-negative *Staphylococcus* subspecies (mainly epidermidis) and Gram-positive cocci (less than 10% of the total; aerococci [2]; micrococci [5], and unspecified [16]).
¶ Although there are limited reports on *S. aureus* contamination originating from endogenous bacteremia in the donor.
** *Bacillus* spp. (roughly 50% *B. cereus*), including some unspecified spore formers (12).
†† Various species, i.e., pseudomonas (1), brevundimonas (1), flavomonas (2), bacteroides spp. (4), salmonella (1), proteus vulgaris (1), and some unspecified (6 aerobic, 1 anaerobic).

the RBCs totally unrelated to the organism as found in the PCs. This number included the 9 cases with no determination culture for the PC, whereas a microorganism could be isolated from one of the associated RBC units. The bacterial species in these cases were CNS plus (4), diphtheroids (4), and *Bacillus* spp. (1).

Of a total of 4505 RBC units (901 PCs each with 5 related RBC units), 741 RBC units had already been released and had to be recalled for culturing. The recall was successful in 68 percent of the cases. A total of 234 units were not available for culture, including 138 RBC units (relating to 99 PC units) that had already been transfused. For 69 of these 138 cases, one of the other related RBC units contained the same bacterium as found in the culture from the PC. From this it might be concluded that only in the remaining 69 cases possibly contaminated RBCs were transfused. These were mainly related to positive PLT cultures in which diphtheroids found (66/69). Because RBCs are stored at 4°C, however, it is not likely that these transfused RBCs contained harmful quantities of bacteria. This is supported by the fact that no transfusion reactions were reported for these units.

DISCUSSION

Based on the results of two calendar years (2002 and 2003) of bacterial screening of all PCs in the Netherlands, it can be concluded that interventions to reduce bacterial contamination were very effective, resulting in a reduction of initially positive cultures for pooled T5 products from 0.95 percent (no interventions) to 0.37 percent (two interventions: diversion and new skin disinfection). The 50 percent reduction in frequency upon diversion is very similar to that found in our previous whole-blood diversion study[10] and also corresponds with the reduction in contamination reported by McDonald and coworkers.[16] The double-swab 70 percent IPA disinfection method slightly enhanced the reducing effect on bacterial contamination of diversion, although this is of marginal significance and without synergy. The final frequency of 0.37 percent (95% CI, 0.24-0.55) positive cultures found for pooled T5 products after introduction of both diversion and new disinfection method is not significantly different from the 0.30 percent contamination rate for single donor apheresis PC (95% CI, 0.19-0.45), whereas the differentiation profile is also similar. This suggests that the relation between number of donor units and degree of bacterial contamination of the final PC, as described by Ness and colleagues,[1] no longer exists if special care is taken to avoid introduction of bacteria during collection. The finding that contamination is reduced to such a large extent by diversion has led to the introduction of the diversion pouch throughout the Netherlands, starting from July 2004.

Our current screening system for bacterial contamination of PC is highly sensitive by use of two bottles. The

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fact that in less than 5 percent of positively flagged units both bottles were positive suggests that positive units have an initial bacterial contamination around the lower detection limit of the culture system. Owing to the high sensitivity, the percentage of initially positive units is relatively high in our screening system compared to other reported rates of bacterial contamination. Most likely, this is due to the fact that other studies use only one culture bottle, with lower inoculation volumes and shorter culture times. Wagner and Robinette[17] showed that higher inoculation volumes lead to shorter detection times. Our results are very similar to those in Belgium, where a similar screening approach is used.[18,19] When reanalyzing our results according to the system used in Denmark, that is, only the aerobic bottle and 5 days of culture, our result of 0.4 percent initially positive for T5 (with double-swab disinfections and without diversion) is very comparable to the Danish results.[20] Also for apheresis units, the recalculated initially positive rate of 0.1 percent (only aerobic bottle, 5 days culturing) resembles the values reported by other groups[1] taken into account that our inoculated volume is larger.

The selectivity of a screening system should be as high as possible, because false-positive samples result in unnecessary recalls and false-negative samples result in possible transfusion of positive units. For some as yet unknown reason, the rate of negative determination cultures is increased after the introduction of interventions for disinfection and diversion. The fraction of negative determination cultures is 0.047 percent of total tested bottles (two per unit), which is in agreement with data from Belgium and Denmark.[18,20] This would result in a false-positive rate by system failure of about 1 of 2000 cultures. Given that in 9 percent of cases with a negative determination culture for PCs, one of the RBC units contained a microorganism, it remains questionable whether a negative determination culture really should be flagged false-positive. Another possibility would be that in some cases the microorganism still has growth capacity (positive signal in BacT/ALERT), but no colony-forming properties (negative determination culture). This possibility is not hypothetical, because experiments from our group showed that after UV-C illumination the survival of bacteria is much higher (about 1.5 log) when measured in liquid culture, compared to measurement of colony formation on solid media (unpublished results). Based on these results, we intend to implement a follow-up procedure for negative determination cultures, with additional attempts to obtain a subculture.

The effect of introducing a standardized double-swab 70 percent IPA disinfection method showed borderline significance in both univariate and multivariate statistical testing with respect to reduction of bacterial contamination. This is in contrast to literature results. McDonald and colleagues[16] reported a possible reduction of approximately 50 percent by the introduction of double-swab disinfection. These results, however, were obtained with a first swab with IPA and a second swab with iodine tincture, which might explain differences in the results. Lee and coworkers[21] recently also reported a significant reduction of the degree of bacterial contamination of PCs prepared from whole blood by the PLT-rich plasma method, as a result of a changed disinfection method. With respect to skin flora, however, as expected, our new disinfection method has a highly significant reducing effect on the CNS plus group, but no effect on diphtheroids. This can be explained by the fact that diphtheroids especially colonize the interior of the sebaceous glands[22] whereas Gram-positive cocci, including CNS, are more on the skin surface. Surface disinfection will therefore be less adequate to remove diphtheroids, whereas diversion will reduce all kind of skin flora, as found in our study.

The various bacteria species detected in 2 years of bacterial screening of PCs in the Netherlands are classified as skin flora, transient skin flora, or gastrointestinal tract flora, with some very rough subclassification. Within the skin flora, the relatively slowly growing diphtheroids (either anaerobic *Propionibacterium* or aerobic *Corynebacterium*) represent the largest group. These bacteria are usually not considered being a clinical hazard[14,23] but there are some reports describing transfusion-transmitted bacterial infection (TTBI) with *Propionibacterium*.[24,25] Diphtheroids also are among the Gram-positive bacteria that can colonize prosthetic valves and intravascular implants, causing infections that are difficult to treat.[26] Upon prolongation of storage time to 7 days or longer, and without a screening system able to detect these bacteria, one should be aware of transmission of slow-growing bacteria, such as *Propionibacterium* spp. This problem is currently not encountered, because PCs containing these bacteria are generally transfused before reaching the threshold for inducing TTBI in the recipient.

The second largest group are the Gram-positive cocci not being *S. aureus* (CNS plus). These commensal skin flora are not considered very pathogenic either. Gram-positive cocci, however, are a regular cause of TTBI[24,27] but seldom responsible for septic fatalities.[28] The small subgroup of *S. aureus* is the type of skin flora with a high clinical hazard profile[1] but all 13 cases found in our surveillance had a positive culture before the products were released.

The *Bacillus* spp. belongs to the transient skin flora and this group includes some not further determined spore formers. Owing to the etiology of infection (we are only considering transmission via transfusion), no further distinction was made between *B. cereus* (known from food poisoning) and other *Bacillus* spp. The new disinfection method has no effect on the frequency of this group, as expected, because spores are not inactivated by 70 percent IPA. Diversion is expected to result in a reduc-

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tion for spore formers, but the observed reduction is not significant, likely because of the low numbers. Because spore formers remain a risk to cause TTBI even with bacterial culturing in place, further research should be focused on improved disinfection also effective in inactivating spores.

Approximately 5 percent of all initial positive samples were determined as normally belonging to the gastrointestinal tract flora, although these bacteria can also be encountered as transient skin flora. The largest subgroup are the anaerobic *Peptostreptococci* spp. (associated with abdominal wound infections) and some *Streptococcus* spp., which are often reported in transfusion-associated sepsis.[26]

The group of Gram-negative rods is very heterogeneous, with *Bacteroides* spp. and *Salmonella* spp. highly likely to have come from the donor's blood circulation. The aerobic Gram-negative rods, although we did not fully determine the species in all cases, are most probably nonfermentative bacilli and are highly likely to have been introduced as transient skin flora. The Gram-negative rods are well known as causative agents for TTBI, especially those cases related to septic fatalities.[1,2,24,25,28] In our study most products positive for the presence of Gram-negative rods were prevented from entering the transfusion chain. In the single case with a transfused RBC unit, the culture turned positive after 5 days.

Among the remaining group, one remarkable microorganism is found, a *Nocordia* spp., well known as transient skin flora present in soil and causing pneumonia, especially in immunocompromised patients or in chronic lung disease.

Despite the absence of a quarantine period, in the Dutch practice more than 90 percent of the units that flagged positive within 2 days could be prevented from being transfused, including the majority of those contaminated with the more dangerous bacteria like Gram-negative bacteria, *B. cereus* and *S. aureus*. Ninety percent of units flagged positive after being released had a positive signal after more than 2 days of culturing. These units were mainly found to be contaminated with diphtheroids, especially *Propionibacterium* spp. and the majority of these units had already been transfused. During the period of the study, two mild transfusion reactions were reported due to transfusion of such units. In general, however, underreporting is noticed in hemovigilance systems, emphasizing the need for improvement. Extension of the storage period of PCs from 5 to 7 days allows for an initial quarantine period as proposed by Munksgaard and colleagues[20] but this will have a very limited impact on the number of PCs already transfused at the time of a positive culture.

In conclusion, it is shown that introduction of diversion and improvement of skin disinfection are effective in reducing the frequency of contaminated blood products. Still, the remaining risk is high enough to warrant screening for bacterial contamination. The screening system in place in the Netherlands proves to be successful in preventing the seriously contaminated PCs from entering the transfusion chain, a similar conclusion to that reported for Belgium[19] with a similar screening system.

ACKNOWLEDGMENT

The authors thank M.P. Janssen, PhD (Julius Center for Health Sciences and Primary Care, UMC, Utrecht, the Netherlands), for help with the statistical analysis.

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Contamination Rates of Blood Cultures Obtained by Dedicated Phlebotomy vs Intravenous Catheter

Alonna Norberg, MD
Norman C. Christopher, MD
Maria L. Ramundo, MD
John R. Bower, MD
Shirley A. Berman, RN

Context Blood culture is the criterion standard for identifying children with bacteremia. However, elevated false-positive rates are common and are associated with substantial health care costs.

Objective To compare contamination rates in blood culture specimens obtained from separate sites vs through newly inserted intravenous catheters.

Design, Setting, and Participants Observational study conducted January 1998 through December 1999 among patients aged 18 years or younger who were seen at a US children's hospital emergency department and had a blood culture obtained as part of their care. Medical records were reviewed in all cases with a positive blood culture. Patients with indwelling vascular catheters were excluded.

Intervention All phlebotomy was performed by emergency department registered nurses. During the baseline phase, blood specimens for culture were obtained simultaneously with intravenous catheter insertion. During the postintervention phase, specimens were obtained by a separate, dedicated procedure.

Main Outcome Measure Contamination rate in the postintervention period compared with the baseline period.

Results A total of 4108 blood cultures were evaluated, including 2108 during the baseline phase and 2000 in the postintervention phase. The false-positive blood culture rate decreased from 9.1% to 2.8% ($P<.001$). A statistical process control chart demonstrated a steady-state process in the baseline phase and the establishment of a significantly improved steady state in the postintervention phase. Young age was associated with increased contamination rate in both the baseline and postintervention periods.

Conclusion Blood culture contamination rates were lower when specimens were drawn from a separate site compared with when they were drawn through a newly inserted intravenous catheter.

JAMA. 2003;289:726-729 www.jama.com

FEVER IS THE PRIMARY COMPLAINT in up to 20% of children presenting to emergency departments,[1] and bacteremia is the source of fever in 1.5% to 2.3% of these patients.[2,3] Blood culture is the criterion standard for identifying children with bacteremia[4-7]; however, false-positive blood cultures are common and may add significantly to health care costs.[8-11] High rates of contamination are common among pediatric patients, likely related to difficulties inherent to phlebotomy in young patients.[12] To minimize the number of venipunctures in children, blood culture specimens are obtained simultaneously with intravenous catheter placement in many emergency departments. The impact of using intravenous catheters to obtain blood cultures is unclear.[13-16] We hypothesized that the blood culture contamination rate would be less when blood culture specimens were obtained from a remote site rather than through a newly inserted intravenous catheter.

METHODS

A preintervention and postintervention observational study of patients who had a blood culture obtained as part of their routine emergency department course was conducted. Patients 18 years old or younger who presented to the emergency department at a free-standing tertiary care children's hospital that evaluates more than 65 000 children annually and required a blood culture as part of their routine care were eligible. Patients were identified by computerized search of the hospital database.

Laboratory specimens were obtained based on clinical and laboratory indications and were drawn by an emergency department registered nurse. The protocols for skin antisepsis and

Author Affiliations: Divisions of Emergency Medicine (Drs Norberg, Christopher, Ramundo, and Ms Berman) and Infectious Diseases (Dr Bower), Department of Pediatrics, Children's Hospital Medical Center of Akron, Akron, Ohio; and Departments of Emergency Medicine and Pediatrics, Northeastern Ohio Universities College of Medicine, Rootstown (Drs Norberg, Christopher, Ramundo, and Bower).
Corresponding Author and Reprints: Norman C. Christopher, MD, Division of Emergency Medicine, Children's Hospital Medical Center, One Perkins Square, Akron, OH 44308 (e-mail: Nchristopher@CHMCA.org).

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for specimen collection and inoculation were standardized and remained unchanged during the study. Nursing staff members were unaware of ongoing data collection and analysis. In cases where a positive blood culture was reported, the patient's medical record was reviewed. Patients with indwelling devices (central venous lines, ventricular catheters) were excluded.

Baseline Phase

During the baseline phase (January 1, 1998-November 19, 1998), culture specimens were obtained through a newly inserted peripheral intravenous catheter using the standard over-the-needle approach. A sterile 5-mL syringe was attached to the catheter hub, and blood for both culture and for laboratory studies was withdrawn; the first portion of the sample was used for culture.

During the first 4 months of the baseline phase, focused efforts to decrease the contamination rate were implemented. Because these interventions failed to reduce the contamination rate, the standard technique was abandoned in favor of obtaining specimens from a separate phlebotomy site. Data from a 6-week implementation phase (November 20, 1998-December 31, 1998) were not included in the analysis.

Postintervention Phase

During the postintervention phase (January 1, 1999-December 31, 1999), culture specimens were obtained by venipuncture at a dedicated site. If a patient required an intravenous catheter, it was placed using the standard approach at a site distant from the blood culture venipuncture site. While laboratory specimens were sometimes obtained through the newly inserted intravenous catheter, all specimens for culture were obtained by phlebotomy dedicated to that procedure.

Classification of Blood Culture Isolates

Blood culture isolates were categorized as contaminants or pathogens. In all cases, *Neisseria meningitidis*, *Streptococcus pneumoniae*, *Salmonella* species, *Haemophilus influenzae*, and group A or group B β-hemolytic streptococci were considered pathogens. A contaminant was defined as a nonpathogenic microorganism.[15] If pathogenicity was uncertain or variable, assignment was made in consultation with an infectious disease expert (J.R.B.), with consideration of patient demographics and the clinical setting. Assignment was made without knowledge of the intervention phase. Because the presence of even a single nonpathogenic species in the blood culture specimen represented improper phlebotomy technique, a specimen with multiple bacteria was considered contaminated.

Decisions regarding treatment and follow-up of patients were made by clinicians in the emergency department based on current practice. The institutional review board of the Children's Hospital Medical Center of Akron approved the study protocol. Consent was not obtained from families. The intervention was adopted as our standard of care, and data was collected in a blinded database for analysis.

Data Analysis

Data were analyzed using STATA Version 7.0 (Dallas, Tex, 2001). Univariate analysis was performed unless stated otherwise. Pearson χ^2 was used to analyze categorical data. Descriptive analysis of continuous data was performed. $P<.05$ was the level of significance.

Statistical process control methodology was also used to examine the impact of the intervention over time. A run chart was constructed showing the blood culture contamination rate for each month of the study ([number of contaminated specimens × 100]/[number of blood cultures obtained]). The mean blood culture contamination rate and the upper and lower control limits were established based on the preintervention data, with control limits representing ±3 SD from the mean.[16-18]

Table 1. Patient Demographics

	Baseline (n = 2106)	Postintervention (n = 2000)
Age, median (IQR), y	1.4 (0.47-3.8)	1.4 (0.42-3.4)
Emergency department disposition, No. (%)		
Admit	1099 (52.0)	1042 (52.0)
Discharge	1009 (48.0)	958 (48.0)
Age category, No. (%)		
<12 wk	385 (18.3)	353 (17.7)
3 mo-≤2 y	887 (42.1)	891 (44.6)
>2 - ≤5 y	391 (18.5)	381 (19.1)
>5 y	445 (21.1)	375 (18.8)

Abbreviation: IQR, interquartile range.

RESULTS

During the study, 4448 blood culture specimens were obtained. We excluded 289 specimens obtained during the 6-week implementation phase, 14 with incomplete data in the medical record and 37 because of the presence of central venous catheters, leaving 4108 emergency department visits for analysis (2108 in the baseline phase and 2000 in the postintervention phase). Overall, there were 324 positive blood culture specimens.

Patient demographics are presented in TABLE 1. There were no statistically or clinically important differences between patients in the baseline and in the postintervention phases.

During the baseline phase, 223 positive blood culture specimens were reported; of these, 32 specimens grew a pathogen. In the 191 blood culture specimens categorized as contaminated, 243 organisms were cultured (TABLE 2). The overall false-positive rate was 9.1% and the true-positive rate was 1.5%. In the postintervention period, there were 101 positive blood cultures; of these, 45 grew a pathogen. In the 56 contaminated specimens, 65 organisms were cultured (Table 2). The overall false-positive rate during the

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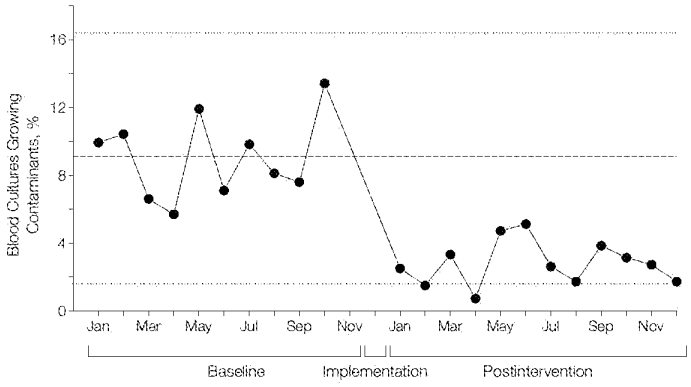
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Table 2. Blood Culture Contaminants in the Baseline and Postintervention Periods of Study

Contaminants	No. of Organisms (% of Total Contaminated Specimens)	
	Baseline*	Postintervention
Coagulase-negative staphylococci	140 (73)	37 (67)
Streptococcus viridans	57 (30)	8 (14)
Corynebacterium species	13 (7)	7 (12)
Micrococcus species	13 (7)	5 (8)
Bacillus species	3 (1.6)	3 (5)
Propionibacterium acnes	4 (2)	0
Neisseria species	3 (1.6)	0
Others	10 (5)	5 (8)
Total No. of Organisms	**243**	**65**

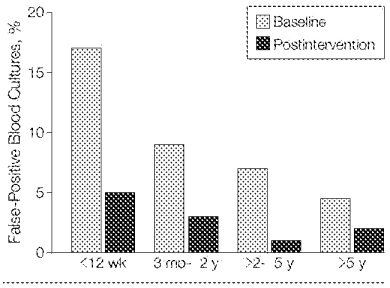
*There were 191 contaminated specimens growing 243 organisms in the baseline phase and 56 contaminated specimens growing 65 organisms in the postintervention phase of the study.

Figure 1. Statistical Process Control Chart Showing the Percentage of All Blood Cultures Growing Contaminants by Month, for the 2-Year Study Period



The upper and lower control limits (dotted lines) represent ±3 SD from the mean (dashed line). The mean, upper control limit, and lower control limit are calculated based on data in the baseline phase of the study.

Figure 2. Blood Culture Contamination Rate, by Age Category, During the Baseline and Postintervention Phases of Study



postintervention period was 2.8%, with a true-positive rate of 2.3%. Using a 2-sample test of proportions, the contaminated blood culture rate in the postintervention phase is significantly decreased when compared with the baseline phase ($P<.001$). The increase in true-positive rates did not reach statistical significance ($P=.20$).

The statistical process control chart (FIGURE 1) shows 12 consecutive data points below the mean established in the baseline phase in the postintervention phase, indicating a special cause effect (the intervention) and a significant change in the measured outcome (the contamination rate).[19]

The contamination rates in the baseline and postintervention phases are higher the younger the child (FIGURE 2). For example, in the baseline phase, the contamination rate in patients younger than 12 weeks was 17%, compared with 4.5% in those older than 5 years.

COMMENT

The contamination rates were significantly lower when blood culture specimens were drawn from a separate and dedicated venipuncture site compared with through a newly inserted intravenous catheter in children seen in a busy emergency department. The low rates have been sustained since the end of the study.

The statistical quality control methodology we applied provides a simple graphical display of process data that enhances our ability to understand outcomes that occur over time.[17] This methodology has been used increasingly in the evaluation of processes occurring in the health care setting.[16,20,21] The premise is that when a process achieves steady state, it is likely to remain there until events cause it to shift to a new steady state.[18,19]

This study addresses a common problem that has been linked to substantial and unnecessary resource utilization.[9,10,22-24] The contamination rate in our emergency department was resistant to change in spite of several specific interventions intended to address the problem. The sole procedural change was in the method by which blood culture specimens were obtained. During the baseline phase, the overall false-positive blood culture rate was 9.1% compared with a rate of 2.8% after the intervention, representing a decrease of 70%. While not statistically significant, the true-positive rate increased from 1.5% at baseline to 2.3% after the intervention. We believe that at least some of this increase is due to more selective ordering of blood cultures during the postintervention phase, when all cultures were obtained in response to other diagnostic tests obtained during the patient's emergency department evaluation. Since it is easier to obtain blood for culture from an intravenous catheter, cultures may have been obtained more indiscriminately in the baseline phase.

Previous studies comparing contamination rates in specimens obtained through newly inserted intravenous catheters or by phlebotomy at a remote

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site suggest that the 2 techniques are essentially equivalent. Smart and Baggoley[22] failed to show a difference in the contamination rate in 940 adult patients randomized to phlebotomy by either venipuncture or by placement of an intravenous catheter. Isaacman and Karasic[14] prospectively evaluated a convenience sample of 99 pediatric patients, each of whom had 2 blood cultures obtained, one by venipuncture and one through a newly inserted intravenous catheter. The authors demonstrated a low contamination rate with both techniques, concluding that newly inserted intravenous catheters offer an alternative to a separate venipuncture procedure in patients requiring blood culture. The small number of patients enrolled and the impact of the nursing staff's awareness of the study protocol may have biased the results.

On the other hand, a study by Ramsook et al[15] suggested that blood culture contamination rates were decreased when using dedicated phlebotomy compared with those obtained through a newly inserted intravenous catheter. Importantly, this study demonstrated the highest contamination rates in patients younger than 3 months of age, regardless of the collection method used, a finding confirmed in our study. Because staff members were aware of ongoing data collection, the potential effect on their phlebotomy technique is unknown.

However, our study also has limitations; because medical records were reviewed only for those patients with positive blood cultures, detailed information about patients with negative blood cultures is not known. In particular, information about antibiotic pretreatment is unknown. While it is likely that some patients were prescribed systemic antibiotic therapy prior to or during their emergency department evaluation, the rates of antibiotic pretreatment in the baseline and postintervention phases of the study are likely to be similar and unlikely to affect the study's conclusions. In addition, this protocol was implemented in a single unit and may not be generalizable to other settings. Finally, no concurrent control group was included to account for secular temporal changes.

Obtaining blood cultures from a separate site requires the patient to undergo an additional procedure for phlebotomy, but the overall benefit in terms of costs associated with a high contamination rate is likely to be substantial. During the baseline period, there were 6 contaminated specimens for every true-positive blood culture, compared with a ratio of 1.2:1 after implementation of the intervention. If subsequent patient management is based on preliminary blood culture results, false-positive test results will result in repeat emergency department visits, unnecessary medical interventions, unnecessary antibiotic therapy, and even hospital admission. One study[5] found that 26% of children followed as outpatients who had false-positive blood cultures were hospitalized unnecessarily, and that unnecessary use of antibiotics was significantly increased in the presence of false-positive blood culture results. Additional costs that are more difficult to quantify include staff effort and time required to arrange follow-up for patients, exposure of patients to unnecessary procedures, and cost and inconvenience related to repeat emergency department and/or hospital visits.[10,24]

Author Contributions: *Study concept and design:* Norberg, Christopher, Ramundo, Berman.
Acquisition of data: Norberg, Christopher, Ramundo, Berman.
Analysis and interpretation of data: Norberg, Christopher, Bower.
Drafting of the manuscript: Norberg, Christopher, Bower.
Critical revision of the manuscript for important intellectual content: Norberg, Christopher, Ramundo, Bower, Berman.
Statistical expertise: Christopher.
Administrative, technical, or material support: Norberg, Berman.
Study supervision: Christopher, Ramundo, Bower.

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Bibliographic data: EP1665986 (A1) — 2006-06-07

Blood collection set with an expanded internal volume

Inventor(s): BENNETT MICHAEL C [US]; CONWAY HUGH T [US] ± (BENNETT, MICHAEL C, ; CONWAY, HUGH T)

Applicant(s): BECTON DICKINSON CO [US] ± (BECTON, DICKINSON AND COMPANY)

Classification: - **international:** ***A61B5/154; A61B5/155***
- **cooperative:** **A61B5/15003 (EP, US); A61B5/150213 (EP, US); A61B5/150221 (EP, US); A61B5/150389 (EP, US); A61B5/150503 (EP, US); A61B5/150572 (EP, US); A61B5/15074 (EP, US); A61B5/150992 (EP, US); A61B5/1545 (EP, US)**

Application number: EP20050111371 20051128 Global Dossier

Priority number(s): US20040631515P 20041129 ; US20050280622 20051116

Also published as: EP1665986 (B1) BRPI0505336 (A) JP2006150083 (A) JP4914601 (B2) US2006129064 (A1)

Abstract of EP1665986 (A1)

The blood collection set includes an IV needle assembly, a length of flexible plastic tubing extending from the IV needle assembly and a non-patient needle assembly. The set is formed with an internal chamber that increases the internal volume of the blood collection set. Thus, the increase in internal volume allowing for greater flash visualization on venous entry.

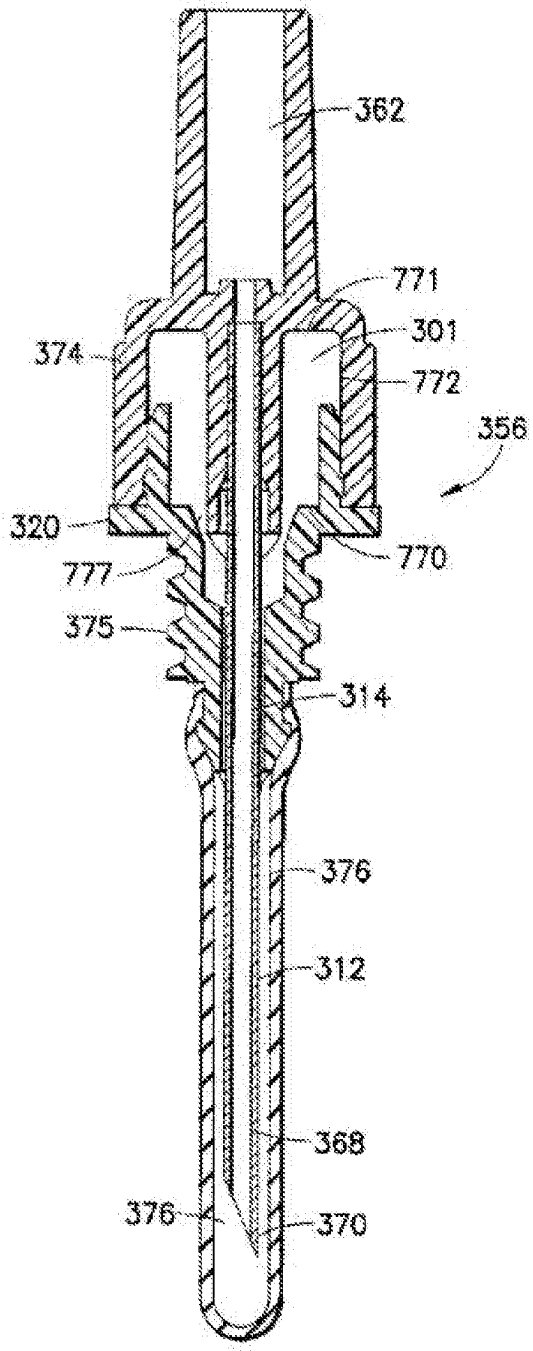


FIG.4

(19) Europäisches Patentamt
European Patent Office
Office européen des brevets

(11) EP 1 665 986 A1

(12) EUROPEAN PATENT APPLICATION

(43) Date of publication:
07.06.2006 Bulletin 2006/23

(51) Int Cl.:
A61B 5/154 *(2006.01)* ***A61B 5/155*** *(2006.01)*

(21) Application number: **05111371.0**

(22) Date of filing: **28.11.2005**

(84) Designated Contracting States:
AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IS IT LI LT LU LV MC NL PL PT RO SE SI SK TR
Designated Extension States:
AL BA HR MK YU

(30) Priority: **29.11.2004 US 631515 P**
16.11.2005 US 280622

(71) Applicant: **Becton, Dickinson and Company**
Franklin Lakes,
New Jersey 07417-1880 (US)
Designated Contracting States:
DE ES FR GB IT

(72) Inventors:
- **Bennett, Michael C.**
Summit, NJ 07901 (US)
- **Conway, Hugh T.**
Verona, NJ 07044 (US)

(74) Representative: **Weber, Thomas**
von Kreisler Selting Werner,
Bahnhofsvorplatz 1,
Deichmannhaus am Dom,
50667 Köln (DE)

(54) Blood collection set with an expanded internal volume

(57) The blood collection set includes an IV needle assembly, a length of flexible plastic tubing extending from the IV needle assembly and a non-patient needle assembly. The set is formed with an internal chamber that increases the internal volume of the blood collection set. Thus, the increase in internal volume allowing for greater flash visualization on venous entry.

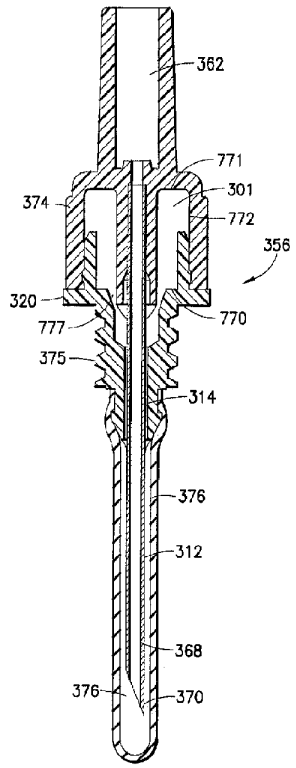


FIG.4

EP 1 665 986 A1

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Description

BACKGROUND OF THE INVENTION

[0001] This application claims priority to U.S. Provisional Application No. 60/631,515, which was filed on November 29, 2004.

1. Field of the Invention

[0002] The subject invention relates to a blood collection set with an internal chamber, which increases the internal volume of the blood collection set thereby improving flash.

2. Description of the Related Art

[0003] Phlebotomy procedures often are carried out using a blood collection set. A typical blood collection set includes an IV needle assembly with an IV cannula that has a proximal end, a sharply pointed distal end and a lumen extending between the ends. The needle assembly also includes a plastic IV hub with a proximal end, a distal end, and a passage extending between the ends. The proximal end of the IV cannula is mounted in the passage of the IV hub so that the lumen through the IV cannula communicates with the passage through the IV hub. The needle assembly may further include a shield for shielding the IV cannula after use (a so called safety blood collection set) and a packaging cover for safely covering the IV cannula prior to use. Packaging covers typically are rigid tubes with a proximal end that can be telescoped over the IV cannula and frictionally engaged with the distal end of the IV hub. Shields for shielding the IV cannula of blood collection sets have taken many forms. Some shields are telescoped over the IV hub and can be moved from a proximal position where the cannula is exposed to a distal position where the cannula is shielded. Other shields are hinged to the IV hub and can be rotated from an open position where the IV cannula is exposed to a closed position where the IV cannula is shielded. A needle assembly for a blood collection set also may include two flexible wings that project transversely from the IV hub or from the shield. The wings can be folded into face-to-face relationship with one another to effectively define a handle that facilitates manipulation of the needle assembly. The wings then can be rotated away from one another and held against the skin of the patient.

[0004] Blood collection sets also include a length of flexible plastic tubing. The tubing has a distal end that is connected to the proximal end of the IV hub, The tubing also has a proximal end that is connected to a plastic fitting. Thus, fluid communication is provided between the lumen of the IV cannula and the plastic fitting at the proximal end of the flexible tubing. The plastic fitting may be a female luer fitting that can be connected to a male luer fitting. The fitting then can be placed in communication with a reservoir or container for collecting a sample of blood.

[0005] Phlebotomy procedures often employ evacuated tubes, such as the VACUTAINER® brand of evacuated tubes sold by Becton Dickinson and Company. Evacuated tubes often are used with a tube holder that has a proximal end, a distal end, and a tubular side wall extending between the ends. The proximal end of the holder is widely open and is configured for slidably receiving the evacuated tube. The distal end of the holder typically includes an end wall with a mounting aperture. The mounting aperture includes internal threads or other mounting structures.

[0006] The tube holder may be used with a non-patient needle assembly that has a non-patient hub with external surface configurations for mounting in the mounting aperture of the holder. The non-patient needle assembly further includes a non-patient cannula extending proximally from the hub and a multiple sample sleeve telescoped over the non-patient cannula and mounted to the proximal end of the hub. The hub of the non-patient needle assembly can be threaded or otherwise engaged in the mounting aperture of the tube holder so that the non-patient needle and the multiple sample sleeve project into the tube receiving chamber of the holder.

[0007] The blood collection set may be used by mounting the fitting at the proximal end of the flexible plastic tubing to the distal end of the hub of the non-patient needle assembly. The packaging shield that covers the non-patient cannula then may be removed, and the hub of the non-patient needle assembly may be engaged with the tube holder. The medical practitioner then grips the IV needle assembly and removes the packaging cover from the IV cannula. The gripping of the IV needle assembly may include folding the flexible wings into face-to-face engagement and gripping the folded wings between a thumb and forefinger. The pointed distal end of the IV cannula then is urged into a targeted blood vessel. The wings then may be folded into engagement with the skin of the patient and may be taped in position. An evacuated tube then is urged into the open proximal end of the blood collection tube holder so that the non-patient needle pierces the stopper of the evacuated tube. As a result, the blood vessel of the patient is placed in communication with the interior of the evacuated tube, and the pressure differential between the blood vessel and the evacuated tube will generate a flow of blood through the IV cannula, through the passage of the IV hub, through the flexible tubing, through the non-patient hub and finally through the non-patient needle and into the evacuated tube.

[0008] The translucent or opaque plastic material of blood collection sets and IV cannula shields, combined with numerous cannula shield mechanism components and the length of the typical needle hub tends to inhibit a clear indication of venous or arterial access. Blood flow into the plastic tubing does provide an indication of venous or arterial access (known as "flash") as the plastic

tubing is often formed from a highly translucent or transparent plastic material. However, because of the existence of the elements associated with the IV needle assembly the length of flash obtained from a typical venous entry may not be sufficient for blood flow to be observed in the flexible tubing at a location proximal to the IV needle assembly itself. Thus, a medical practitioner may have a delayed indication of venous or arterial access and may incorrectly assume that the blood vessel was not accessed properly. In these situations, the medical practitioner may try to access the blood vessel again even though the initial access was successful. Accordingly, the patient may be subjected to unnecessary trauma during a repeated attempt to access the targeted blood vessel. Thus, improved techniques for increasing the length of flash such that initial blood flow will be observable in the flexible tubing proximal the IV needle assembly and associated shielding elements would be desirable.

SUMMARY OF THE INVENTION

[0009] The invention relates to a blood collection set with an internal chamber provided to increase the internal volume of the blood collection set when compared to a prior art blood collection set which does not have an internal chamber. In this manner, improved flash visualization, can be provided.

[0010] "Internal chamber" as used herein means an enclosed space or compartment, which is in communication with the fluid passage of the blood collection set. The "fluid passage" is defined as any part of the blood collection set in which blood flows and can include the lumen through the IV cannula, the passage through the IV hub, the passage through the flexible tubing, the passage through the non-patient hub and lumen through the non-patient cannula. "Flash" is defined as the initial blood flow into the fluid passage on venous entry, which provides an indication of venous or arterial access before an evacuated tube is urged into the open proximal end of the blood collection tube holder. "Flash length" is the linear distance that blood flows in a proximal direction along the fluid passage on venous entry. "Flash volume" is the volume of blood that flows into the fluid passage on venous entry expressed as a percentage of the total internal volume of the blood collection set.

[0011] In one embodiment, the blood collection set includes an IV needle assembly, a length of flexible plastic tubing extending from the IV needle assembly and a non-patient needle assembly. The internal chamber is advantageously disposed on or near the non-patient needle assembly to permit an increase in the internal volume of the blood collection set without being located directly in the blood flow path.

[0012] The IV needle assembly typically comprises an IV hub having a proximal end, a distal end and a passage extending between the ends. The IV needle assembly typically further comprises an IV cannula having a proximal end mounted in the passage of the IV hub, a pointed distal end projecting distally from the IV hub and a lumen that communicates with the passage through the IV hub. The flexible tubing is typically connected to the proximal end of the IV hub. The IV needle assembly typically includes a packaging cover that protectively encloses the IV needle cannula prior to use. The packaging cover is removed immediately prior to use to permit access to the IV cannula. The IV needle assembly may further include a protective shield that is moveable relative to the IV cannula from an open position where the IV cannula is exposed to a closed position where the IV cannula is substantially shielded. The shield protects against accidental sticks with the used IV cannula. A pair of flexible wings may be mounted to the IV hub or to the shield to facilitate manipulation of the IV needle assembly.

[0013] In this embodiment, the non-patient needle assembly includes a non-patient hub having a proximal end and a distal end. The non-patient needle assembly further includes a non-patient cannula having a distal end securely mounted in the hub, a proximal end projecting proximally from the non-patient hub and a lumen that communicates with the passage through the non-patient hub. A multiple sample sleeve is typically mounted over the non-patient cannula and secured to the proximal end of the non-patient hub. External portions of the non-patient hub near the proximal end thereof may be formed with an array of external threads or other mounting structure to enable the non-patient needle assembly to be mounted to a collection tube holder or other such medical device. Or, the holder may be pre-attached with the non-patient needle assembly. The blood collection set may further include a fitting mounted to the proximal end of the flexible plastic tubing and configured for mating with the distal end of the non-patient hub. For example, the fitting may be a female luer fitting that can be engaged with the male luer taper at the distal end of the non-patient hub.

[0014] In one embodiment, the internal chamber is located in the non-patient assembly beyond the non-patient cannula proximal end, which means that the air passes through the non-patient cannula proximal end from which blood is drawn, and then into the internal chamber. Specifically, on venous entry air is compressed and flows from the fluid passage and out of the non-patient cannula proximal end where it further flows through the space between needle exterior and multiple sample sleeve. The air then flows into the internal chamber, which may be at the non-patient barb, the non-patient hub thread, the non-patient hub body, or other location or combination of locations that are beyond the non-patient cannula proximal end. The collection tube, which is applied at the non-patient cannula proximal end, draws blood from only the fluid passage and not from the internal chamber.

[0015] In another embodiment, a one-way check valve is located within the internal chamber. The valve allows air and blood to enter the internal chamber but shuts closed both when vacuum is applied. Thus, when an

evacuated collection tube is applied at the non-patient needle tip, the tube draws blood from the fluid passage but not from the internal chamber, and upon removal of the IV needle from the targeted blood vessel, the check valve closes and inhibits blood from dripping from the IV needle tip.

[0016] In a further embodiment, the internal chamber utilizes a branch in the fluid passage, e.g., a "Y" or "T". The branching may be at any location or locations along the fluid passage, but is advantageously at the proximal end such as at the non-patient hub. The branching may be in the form of a separate component added into the fluid passage such as in between the female and male luer fittings or it may be integral within the hub. The branching includes some type of internal chamber as discussed herein.

BRIEF DESCRIPTION OF THE DRAWINGS

[0017] FIG. 1A is a perspective view of a prior art blood collection set and collection tube holder.

[0018] FIG. 1B is a top plan view of the blood collection set and collection tube holder shown in FIG. 1A.

[0019] FIG. 2 is an exploded perspective view of a prior art blood collection set.

[0020] FIG. 3 is side elevation view of a prior art non-patient needle assembly, partly in section.

[0021] FIG. 4 is a cross-sectional side view of an embodiment of the non-patient needle assembly of the blood collection set.

[0022] FIG. 5 is a perspective view of the same embodiment shown in FIG. 4

[0023] FIG. 6 is a cross-sectional side view of an embodiment of the non-patient needle assembly of the blood collection set.

[0024] FIG. 7 is a perspective view of the same embodiment shown in FIG. 6

[0025] FIG. 8 is a cross-sectional side view of an embodiment of the non-patient needle assembly of the blood collection set.

[0026] FIG. 9 is an expanded view of the same embodiment shown in FIG. 8

[0027] FIG. 10 is a perspective view of one embodiment of a one way check valve.

[0028] FIG. 11 is a plan view of the same embodiment shown in FIG. 10

[0029] FIG. 12 is a cross-sectional side view of the same embodiment shown in FIG. 10

[0030] FIG. 13 is a perspective view of one embodiment of the blood collection set.

[0031] FIG. 14 is a perspective view of one embodiment of the blood collection set.

DETAILED DESCRIPTION

[0032] A prior art blood collection set that contains IV cannula shielding is identified generally by the numeral **10** in FIGS. 1A and 1B. Blood collection set **10** is employed in this embodiment with a collection tube holder **12.** Holder **12** has a proximal end **14,** a distal end **16** and a tubular sidewall **18** extending between the ends. Proximal end **14** of holder **12** is widely open and defines an entry to a tube receptacle within sidewall **18.** Thus, an evacuated collection tube can be slid in a proximal-to-distal direction through open proximal end **14** of holder **12** toward distal end **16.** Distal end **16** of holder **12** is characterized by an end wall **20.** End wall **20** is formed with an internally threaded mounting aperture **22,** as shown in FIG. 3.

[0033] Blood collection set **10** includes an IV needle assembly **24** that comprises an IV hub **26.** IV hub **26** includes a proximal end **28,** a distal end **30** and a passage (not shown) extending between the ends. IV needle assembly **24** further includes an IV cannula **32** with a proximal end **34,** a pointed distal end **36** and a lumen **38** extending between the ends. Proximal end **34** of IV cannula **32** is mounted securely in the passage of IV hub **26.** Thus, lumen **38** through IV cannula **32** communicates with the passage through IV hub **26.** Flexible wings **40** are mounted to IV hub **26** at a location near distal end **30.** Wings **40** can be folded into face-to-face relationship with one another for convenient gripping between a thumb and forefinger to enable manipulation of IV needle assembly **24.** Wings **40,** however, also can be rotated into a substantially coplanar disposition for taping to the skin of a patient.

[0034] IV needle assembly **24** further includes a tubular shield **42** that is telescoped over IV hub **26.** Shield **42** is formed with transverse slots **44** that slidably receive wings **40.** Thus, shield **42** can be slid from a proximal position, as shown in FIGS. 1A and 1B to a distal position. IV cannula **32** is exposed for use when shield **42** is in the proximal position shown in FIGS. 1A and 1B. However, IV cannula **32** is substantially surrounded by shield **42** when shield **42** is moved to the distal position. Additionally, slots **44** in shield **42** are configured to lockingly engage wings **40** when shield **42** is in the distal position to prevent or complicate a re-exposure of IV cannula **32.** In this case the presence of a shield does not inhibit flash visualization within the IV needle assembly. The shield illustrated in FIGS. 1A and 1B is one of many optional shield designs that can be incorporated into blood collection set **10.** Other designs may provide wings mounted directly to the shield. Still other designs may provide a hinged shield mounted to IV hub **26.** In still other designs, a shield may be entirely separate from IV needle assembly **24.**

[0035] Another prior art blood collection set is identified generally by the numeral **110** in FIG. 2. Fluid collection/infusion set **110** includes a length of flexible plastic tubing **112,** a proximal fitting **114,** a needle assembly **116,** a spring **118** and a barrel assembly that comprises a front barrel **120,** a rear barrel **122** and a wing **124.** Needle assembly **116** includes a needle cannula **134,** a needle hub **136** and a needle protector **138.** Needle cannula **134** has a proximal end **140,** a distal end **142** and a lumen

144 extending between the ends. Distal end 142 of needle cannula 134 is beveled to a sharp tip.

[0036] FIGS. 1 A and 1B also show that a blood collection set 10 further includes a length of flexible plastic tubing 46. Tubing 46 includes opposite proximal and distal ends 48 and 50 and a passage extending between the ends. Distal end 50 of tubing 46 is securely mounted to proximal end 28 of IV hub 26 so that the passage through IV hub 26 communicates with the passage through tubing 46. A female luer fitting 52 is securely mounted to proximal end 48 of tubing 46.

[0037] Blood collection set 10 further includes a non-patient needle assembly 54, as shown in FIG. 3. Non-patient needle assembly 54 includes a non-patient hub 56 with a proximal end 58, a distal end 60 and a fluid passage 62 extending between the ends. Exterior surface regions of non-patient hub 56 substantially adjacent proximal end 58 define an array of external threads 64 configured for threaded engagement with the internal threads formed in mounting aperture 22 of collection tube holder 12. External surface regions of non-patient hub 56 adjacent distal end define a male luer taper 66 configured for mating with female luer fitting 52. Non-patient needle assembly 54 further includes a non-patient cannula 68 having a pointed proximal end 70, a distal end 72 and a lumen 74 extending between the ends. Distal end 72 of non-patient cannula 68 is mounted securely in passage 62 through non-patient hub 56 and aligns substantially with external threads 64 on non-patient hub 56. Non-patient needle assembly 54 further includes a multiple sample sleeve 76 mounted over non-patient cannula 68 and securely engaged with proximal end 58 of non-patient hub 56. Multiple sample sleeve 76 effectively functions as a valve that prevents a flow of fluid from non-patient cannula 68. However, multiple sample sleeve 76 can be pierced by pointed proximal end 70 of non-patient cannula 68 in response to forces generated by a stopper on an evacuated collection tube.

[0038] It should be noted that flash visualization maybe acceptable in certain blood collection sets with safety features, such as the type shown in FIGS. 1A and 1B. The IV needle assembly and safety shield tend to be made from a translucent plastic material, and may only contain the IV cannula and flexible tubing, which may allow flash to be seen through the IV cannula hub walls. Therefore a minimum length of flash maybe sufficient, such that initial blood flow on venous entry maybe observed at the proximal end of the IV cannula. However in more advanced and complex IV cannula shielding mechanisms, such as the blood collection set shown in FIG. 2, the length of flash obtained from a typical venous entry may not be sufficient for blood flow to be observed in the flexible tubing at a location proximal to the IV needle assembly itself, therefore flash visualization tends to be inhibited within the IV needle assembly.

[0039] According to one embodiment of the invention, a blood collection set, for example of the type disclosed above, contains an internal chamber that increases the internal volume of the blood collection set. The increase in internal volume of the blood collection set provides a greater length of flash and therefore improved flash visualization, such that, advantageously, blood is observed in the flexible tubing proximal the IV needle assembly on the initial venous entry. While such improved or lengthened flash is particularly advantageous for such complex blood collection sets as shown in FIG 2, application in any blood collection set is contemplated.

[0040] According to this embodiment of the invention, a blood collection set includes a plurality of internal spaces that will initially be at ambient air pressure. These internal spaces include the lumen through the IV cannula, the passage through the IV hub, the passage through the flexible tubing, the passage through the non-patient hub and lumen through the non-patient cannula. The blood collection set is employed by folding wings into face-to-face engagement with one another and gripping the wings between a thumb and forefinger. Any packaging cover that may be mounted over IV cannula then is removed and discarded. The pointed distal end of the IV cannula then is urged into a targeted blood vessel. The healthcare practitioner then may release the grip on the wings, and if long term access to the blood vessel is required, the wings may be taped into face-to-face engagement with the skin of the patient. The venous or arterial access achieved with the IV cannula places the plurality of interior spaces of the blood collection set in communication with the pressure of the blood in the patient. Blood pressure exceeds the ambient air pressure. Accordingly, the pressure of air in the above-referenced internal spaces will increase, and blood will begin to flow into these internal spaces. The system will reach equilibrium as the air pressure within the blood collection set increases in response to a reduction of volume caused by the inflow of blood. Hence, a portion of the internal spaces in the system will remain filled with air at a pressure substantially equal to the venous or arterial pressure thereby preventing blood from flowing any further to or into the tubing. Stated differently, the system will include its original volume of air in the space between the proximal end of the non-patient needle and the blood that enters the blood collection set. This pressurized air will prevent any further flow of blood toward the non-patient assembly, thereby stopping flash. In prior art systems the total volume of the internal spaces maybe insufficient, such that flash maybe stopped before it can be observed. According to embodiments of the invention, however, the internal chamber which lacks direct communication to the exterior, provides more internal volume into which the air can be pushed, allowing blood to push further into the device before the pressure of the blood equals the pressure of the air. This increase in interior space thereby allows a greater length of flash to occur. Various embodiments of such internal chambers are described in detail below.

[0041] FIGS. 4 and 5 show an embodiment of the invention, where the internal chamber 301 is located be-

yond the proximal end **370** of the non-patient cannula in the non-patient hub **356** and lacks direct communication to the exterior. The internal chamber **301** is annular in cross-section and has opposite proximal **770** and distal ends **771** and a wall **772** extending therebetween; the proximal end **770** has an inlet **777** in communication with the passage. However all internal chamber geometries can be considered for the invention. The non-patient hub **356** is generally made from 2 separate parts; the male luer **374** and the non-patient thread assembly **375.** Other configurations are possible. On venous entry, air is compressed and flows from the fluid passage **362** and out of the non-patient cannula proximal end **370** where it further flows through the space **312** between needle exterior **368** and multiple sample sleeve interior **376,** then through a passage **314** through the non-patient barb and the male luer wall **320** into the internal chamber **301** through the inlet **777** in the male luer **374.**

[0042] FIGS 6 and 7 show another embodiment of the invention, with an elongated internal chamber to further increase the flash length. The internal chamber **301a** is annular in cross-section and has opposite proximal **770a** and distal ends **771a** and a wall **772a** extending therebetween, the proximal end **770a** has an inlet **777a** in communication with the passage. However all internal chamber geometries can be considered for the invention. The non-patient hub is made from 2 separate parts; the male luer **374a** and the non-patient thread assembly **375a.** The longer internal chamber **301a** is located beyond the proximal end **370a** of the non-patient cannula in the non-patient thread assembly **375a** and has no direct communication to the exterior. Other configurations are possible. On venous entry, air is compressed and flows from the fluid passage **362a** and out of the non-patient cannula proximal end **370a** where it further flows through the space **312a** between needle exterior **368a** and multiple sample sleeve interior **376a**, then through a passage **314a** through the non-patient barb into an internal chamber **301a** through an inlet **777a** in the non-patient thread assembly **375a.**

[0043] FIGS 8 to 12 show a further embodiment of the invention, in which a one-way valve **555** is located within an internal chamber similar to that shown in FIG. 6. The one way valve has a central core **550** surrounded by an annular flange **551** that has a sealing ring **552** around its outer diameter. The central core **550** is located around the non-patient needle exterior **368b** within the internal chamber **301b** and has a tapered base **553** which mates to the taper of inlet **777b.** Typically the one way valve **555** is formed from a resilient polymer such as an elastomer or thermoplastic.

[0044] As apparent to one skilled in the art, on venous entry, air flows from the fluid passage **362b** and out of the non-patient cannula proximal end **370b** where it further flows through the space **312b** between needle exterior **368b** and multiple sample sleeve interior **376b,** then through a passage **314b**, through the non-patient barb and the male luer wall **320b,** through the inlet **777b** where it moves the one-way valve **555,** flowing past the valve core base **553,** valve sealing ring **552** and into an internal chamber **301b** in the male luer **374b.** A vacuum is applied to the fluid passage, when an evacuated collection tube is applied at the non-patient needle tip. The resultant positive pressure differential between the internal chamber and the fluid passage causes the one way valve **555** to close, by the valve sealing ring **552** being pressed against the proximal end of the internal chamber **770b** and the valve core tapered base **553** being pressed into inlet 777b thereby preventing outflow of air or blood from the internal chamber,. It should be noted that the one way valve is not limited to the particular design described in this embodiment as all types of one way valves can be contemplated for this invention.

[0045] The one way valve **555** also inhibits blood from dripping from the IV needle tip upon removal of the IV needle from the targeted blood vessel after the blood collection has been completed. In prior art blood collection sets, at the instance of removal of the IV needle, the fluid passage of the blood collection set, will contain a reservoir of air and blood at venous pressure, which will be greater than the ambient atmospheric pressure. Thus a back pressure is created within the fluid passage which may cause a back-flow of blood to drip from the IV needle tip. In the embodiment of the invention shown in FIGS 8 to 12, the reservoir of air at venous pressure is within the internal chamber **301b**, therefore the back pressure causes the one way valve **555** to shut upon removal of the IV needle thereby preventing such a back-flow of blood in the fluid passage **362b.**

[0046] FIGS 13 and 14 show another embodiment of an internal chamber **401** which is branched from the fluid passage using a "Y" or "T" branched internal chamber in the fluid passage into which air is displaced. The branching may be at any location or locations along the fluid passage, but is typically near the proximal end such as at the non-patient hub. FIG 13 shows a "Y" branched internal chamber **454** in the form of a separate component added into the fluid passage **462** such as in between the female **455** and male luer **456** fittings. FIG 14 shows a "T" branched internal chamber **457,** which is an integral part of the non-patient hub, thus reducing the number of components. The use of a "Y" or "T" branched internal chamber may be accomplished with any convenient terminal shapes at the interfaces of each component. The embodiments exemplified previously are shown with luer tapered fittings but other interface designs such as direct connection to the flexible tubing may also be applied. Although typical applications use a three port "Y" or "T" branched internal chamber the use of a multiple port branched internal chamber system is also possible. The internal chamber **401**, can be a separate component which is affixed into a port **460** of the branch system as shown in FIG 13 or an integral part of the branched system as shown in FIG 14. All internal chamber geometries can also be contemplated.

Claims

1. A blood collection set comprising;
a first needle assembly comprising a first hub and a first cannula having a lumen therethrough, wherein said cannula is mounted to said first hub,
a length of flexible tubing having opposite first and second ends and a tubing passage extending between said ends, said first hub located proximate said first end for providing communication between said lumen of said first cannula and said tubing passage,
a second hub located proximate said second end and having a passage extending therethrough, said second hub passage being in fluid communication with said tubing passage,
a non-patient cannula having opposite proximal and distal ends and a lumen extending between said ends, said distal end of said non-patient cannula being mounted to said second hub such that said lumen through said non-patient cannula communicates with said second hub passage,
a multiple sample sleeve covering said non-patient cannula and mounted to said second hub, and
an internal chamber in communication with said second hub passage, wherein said internal chamber is located within said second hub or is branched from said second hub passage, and wherein said internal chamber lacks direct communication to the exterior.

2. The blood collection set of claim 1, wherein said second hub further comprises a male luer and a non-patient thread assembly, which form said internal chamber.

3. The blood collection set of claim 1, wherein said internal chamber communicates with said second hub passage beyond said proximal end of said non-patient cannula.

4. The blood collection set of claim 1, further comprising a one way valve, wherein said one way valve inhibits an outflow of air or fluid from said internal chamber.

5. The blood collection set of claim 4, wherein said one way valve is located within said internal chamber.

6. The blood collection set of claim 1, wherein upon venous access by said first needle cannula, venous pressure causes blood to flow into said tubing passage, such that the total internal volume of said internal chamber and tubing passage results in a flash length of at least approximately 0.25 inches in linear distance in a proximal direction along said tubular passage from said first end of said flexible tubing.

7. The blood collection set of claim 1, wherein upon venous access by said first needle cannula, venous pressure causes blood to flow into said tubing passage, such that the total internal volume of said internal chamber and tubing passage results in a flash length of at least approximately 0.50 inches in linear distance in a proximal direction along said tubular passage from said first end of said flexible tubing.

8. The blood collection set of claim 1, wherein said internal chamber is branched from said second hub passage.

9. The blood collection set of claim 8, wherein said internal chamber is a Y branched internal chamber or a T branched internal chamber.

10. The blood collection set of claim 1, wherein the volume of said internal chamber is at least approximately 1.0 ml.

11. The blood collection set of claim 10, wherein said volume of said internal chamber is approximately 1.0 ml to approximately 3.0 ml.

12. The blood collection set of claim 11, wherein said volume of said internal chamber is approximately 1.0 ml to approximately 2.0 ml.

13. A blood collection set comprising;
a first needle assembly comprising a first hub and a first cannula having a lumen therethrough, wherein said cannula is mounted to said first hub,
a length of flexible tubing having opposite first and second ends and a tubing passage extending between said ends, said first hub located proximate said first end for providing communication between said lumen of said first cannula and said tubing passage,
a second hub located proximate said second end and having a passage extending therethrough, said second hub passage being in fluid communication with said tubing passage,
a non-patient cannula having opposite proximal and distal ends and a lumen extending between said ends, said distal end of said non-patient cannula being mounted to said second hub such that said lumen through said non-patient cannula communicates with said second hub passage,
a multiple sample sleeve covering said non-patient cannula and mounted to said second hub, and
an internal chamber in communication with said second hub passage, wherein said internal chamber is located within said second hub or is branched from said second hub passage, and wherein said internal chamber lacks direct communication to the exterior,
wherein upon on venous access by said first needle cannula, venous pressure causes blood to flow into said tubing passage, such that the total internal volume of said internal chamber and tubing passage

results in flash being observed within said flexible tubing.

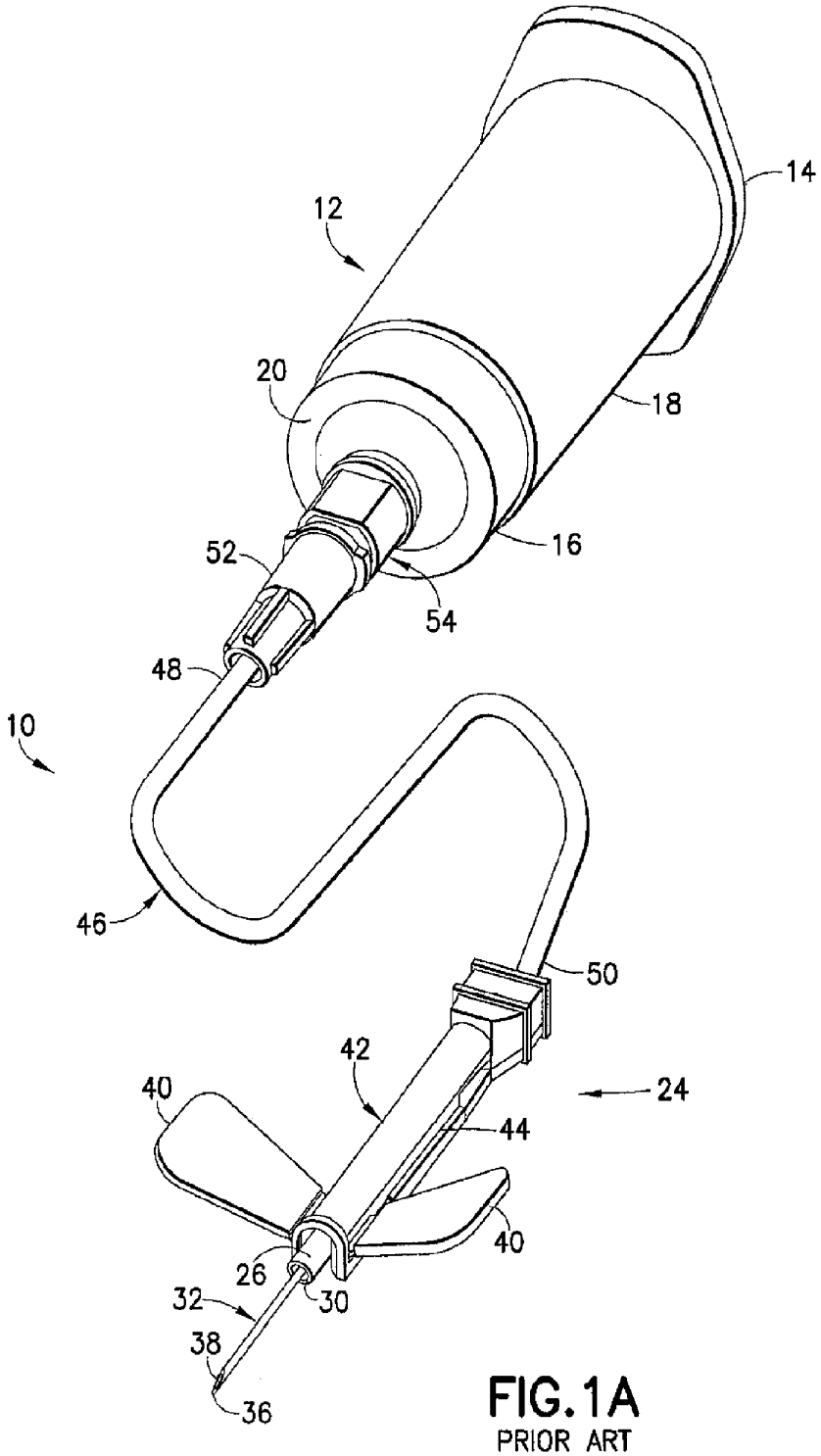


FIG. 1A
PRIOR ART

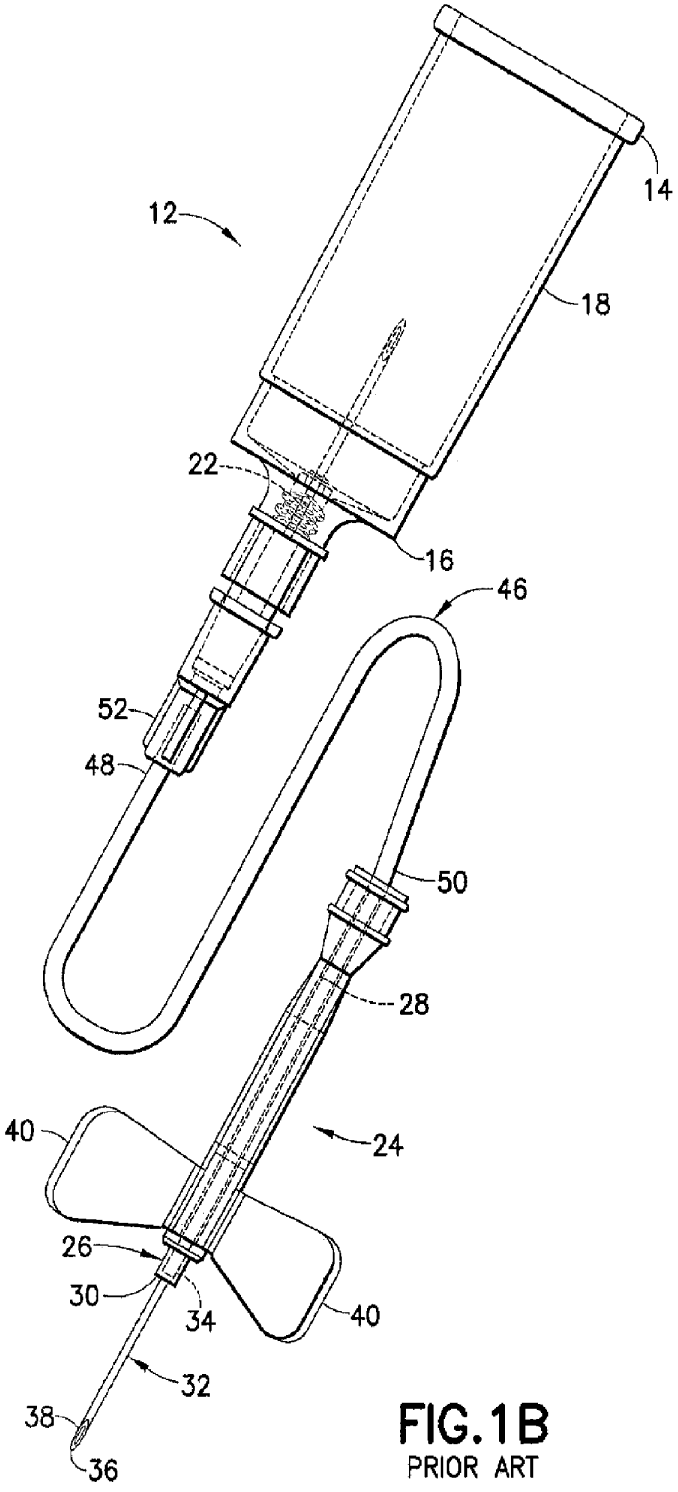


FIG.1B
PRIOR ART

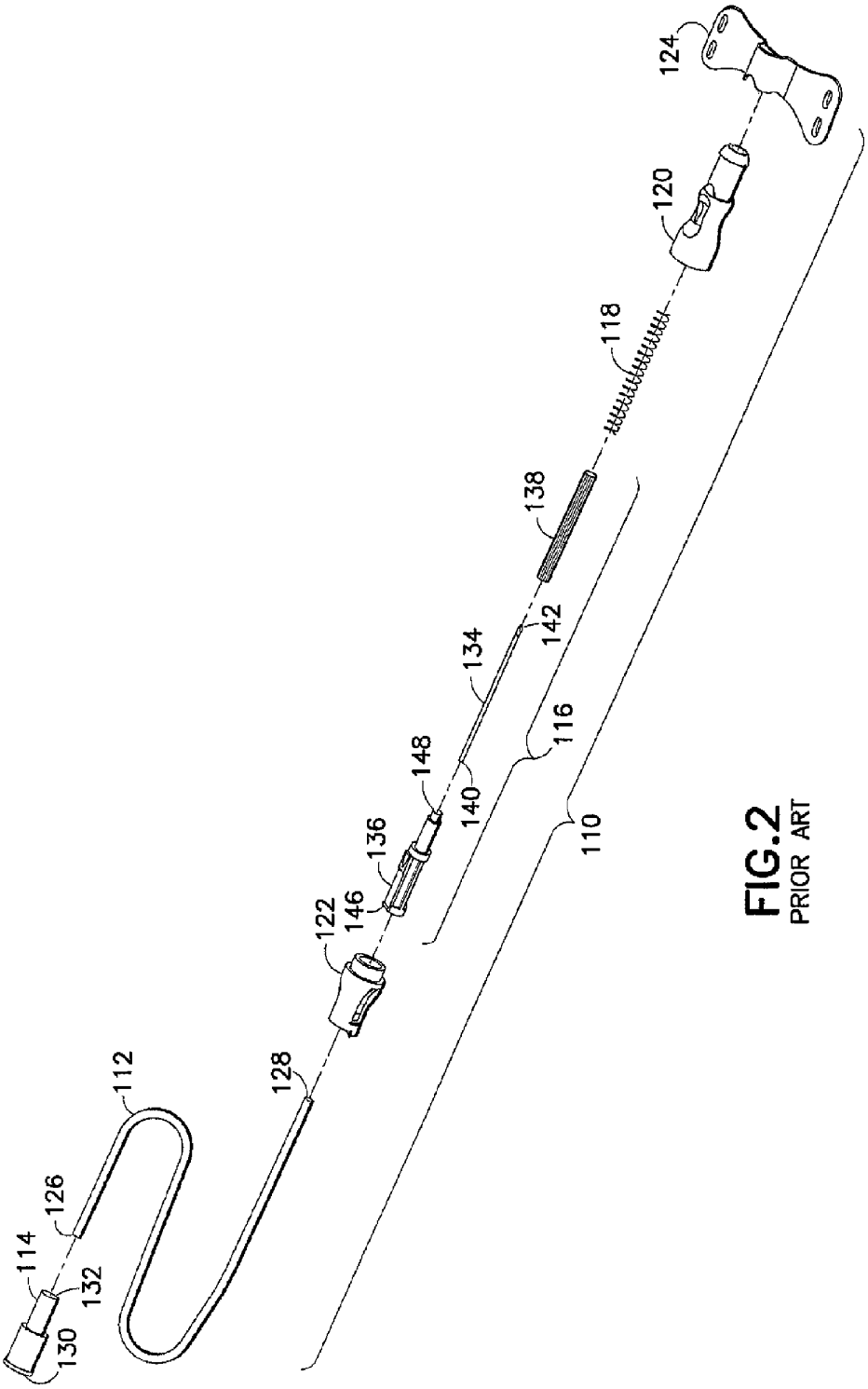


FIG.2
PRIOR ART

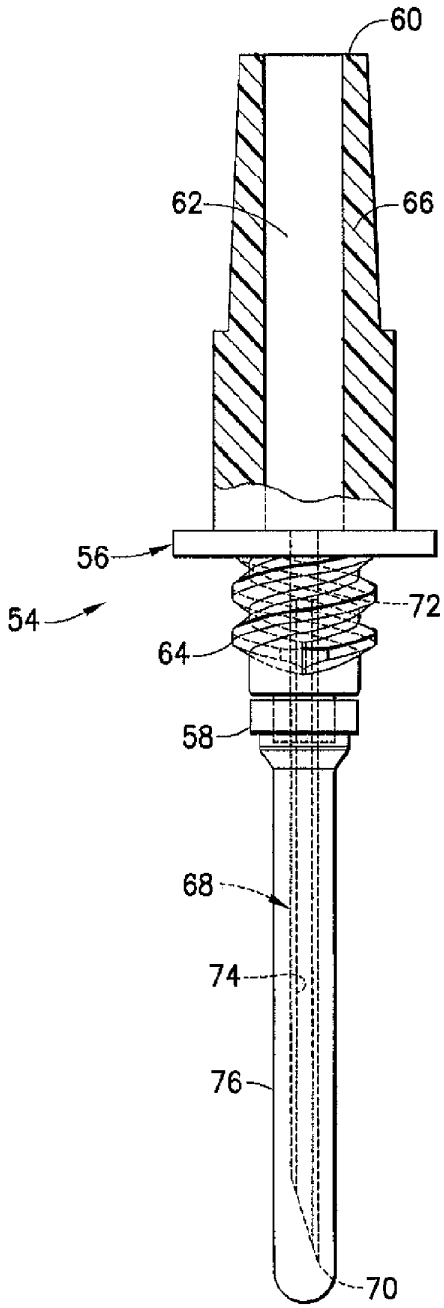


FIG.3
PRIOR ART

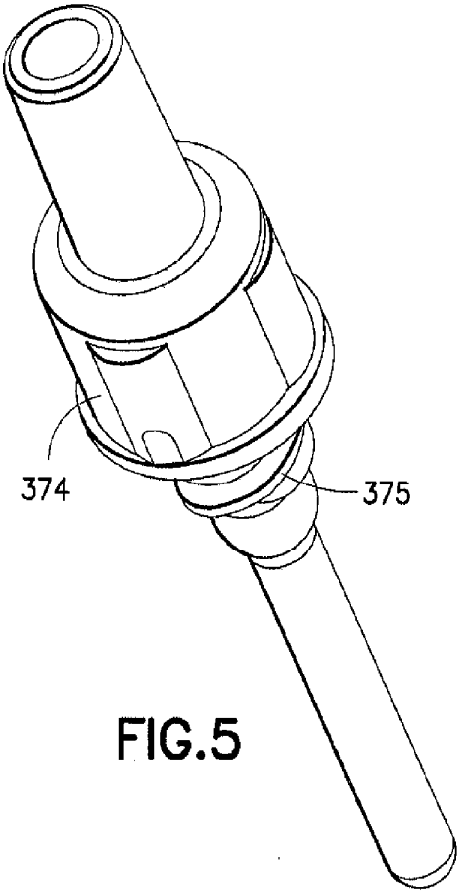

374
375

FIG.5

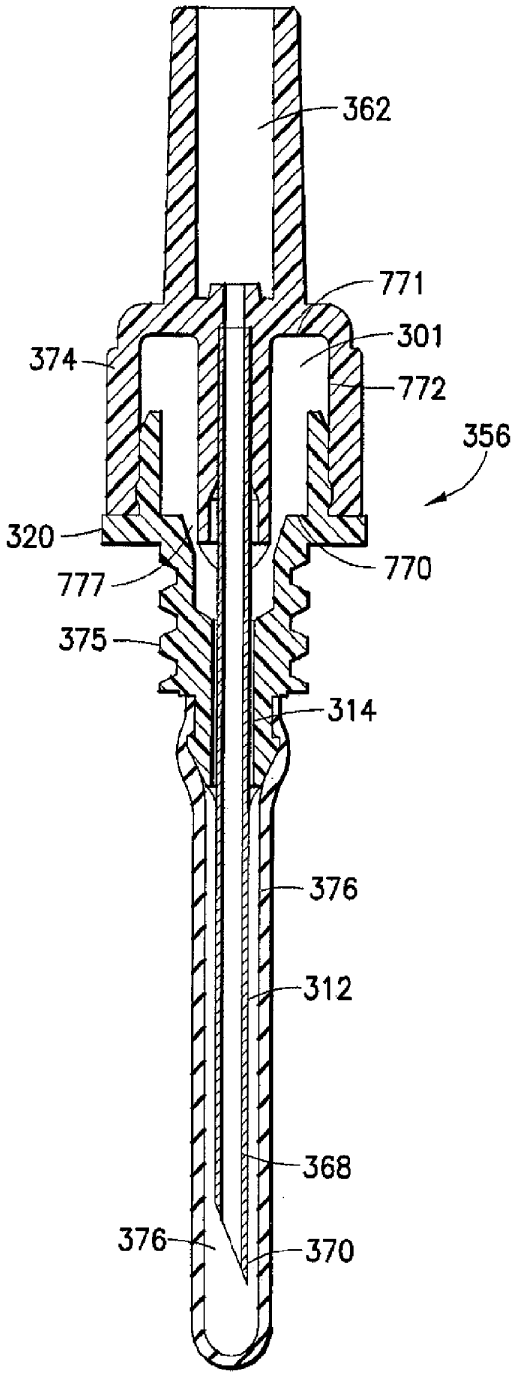

362
771
301
374
772
356
320
770
777
375
314
376
312
368
376
370

FIG.4

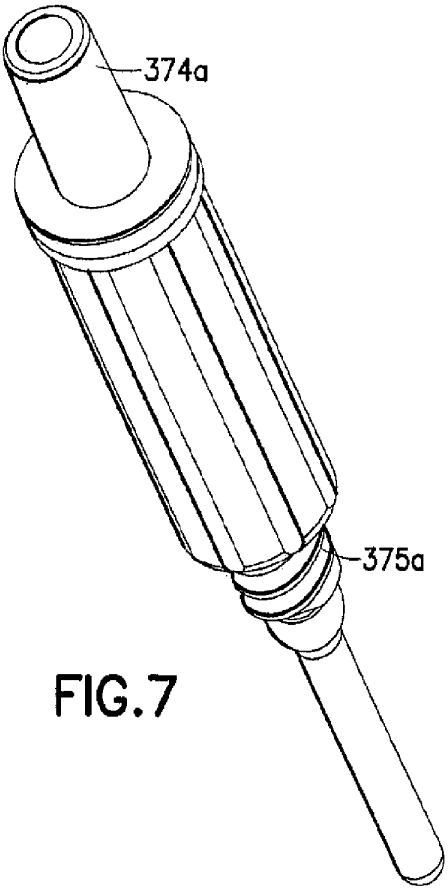

374a
375a

FIG.7

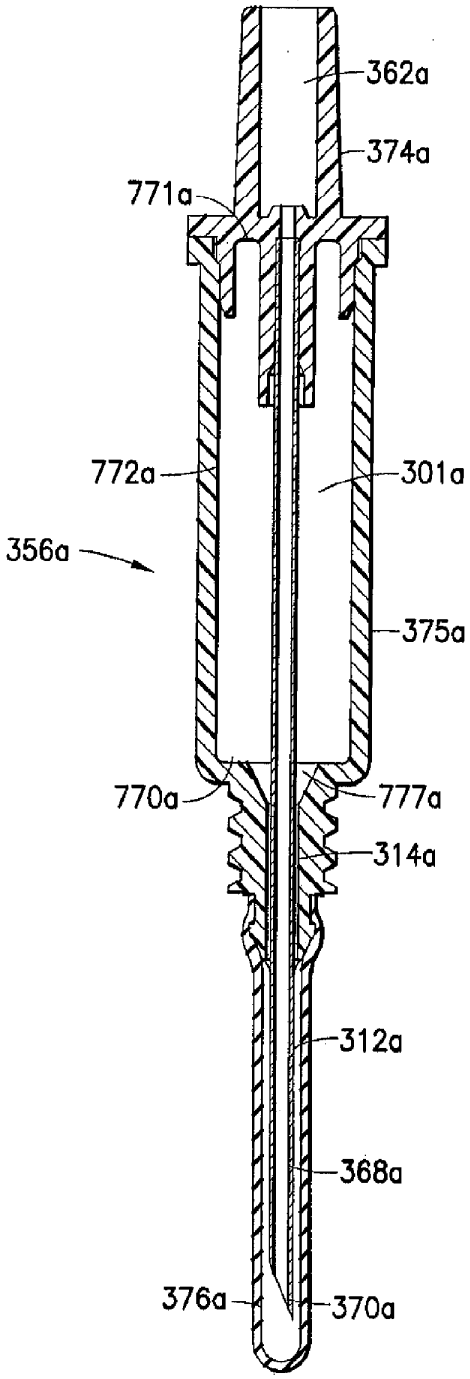

362a
374a
771a
772a
301a
356a
375a
770a
777a
314a
312a
368a
376a
370a

FIG.6

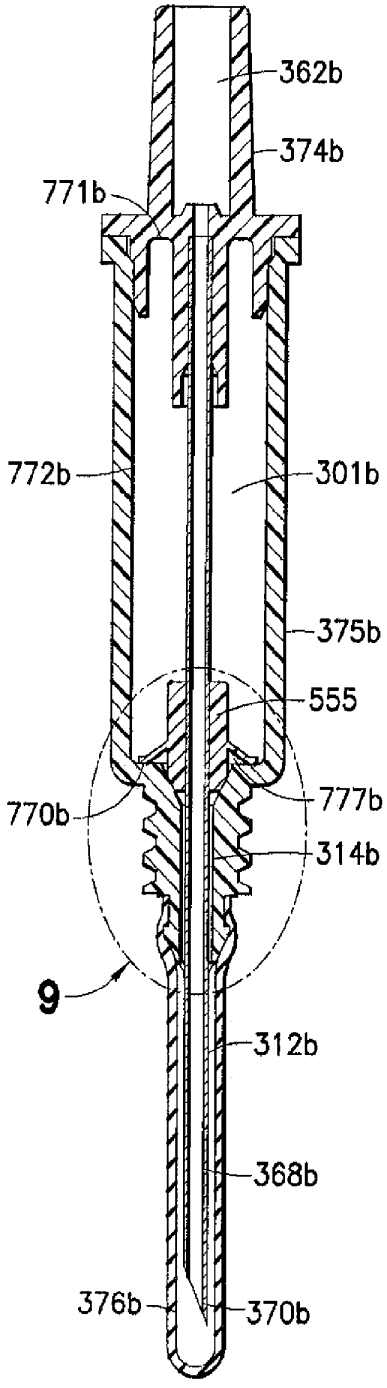

362b
374b
771b
772b
301b
375b
555
770b
777b
314b
9
312b
368b
376b
370b

FIG.8

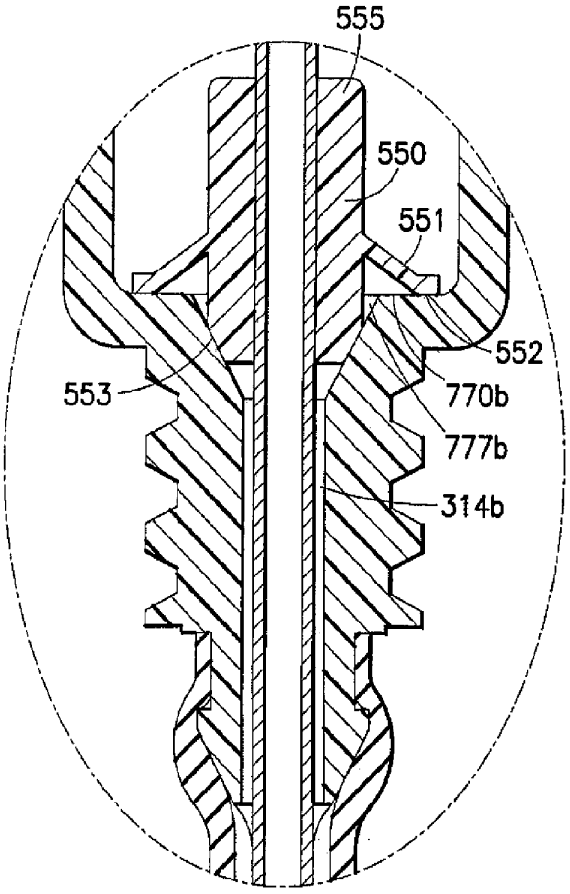

555
550
551
552
553
770b
777b
314b

FIG.9

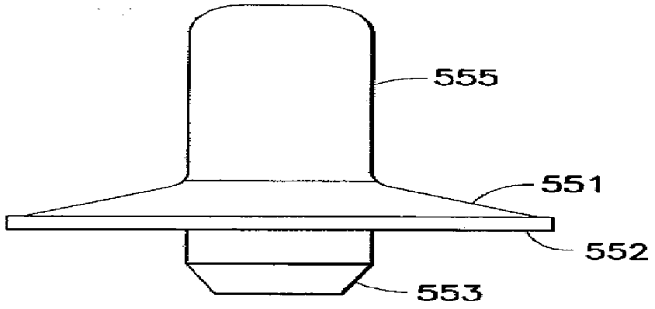


FIG. 10

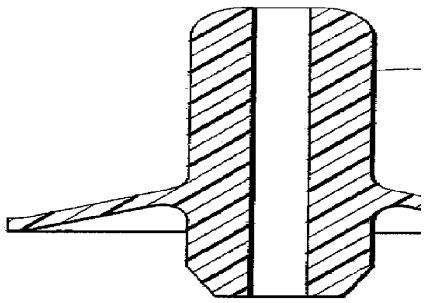


FIG. 12

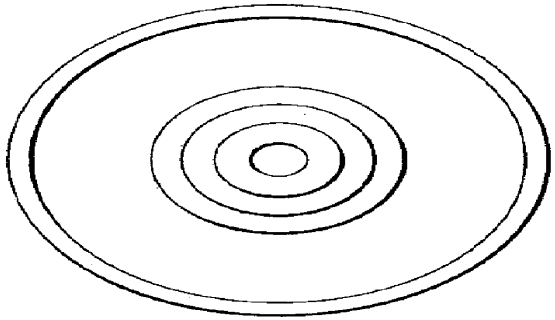


FIG. 11

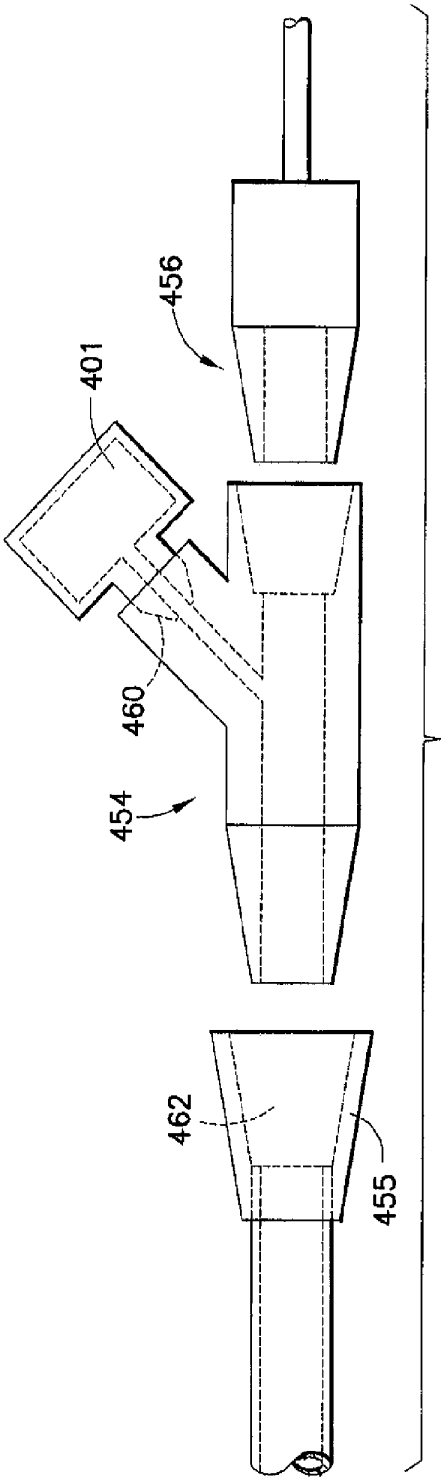


FIG.13

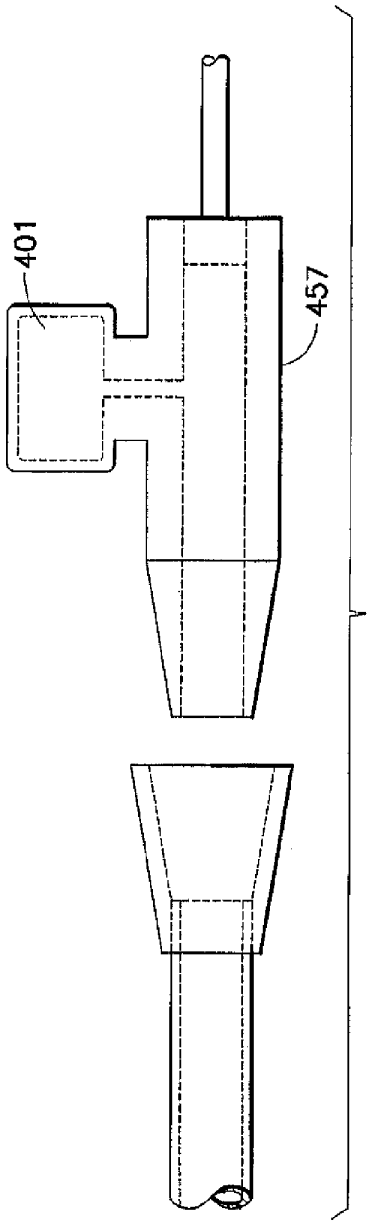


FIG.14

European Patent Office

EUROPEAN SEARCH REPORT

Application Number
EP 05 11 1371

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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)

A61B
A61M

The present search report has been drawn up for all claims

Place of search	Date of completion of the search	Examiner
Munich	16 March 2006	Ceccarelli, D

CATEGORY OF CITED DOCUMENTS

X : particularly relevant if taken alone
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P : intermediate document

T : theory or principle underlying the invention
E : earlier patent document, but published on, or after the filing date
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ANNEX TO THE EUROPEAN SEARCH REPORT ON EUROPEAN PATENT APPLICATION NO. EP 05 11 1371

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(19) [Country of issue] Japan Patent Office (JP)
(12) [Type of publication] Published patent publication (A)
(11) [Publication number] Special table 2019-534792 (P2019-534792A)
(43) [Publication date] December 5, 2019 (2019.12.5)
(54) [Title of invention] Cooling of rolls in rolling stands
(51) [International patent classification]
B21B 27/10 (2006.01)
[FI]
B21B 27/10 A
B21B 27/10 C
B21B 27/10 D
[Request for examination] Yes
[Request for preliminary examination] Not yet requested
[Total number of pages] 21
(21
) 22) [Filing date] October 12, 2017 (2017.10.12)
(85) [Translation submission date] June 13, 2019 (2019.6.13)

(86) [International application number] PCT/ EP2017/076000
(87) [International publication number] WO2018/073086 (87) [International publication date] April 26, 2018 (2018.4.26) (31) [Priority claim number] 16194099.4 (32) [Priority date] October 17, 2016 (2016.10.17) (33) [Country/region or organization claiming priority] European Patent Office (EP)

(81) [Designated countries/regions] AP (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), EA (AM, AZ, BY, KG, KZ, RU, TJ, TM), EP (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR ,HU,IE,IS,IT,LT,LU,LV,MC,MK,MT,NL,NO,PL,PT,RO,RS,SE,SI,SK,SM,TR),OA(BF,BJ, CF,CG,CI,CM,GA,GN,GQ,GW,KM,ML,MR,NE,SN,TD,TG),AE,AG,AL,AM,AO,AT,AU,AZ,BA,BB , BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES ,FI,GB,GD,GE,GH,GM,GT,HN,HR,HU,ID,IL,IN,IR,IS,JO,JP,KE,KG,KH,KN,KP,KR,KW,KZ ,LA,LC,LK,LR,LS,LU,LY,MA,MD,ME,MG,MK,MN,MW,MX,MY,MZ,NA,NG,NI,NO,NZ,OM,PA,PE ,PG,PH,PL,PT,QA,RO,RS,RU,RW,SA,SC,SD,SE,SG,SK,SL,SM,ST,SV,SY,TH,TJ,TM,TN,TR , TT
(71) [Applicant]
[Identification number] 515153152
[Name] Primetals Technologies Austria GmbH
(74) [Agent]
[Identification number] 100133400 [
Patent attorney]
[Name] Tatsuhiko Abe
(74) [Agent]
[Identification number] 100110364
[Patent Attorney]
[Name] Shinya Sanehiro
(72) [Inventor]
[Name] Alois Seilinger
(72) [Inventor]
[Name] Erich Orpits
(72) [Inventor]
[Name] Lucas Pichler

wrap up close

(57) [Summary]

The present invention relates to a cooling device (7) for cooling the rolls (5) of the rolling sta nd (1). The cooling device (7) comprises cooling beams (13) for receiving and discharging coo lant. The cooling beam (13) has a plurality of full jet nozzles (21) arranged on the discharge si de (19) of said cooling beam (13), said side facing the roll (5).) extending parallel to the roll axis (17). A jet of coolant with a substantially constant jet diameter can be sprayed through e ach of the full jet nozzles from the cooling beam (13) towards the roll (5) in the discharge dire ction (23).

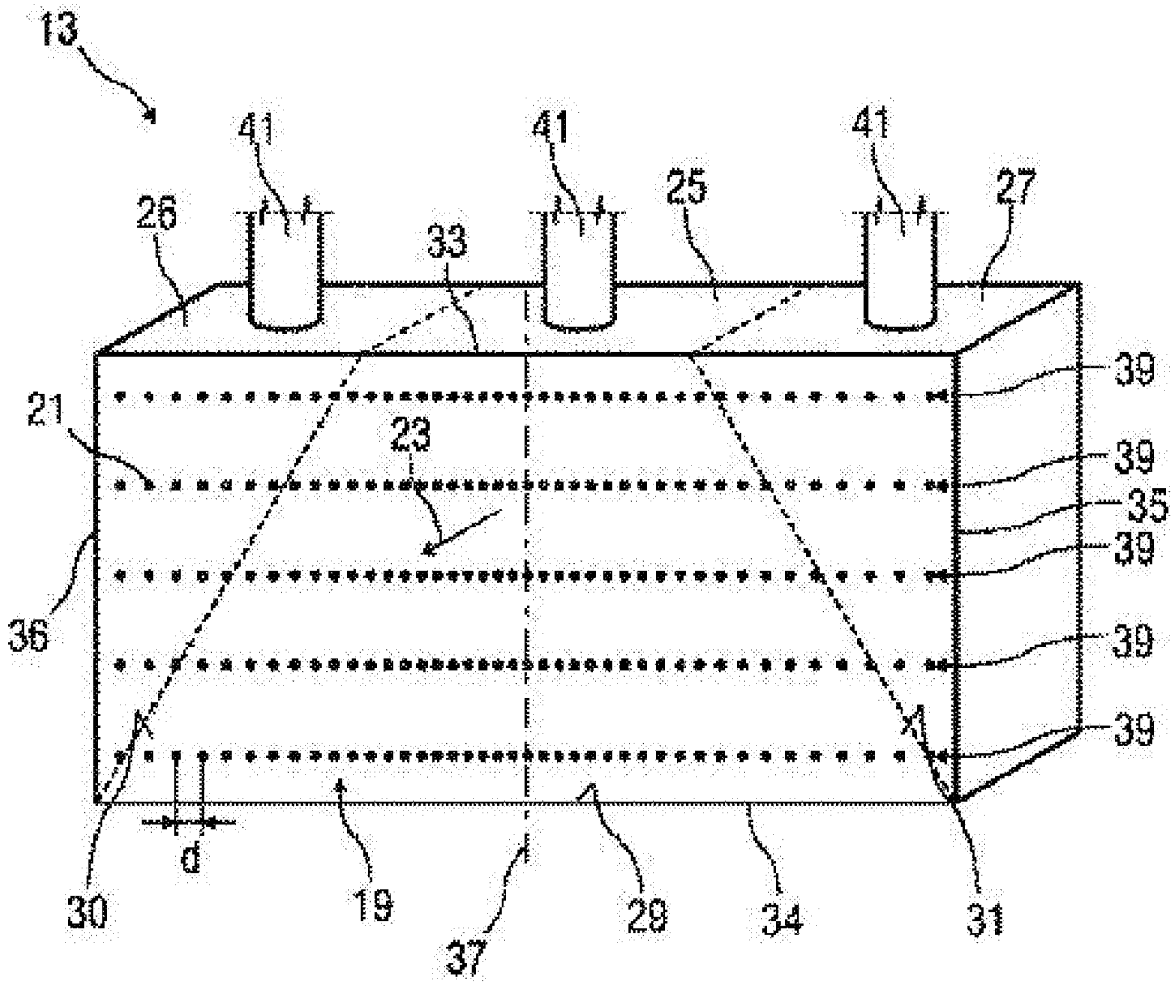


FIG 2

The scope of the claims open

We claim:

1.

A cooling device (7) for cooling rolls (5) of a rolling stand (1) comprising cooling bars (13) fo r receiving and discharging a coolant. wherein

said cooling rod (13) has a plurality of full jet nozzles (21) arranged on a discharge side (19) of said cooling rod (13), said discharge side facing a roll (5). , extending parallel to the roll axi s (17) of said roll (5) and sending coolant jets of substantially constant jet diameter through e ach of the full jet nozzles from said cooling rods (13) to said roll. A cooling device (7) capable of discharging in a discharge direction (23) towards (5).

2.

The cooling rod (13) is divided into at least two mutually separated coolant chambers (25-2 7) for receiving coolant, each coolant chamber (25-27) comprising: Corresponding sub-region s (29-31) of said discharge side (19) of said cooling rod (13) where a plurality of full-jet nozzl es (21) are arranged, through each of said full-jet nozzles (21), coolant Cooling device (7) acc ording to claim 1, characterized in that a jet can be discharged from the coolant chamber (25-27) towards the roll (5).

3.

A first coolant chamber (25) corresponds to a first partial area (29) of said discharge side (1 9) of said cooling rod (13), said first partial area (29)) is mirror symmetrical with respect to t he centerline (37) of the discharge side (19) of the cooling rod (13), the axis being perpendic ular to the roll axis (17). 3. Cooling device (7) according to claim 2.

[Claim 4]

characterized in that the extent of the first sub-region (29) parallel to the center line (37) va ries along the direction of said roll axis (17) and is greatest along said center line (37). A cooli ng device (7) according to claim 2 or 3, wherein

5.

A cooling device (7) according to any one of claims 2 to 4, characterized in that the first part ial area (29) is polygonal.

6.

Each coolant chamber (25-27) is connected to a coolant supply line (41) for supplying coola nt into said coolant chamber (25-27), said coolant supply line (41) opens into said coolant cha mber (25-27) substantially perpendicular to said discharge direction (23) of said coolant. A co oling device (7) according to claim 1.

7.

The amount of coolant supplied into the coolant chambers (25-27) is controlled independentl y of each other by respective control valves (43) and/or respective pumps (45). A cooling devi ce (7) according to any one of claims 2 to 6, characterized in that it is capable of

8. A

system according to any one of claims 2 to 7, characterized by an automated system for con trolling the amount of coolant fed into the coolant chamber (25-27). Cooling device (7).

9.

Characterized in that the nozzle spacing (d) of full jet nozzles (21) adjacent to each other al ong a direction parallel to said roll axis (17) varies along said direction. A cooling device (7) a ccording to any one of claims 1 to 8.

[Claim 10]

10. Cooling device (7) according to claim 9, characterized in that said nozzle spacing (d) is n arrowest in a central region of said discharge side (19) of said cooling rod (13).

11.

The nozzle spacing (d) is between about 25 mm and about 50 mm.

Cooling device (7) according to claim 9 or 10.

12. The method

according to any one of claims 1 to 11, characterized in that said full jet nozzles (21) are arr anged in a plurality of mutually parallel nozzle rows (39). A cooling device (7) as described.

13.

Characterized in that said cooling rod (13) has a nozzle opening for each full jet nozzle (21) to which said full jet nozzle (21) is detachably fixed. A cooling device (7) according to any one of claims 1 to 12.

14.

A wiper (15) for wiping coolant from said roll (5), characterized by a wiper (15) which can be pivoted together with said cooling rod (13). A cooling device (7) according to any one of claim s 1 to 13.

15. A

rolling stand (1) with rolls (5) and two cooling devices (7) each designed as claimed in any o ne of claims 1 to 13. A rolling stand (1), wherein said two cooling devices (7) are arranged on either side of said rolls (5).

detailed description open —

Description: BACKGROUND OF THE INVENTION 1.

Field of the Invention The present invention relates to a cooling device for cooling the rolls of a rolling stand. BACKGROUND OF THE INVENTION Rolling stands for rolling rolling stock hav e rolls which are cooled with a cooling liquid, generally cooling water. [0003] US Pat. No. 6,2 00,000 discloses a stiff, concave shell that allows low-pressure cooling liquid to be applied to t he rolls of a rolling stand. [0004] US Pat. No. 6,200,000 discloses fluid cooling of the work r

olls of a roll stand by means of movable, articulated cooling shells. In this case, the cooling liq uid is applied mainly at low pressure using the cooling shell, but in addition the cooling liquid i s applied at high pressure to produce a sufficient cooling effect. [0005] US Pat. No. 5,300,00 9 discloses a cooling device for cooling the work rolls of a rolling stand, which device comprise s a fixed spray that is slightly narrower than the narrowest strip produced using the relevant r olling stand. It has axially displaceable spray bars for cooling only those portions of the work r olls which have bars and which correspond to the width of the strip being rolled at the time. [0006] US Pat. No. 6,200,403 discloses a method for cooling the work rolls of a rolling stan d, in which cooling water is sprayed onto the work rolls at low pressure rather than high press ure, but at the same time, The range that can be used is widened. [0007]

US Pat. No. 5,300,003 discloses a spray bar for cooling rolled stock, the spray bar extending transversely to the direction of travel of the rolled stock and having a central region and two e dge regions. , the cooling medium can be supplied to each of them separately.
[0008]
[Patent Document 1] US Patent Application Publication No. 2010/0089112 [Patent Document 2] German Patent Application Publication No. 102009053074

[Patent Document 3] JP-A-6-170420 [Patent Document 4] JP-A-59-156506 [Patent Document 5] International Publication No. 2014/170139 [Outline of the Invention] [Problems to be Solve d by the Invention] [SUMMARY OF THE INVENTION It is a principal object of the present inv ention to identify an improved cooling device for cooling the rolls of a rolling stand. [0010] Ac cording to the invention , this object is achieved by the features of claim 1 . Advantageous embodiments of the invention form the subject matter of the dependent claims . A cooling de

vice according to the invention for cooling the rolls of a rolling stand comprises cooling rods f or receiving and discharging coolant. The cooling rod has a plurality of full jet nozzles located on the discharge side of the cooling rod, said side facing the roll and extending parallel to the roll axis of the roll. A coolant jet of coolant of substantially constant jet diameter can be disch arged through each full jet nozzle from the cooling rod toward the roll in the discharge directi on. [0013]

A full jet nozzle shall mean a nozzle capable of delivering a substantially straight jet of coola nt with a substantially constant jet diameter. By virtue of the concentrated coolant discharge, the full jet nozzle produces a higher roll impact pressure at the same coolant pressure at the c ooling rod than the conventionally used fan jet nozzle. Due to the large amount of coolant app lied throughout, there is always a specific coolant film, typically a few millimeters to a few cen timeters thick, by impinging coolant jets for good heat dissipation. Since this film should be p enetrated as completely as possible, a higher impact pressure has a direct positive effect on t he cooling action at the roll surface. Thanks to the high impact pressure of the coolant jets on the rolls produced by the full-jet nozzles, the coolant pressure in the cooling rods can be signif icantly reduced compared to when fan-jet nozzles are used, thereby increasing the cooling sys tem It is advantageous to be able to significantly reduce the energy consumption and operatin g costs of

[0014]

Since the coolant is discharged through a full-jet nozzle, the distance from the roll to the spr ay bar is also less critical over a wider range and therefore does not have to be adapted to the roll diameter. Thus, for example, a substantially straight coolant jet can cool the roll surface to be cooled at distances between 50 mm and 500 mm without any significant change in the coo ling effect of the coolant jet.

[0015]

Since the reduction in coolant pressure is also associated with reduced loading and conseque nt wear on the nozzles, this also results in reduced maintenance costs as a result of reduced c oolant pressure in the cooling rods, which Another advantage of using a full jet nozzle.

[0016]

In one embodiment of the invention, it is envisioned that the cooling rod is divided into at le ast two mutually separated coolant chambers for receiving coolant. Each coolant chamber cor responds to a sub-region of the discharge side of the cooling rod with a plurality of full-jet noz zles arranged through each of the full-jet nozzles to discharge a coolant jet from the coolant c hamber toward the roll. can. Dividing the cooling rod into a plurality of mutually separated co olant chambers corresponding to different subregions of the discharge side of the cooling rod controls the coolant pressure in the subregions independently of each other, resulting in It is a dvantageous to be able to control the cooling effect of the subregions independently of each o ther by controlling the coolant flow rate delivered by the . Thereby, depending on the position, the roll

It is advantageous to be able to influence the cooling and ensure that the more strongly heate d areas of the roll surface, for example the central area of the roll surface, are cooled more st rongly than the less intensely heated areas. . A development of the above-described embodi ment of the invention is that the first coolant chamber corresponds to a first partial area of th e discharge side of the cooling rod, the first partial area being the discharge side of the coolin g rod

.

is assumed to be mirror-symmetrical about the centerline of the roll, and its axis is perpendic ular to the roll axis. For example, the extent of the first subregion parallel to the centerline va ries along the direction of the roll axis and is greatest along the centerline. For example, the fi rst partial area is polygonal. Embodiments in which the first sub-region is mirror-symmetrical about the center line take into account the fact that the rolls are generally also heated symme trically about the center line. The fact that the extent of the first subregion parallel to the cent er line varies along the direction of the roll axis and has a maximum extent along the center li ne means that the roll is generally heated most strongly at the center and the heating of the r oll decreases towards the edge region. A corresponding configuration of the first subregion th us makes it possible to adapt the cooling of the rolls to the position-dependent thermal load o f the rolls by means of the first subregions.

[0018]

In another embodiment of the invention, each coolant chamber is connected to a coolant sup ply line for supplying coolant into the coolant chamber, the coolant supply line supplying coola nt into the coolant chamber. It is assumed that the opening is substantially perpendicular to t he ejection direction of the . The coolant supply lines opening into the cooling rods substantial ly perpendicular to the direction of discharge allow for a substantially uniform coolant pressur e distribution in each coolant chamber. Advantageously, the pressure gradient between the ful

l jet nozzle near the opening and the full jet nozzle away from the opening is thereby eliminat ed.

[0019]

Another embodiment of the invention envisions that the amount of coolant supplied into the coolant chambers can be controlled independently of each other by respective control valves a nd/or respective pumps. This allows the cooling effectiveness of the coolant jets discharged fr om the individual coolant chambers to be controlled independently of each other, as described above. If, for example, a conventional coolant supply system present at any given time can be used in the relevant rolling system, for example a water supply system that normally delivers cooling water at a pressure of 4 bar, the control It is particularly advantageous to control the amount of coolant by means of a valve. In this case, complex and expensive pressure boost s ystems can be dispensed with for roll cooling. By controlling the amount of coolant by the pu mps, if appropriate in conjunction with control valves, individual pumps can be turned off or t urned on during breaks between rolling or in the case of rolling operations requiring only a lo w cooling capacity. Power can be lowered, thereby reducing energy consumption. Another e mbodiment of the present invention contemplates an automated system for controlling the a mount of coolant supplied into the coolant chamber

.

Thereby, it is advantageous to be able to automatically control the volumetric flow rate of the coolant discharged from the coolant chamber onto the roll in order to adapt the volumetric flo w rate to the temperature distribution of the roll surface. In this case, the amount of coolant s upplied into the coolant chamber is preferably controlled by an automated system through co ntrolling the control valves and/or pumps mentioned above.

[0021]

In another embodiment of the invention, it is envisaged that the nozzle spacing of full jet no zzles adjacent to each other along a direction parallel to the roll axis varies along said directio n. In this case, the nozzle spacing is preferably the narrowest in the central region of the disc harge side of the cooling rod. For example, the nozzle spacing along the direction parallel to t he roll axis is between about 25mm and about 50mm. These embodiments of the present inve ntion also allow the nozzle spacing along the direction parallel to the roll axis to be varied acc ording to the position-dependent thermal load of the roll surface, so that the placement of the full-jet nozzles can also be adapted to this thermal load. can. The minimum nozzle spacing in the central region of the discharge side of the cooling rods takes into account the fact that the central region of the roll surface generally experiences the greatest heat load.

Another

embodiment of the present invention envisions that the full jet nozzles are arranged in parall el rows of nozzles. Advantageously, this allows the coolant to be applied to the roll over a wid er area and evenly as the roll rotates.

Another

embodiment of the invention envisions that the cooling rod has a nozzle opening for each full jet nozzle to which the full jet nozzle is removably secured. Advantageously, this embodiment of the present invention allows for easy replacement of defective jet nozzles.

In another embodiment of the invention, a wiper is provided for wiping coolant from the roll, and the wiper and cooling bar can be pivoted together. For example, wipers direct excess coolant to the rolled stock and/or to the roll nip where the rolled stock is guided between two rolls to reduce friction between the rolled stock and the rolls. It is advantageous to be able to prevent the lubricant from washing away. Advantageously, the ability to pivot the wiper and cooling rods together obviates the need for additional equipment to move the cooling rods. In this case, the advantages of using full-jet nozzles already mentioned above are also in effect here. That is, by using a full-jet nozzle, the distance between the spray bar and the roll becomes less critical over a wider range and therefore no longer needs to be adapted to the roll diameter. Furthermore, the present invention is also particularly suitable as a retrofit to existing rolling systems with wipers, for example only conventional high pressure spray rods need to be replaced with cooling rods according to the invention.

[0025]

The rolling stand according to the invention comprises rolls and two cooling devices according to the invention, the two cooling devices being arranged on opposite sides of the rolls. The advantages of the rolling stand according to the invention result from the advantages of the cooling device according to the invention already mentioned above.

The above-described properties, features, and advantages of the present invention, as well as the manner in which they are achieved, will become clearer and will be clearly understood.

BRIEF DESCRIPTION OF THE DRAWINGS

[0027]

FIG. 1 is a schematic view of a rolling stand with cooling device;

2 is a schematic perspective view of a first exemplary embodiment of a cooling rod; FIG.

3 shows the volumetric flow rate of coolant delivered by the cooling rods shown in FIG. 2 as a function of position; FIG.

FIG. 4 is a discharge side view of a second exemplary embodiment of a cooling rod;

FIG. 5 is a discharge side view of a third exemplary embodiment of a cooling rod;

FIG. 6 is a discharge side view of a fourth exemplary embodiment of a cooling rod;

FIG. 7 is a view of the discharge side of the fifth exemplary embodiment of the cooling rod;

FIG. 8 is a view of the discharge side of the sixth exemplary embodiment of the cooling rod;

FIG. 9 is a view of the discharge side of the seventh exemplary embodiment of the cooling rod;

FIG. 10 is a discharge side view of an eighth exemplary embodiment of a cooling rod;

FIG. 11 is a discharge side view of a ninth exemplary embodiment of a cooling rod;

FIG. 12 is a discharge side view of a tenth exemplary embodiment of a cooling rod;

[Mode for carrying out the invention]

[0028]

In all drawings, the same parts are provided with the same reference numerals.

[0029]

FIG. 1 is a schematic diagram of a rolling stand 1 for rolling a rolling stock 3. FIG. The rolling stand 1 comprises two rolls 5 designed as work rolls and two cooling devices 7 for each roll 5 , said devices being arranged on either side of the rolls 5 . The rolls 5 are spaced apart by a r oll nip 9 and pass the rolling stock 3 through the roll nip 9 in the rolling direction 11 to form t he rolled stock 3 . Each cooling device 7 comprises cooling bars 13 and wipers 15 . Each cool ing rod 13 is designed to receive and discharge coolant

.

For discharging the coolant, the cooling rod 13 has a plurality of full jet nozzles 21 arranged o n the discharge side 19 of the cooling rod 13, said side facing the respective roll 5 and the roll of the roll 5. A coolant jet extending parallel to axis 17 and having a substantially constant jet diameter can be discharged in discharge direction 23 from cooling rod 13 towards roll 5 throu gh each of the full-jet nozzles. Coolant may be supplied into the cooling rods 13 via coolant su pply lines 41, the amount of coolant supplied into the cooling rods 13 being controlled by a co ntrol valve 43 and/or a frequency controlled pump 45, for example. can be controlled by A co olant is, for example, water. Each wiper 15 is designed to wipe coolant from the respective r oll 5 and can be pivoted toward and away from the roll 5

.

The cooling rods 13 and wipers 15 of each cooling device 7 are fixed to the pivoting device of the cooling device 7 , thus pivoting the cooling rods 13 and wipers 15 together toward and aw ay from the rolls 5 . Preferably, it can be moved.

[0032]

FIG. 2 is a schematic perspective view of a first exemplary embodiment of cooling rods 13 fo r delivering coolant to rolls 5. As shown in FIG. The cooling rod 13 is divided into three mutual ly separated coolant chambers 25-27 to receive coolant. Each coolant chamber 25-27 corresp onds to a sub-region 29-31 of the discharge side 19 in which a plurality of full jet nozzles 21 a re arranged to roll coolant jets from the coolant chambers 25-27 through each of the full jet n ozzles. 5 can be discharged in the discharge direction 23 . The discharge side 19 is rectangula r with two longitudinal sides 33 , 34 parallel to the roll axis 17 and two lateral sides 35 , 36 pe rpendicular to the roll axis 17 . The first coolant chamber 25 corresponds to a first partial ar ea 29 of the discharge side 19 of the cooling rod 13 forming the central area of the discharge side 19

.

The first partial region 29 is mirror-symmetrical to the centerline 37 of the discharge side 19 o f the cooling rod 13, said axis being perpendicular to the roll axis 17 and arranged on the first longitudinal side 33. It is a trapezoid with four vertices and two vertices each located at the e

ndpoint of the second longitudinal side 34 .

[0034]

The full jet nozzles 21 are arranged on the discharge side surface 19 in a plurality of nozzle r ows 39 each extending parallel to the roll axis 17 . In this case, the nozzle spacing d between the adjacent full jet nozzles 21 of each nozzle row 39 varies symmetrically with respect to the center line 37, so that the nozzle spacing d is is narrowest at and widens towards the edge re gion of the outlet side 19, for example parabolically. In the exemplary embodiment shown in F IG. 2, the nozzle spacing d is twice as large at the ends of each nozzle row 39 as it is at the c enter of the nozzle row 39 . The nozzle spacing d varies, for example, between 25mm and 50 mm. The nozzle rows 39 extend substantially evenly over the entire extent of the discharge si de 19 and thus produce a relatively uniform cooling effect on the roll surface of the roll 5 . A further development of the exemplary embodiment shown in FIG. 2 envisions arranging the n ozzle rows 39 staggered with respect to each other, so that the full jet nozzles 21 of the vario us nozzle rows 39 are arranged in

roll

It is not arranged along a direction perpendicular to the axis 17. A "cooling channel" extends perpendicular to the row of nozzles 39 where no coolant is ejected onto the roll 5, resulting in a reduced cooling effect, but this "cooling channel" can be avoided. so that the nozzle row 39 has a particularly uniform

Advantageously, a good cooling effect is achieved. Furthermore, the full jet nozzles 21 very c lose to or on the boundary between two adjacent sub-regions 29-31 in FIG

.

Displaced with respect to the arrangement, they are arranged to fall into one of the adjacent s ub-regions 29-31, which subdivide into the coolant chambers 25-27 inside the cooling tube 13 by the separating plate such a boundary line. because it extends along Each full jet nozzle 2 1 is removably attached to the nozzle opening of the cooling rod 13, for example by a threade d joint

.

Each full jet nozzle 21 has a minimum diameter nozzle cross-section of, for example, about 4 mm. Each coolant chamber 25-27 is connected to a coolant supply line 41 for supplying cool ant into the coolant chambers 25-27

.

, it is open substantially perpendicular to the discharge direction 23 of the coolant. The cross-sections of the coolant supply lines 41 each have a diameter of, for example, between 100 m m and 150 mm. The amount of coolant supplied into coolant chambers 25-27 via coolant su pply line 41 is controlled by respective control valves 43 (not shown in FIG. 2) and/or respecti ve pumps

.

can be controlled independently of each other by 45 (not shown in FIG. 2). Advantageously, t

his allows the amount of coolant discharged from the coolant chambers 25-27 to be adapted t o different heat loads in different regions of the roll surface.

FIG . 3 shows, by way of example, the volume flow rate V_1 of three coolants discharged from the cooling rod 13 shown in FIG. , V_2 , V_3 as a function o f the position y along the direction parallel to the roll axis 17 . Here, the volumetric flows V_1 , V_2 , V_3 are expressed as a percentage of the rated flow.

The rated flow is the first volumetric flow V_1 at the center position y_m . A first volumetric flow rate V_1 occur s when coolant is fed into all three coolant chambers 25-27 at the same specified pressure rat ing for all coolant chambers 25-27. The first volume flow rate V_1 has a parabolic shape with a maximum at the central position y_m and decreases from the central position y_m towards the two end regions to half the value of the central position y_m Become. The reason for this shap e of the first volumetric flow rate V1 is that from the center of the nozzle row 39 to the two en ds, the nozzle spacing d of the full jet nozzles 21 along the nozzle row 39 doubles . , a parabo lic increase in the nozzle spacing d is assumed. Second volumetric flow rate V_2 supplies coolant into the first coolant chamber 25 at a coolant pressure of approximately twic e the rated pressure and into the other two coolant chambers 26, at a coolant pressure of app roximately half the rated pressure. 27 when supplied to each of them. The third volume flow rate V3 supplies coolant into the first coolant chamber 25 at a coolant pressure approximately h alf the rated pressure and supplies coolant at a coolant pressure approximately twice the rate d pressure . into each of the other two coolant chambers 26, 27. FIG . 3 illustrates the volumetric flow ra tes V_1 , V_2 , V_3 with different patterns of dependence on position y along the direction par allel to the roll axis 17 at different coolant pressures in the coolant chambers 25-27. , so that the volume flows V_1 , V_2 , V_3 discharged from the cooling rods 13 can be adapted to the te mperature distribution of the roll surfaces. The coolant pressure in each coolant chamber 25 - 27 is set by a respective control valve 43 and/or a respective pump 45 . FIGS. 4-12 each sh ow the discharge side 19 of another exemplary embodiment of the cooling rod 13. FIG. these differs from the exemplary embodiment shown in FIG. 2 only in the shape and number of the coolant chambers 25-27 and the corresponding partial areas 29-31 of the discharge side 19. F IG. As in the exemplary embodiment shown in FIG. 2, the full jet nozzles 21 are each arrange d in a plurality of nozzle rows 39, with the nozzle spacing d in each case extending from the c enter along it to the two ends. increase towards the part. Therefore, the full jet nozzle 21 of Fi

gures 4-12 will not be described here again. Due to the distribution of the full jet nozzles 21 o n the discharge side 19 similar to the exemplary embodiment shown in FIG. 2, each of the ex emplary embodiments shown in FIGS. V_1 , V_2 , V_3 can be produced. Like the exemplary e mbodiment shown in FIG. 2, the exemplary embodiments shown in FIGS. 4-10 each correspo nd to three coolant chambers 25-27 and a discharge side 19

.

It has partial regions 29-31. Similar to the exemplary embodiment shown in FIG. 2, the first s ubregion 29 is mirror-symmetrical about the centerline 37 of the discharge side 19 of the cool ing rod 13, perpendicular to the roll axis 17, and the other The two partial areas 30 , 31 adjoi n the first partial area 29 and on different sides of the centerline 37 .

FIG.

4 shows that the first partial area 29 is trapezoidal with two vertices located on the first long itudinal side 33 and two vertices located on the second longitudinal side 34 . 1 illustrates an e xemplary embodiment;

[0048]

FIG. 5 shows that the first partial region 29 has one vertex arranged at the intersection of th e centerline 37 and the first longitudinal side 33 and two corners arranged at the end of the s econd longitudinal side 34 . 2 shows an exemplary embodiment that is a triangle with four ver tices.

FIG.

6 shows that the first partial area 29 has one vertex located at the intersection of the centerl ine 37 and the first longitudinal side 33 and two corners located at the second longitudinal sid e 34 . 2 shows an exemplary embodiment that is a triangle with four vertices.

FIG .

7 shows an exemplary embodiment in which the first partial area 29 is a rectangle with verti ces located on the longitudinal sides 33,34. In this exemplary embodiment, no coolant is disc harged via the two outer partial regions 30 , 31 , so that the discharge of coolant can only occ ur from the central region of the discharge side 19 . This exemplary embodiment is therefore particularly suitable for rolling rolling blanks 3 of different widths.

FIG .

8 shows that the second partial area 30 and the third partial area 31 each have a vertex on t he first longitudinal side 33 and a vertex located at one end of the first longitudinal side 33. , and vertices located on the lateral sides 35, 36. FIG.

FIG.

9 shows that the first partial region 29 has two vertices on the first longitudinal side 33 and t wo vertices located at the ends of the second longitudinal side 34, respectively. Figure 10 sho ws an exemplary embodiment that is a hexagon with vertices on its short sides 35,36.

[0053]

FIG. 10 shows that the first partial regions 29 are arranged at one vertex arranged at the int

ersection of the centerline 37 and the first longitudinal side 33 and at the end of the second lo ngitudinal side 34 respectively. An exemplary embodiment is shown that is a pentagon with t wo vertices and one vertex on each of the short sides 35,36. The exemplary embodiments s hown in FIGS. 11 and 12 each have two coolant chambers 25 , 26 and corresponding subregi ons 29 , 30 of the discharge side 19

.

Both partial regions 29 are mirror-symmetrical with respect to a centerline 37 of the discharg e side 19 of the cooling rod 13 perpendicular to the roll axis 17 .

FIG .

11 shows that the first partial area 29 is triangular with one vertex located at the centerline 37 and two vertices located at the ends of the second longitudinal sides 34 respectively. show s an exemplary embodiment

.

FIG.

12 shows that the first partial area 29 has one vertex located on the centerline 37 and two v ertices located respectively at the ends of the second longitudinal sides 34 and each short edg e. 4 shows an exemplary embodiment that is a pentagon with vertices on hand sides 35,36.

Although the present invention has been illustrated and described in more detail by way of p referred exemplary embodiments, the present invention is not limited to the disclosed exampl es, and a person skilled in the art can fully understand the scope of protection of the present i nvention

.

Other variations can be obtained from these without exceeding.

[Description of Symbols]

1

Rolling stand

3 Rolling material, rolling material

5 Roll

7 Cooling device

9 Roll gap

11 Rolling direction 13

Cooling bar

15 Wiper

17 Roll shaft

19 Discharge side surface

21 Full jet nozzle

23 Discharge direction

25-27 Cooling Agent chambers

29 to 31 Partial areas

33, 34 Longitudinal sides

35, 36 Short side

37 Center line

39 Nozzle row

41 Coolant supply line

43 Control valve

45 Pump

d Nozzle spacing

drawing open —

[Fig. 1]

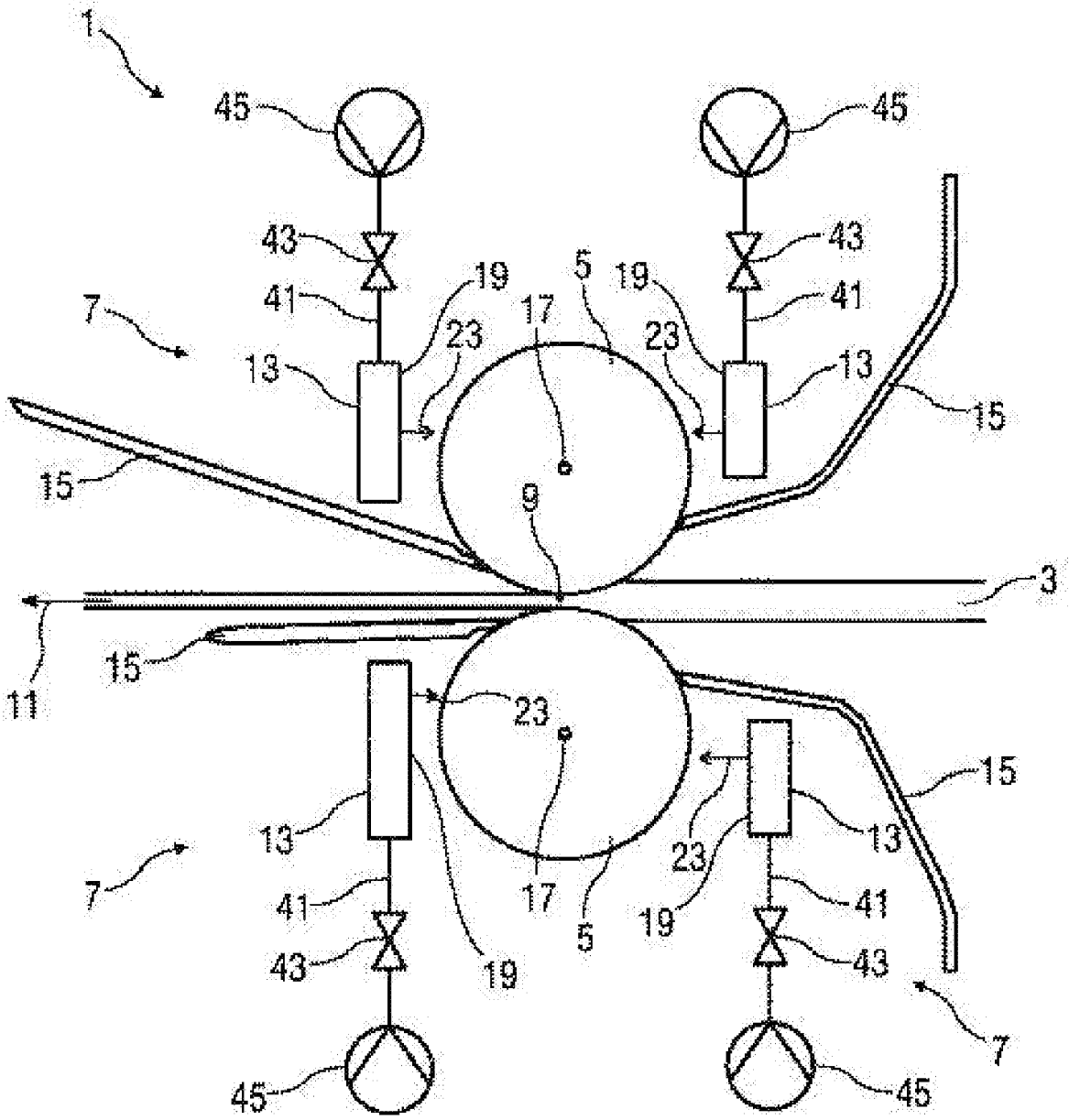


FIG 1

[Figure 2]

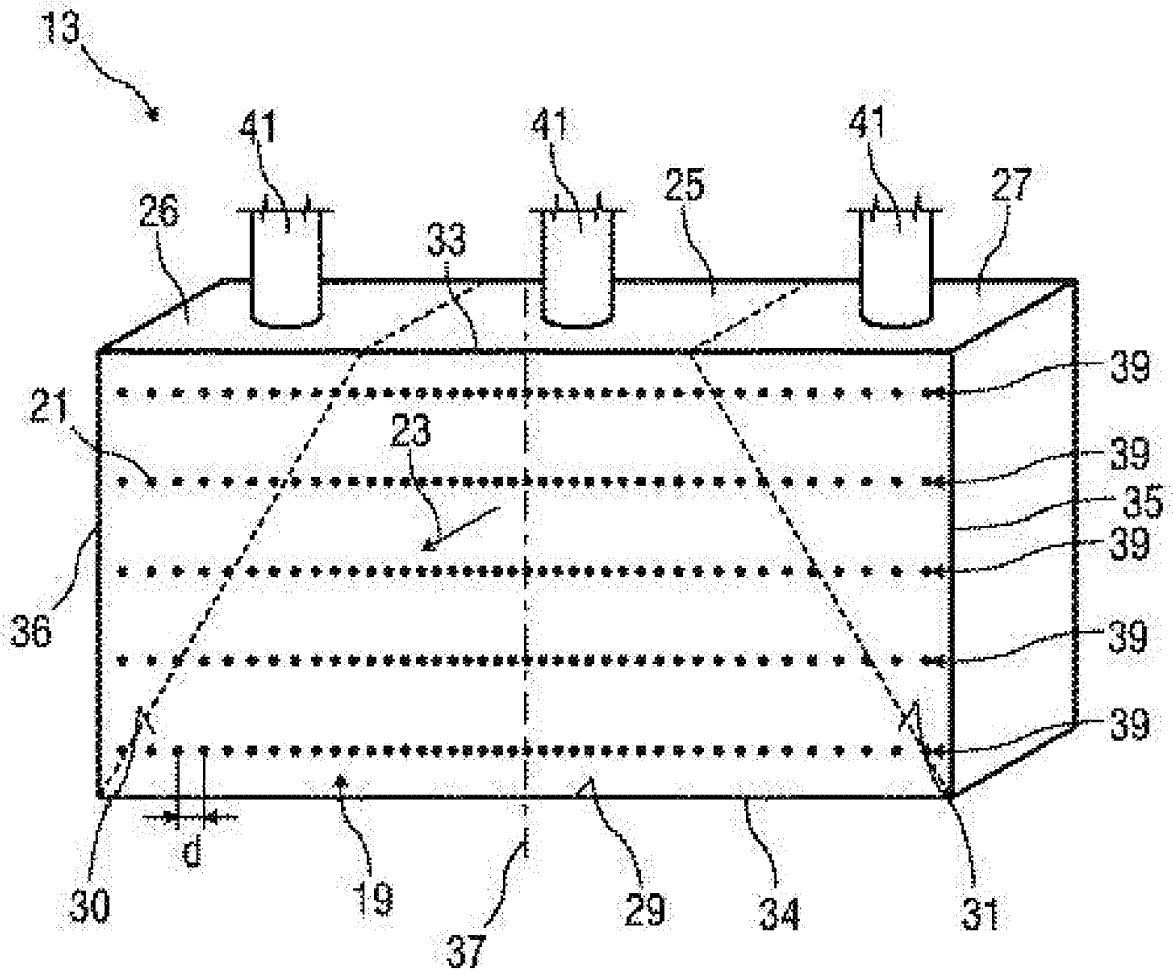


FIG 2

[Figure 3]

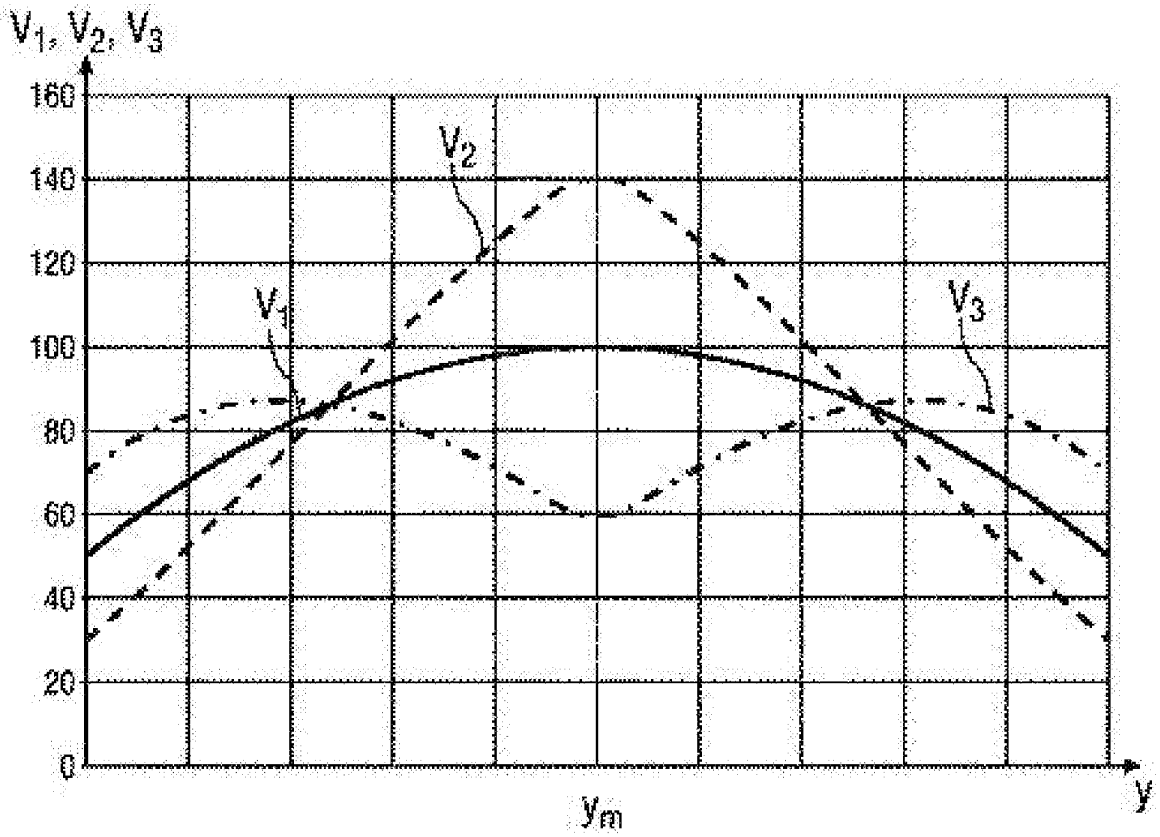


FIG 3

[Figure 4]

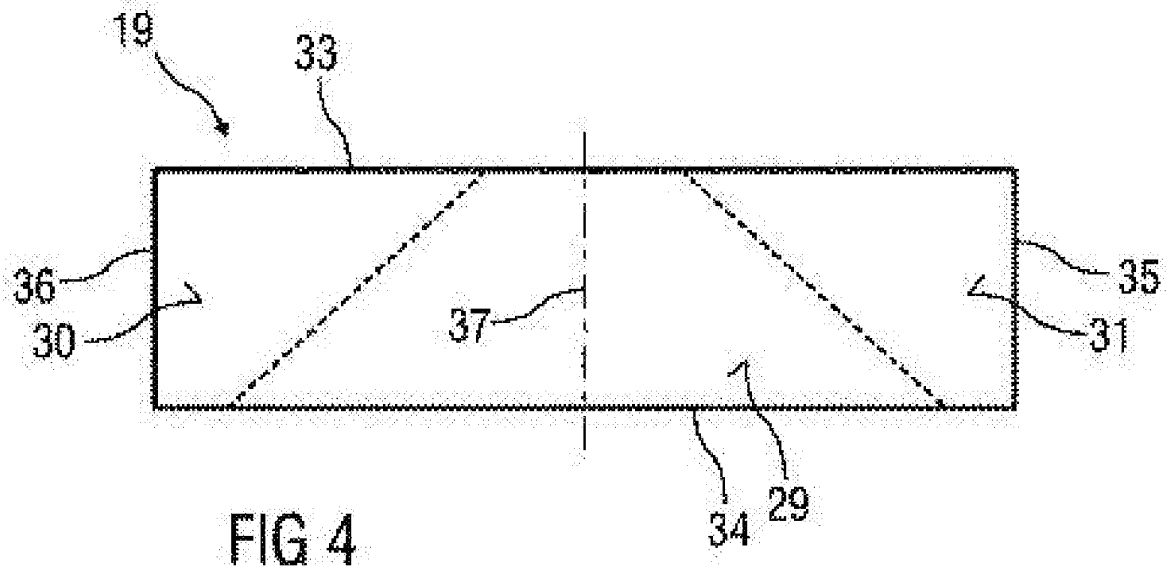


FIG 4

[Figure 5]

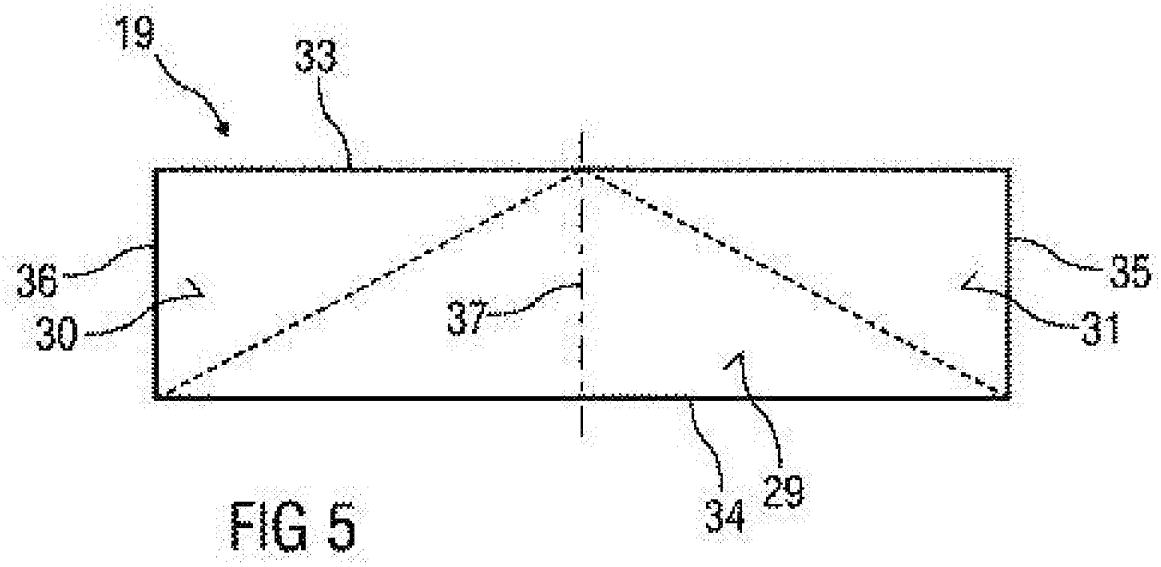


FIG 5

[Fig. 6]

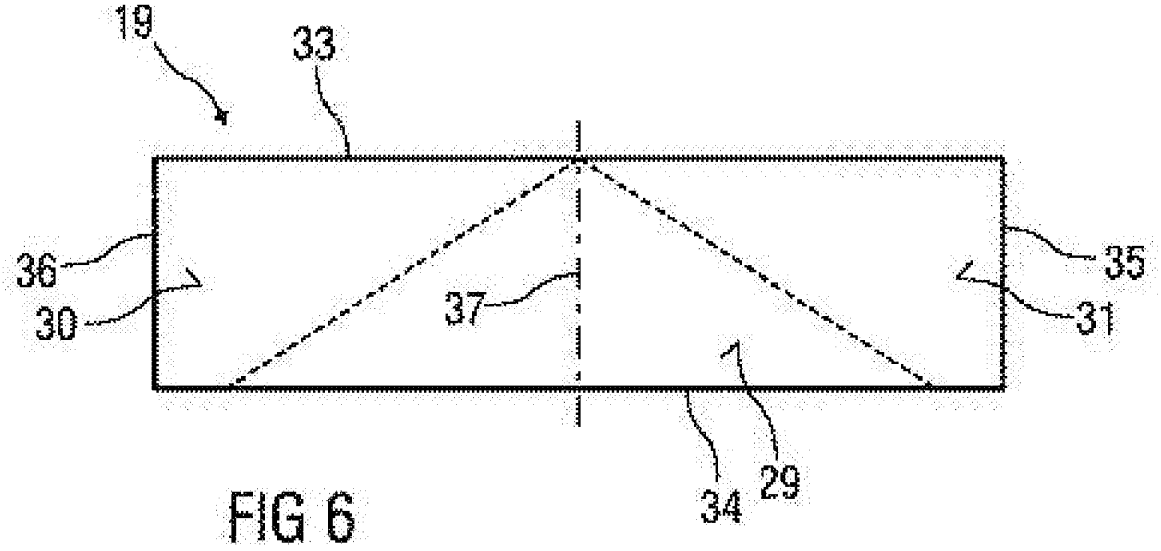


FIG 6

[Fig. 7]

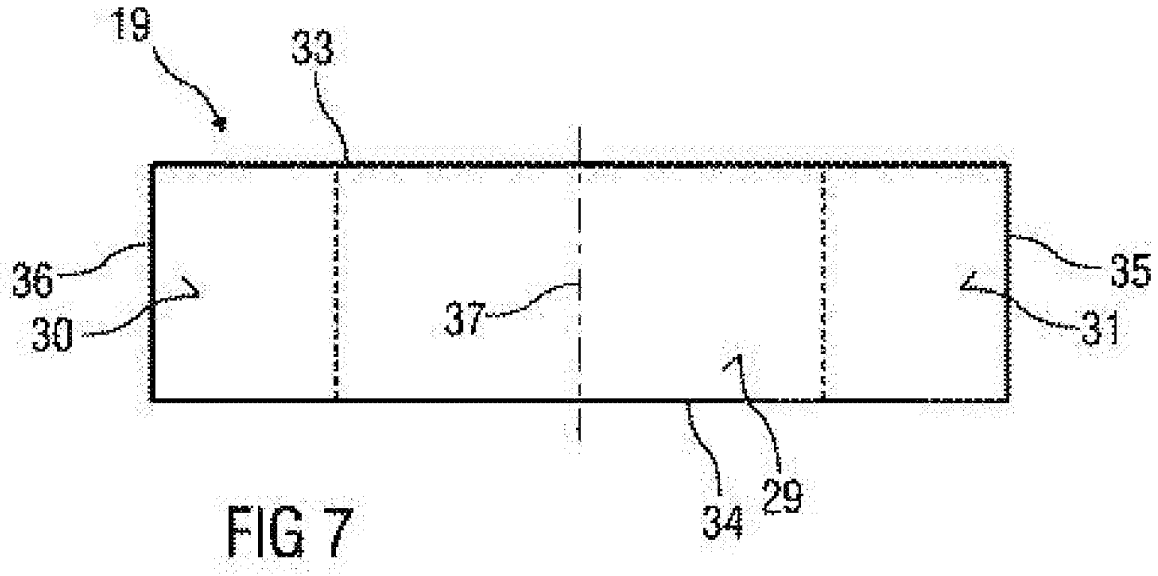


FIG 7

[Fig. 8]

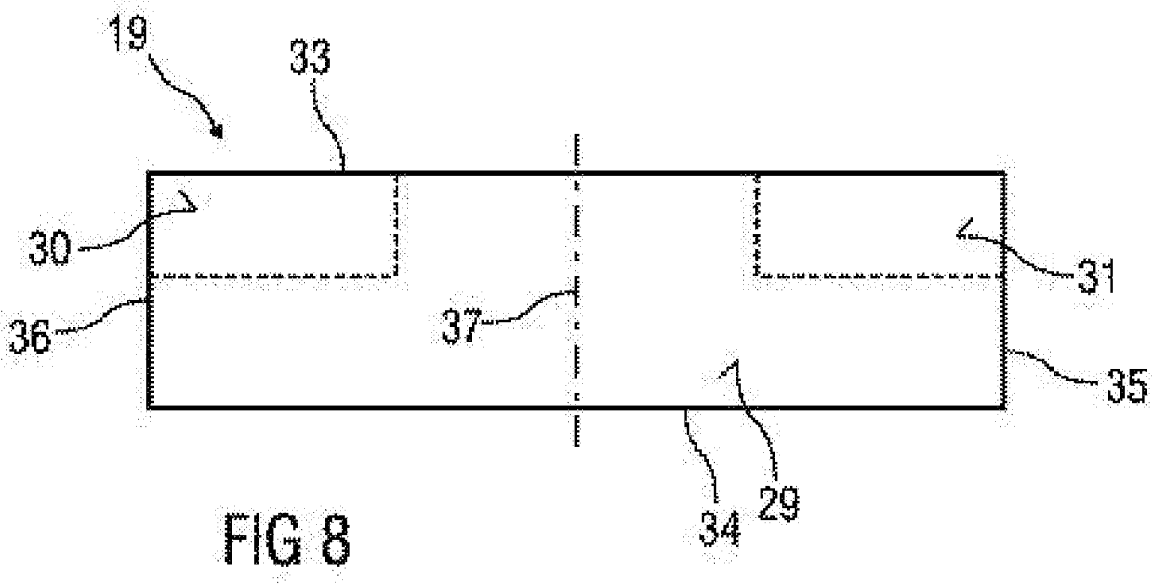


FIG 8

[Fig. 9]

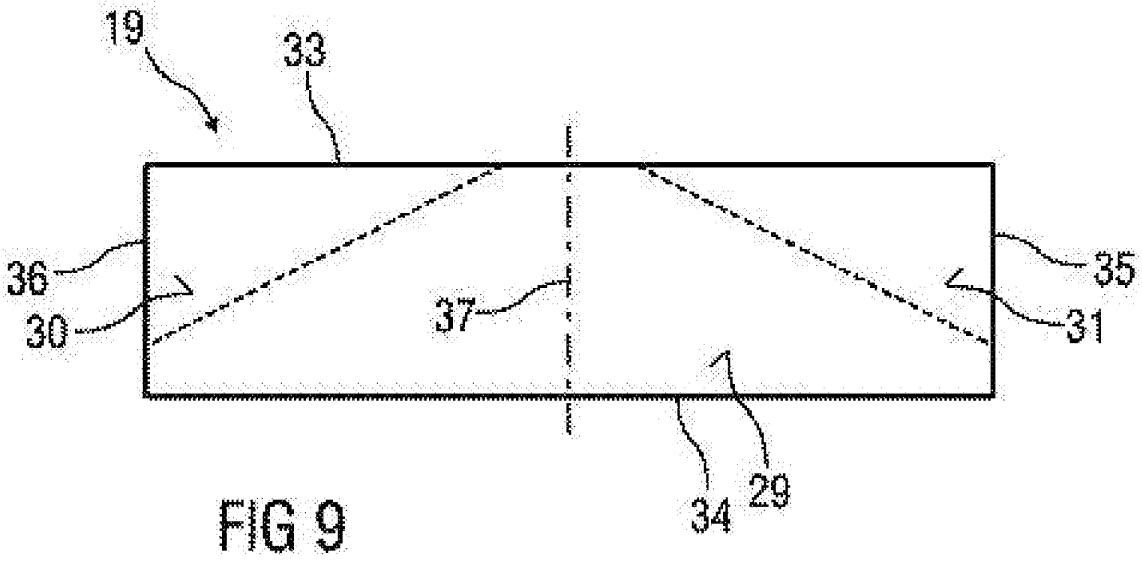


FIG 9

[Fig. 10]

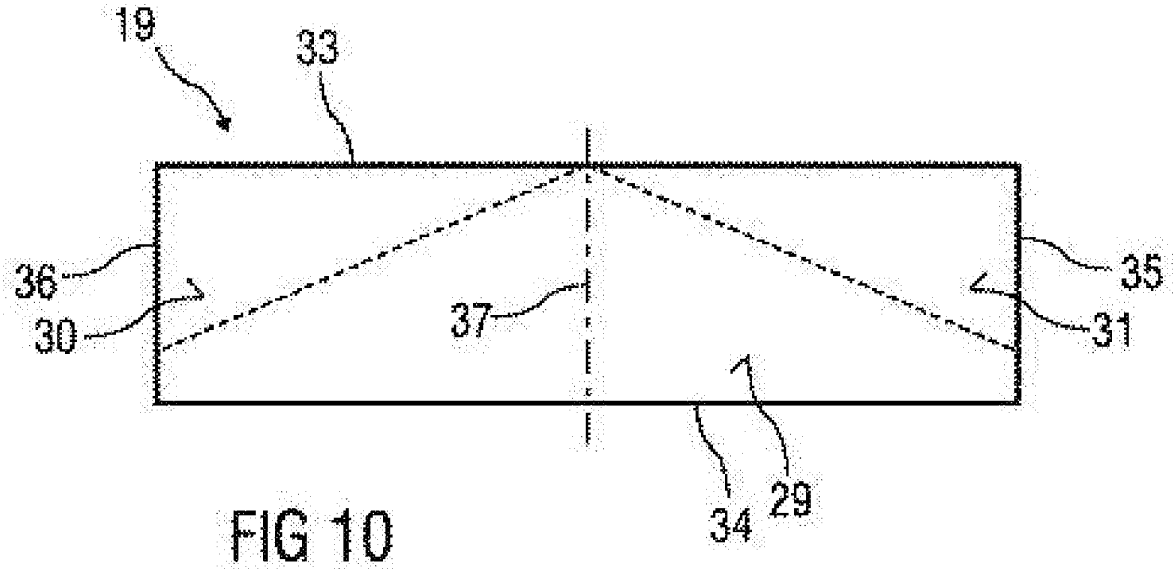


FIG 10

[Fig. 11]

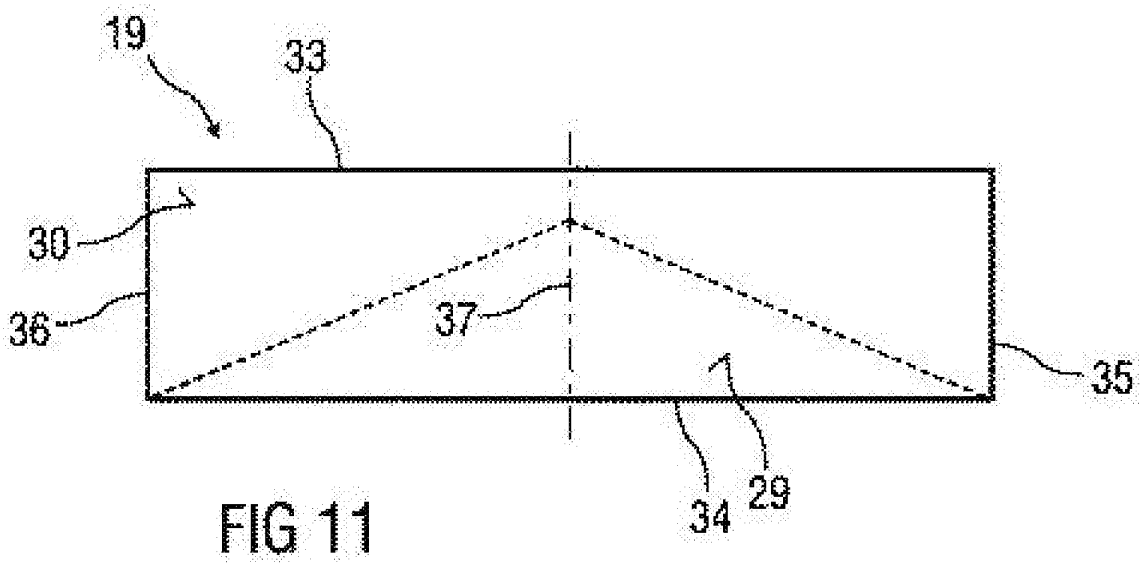


FIG 11

[Fig. 12]

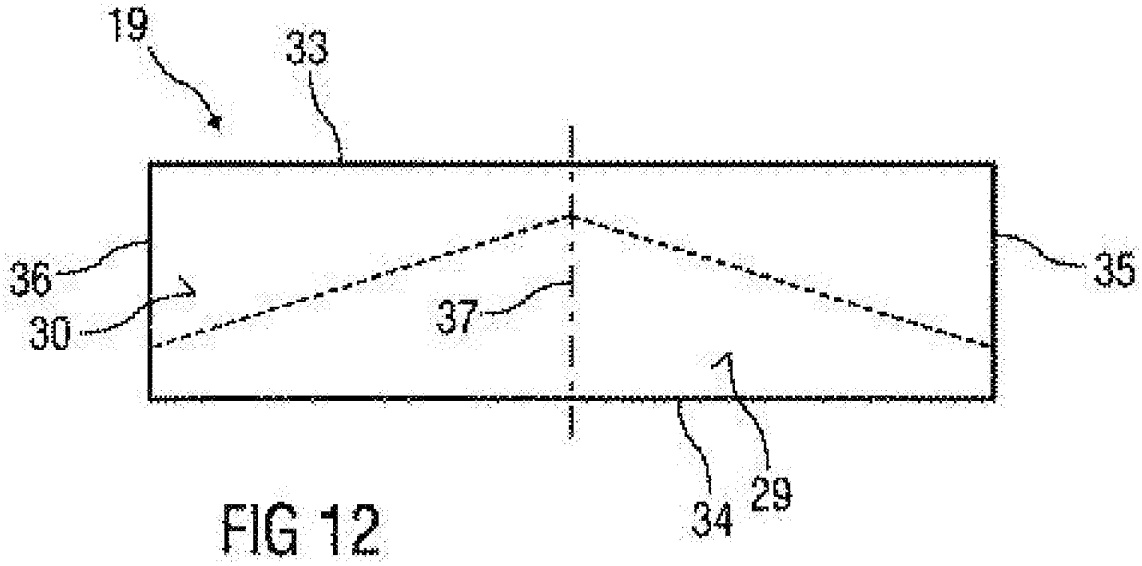


FIG 12

search report open

[International search report]

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2017/076000

A. CLASSIFICATION OF SUBJECT MATTER
INV. B21B27/10
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)
B21B

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.
X	DE 200 06 508 U1 (ACHENBACH BUSCHHUETTEN GMBH [DE]) 31 August 2000 (2000-08-31)	1,15
Y	page 5, paragraph 3 - page 7, paragraph 3	2-5
X	WO 2008/149195 A1 (ARCELORMITTAL FRANCE [FR]; VANDERSCHUEREN DIRK [BE]; VAN POECKE PATRIC) 11 December 2008 (2008-12-11)	1,15
Y	page 3, line 20 - page 4, line 12; figures 1,2	2-5
Y	EP 2 792 428 A1 (SIEMENS VAI METALS TECH GMBH [AT]) 22 October 2014 (2014-10-22) paragraph [0017] - paragraph [0027]; figures 1-3	2-5
A	WO 2015/113832 A1 (LOI THERMPROCESS GMBH [DE]) 6 August 2015 (2015-08-06) page 4, line 8 - line 17	1

☐ Further documents are listed in the continuation of Box C.

☒ 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

"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
11 January 2018	06/03/2018

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	Frisch, Ulrich

2

Form PCT/ISA/210 (second sheet) (April 2005)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2017/076000

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:

see additional sheet

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, 15

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.

Form PCT/ISA/210 (continuation of first sheet (2)) (January 2015)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2017/076000

The International Searching Authority has found that the international application contains multiple (groups of) inventions, as follows:

1. Claims 1-5, 15

Cooling device for cooling a roller, wherein two coolant chambers are provided which are separated from each other.

---

2. Claims 1, 6-8

Cooling device for cooling a roller, wherein the feed/control of the coolant is further defined.

---

3. Claims 1, 9-13

Cooling device for cooling a roller, wherein the distance of the nozzles is defined.

---

4. Claims 1, 14

Cooling device for cooling a roller, wherein an additional stripper is defined.

Form PCT/ISA/210 (extra sheet) (January 2015)

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/EP2017/076000

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
DE 20006508 U1	31-08-2000	DE 20006508 U1	31-08-2000
		EP 1142652 A2	10-10-2001
		JP 2001347307 A	18-12-2001
		US 2001027672 A1	11-10-2001
WO 2008149195 A1	11-12-2008	AU 2008259470 A1	11-12-2008
		BR PI0812201 A2	25-11-2014
		CA 2690098 A1	11-12-2008
		CN 101702888 A	05-05-2010
		EP 2014379 A1	14-01-2009
		EP 2164651 A1	24-03-2010
		JP 5380438 B2	08-01-2014
		JP 2010528870 A	26-08-2010
		KR 20100020462 A	22-02-2010
		RU 2009149178 A	20-07-2011
		SI 2164651 T1	30-08-2013
		UA 99295 C2	10-08-2012
		US 2010180657 A1	22-07-2010
		WO 2008149195 A1	11-12-2008
		ZA 200908405 B	28-07-2010
EP 2792428 A1	22-10-2014	CN 105188975 A	23-12-2015
		EP 2792428 A1	22-10-2014
		EP 2986400 A1	24-02-2016
		JP 6110015 B2	05-04-2017
		JP 2016515474 A	30-05-2016
		KR 20150143746 A	23-12-2015
		RU 2015141167 A	17-05-2017
		US 2016052033 A1	25-02-2016
		WO 2014170139 A1	23-10-2014
WO 2015113832 A1	06-08-2015	DE 102014001146 A1	06-08-2015
		EP 3099829 A1	07-12-2016
		WO 2015113832 A1	06-08-2015

Form PCT/ISA/210 (patent family annex) (April 2005)

INTERNATIONALER RECHERCHENBERICHT

Internationales Aktenzeichen
PCT/EP2017/076000

A. KLASSIFIZIERUNG DES ANMELDUNGSGEGENSTANDES
INV. B21B27/10
ADD.

Nach der Internationalen Patentklassifikation (IPC) oder nach der nationalen Klassifikation und der IPC

B. RECHERCHIERTE GEBIETE

Recherchierter Mindestprüfstoff (Klassifikationssystem und Klassifikationssymbole)
B21B

Recherchierte, aber nicht zum Mindestprüfstoff gehörende Veröffentlichungen, soweit diese unter die recherchierten Gebiete fallen

Während der internationalen Recherche konsultierte elektronische Datenbank (Name der Datenbank und evtl. verwendete Suchbegriffe)
EPO-Internal, WPI Data

C. ALS WESENTLICH ANGESEHENE UNTERLAGEN

Kategorie*	Bezeichnung der Veröffentlichung, soweit erforderlich unter Angabe der in Betracht kommenden Teile	Betr. Anspruch Nr.
X	DE 200 06 508 U1 (ACHENBACH BUSCHHUETTEN GMBH [DE]) 31. August 2000 (2000-08-31)	1,15
Y	Seite 5, Absatz 3 - Seite 7, Absatz 3	2-5
X	WO 2008/149195 A1 (ARCELORMITTAL FRANCE [FR]; VANDERSCHUEREN DIRK [BE]; VAN POECKE PATRIC) 11. Dezember 2008 (2008-12-11)	1,15
Y	Seite 3, Zeile 20 - Seite 4, Zeile 12; Abbildungen 1,2	2-5
Y	EP 2 792 428 A1 (SIEMENS VAI METALS TECH GMBH [AT]) 22. Oktober 2014 (2014-10-22) Absatz [0017] - Absatz [0027]; Abbildungen 1-3	2-5
A	WO 2015/113832 A1 (LOI THERMPROCESS GMBH [DE]) 6. August 2015 (2015-08-06) Seite 4, Zeile 8 - Zeile 17	1

☐ Weitere Veröffentlichungen sind der Fortsetzung von Feld C zu entnehmen ☒ Siehe Anhang Patentfamilie

* Besondere Kategorien von angegebenen Veröffentlichungen :
"A" Veröffentlichung, die den allgemeinen Stand der Technik definiert, aber nicht als besonders bedeutsam anzusehen ist
"E" frühere Anmeldung oder Patent, die bzw. das jedoch erst am oder nach dem internationalen Anmeldedatum veröffentlicht worden ist
"L" Veröffentlichung, die geeignet ist, einen Prioritätsanspruch zweifelhaft erscheinen zu lassen, oder durch die das Veröffentlichungsdatum einer anderen im Rechercherenbericht genannten Veröffentlichung belegt werden soll oder die aus einem anderen besonderen Grund angegeben ist (wie ausgeführt)
"O" Veröffentlichung, die sich auf eine mündliche Offenbarung, eine Benutzung, eine Ausstellung oder andere Maßnahmen bezieht
"P" Veröffentlichung, die vor dem internationalen Anmeldedatum, aber nach dem beanspruchten Prioritätsdatum veröffentlicht worden ist
"T" Spätere Veröffentlichung, die nach dem internationalen Anmeldedatum oder dem Prioritätsdatum veröffentlicht worden ist und mit der Anmeldung nicht kollidiert, sondern nur zum Verständnis des der Erfindung zugrundeliegenden Prinzips oder der ihr zugrundeliegenden Theorie angegeben ist
"X" Veröffentlichung von besonderer Bedeutung; die beanspruchte Erfindung kann allein aufgrund dieser Veröffentlichung nicht als neu oder auf erfinderischer Tätigkeit beruhend betrachtet werden
"Y" Veröffentlichung von besonderer Bedeutung; die beanspruchte Erfindung kann nicht als auf erfinderischer Tätigkeit beruhend betrachtet werden, wenn die Veröffentlichung mit einer oder mehreren Veröffentlichungen dieser Kategorie in Verbindung gebracht wird und diese Verbindung für einen Fachmann naheliegend ist
"&" Veröffentlichung, die Mitglied derselben Patentfamilie ist

Datum des Abschlusses der internationalen Recherche	Absendedatum des internationalen Recherchenberichts
11. Januar 2018	06/03/2018

Name und Postanschrift der Internationalen Recherchenbehörde	Bevollmächtigter Bediensteter
Europäisches Patentamt, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Frisch, Ulrich

2

Formblatt PCT/ISA/210 (Blatt 2) (April 2005)

INTERNATIONALER RECHERCHENBERICHT

Internationales Aktenzeichen
PCT/EP2017/076000

Feld Nr. II Bemerkungen zu den Ansprüchen, die sich als nicht recherchierbar erwiesen haben (Fortsetzung von Punkt 2 auf Blatt 1)

Gemäß Artikel 17(2)a) wurde aus folgenden Gründen für bestimmte Ansprüche kein internationaler Recherchenbericht erstellt:

1. ☐ Ansprüche Nr.
weil sie sich auf Gegenstände beziehen, zu deren Recherche diese Behörde nicht verpflichtet ist, nämlich

2. ☐ Ansprüche Nr.
weil sie sich auf Teile der internationalen Anmeldung beziehen, die den vorgeschriebenen Anforderungen so wenig entsprechen, dass eine sinnvolle internationale Recherche nicht durchgeführt werden kann, nämlich

3. ☐ Ansprüche Nr.
weil es sich dabei um abhängige Ansprüche handelt, die nicht entsprechend Satz 2 und 3 der Regel 6.4 a) abgefasst sind.

Feld Nr. III Bemerkungen bei mangelnder Einheitlichkeit der Erfindung (Fortsetzung von Punkt 3 auf Blatt 1)

Diese Internationale Recherchenbehörde hat festgestellt, dass diese internationale Anmeldung mehrere Erfindungen enthält:

siehe Zusatzblatt

1. ☐ Da der Anmelder alle erforderlichen zusätzlichen Recherchengebühren rechtzeitig entrichtet hat, erstreckt sich dieser internationale Recherchenbericht auf alle recherchierbaren Ansprüche.

2. ☐ Da für alle recherchierbaren Ansprüche die Recherche ohne einen Arbeitsaufwand durchgeführt werden konnte, der zusätzliche Recherchengebühr gerechtfertigt hätte, hat die Behörde nicht zur Zahlung solcher Gebühren aufgefordert.

3. ☐ Da der Anmelder nur einige der erforderlichen zusätzlichen Recherchengebühren rechtzeitig entrichtet hat, erstreckt sich dieser internationale Recherchenbericht nur auf die Ansprüche, für die Gebühren entrichtet worden sind, nämlich auf die Ansprüche Nr.

4. ☒ Der Anmelder hat die erforderlichen zusätzlichen Recherchengebühren nicht rechtzeitig entrichtet. Dieser internationale Recherchenbericht beschränkt sich daher auf die in den Ansprüchen zuerst erwähnte Erfindung; diese ist in folgenden Ansprüchen erfasst:
1-5, 15

Bemerkungen hinsichtlich eines Widerspruchs

☐ Der Anmelder hat die zusätzlichen Recherchengebühren unter Widerspruch entrichtet und die gegebenenfalls erforderliche Widerspruchsgebühr gezahlt.

☐ Die zusätzlichen Recherchengebühren wurden vom Anmelder unter Widerspruch gezahlt, jedoch wurde die entsprechende Widerspruchsgebühr nicht innerhalb der in der Aufforderung angegebenen Frist entrichtet.

☐ Die Zahlung der zusätzlichen Recherchengebühren erfolgte ohne Widerspruch.

Formblatt PCT/ISA/210 (Fortsetzung von Blatt 1 (2)) (April 2005)

Internationales Aktenzeichen PCT/ EP2017/ 076000

WEITERE ANGABEN **PCT/ISA/ 210**

Die internationale Recherchenbehörde hat festgestellt, dass diese internationale Anmeldung mehrere (Gruppen von) Erfindungen enthält, nämlich:

1. Ansprüche: 1-5, 15

   Kühlvorrichtung zur Kühlung einer Walze, wobei zwei voneinander getrennte Kühlmittelkammern vorgesehen sind.

   ---

2. Ansprüche: 1, 6-8

   Kühlvorrichtung zur Kühlung einer Walze, wobei die Zuleitung / Steuerung des Kühlmittels weiter definiert wird.

   ---

3. Ansprüche: 1, 9-13

   Kühlvorrichtung zur Kühlung einer Walze, wobei der Abstand der Düsen definiert wird.

   ---

4. Ansprüche: 1, 14

   Kühlvorrichtung zur Kühlung einer Walze, wobei ein zusätzlicher Abstreifer definiert wird

   ---

INTERNATIONALER RECHERCHENBERICHT

Angaben zu Veröffentlichungen, die zur selben Patentfamilie gehören

Internationales Aktenzeichen
PCT/EP2017/076000

Im Recherchenbericht angeführtes Patentdokument	Datum der Veröffentlichung	Mitglied(er) der Patentfamilie	Datum der Veröffentlichung
DE 20006508 U1	31-08-2000	DE 20006508 U1	31-08-2000
		EP 1142652 A2	10-10-2001
		JP 2001347307 A	18-12-2001
		US 2001027672 A1	11-10-2001
WO 2008149195 A1	11-12-2008	AU 2008259470 A1	11-12-2008
		BR PI0812201 A2	25-11-2014
		CA 2690098 A1	11-12-2008
		CN 101702888 A	05-05-2010
		EP 2014379 A1	14-01-2009
		EP 2164651 A1	24-03-2010
		JP 5380438 B2	08-01-2014
		JP 2010528870 A	26-08-2010
		KR 20100020462 A	22-02-2010
		RU 2009149178 A	20-07-2011
		SI 2164651 T1	30-08-2013
		UA 99295 C2	10-08-2012
		US 2010180657 A1	22-07-2010
		WO 2008149195 A1	11-12-2008
		ZA 200908405 B	28-07-2010
EP 2792428 A1	22-10-2014	CN 105188975 A	23-12-2015
		EP 2792428 A1	22-10-2014
		EP 2986400 A1	24-02-2016
		JP 6110015 B2	05-04-2017
		JP 2016515474 A	30-05-2016
		KR 20150143746 A	23-12-2015
		RU 2015141167 A	17-05-2017
		US 2016052033 A1	25-02-2016
		WO 2014170139 A1	23-10-2014
WO 2015113832 A1	06-08-2015	DE 102014001146 A1	06-08-2015
		EP 3099829 A1	07-12-2016
		WO 2015113832 A1	06-08-2015

Formblatt PCT/ISA/210 (Anhang Patentfamilie) (April 2005)

drawing open

Representative drawing | 1 | 2 | 3 | Four | Five | 6 | 7 | 8 | 9 | ...

Magnify and Rotate

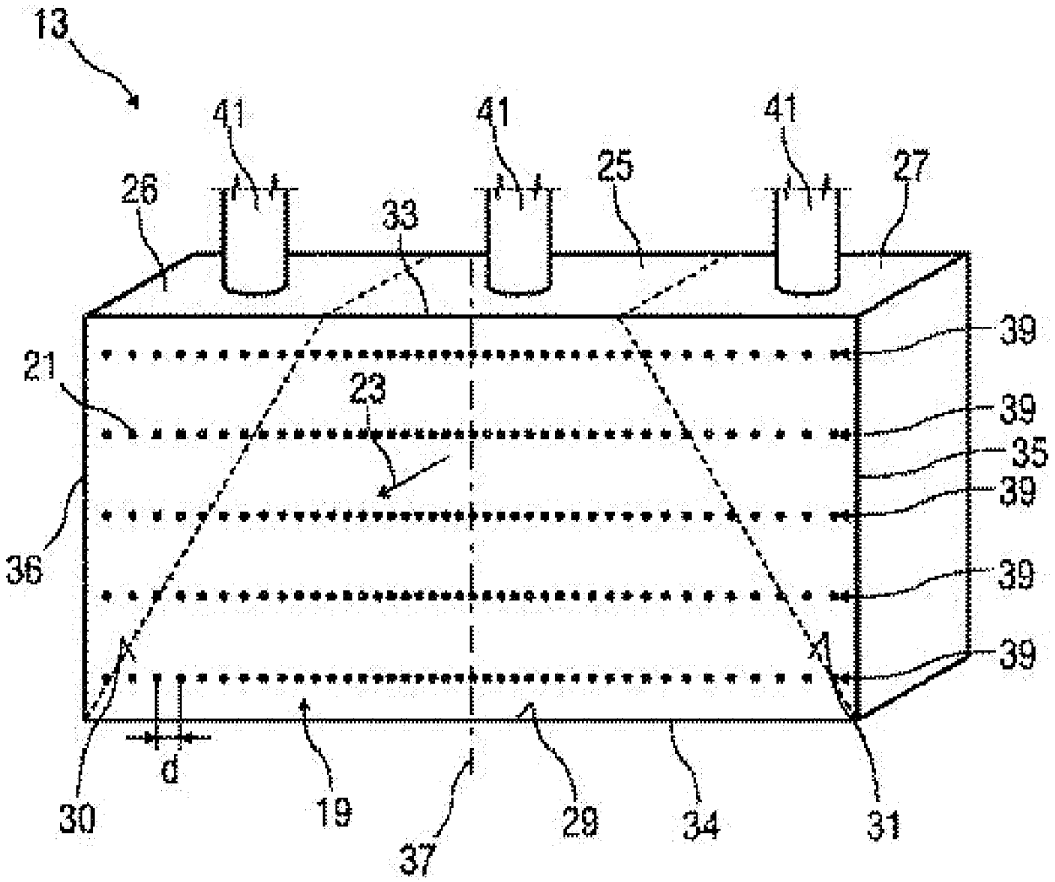


FIG 2

Representative drawing

1 / 1 display

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Notice

This translation is machine-generated. It cannot be guaranteed that it is intelligible, accurate, complete, reliable or fit for specific purposes. Critical decisions, such as commercially relevant or financial decisions, should not be based on machine-translation output.

ABSTRACT JP2019534792A

[0001]

The present invention relates to a cooling device (7) for cooling the rolls (5) of the rolling stand (1). The cooling device (7) comprises cooling beams (13) for receiving and discharging coolant. The cooling beam (13) has a plurality of full jet nozzles (21) arranged on the discharge side (19) of said cooling beam (13), said side facing the roll (5).) parallel to the roll axis (17). A jet of coolant with a substantially constant jet diameter can be sprayed through each of the full jet nozzles from the cooling beam (13) towards the roll (5) in the discharge direction (23).



(19)日本国特許庁(JP)　(12)公表特許公報(A)　(11)特許出願公表番号
特表2019-534792
(P2019-534792A)
(43)公表日　令和1年12月5日(2019.12.5)

(51)Int.Cl.		F I			テーマコード（参考）
B21B 27/10	(2006.01)	B21B	27/10	A	
		B21B	27/10	C	
		B21B	27/10	D	

審査請求 有　予備審査請求 未請求　（全 21 頁）

(21)出願番号　特願2019-520550 (P2019-520550)
(86)(22)出願日　平成29年10月12日 (2017.10.12)
(85)翻訳文提出日　令和1年6月13日 (2019.6.13)
(86)国際出願番号　PCT/EP2017/076000
(87)国際公開番号　WO2018/073086
(87)国際公開日　平成30年4月26日 (2018.4.26)
(31)優先権主張番号　16194099.4
(32)優先日　平成28年10月17日 (2016.10.17)
(33)優先権主張国・地域又は機関
欧州特許庁 (EP)

(71)出願人　515153152
プライメタルズ・テクノロジーズ・オーストリア・ゲーエムベーハー
オーストリア・４０３１・リンツ・ツームシュトラーセ・４４
(74)代理人　100133400
弁理士　阿部　達彦
(74)代理人　100110364
弁理士　実広　信哉
(72)発明者　アロイス・ザイリンガー
オーストリア・４０４０・リンツ・ハーゼルグラーベンヴェーク・１７
(72)発明者　エリッヒ・オービッツ
オーストリア・７１２３・メンヒーホフ・アンガーガッセ・４６

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(54)【発明の名称】圧延スタンドのロールの冷却

【要約】
本発明は、圧延スタンド　のロール　を冷却するための冷却装置　に関する。冷却装置　は、冷却剤を受け入れて吐出するための冷却ビーム　を備える。冷却ビーム　は、前記冷却ビーム　の吐出側面　に配置された複数のフルジェットノズル　を有し、前記側面は、ロール　に面してロール　のロール軸　に平行に延在する。ほぼ一定のジェット径を有する冷却剤のジェットを、フルジェットノズルのそれぞれを通して、冷却ビーム　からロール　に向けて吐出方向　に噴霧することができる。

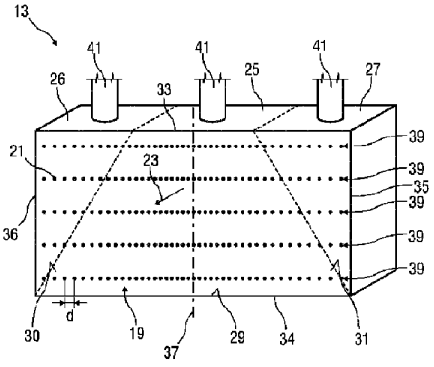


FIG 2

【特許請求の範囲】
【請求項１】
冷却剤を受け入れて吐出するための冷却棒（１３）を備えた、圧延スタンド（１）のロール（５）を冷却するための冷却装置（７）であって、
前記冷却棒（１３）が、前記冷却棒（１３）の吐出側面（１９）に配置された複数のフルジェットノズル（２１）を有し、前記吐出側面が、ロール（５）に面して前記ロール（５）のロール軸（１７）に平行に延在し、ほぼ一定のジェット径の冷却剤の冷却剤ジェットを、フルジェットノズルのそれぞれを通して、前記冷却棒（１３）から前記ロール（５）に向けて吐出方向（２３）に吐出することができる、冷却装置（７）。
【請求項２】
前記冷却棒（１３）が、冷却剤を受け入れるための、相互に分離した少なくとも２つの冷却剤室（２５～２７）に分割され、各冷却剤室（２５～２７）が、複数のフルジェットノズル（２１）が配置された前記冷却棒（１３）の前記吐出側面（１９）の部分領域（２９～３１）に対応し、前記フルジェットノズル（２１）のそれぞれを通して、冷却剤ジェットを前記冷却剤室（２５～２７）から前記ロール（５）に向けて吐出することができることを特徴とする、請求項１に記載の冷却装置（７）。
【請求項３】
第１の冷却剤室（２５）が、前記冷却棒（１３）の前記吐出側面（１９）の第１の部分領域（２９）に対応し、前記第１の部分領域（２９）が、前記冷却棒（１３）の前記吐出側面（１９）の中心線（３７）に対して鏡面対称であり、軸が前記ロール軸（１７）に垂直であることを特徴とする、請求項２に記載の冷却装置（７）。
【請求項４】
中心線（３７）に並行する第１の部分領域（２９）の範囲が、前記ロール軸（１７）の方向に沿って変化し、前記中心線（３７）に沿って最大であることを特徴とする、請求項２または３に記載の冷却装置（７）。
【請求項５】
第１の部分領域（２９）が多角形であることを特徴とする、請求項２から４のいずれか一項に記載の冷却装置（７）。
【請求項６】
各冷却剤室（２５～２７）が、前記冷却剤室（２５～２７）内に冷却剤を供給するための冷却剤供給ライン（４１）に接続され、前記冷却剤供給ライン（４１）が、前記冷却剤室（２５～２７）内に、前記冷却剤の前記吐出方向（２３）に実質的に垂直に開口していることを特徴とする、請求項２から５のいずれか一項に記載の冷却装置（７）。
【請求項７】
前記冷却剤室（２５～２７）内に供給される前記冷却剤の量を、それぞれの制御弁（４３）、および／または、それぞれのポンプ（４５）によって互いに独立して制御することができることを特徴とする、請求項２から６のいずれか一項に記載の冷却装置（７）。
【請求項８】
前記冷却剤室（２５～２７）内に供給される前記冷却剤の量を制御するための自動化システムによって特徴付けられた、請求項２から７のいずれか一項に記載の冷却装置（７）。
【請求項９】
前記ロール軸（１７）に平行な方向に沿って相互に隣り合うフルジェットノズル（２１）のノズル間隔（ｄ）が、前記方向に沿って変化していることを特徴とする、請求項１から８のいずれか一項に記載の冷却装置（７）。
【請求項１０】
前記ノズル間隔（ｄ）が、前記冷却棒（１３）の前記吐出側面（１９）の中央領域において最も狭いことを特徴とする、請求項９に記載の冷却装置（７）。
【請求項１１】
前記ノズル間隔（ｄ）が、約２５ｍｍから約５０ｍｍの間であることを特徴とする、請

求項９または１０に記載の冷却装置（７）。
【請求項１２】
前記フルジェットノズル（２１）が、相互に平行な複数のノズル列（３９）になるように配置されていることを特徴とする、請求項１から１１のいずれか一項に記載の冷却装置（７）。
【請求項１３】
前記冷却棒（１３）が、前記フルジェットノズル（２１）が取り外し可能に固定された、各フルジェットノズル（２１）のためのノズル開口を有していることを特徴とする、請求項１から１２のいずれか一項に記載の冷却装置（７）。
【請求項１４】
前記ロール（５）から冷却乳をぬぐい取るためのワイパ（１５）であって、前記冷却棒（１３）と一緒に枢動させることができるワイパ（１５）によって特徴付けられた、請求項１から１３のいずれか一項に記載の冷却装置（７）。
【請求項１５】
ロール（５）と、請求項１から１３のいずれか一項に記載されたようにそれぞれ設計された２つの冷却装置（７）と、を備えた圧延スタンド（１）であって、前記２つの冷却装置（７）が、前記ロール（５）の両側に配置されている、圧延スタンド（１）。
【発明の詳細な説明】
【技術分野】
【０００１】
本発明は、圧延スタンドのロールを冷却するための冷却装置に関する。
【背景技術】
【０００２】
圧延素材を圧延するための圧延スタンドは、冷却液体、一般的には冷却水を用いて冷却されるロールを有する。
【０００３】
特許文献１には、低圧の冷却液体を圧延スタンドのロールにかけることができる、剛性の高い凹状のシェルが開示されている。
【０００４】
特許文献２には、移動可能な関節式冷却シェルによる圧延スタンドのワークロールの流動冷却が開示されている。この場合、冷却液体は、冷却シェルを用いて主として低圧でかけられるが、さらに、冷却液体は、高圧でかけられて十分な冷却効果を生じる。
【０００５】
特許文献３には、圧延スタンドのワークロールを冷却するための冷却装置が開示されており、この装置は、関係する圧延スタンドを用いて生産される最も狭い片よりもやや狭い固定スプレー棒を有し、そのときに圧延されている片の幅に対応するワークロールのこれらの部分のみを冷却するための、軸方向に移動可能なスプレー棒を有する。
【０００６】
特許文献４には、圧延スタンドのワークロールを冷却するための方法が開示されており、この方法では、冷却水が、高圧ではなく低圧でワークロールに噴霧されるが、同時に、かけられる範囲が広くされている。
【０００７】
特許文献５には、圧延材を冷却するためのスプレー棒が開示されており、このスプレー棒は、圧延材の移動方向に横断して延在し、中央領域および つの縁領域を有して、冷却媒体をそれらのそれぞれに別々に供給することができる。
【先行技術文献】
【特許文献】
【０００８】
【特許文献１】米国特許出願公開第　　号
【特許文献２】独国特許出願公開第　　号

【特許文献３】特開平　　号
【特許文献４】特開昭　　号
【特許文献５】国際公開第　　号
【発明の概要】
【発明が解決しようとする課題】
【０００９】
圧延スタンドのロールを冷却するための改善された冷却装置を特定することが本発明の基本的な目的である。
【課題を解決するための手段】
【００１０】
本発明によれば、この目的は、請求項　の特徴によって達成される。
【００１１】
本発明の有利な実施形態は、従属請求項の主題を形成する。
【００１２】
圧延スタンドのロールを冷却するための本発明による冷却装置は、冷却剤を受け入れて吐出するための冷却棒を備える。冷却棒は、冷却棒の吐出側面に配置された複数のフルジェットノズルを有し、前記側面は、ロールに面してロールのロール軸に平行に延在する。ほぼ一定のジェット径の冷却剤の冷却剤ジェットを、各フルジェットノズルを通して、冷却棒からロールに向けて吐出方向に吐出することができる。
【００１３】
フルジェットノズルとは、ほぼ一定のジェット径で実質的に直線状の冷却剤ジェットを吐出することができるノズルを意味するものとする。冷却剤を集中させて吐出するおかげで、フルジェットノズルは、従来使用されてきたファンジェットノズルよりも、冷却棒での同じ冷却剤圧力でより高いロールへの衝撃圧を生じる。全体にかけられた大量の冷却剤の量により、典型的には、数ミリメートルから数センチメートルの厚さの特定の冷却剤膜が常にあり、良好な放熱のために冷却剤ジェットを衝突させることによって、この膜はできるだけ完全に貫通されるべきであるので、より高い衝撃圧は、ロール表面での冷却作用に直接良い効果を生じる。フルジェットノズルによって生じた、ロールへの冷却剤ジェットの高い衝撃圧のおかげで、冷却棒の冷却剤圧力は、ファンジェットノズルを使用した場合に比べて大きく下げることができ、それによって、冷却装置のＴネルギー消費および運用コストを大きく下げることができることは有利である。
【００１４】
冷却剤はフルジェットノズルを通って吐出されるので、ロールからスプレー棒までの間隔はさらに、広い範囲にわたってそれほど重要ではなくなり、したがって、ロール直径に適合させる必要はない。したがって、例えば、実質的に直進する冷却剤ジェットによって、冷却剤ジェットの冷却効果に何ら大きな変化もなしに、　　から　　の間の距離で、冷却されるべきロール表面を冷却することができる。
【００１５】
冷却剤圧力の低下はまた、負荷の低減、その結果としてノズルの摩耗の低減に関係するので、これもまた、冷却棒の冷却剤圧力の低下の結果、保守費用が低減され、これがフルジェットノズルの使用の別の利点である。
【００１６】
本発明の一実施形態では、冷却棒が、冷却剤を受け入れるための、相互に分離した少なくとも　つの冷却剤室に分割されることが想定されている。各冷却剤室は、複数のフルジェットノズルが配置された冷却棒の吐出側面の部分領域に対応し、フルジェットノズルのそれぞれを通して、冷却剤ジェットを冷却剤室からロールに向けて吐出することができる。冷却棒の吐出側面の異なる部分領域に対応する、相互に分離した複数の冷却剤室に、冷却棒を分割すると、互いに独立して、部分領域の冷却剤圧力を制御し、その結果、部分領域によって吐出される冷却剤流量を制御することによって、部分領域の冷却効果を互いに独立して制御することができることは有利である。それによって、位置に応じてロールの

冷却に影響を与えることが可能となり、ロール表面のより強く加熱された領域、例えば、ロール表面の中央領域を、それほど強く加熱されていない領域よりも確実に強く冷却することができることは有利である。

【００１７】

本発明の上記の実施形態の展開としては、第 の冷却剤室が、冷却棒の吐出側面の第 の部分領域に対応し、第 の部分領域が、冷却棒の吐出側面の中心線に対して鏡面対称であり、その軸がロール軸に垂直であることが想定されている。例えば、中心線に並行する第 の部分領域の範囲は、ロール軸の方向に沿って変化し、中心線に沿って最大である。例えば、第 の部分領域は多角形である。第 の部分領域が中心線に対して鏡面対称の実施形態は、ロールが概ね同様に、中心線に対して対称的に加熱されるという事実を考慮している。中心線に並行する第 の部分領域の範囲がロール軸の方向に沿って変化し、中心線に沿って最大範囲を有することは、ロールが、一般に、中心において最も強く加熱され、ロールの加熱が縁領域に向けて減少するという事実を考慮している。したがって、これに対応した第 の部分領域の構成は、第 の部分領域によって、位置に依存したロールの熱負荷にロールの冷却を適合させることを可能にする。

【００１８】

本発明の別の実施形態では、各冷却剤室が、冷却剤室内に冷却剤を供給するための冷却剤供給ラインに接続され、冷却剤供給ラインが、冷却剤室内に、冷却剤の吐出方向に実質的に垂直に開口していることが想定されている。冷却剤供給ラインが、冷却棒内に、吐出方向に実質的に垂直に開口していることによって、各冷却剤室内の冷却剤の圧力分布をほとんど均一にすることができる。それによって、開口近くのフルジェットノズルと開口から離れたノルジェットノズルとの間の圧力勾配がなくなることは有利である。

【００１９】

本発明の別の実施形態では、冷却剤室内に供給される冷却剤の量を、それぞれの制御弁、および／または、それぞれのポンプによって互いに独立して制御することができることが想定されている。これによって、上記のように、個々の冷却剤室から吐出される冷却剤ジェットの冷却効果を互いに独立して制御することができる。例えば、通常、 の圧力で冷却水を送出する水供給システムなどの、例えば、いかなるときにも存在する従来の冷却剤供給システムを、関連する圧延システムにおいて使用することができる場合には、制御弁によって冷却剤の量を制御することが特に有利である。この場合、ロール冷却をするために複雑で高価な昇圧システム無しで済ますことができる。適当であれば、制御弁と共に、ポンプによって冷却剤の量を制御することによって、圧延間の休止時、または、低い冷却能力しか必要でない圧延作業の場合に、個々のポンプを止める、またはポンプの動力を下げることができ、それによって、エネルギー消費を低減することができる。

【００２０】

本発明の別の実施形態では、冷却剤室内に供給される冷却剤の量を制御するための自動化システムが想定されている。それによって、体積流量をロール表面の温度分布に適合させるために、冷却剤室からロールに吐出される冷却剤の体積流量を自動的に制御することができることは有利である。この場合、冷却剤室内に供給される冷却剤の量は、上記の制御弁および／またはポンプを制御することを通じて、自動化システムによって制御されることが好ましい。

【００２１】

本発明の別の実施形態では、ロール軸に平行な方向に沿って相互に隣り合うフルジェットノズルのノズル間隔が前記方向に沿って変化していることが想定されている。この場合、ノズル間隔は、冷却棒の吐出側面の中央領域において最も狭いことが好ましい。例えば、ロール軸に平行な方向に沿うノズル間隔は、約 から約 の間である。本発明のこれらの実施形態によって、また、ロール軸に平行な方向に沿うノズル間隔が位置に依存したロール表面の熱負荷に従って変えられるので、フルジェットノズルの配置をこの熱負荷に適合させることもできる。最小のノズル間隔が冷却棒の吐出側面の中央領域にあるのは、ロール表面の中央領域が一般に、最大の熱負荷を受けるという事実を考慮している。

【００２２】
本発明の別の実施形態では、フルジェットノズルが、相互に平行な複数のノズル列になるように配置されていることが想定されている。これによって、冷却剤をより広い範囲にわたって、かつ、ロールが回転することと併せて、均一にロールにかけることができることは有利である。
【００２３】
本発明の別の実施形態では、冷却棒が、フルジェットノズルが取り外し可能に固定された、各フルジェットノズルのためのノズル開口を有していることが想定されている。本発明のこの実施形態によって、不良なジェットノズルを容易に交換することができることは有利である。
【００２４】
本発明の別の実施形態では、ロールから冷却剤をぬぐい取るためのワイパが提供され、ワイパと冷却棒を一緒に枢動させることができる。例えば、ワイパによって、過剰な冷却剤が、圧延材に、および／または、圧延材が つのロール間を案内されるロール間隙に導かれて、圧延材とロールとの間の摩擦を低減するための潤滑剤を洗い流すことを防ぐことができることは有利である。ワイパと冷却棒が一緒に枢動することができることによって、冷却棒を動かすための追加の装置の必要が除かれることは有利である。この場合、上記ですでに言及したフルジェットノズルを使用する利点は、この場合にもまた効果がある。すなわち、フルジェットノズルを使用することによって、スプレー棒とロールとの間の距離は、広い範囲にわたってそれほど重要ではなくなり、したがって、ロール直径に適合させる必要がなくなる。さらに、本発明はまた、ワイパを有する既存の圧延システムに対しては改造策として特に適しており、例えば、従来の高圧スプレー棒のみを本発明による冷却棒に交換するだけでよい。
【００２５】
本発明による圧延スタンドは、ロール、および本発明による つの冷却装置を備え、 つの冷却装置は、ロールの反対側に配置される。本発明による圧延スタンドの利点は、上記ですでに言及した、本発明による冷却装置の利点から生じる。
【００２６】
この発明の上記の特性、特徴、および利点、ならびにこれらを達成する態様は、図面と併せてより詳細に説明される例示的な実施形態の以下の説明と関連して、より明確かつ明瞭に理解されるであろう。
【図面の簡単な説明】
【００２７】
【図１】冷却装置を有する圧延スタンドの概略図である。
【図２】冷却棒の第 の例示的な実施形態の概略斜視図である。
【図３】図 に示した冷却棒によって吐出される冷却剤の体積流量を位置の関数として示した図である。
【図４】冷却棒の第 の例示的な実施形態の吐出側面の図である。
【図５】冷却棒の第 の例示的な実施形態の吐出側面の図である。
【図６】冷却棒の第 の例示的な実施形態の吐出側面の図である。
【図７】冷却棒の第 の例示的な実施形態の吐出側面の図である。
【図８】冷却棒の第 の例示的な実施形態の吐出側面の図である。
【図９】冷却棒の第 の例示的な実施形態の吐出側面の図である。
【図１０】冷却棒の第 の例示的な実施形態の吐出側面の図である。
【図１１】冷却棒の第 の例示的な実施形態の吐出側面の図である。
【図１２】冷却棒の第 の例示的な実施形態の吐出側面の図である。
【発明を実施するための形態】
【００２８】
すべての図面で、同じ部品には同じ参照符号が付けられている。
【００２９】

図 は、圧延素材 を圧延するための圧延スタンド の概略図である。圧延スタンド は、ワークロールとして設計された つのロール 、および各ロール に対して つの冷却装置 を備え、前記装置は、ロール の両側に配置されている。ロール は、ロール間隙 だけ間隔を置いて配置され、圧延材 を形成するために、圧延素材 をロール間隙 に圧延方向 に通す。各冷却装置 は、冷却棒 およびワイパ を備える。

【００３０】

各冷却棒 は、冷却剤を受け入れて吐出するように設計されている。冷却剤を吐出するために、冷却棒 は、冷却棒 の吐出側面 に配置された複数のフルジェットノズル を有し、前記側面は、それぞれのロール に面してロール のロール軸 に平行に延在し、ほぼ一定のジェット径の冷却剤ジェットを、フルジェットノズルのそれぞれを通して、冷却棒 からロール に向けて吐出方向 に吐出することができる。冷却剤は、冷却剤供給ライン を経て冷却棒 内に供給することができ、冷却棒 内に供給される冷却剤の量は、制御弁 、および／または、例えば周波数制御のポンプ によって制御することができる。冷却剤は、例えば、水である。

【００３１】

各ワイパ は、それぞれのロール から冷却剤をぬぐい取るように設計され、ロール に向かうように、またこれから離れるように枢動させることができる。各冷却装置 の冷却棒 およびワイパ は、冷却装置 の枢動装置に固定され、したがって、冷却棒 およびワイパ をロール に向かうように、またロール から離れるように一緒に枢動させることができることが好ましい。

【００３２】

図 は、ロール に冷却剤を吐出するための冷却棒 の第 の例示的な実施形態の概略斜視図である。冷却棒 は、相互に分離した つの冷却剤室 ～ に分割されて、冷却剤を受け入れる。各冷却剤室 ～ は、複数のフルジェットノズル が配置された吐出側面 の部分領域 ～ に対応し、冷却剤ジェットを冷却剤室 ～ からフルジェットノズルのそれぞれを通してロール に向けて吐出方向 に吐出することができる。吐出側面 は、ロール軸 に平行な つの長手方向辺 、 、およびロール軸 に垂直な つの短手方向辺 、 を有する長方形である。

【００３３】

第 の冷却剤室 は、吐出側面 の中央領域を形成する、冷却棒 の吐出側面 の第 の部分領域 に対応する。第 の部分領域 は、冷却棒 の吐出側面 の中心線 に対して鏡面対称であり、前記軸はロール軸 に垂直であり、第 の長手方向辺 に配置された つの頂点と、第 の長手方向辺 の端点にそれぞれ配置された つの頂点とを有する台形である。

【００３４】

フルジェットノズル は、それぞれがロール軸 に平行に延在する複数のノズル列 になって、吐出側面 に配置されている。この場合、各ノズル列 の相互に隣り合うフルジェットノズル のノズル間隔ｄは、中心線 に対して対称的に変化しており、その結果、ノズル間隔ｄは、吐出側面 の中央領域において最も狭く、吐出側面 の縁領域に向かって、例えば、放物線状に広くなっている。図 に示した例示的な実施形態では、ノズル間隔ｄは、各ノズル列 の端部ではノズル列 の中心での間隔の 倍大きくなっている。ノズル間隔ｄは、例えば、 から の間を変化する。ノズル列 は、吐出側面 の全範囲にわたって実質的に等間隔に延在し、したがって、ロール のロール表面に比較的均一な冷却効果を生じる。

【００３５】

図 に示した例示的な実施形態のさらなる展開としては、ノズル列 を互いに対してずらして配置することが想定され、したがって、様々なノズル列 のフルジェットノズル が、ロール軸 に垂直な方向に沿って配置されてはいない。「冷却チャネル」は、ノズル列 に垂直に延在して、そこでは、ロール に冷却剤が吐出されず、その結果、冷却効果が低下するが、この「冷却チャネル」を避けることができるので、ノズル列 の特に均一

な冷却効果が達成されることは有利である。
【００３６】
さらに、図 の隣り合う つの部分領域 ～ 間の境界線に非常に近い、または境界線上にあるフルジェットノズル は、完全に省かれるか、または、図 に示した配置に対してずらされて、隣接した部分領域 ～ の つに入るように配置され、それは分離板による冷却筒 の内部の冷却剤室 ～ への細分がこのような境界線に沿って延在するからである。
【００３７】
各フルジェットノズル は、冷却棒 のノズル開口に、例えば、ねじ込み継手によって取り外し可能に取り付けられる。フルジェットノズル はそれぞれ、例えば、約 の最小直径のノズル断面を有する。
【００３８】
各冷却剤室 ～ は、冷却剤室 ～ 内に冷却剤を供給するための冷却剤供給ライン に接続され、冷却剤供給ライン は、冷却剤室 ～ 内に、冷却剤の吐出方向 に実質的に垂直に開口している。冷却剤供給ライン の断面はそれぞれ、例えば、 からの間の直径を有する。
【００３９】
冷却剤供給ライン を経て冷却剤室 ～ 内に供給される冷却剤の量を、それぞれの制御弁 図 には示されていない 、および／または、それぞれのポンプ 図 には示されていない によって互いに独立して制御することができる。これによって、冷却剤室 ～ から吐出される冷却剤の量を、ロール表面の様々な領域の異なる熱負荷に対して適合させることができることは有利である。
【００４０】
図 は、一例として、図 に示した冷却棒 から吐出される つの冷却剤の体積流量 、 、 を、ロール軸 に平行な方向に沿う位置ｙの関数として示す。ここで、体積流量 、 、 は定格流量に対する比率で示されている。
【００４１】
定格流量は、中央位置ｙにおける第 の体積流量 である。第 の体積流量 は、冷却剤が、すべての冷却剤室 ～ に対して同じ与定の定格圧力で、すべての つの冷却剤室 ～ 内に供給された場合に生じる。第 の体積流量 は、中央位置ｙで最大となる放物線の形状を有し、中央位置ｙから つの端部領域に向かって減少して、中央位置ｙの値の半分になる。第 の体積流量 がこのような形状になる理由は、ノズル列 の中心から２つの端部へ、ノズル列 に沿うフルジェットノズル のノズル間隔ｄが 倍になるからであり、ノズル間隔ｄの放物線状の増大が仮定される。
【００４２】
第 の体積流量 は、定格圧力のほぼ 倍の冷却剤圧力で冷却剤を第 の冷却剤室 内に供給し、定格圧力のほぼ半分の冷却剤圧力で冷却剤を他の つの冷却剤室 、 内のそれぞれに供給した場合に生じる。
【００４３】
第 の体積流量 は、定格圧力のほぼ半分の冷却剤圧力で冷却剤を第 の冷却剤室 内に供給し、定格圧力のほぼ 倍の冷却剤圧力で冷却剤を他の つの冷却剤室 、 内のそれぞれに供給した場合に生じる。
【００４４】
図 は、ロール軸 に平行な方向に沿う位置ｙへの依存性が異なるパターンを有する体積流量 、 、 を、冷却剤室 ～ の異なる冷却剤圧力によって生じさせることができ、その結果、冷却棒 から吐出される体積流量 、 、 を、ロール表面の温度分布に適合させることができることを示している。各冷却剤室 ～ の冷却剤圧力は、それぞれの制御弁 および／またはそれぞれのポンプ によって設定される。
【００４５】
図 ～図 はそれぞれ、冷却棒 の別の例示的な実施形態の吐出側面 を示す。これら

の例示的な実施形態は、図 に示した例示的な実施形態とは、冷却剤室 ～ 、およびそれに対応する吐出側面 の部分領域 ～ の形状および数だけが異なる。図 に示した例示的な実施形態のように、フルジェットノズル はそれぞれ、複数のノズル列 になるように配置され、それぞれの場合のノズル間隔ｄは、それに沿って中央から つの端部に向かって増大する。したがって、図 ～図 のフルジェットノズル はここでまた説明することはしない。吐出側面 のフルジェットノズル の、図 に示した例示的な実施形態と同様な分布によって、図 ～図 に示される例示的な実施形態のそれぞれで、図 と同様な体積流量 、 、 を生じさせることができる。

【００４６】

図 に示した例示的な実施形態のように、図 ～図 に示した例示的な実施形態はそれぞれ、 つの冷却剤室 ～ 、および吐出側面 にそれに対応する部分領域 ～ を有する。図 に示した例示的な実施形態と同様に、第 の部分領域 は、冷却棒 の吐出側面 の、ロール軸 に垂直な中心線 に対して鏡面対称であり、他の つの部分領域 、 は、第 の部分領域 と中心線 の異なる側で隣接する。

【００４７】

図 は、第 の部分領域 が、第 の長手方向辺 に配置された つの頂点と、第 の長手方向辺 に配置された つの頂点とを有する台形である例示的な実施形態を示す。

【００４８】

図 は、第 の部分領域 が、中心線 と第 の長手方向辺 との交点に配置された つの頂点と、第 の長手方向辺 の端部に配置された つの頂点とを有する三角形である例示な実施形態を示す。

【００４９】

図 は、第 の部分領域 が、中心線 と第 の長手方向辺 との交点に配置された つの頂点と、第 の長手方向辺 に配置された つの頂点とを有する三角形である例示的な実形態を示す。

【００５０】

図 は、第 の部分領域 が、頂点が長手方向辺 、 に配置された長方形である例示的な実施形態を示す。この例示的な実施形態では、 つの外側の部分領域 、 を経て冷却剤を吐出しないので、冷却剤の吐出を吐出側面 の中央領域からのみ生じさせることができる。したがって、この例示的な実施形態は、異なる幅の圧延素材 を圧延するのに特に適している。

【００５１】

図 は、第 の部分領域 および第 の部分領域 がそれぞれ、第 の長手方向辺 上の頂点と、第 の長手方向辺 の一端に配置された頂点と、短手方向辺 、 に配置された頂点とを有する長方形である例示的な実施形態を示す。

【００５２】

図 は、第 の部分領域 が、第 の長手方向辺 上の つの頂点と、第 の長手方向辺 の端部にそれぞれ配置された つの頂点と、それぞれの短手方向辺 、 上の頂点とを有する六角形である例示的な実施形態を示す。

【００５３】

図 は、第 の部分領域 が、中心線 と第 の長手方向辺 との交点に配置された つの頂点と、第 の長手方向辺 の端部にそれぞれ配置された つの頂点と、それぞれの短手方向辺 、 上の つの頂点とを有する五角形である例示的な実施形態を示す。

【００５４】

図 および図 に示した例示的な実施形態はそれぞれ、 つの冷却剤室 、 、およびそれに対応する、吐出側面 の部分領域 、 を有する。両方の部分領域 は、冷却棒 の吐出側面 の、ロール軸 に垂直な中心線 に対して鏡面対称である。

【００５５】

図 は、第 の部分領域 が、中心線 に配置された つの頂点と、第 の長手方向辺 の端部にそれぞれ配置された つの頂点とを有する三角形である例示的な実施形態を示す

。
【００５６】
図　は、第　の部分領域　が、中心線　に配置された　つの頂点と、第　の長手方向辺　の端部にそれぞれ配置された　つの頂点と、それぞれの短手方向辺　、　上の頂点とを有する五角形である例示的な実施形態を示す。
【００５７】
本発明を、好ましい例示的な実施形態によって、より詳細に例示および説明したが、本発明は、開示した例に限定されるものではなく、当業者は、本発明の保護の範囲を超えずにこれらから他の変形を得ることができる。
【符号の説明】
【００５８】
圧延スタンド
圧延素材、圧延材
ロール
冷却装置
ロール間隙
圧延方向
冷却棒
ワイパ
ロール軸
吐出側面
ノルジェットノズル
吐出方向
～　冷却剤室
～　部分領域
、　長手方向辺
、　短手方向辺
中心線
ノズル列
冷却剤供給ライン
制御弁
ポンプ
ノズル間隔

【図１】

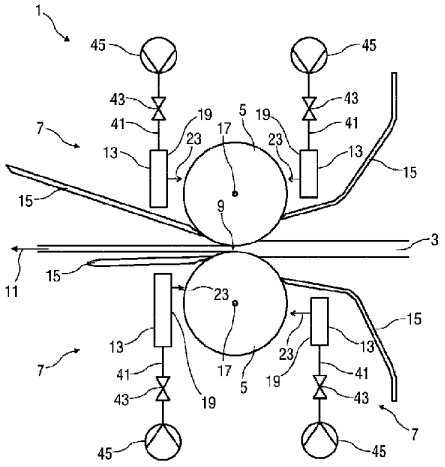


FIG 1

【図２】

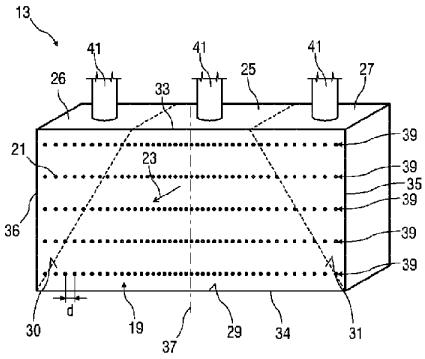


FIG 2

【図３】

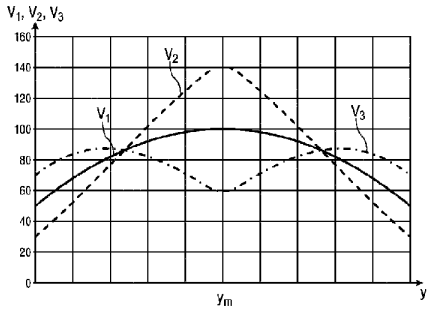


FIG 3

【図４】

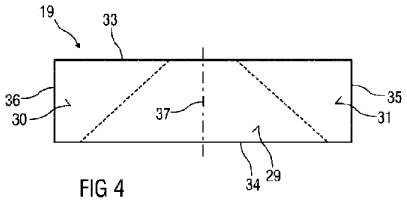


FIG 4

【図５】

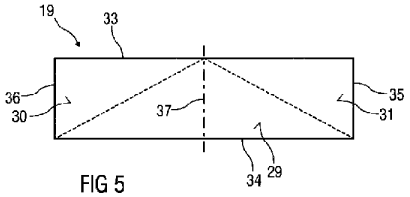


FIG 5

【図６】

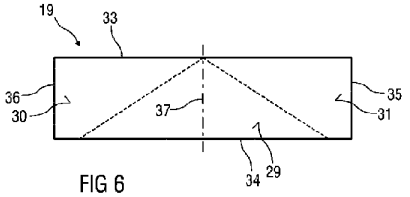


FIG 6

【図７】

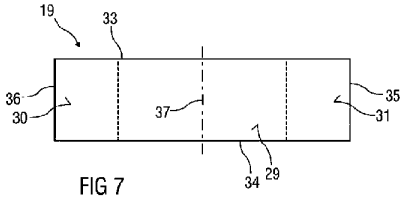


FIG 7

【図８】

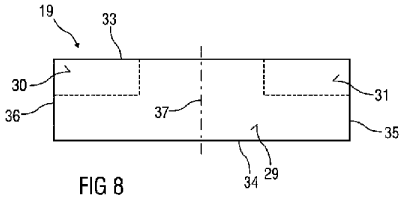


FIG 8

【図９】

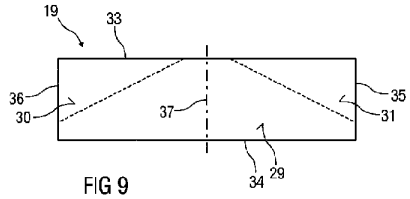


FIG 9

【図１０】

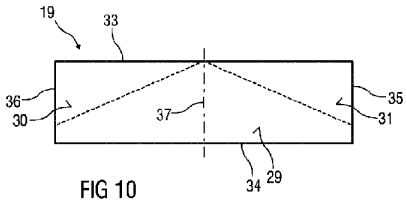


FIG 10

【図１１】

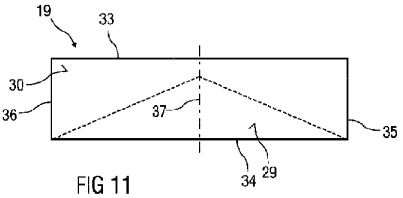


FIG 11

【図１２】

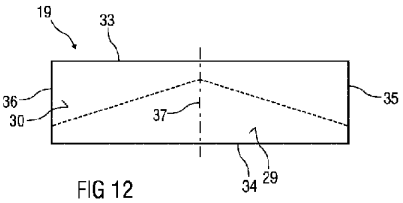


FIG 12

【国際調査報告】

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2017/076000

A. CLASSIFICATION OF SUBJECT MATTER
INV. B21B27/10
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)
B21B

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.
X	DE 200 06 508 U1 (ACHENBACH BUSCHHUETTEN GMBH [DE]) 31 August 2000 (2000-08-31)	1,15
Y	page 5, paragraph 3 - page 7, paragraph 3	2-5

X	WO 2008/149195 A1 (ARCELORMITTAL FRANCE [FR]; VANDERSCHUEREN DIRK [BE]; VAN POECKE PATRIC) 11 December 2008 (2008-12-11)	1,15
Y	page 3, line 20 - page 4, line 12; figures 1,2	2-5

Y	EP 2 792 428 A1 (SIEMENS VAI METALS TECH GMBH [AT]) 22 October 2014 (2014-10-22) paragraph [0017] - paragraph [0027]; figures 1-3	2-5

A	WO 2015/113832 A1 (LOI THERMPROCESS GMBH [DE]) 6 August 2015 (2015-08-06) page 4, line 8 - line 17	1

☐ Further documents are listed in the continuation of Box C. ☒ 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

"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
11 January 2018	06/03/2018

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	Frisch, Ulrich

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Form PCT/ISA/210 (second sheet) (April 2005)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2017/076000

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:

see additional sheet

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, 15

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.

The International Searching Authority has found that the international application contains multiple (groups of) inventions, as follows:

1. Claims 1-5, 15

Cooling device for cooling a roller, wherein two coolant chambers are provided which are separated from each other.

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2. Claims 1, 6-8

Cooling device for cooling a roller, wherein the feed/control of the coolant is further defined.

---

3. Claims 1, 9-13

Cooling device for cooling a roller, wherein the distance of the nozzles is defined.

---

4. Claims 1, 14

Cooling device for cooling a roller, wherein an additional stripper is defined.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/EP2017/076000

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
DE 20006508 U1	31-08-2000	DE 20006508 U1	31-08-2000
		EP 1142652 A2	10-10-2001
		JP 2001347307 A	18-12-2001
		US 2001027672 A1	11-10-2001
WO 2008149195 A1	11-12-2008	AU 2008259470 A1	11-12-2008
		BR PI0812201 A2	25-11-2014
		CA 2690098 A1	11-12-2008
		CN 101702888 A	05-05-2010
		EP 2014379 A1	14-01-2009
		EP 2164651 A1	24-03-2010
		JP 5380438 B2	08-01-2014
		JP 2010528870 A	26-08-2010
		KR 20100020462 A	22-02-2010
		RU 2009149178 A	20-07-2011
		SI 2164651 T1	30-08-2013
		UA 99295 C2	10-08-2012
		US 2010180657 A1	22-07-2010
		WO 2008149195 A1	11-12-2008
		ZA 200908405 B	28-07-2010
EP 2792428 A1	22-10-2014	CN 105188975 A	23-12-2015
		EP 2792428 A1	22-10-2014
		EP 2986400 A1	24-02-2016
		JP 6110015 B2	05-04-2017
		JP 2016515474 A	30-05-2016
		KR 20150143746 A	23-12-2015
		RU 2015141167 A	17-05-2017
		US 2016052033 A1	25-02-2016
		WO 2014170139 A1	23-10-2014
WO 2015113832 A1	06-08-2015	DE 102014001146 A1	06-08-2015
		EP 3099829 A1	07-12-2016
		WO 2015113832 A1	06-08-2015

Form PCT/ISA/210 (patent family annex) (April 2005)

INTERNATIONALER RECHERCHENBERICHT

Internationales Aktenzeichen
PCT/EP2017/076000

A. KLASSIFIZIERUNG DES ANMELDUNGSGEGENSTANDES
INV. B21B27/10
ADD.

Nach der Internationalen Patentklassifikation (IPC) oder nach der nationalen Klassifikation und der IPC

B. RECHERCHIERTE GEBIETE

Recherchierter Mindestprüfstoff (Klassifikationssystem und Klassifikationssymbole)
B21B

Recherchierte, aber nicht zum Mindestprüfstoff gehörende Veröffentlichungen, soweit diese unter die recherchierten Gebiete fallen

Während der internationalen Recherche konsultierte elektronische Datenbank (Name der Datenbank und evtl. verwendete Suchbegriffe)
EPO-Internal, WPI Data

C. ALS WESENTLICH ANGESEHENE UNTERLAGEN

Kategorie*	Bezeichnung der Veröffentlichung, soweit erforderlich unter Angabe der in Betracht kommenden Teile	Betr. Anspruch Nr.
X Y	DE 200 06 508 U1 (ACHENBACH BUSCHHUETTEN GMBH [DE]) 31. August 2000 (2000-08-31) Seite 5, Absatz 3 - Seite 7, Absatz 3 -----	1,15 2-5
X Y	WO 2008/149195 A1 (ARCELORMITTAL FRANCE [FR]; VANDERSCHUEREN DIRK [BE]; VAN POECKE PATRIC) 11. Dezember 2008 (2008-12-11) Seite 3, Zeile 20 - Seite 4, Zeile 12; Abbildungen 1,2 -----	1,15 2-5
Y	EP 2 792 428 A1 (SIEMENS VAI METALS TECH GMBH [AT]) 22. Oktober 2014 (2014-10-22) Absatz [0017] - Absatz [0027]; Abbildungen 1-3 -----	2-5
A	WO 2015/113832 A1 (LOI THERMPROCESS GMBH [DE]) 6. August 2015 (2015-08-06) Seite 4, Zeile 8 - Zeile 17 -----	1

☐ Weitere Veröffentlichungen sind der Fortsetzung von Feld C zu entnehmen ☒ Siehe Anhang Patentfamilie

* Besondere Kategorien von angegebenen Veröffentlichungen :
"A" Veröffentlichung, die den allgemeinen Stand der Technik definiert, aber nicht als besonders bedeutsam anzusehen ist
"E" frühere Anmeldung oder Patent, die bzw. das jedoch erst am oder nach dem internationalen Anmeldedatum veröffentlicht worden ist
"L" Veröffentlichung, die geeignet ist, einen Prioritätsanspruch zweifelhaft erscheinen zu lassen, oder durch die das Veröffentlichungsdatum einer anderen im Recherchenbericht genannten Veröffentlichung belegt werden soll oder die aus einem anderen besonderen Grund angegeben ist (wie ausgeführt)
"O" Veröffentlichung, die sich auf eine mündliche Offenbarung, eine Benutzung, eine Ausstellung oder andere Maßnahmen bezieht
"P" Veröffentlichung, die vor dem internationalen Anmeldedatum, aber nach dem beanspruchten Prioritätsdatum veröffentlicht worden ist
"T" Spätere Veröffentlichung, die nach dem internationalen Anmeldedatum oder dem Prioritätsdatum veröffentlicht worden ist und mit der Anmeldung nicht kollidiert, sondern nur zum Verständnis des der Erfindung zugrundeliegenden Prinzips oder der ihr zugrundeliegenden Theorie angegeben ist
"X" Veröffentlichung von besonderer Bedeutung; die beanspruchte Erfindung kann allein aufgrund dieser Veröffentlichung nicht als neu oder auf erfinderischer Tätigkeit beruhend betrachtet werden
"Y" Veröffentlichung von besonderer Bedeutung; die beanspruchte Erfindung kann nicht als auf erfinderischer Tätigkeit beruhend betrachtet werden, wenn die Veröffentlichung mit einer oder mehreren Veröffentlichungen dieser Kategorie in Verbindung gebracht wird und diese Verbindung für einen Fachmann naheliegend ist
"&" Veröffentlichung, die Mitglied derselben Patentfamilie ist

Datum des Abschlusses der internationalen Recherche	Absendedatum des internationalen Recherchenberichts
11. Januar 2018	06/03/2018

Name und Postanschrift der Internationalen Recherchenbehörde	Bevollmächtigter Bediensteter
Europäisches Patentamt, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Frisch, Ulrich

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Formblatt PCT/ISA/210 (Blatt 2) (April 2005)

INTERNATIONALER RECHERCHENBERICHT

Internationales Aktenzeichen
PCT/EP2017/076000

Feld Nr. II Bemerkungen zu den Ansprüchen, die sich als nicht recherchierbar erwiesen haben (Fortsetzung von Punkt 2 auf Blatt 1)

Gemäß Artikel 17(2)a) wurde aus folgenden Gründen für bestimmte Ansprüche kein internationaler Recherchenbericht erstellt:

1. ☐ Ansprüche Nr.
weil sie sich auf Gegenstände beziehen, zu deren Recherche diese Behörde nicht verpflichtet ist, nämlich

2. ☐ Ansprüche Nr.
weil sie sich auf Teile der internationalen Anmeldung beziehen, die den vorgeschriebenen Anforderungen so wenig entsprechen, dass eine sinnvolle internationale Recherche nicht durchgeführt werden kann, nämlich

3. ☐ Ansprüche Nr.
weil es sich dabei um abhängige Ansprüche handelt, die nicht entsprechend Satz 2 und 3 der Regel 6.4 a) abgefasst sind.

Feld Nr. III Bemerkungen bei mangelnder Einheitlichkeit der Erfindung (Fortsetzung von Punkt 3 auf Blatt 1)

Diese Internationale Recherchenbehörde hat festgestellt, dass diese internationale Anmeldung mehrere Erfindungen enthält:

siehe Zusatzblatt

1. ☐ Da der Anmelder alle erforderlichen zusätzlichen Recherchengebühren rechtzeitig entrichtet hat, erstreckt sich dieser internationale Recherchenbericht auf alle recherchierbaren Ansprüche.

2. ☐ Da für alle recherchierbaren Ansprüche die Recherche ohne einen Arbeitsaufwand durchgeführt werden konnte, der zusätzliche Recherchengebühr gerechtfertigt hätte, hat die Behörde nicht zur Zahlung solcher Gebühren aufgefordert.

3. ☐ Da der Anmelder nur einige der erforderlichen zusätzlichen Recherchengebühren rechtzeitig entrichtet hat, erstreckt sich dieser internationale Recherchenbericht nur auf die Ansprüche, für die Gebühren entrichtet worden sind, nämlich auf die Ansprüche Nr.

4. ☒ Der Anmelder hat die erforderlichen zusätzlichen Recherchengebühren nicht rechtzeitig entrichtet. Dieser internationale Recherchenbericht beschränkt sich daher auf die in den Ansprüchen zuerst erwähnte Erfindung; diese ist in folgenden Ansprüchen erfasst:
1-5, 15

Bemerkungen hinsichtlich eines Widerspruchs

☐ Der Anmelder hat die zusätzlichen Recherchengebühren unter Widerspruch entrichtet und die gegebenenfalls erforderliche Widerspruchsgebühr gezahlt.

☐ Die zusätzlichen Recherchengebühren wurden vom Anmelder unter Widerspruch gezahlt, jedoch wurde die entsprechende Widerspruchsgebühr nicht innerhalb der in der Aufforderung angegebenen Frist entrichtet.

☐ Die Zahlung der zusätzlichen Recherchengebühren erfolgte ohne Widerspruch.

WEITERE ANGABEN PCT/ISA/ 210

Die internationale Recherchenbehörde hat festgestellt, dass diese internationale Anmeldung mehrere (Gruppen von) Erfindungen enthält, nämlich:

1. Ansprüche: 1-5, 15

   Kühlvorrichtung zur Kühlung einer Walze, wobei zwei voneinander getrennte Kühlmittelkammern vorgesehen sind.

   ---

2. Ansprüche: 1, 6-8

   Kühlvorrichtung zur Kühlung einer Walze, wobei die Zuleitung / Steuerung des Kühlmittels weiter definiert wird.

   ---

3. Ansprüche: 1, 9-13

   Kühlvorrichtung zur Kühlung einer Walze, wobei der Abstand der Düsen definiert wird.

   ---

4. Ansprüche: 1, 14

   Kühlvorrichtung zur Kühlung einer Walze, wobei ein zusätzlicher Abstreifer definiert wird

   ---

INTERNATIONALER RECHERCHENBERICHT

Angaben zu Veröffentlichungen, die zur selben Patentfamilie gehören

Internationales Aktenzeichen
PCT/EP2017/076000

Im Recherchenbericht angeführtes Patentdokument	Datum der Veröffentlichung	Mitglied(er) der Patentfamilie	Datum der Veröffentlichung
DE 20006508 U1	31-08-2000	DE 20006508 U1	31-08-2000
		EP 1142652 A2	10-10-2001
		JP 2001347307 A	18-12-2001
		US 2001027672 A1	11-10-2001
WO 2008149195 A1	11-12-2008	AU 2008259470 A1	11-12-2008
		BR PI0812201 A2	25-11-2014
		CA 2690098 A1	11-12-2008
		CN 101702888 A	05-05-2010
		EP 2014379 A1	14-01-2009
		EP 2164651 A1	24-03-2010
		JP 5380438 B2	08-01-2014
		JP 2010528870 A	26-08-2010
		KR 20100020462 A	22-02-2010
		RU 2009149178 A	20-07-2011
		SI 2164651 T1	30-08-2013
		UA 99295 C2	10-08-2012
		US 2010180657 A1	22-07-2010
		WO 2008149195 A1	11-12-2008
		ZA 200908405 B	28-07-2010
EP 2792428 A1	22-10-2014	CN 105188975 A	23-12-2015
		EP 2792428 A1	22-10-2014
		EP 2986400 A1	24-02-2016
		JP 6110015 B2	05-04-2017
		JP 2016515474 A	30-05-2016
		KR 20150143746 A	23-12-2015
		RU 2015141167 A	17-05-2017
		US 2016052033 A1	25-02-2016
		WO 2014170139 A1	23-10-2014
WO 2015113832 A1	06-08-2015	DE 102014001146 A1	06-08-2015
		EP 3099829 A1	07-12-2016
		WO 2015113832 A1	06-08-2015

Formblatt PCT/ISA/210 (Anhang Patentfamilie) (April 2005)

フロントページの続き

指定国・地域

発明者　ルーカス・ピヒラー
オーストリア・４０４０・リンツ・シュトライムリングヴェーク・７

United States District Court,
E.D. Texas, Marshall Division.

RETRACTABLE TECHNOLOGIES, INC., and Thomas J. Shaw,
Plaintiffs.
v.
BECTON DICKINSON & CO,
Defendant.

Civil Action No. 2:07-CV-250 (DF)

Jan. 20, 2009.

Bradley Carroll Weber, Paul Featherstone Schuster, Locke Liddell & Sapp, George E. Bowles, Mark Richard Backofen, Michael V. Powell, Monty Lee Ross, Roy William Hardin, Locke Lorde Bissell & Liddell LLP, Dallas, TX, Deborah J. Race, Otis W. Carroll, Jr., Ireland Carroll & Kelley, Tyler, TX, G. William Lavender, Lavender Law, Texarkana, AR, for Plaintiffs.

Robert A. Atkins, Jacqueline Pilar Rubin, Paul Weiss Rifkind Wharton & Garrison, Alexandra B. McTague, Wilmer Cutler Pickering Hale & Dorr, New York, NY, Alistair Byrne Dawson, David J. Beck, Beck Redden & Secrest, Houston, TX, Heath A. Brooks, Mark L. Rienzi, Stephanie K. Wood, William G. McElwain, Los Angeles, CA, Lisa J. Pirozzolo, William F. Lee, Wilmer Cutler Pickering Hale & Dorr, Boston, MA, William David Carter, Sr., Mercy Carter Tidwell, L.L.P., Texarkana, TX, for Defendant.

Stephen David Wilson, Locke Lord Bissell & Liddell LLP, Dallas, TX.

CLAIM CONSTRUCTION ORDER

Construing Terms in U.S. Patent Nos. 5,632,733**,** 6,090,077**, and** 7,351,224

DAVID FOLSOM**, District Judge.**

Before the Court are RTI's Opening Brief on Claim Construction (Dkt. No. 111), BD's Opening Claim Construction Brief (Dkt. No. 112), RTI's Reply Brief on Claim Construction (Dkt. No. 113) and BD's Notice of Supplemental Authority (Dkt. No. 116). Also before the Court are the Local Patent Rule (LPR) 4-3 Joint Claim Construction and Prehearing Statement (Dkt. No. 110) and the LPR 4-5 Joint Claim Construction Chart (Dkt. No. 114). A claim-construction hearing, in accordance with Markman v. Westview Instruments, 52 F.3d 967 (Fed.Cir.1995) (en banc), *aff'd,* 517 U.S. 370 (1996), was held in Texarkana on December 4, 2008. *See* Dkt. No. 118 (hearing transcript). After hearing the arguments of counsel and reviewing the relevant pleadings, presentation materials, other papers, and case law, the Court finds the disputed terms of the patents-in-suit should be construed as set forth herein.

TABLE OF CONTENTS

I.	BACKGROUND	-1-
II.	LEGAL PRINCIPLES	-1-
III.	PATENTS-IN-SUIT	-2-
IV.	U.S. PATENT NO. 5,632,733	-3-

A. Overview -3-
B. Claim Construction -5-
1. "body" -5-
2. "barrel" -6-
3. "nose"/"nose portion" -9-
4. "transition zone" -10-
5. "inwardly facing surface" -11-
6. "retraction mechanism sealingly disposed in the nose" -12-
7. "retainer member" -12-
8. "bridging portion" -16-
9. "releaseably installed by sliding engagement of said retaine r member and said inwardly facing surface" -18-
10. "sliding engagement producing a holding force" -20-
11. "outwardly facing surface" -20-
V. U.S. PATENT NO. 6,090,077 -21-
A. Overview -21-
B. Claim Construction -22-
1. "body"/"barrel" -22-
2. "vent" -22-
3. "the barrel having a front end portion containing a retraction mechanism configured for operation by a plunger" -22-
4. "a front end configured to operate the retraction mechanism" -23-
VI. U.S. PATENT NO. 7,351,224 -23-
A. Overview -23-
B. Claim Construction -24-
1. "body"/"barrel"/"bridging portion"/"retainer member" -24-
2. "continuous retainer member surrounding the inner head" -25-
3. "end cap" -25-
4. "wherein the continuous retainer member is releasable from the inner head" -27-

I. BACKGROUND

In the present lawsuit, Retractable Technologies, Inc. and Thomas Shaw (collectively "RTI") contend certain safety syringes made by Becton, Dickinson and Co. ("BD") infringe claims of U.S. Patent Nos. 5,578,011 ("the '011 Patent), 5,632,733 ("the '733 Patent"), 6,090,077 ("the '077 Patent"), and 7,351,224 ("the '224 Patent"). Both the '011 and '733 Patents are entitled "Tamperproof retractable syringe," while the '077 Patent is entitled "Syringe plunger assembly and barrel," and the '224 Patent is entitled "Retractable syringe assembly designed for one use." All three later patents are continuations-in-part of the '011 Patent. '733 at [63]; '077 at [63]; '224 at [63]. FN1

FN1. The parties have agreed on the construction of one term in the ' 011 Patent. The parties agree that "frictionally held retraction mechanism" will be construed as "a retraction mechanism held by friction." The Court has no reason to disagree and therefore adopts the parties' construction. Because no terms from the '011 Patent are in dispute this Claim Construction Order will not address the '011 Patent further.

II. LEGAL PRINCIPLES

A determination of patent infringement involves two steps: first, the patent claims are construed, and, second, the claims are compared to the allegedly infringing device. Cybor Corp. v. FAS Techs., Inc., 138 F.3d 1448, 1455 (Fed.Cir.1998) (en banc). The legal principles of claim construction were reexamined by the Federal Circuit in Phillips v. AWH Corp., 415 F.3d 1303 (Fed.Cir .2005) (en banc). The Federal Circuit in *Phillips* expressly reaffirmed the principles of claim construction as set forth in Markman v. Westview Instruments, Inc., 52 F.3d 967 (Fed.Cir.1995) (en banc), *aff'd,* 517 U.S. 370 (1996), Vitronics Corp. v. Conceptronic, Inc., 90 F.3d 1576 (Fed.Cir.1996), and Innova/Pure Water, Inc. v. Safari Water Filtration Sys., Inc., 381 F.3d 1111 (Fed.Cir.2004). Claim construction is a legal question for the courts. Markman, 52 F.3d at 979.

The Court, in accordance with the doctrines of claim construction that it has outlined in the past, will construe the claims of the RTI Patents below. *See Pioneer v. Samsung,* No. 2:07-CV-170, Dkt. No. 94, at 2-8 (E.D. Tex. filed Mar. 10, 2008) (claim-construction order).

III. PATENTS-IN-SUIT

The patents-in-suit are directed to particular features of a retractable syringe. The '773 Patent issued on May 27, 1997 from an application filed on September 29, 1995. The '773 Patent is a continuation-in-part of U.S. Patent App. No. 438,954, which was eventually issued as the '011 Patent. '733 at [63]. The '773 Patent abstract reads:

A tamperproof retractable non-reusable syringe has a one piece hollow outer body with a barrel for a slidable plunger, a transition zone and a smaller diameter nose portion. An elongated needle holder and spring combination is installable from the rear of the outer body, guided into the nose portion and held by cooperating inwardly and outwardly facing surfaces oriented in the direction of retraction at the most constricted part of the transition zone where the nose begins. The plunger has an opening with a dislodgable stopper for receiving parts of the retraction mechanism. The stopper and the head of the needle holder are of significantly reduced diameter from the injection fluid chamber to resist blowing out prematurely. In one embodiment the head of the needle holder is surrounded by a separable retainer member which is slidingly removed by contact with the tip of the plunger after the stopper is mostly or fully removed to avoid cumulation of force required for retraction after the injection. In a second embodiment the head of the

needle holder is clamped and held by constricting forces imposed by stress on the outer body induced by interference fit. Release occurs by slight expansion on the barrel by contact of the plunger tip with a small internal ramp in the outer barrel. Both embodiments have a plunger cap configured to enter an opening in the outer body to provide an additional tamperproof feature.

'773 Patent at [57].

The '077 Patent issued July 18, 2000 from an application filed on April 25, 1997. The '077 Patent is a continuation-in-part of both the '773 and '011 Patents. '077 at [63]. The abstract from the '077 Patent mirrors that of the '773 Patent, but contains one additional sentence: "The retraction cavity is provided with venting structure to assure that all uninjected fluid is retained within the syringe body." Id. at [57].

The '224 Patent issued April 1, 2008 from an application filed July 17, 2000. The '224 Patent is a continuation-in-part of the '007, '773, and ' 011 Patents. '224 at [63]. The '773 Patent abstract reads:

A syringe assembly having a retractable needle, the syringe assembly being rendered unusable after a single injection and having a hollow syringe body, a retraction mechanism with a spring disposed in the front portion of the syringe and an inner head, a continuous retainer member surrounding the inner head, and a bridging portion disposed between the continuous retainer member and the inner head, wherein the bridging portion couples the continuous retainer member and the inner head to form a fluid seal between a fluid passageway and the barrel prior to retraction, and a plunger reciprocally disposed inside the barrel and forming a variable chamber between the plunger and the needle holder prior to and during retraction, wherein the continuous retainer member is releasable from the inner head of the needle holder when the plunger is further depressed inside the barrel following injection.

Id. at [57].

IV. U.S. PATENT NO. 5,632,733

A. Overview

RTI has asserted claims 1, 24, and 36 of the '733 Patent against BD in this lawsuit. Dkt. No. 114. For reference, asserted claims 1 and 24 are reproduced below (terms to be construed emphasized):

1. A tamperproof retractable syringe for injecting fluid wherein the syringe has a one piece **body** and a retraction mechanism assembleable from the rear which resists high blowout pressure during an injection but can be retracted with low plunger force after injection comprising:

a one piece hollow outer **body** having a longitudinally extending wall, comprising an elongated **barrel** and **nose,** with a **transition zone** connecting the **barrel** and **nose,** the **nose** having a reduced cross sectional area relative to the **barrel** and an **inwardly facing surface** in the wall at the most constricted part of the **transition zone** where the nose begins;

a plunger assembly disposed partially within the elongated **barrel,** the plunger having a head in slidable sealed contact with the interior of the outer **body,** a forward portion and a retraction cavity therein for receiving parts of a retraction mechanism;

a **retraction mechanism sealingly disposed in the nose,** the retraction mechanism having a retractable part comprising a needle holder having an elongated **body** having a needle holding tip portion in front and a head in back, a passageway defining a fluid path into a variable fluid chamber in the **barrel** below the plunger, and a spring applying retraction force to the retractable part, said retractable part being configured to be able to retract into the retraction cavity of the plunger when retraction is initiated;

the retraction mechanism further including a nonretractable part comprising a **retainer member** surrounding the head of the needle holder, the retainer member and said head of the needle holder being removably coupled by a **bridging portion** between them;

the needle holder and spring being installable into the **nose** from the rear of the **barrel** and **releaseably installed by sliding engagement of said retainer member and said inwardly facing surface** while compressing said spring, said **sliding engagement producing a holding force** in opposition to the retraction force applied to the needle holder by said spring; and

the plunger being depressible to a first position which comprises the end of an injection cycle whereby fluid previously drawn into the variable chamber is expelled through said fluid path, and a retraction position beyond said first position wherein retraction is initiated by the forward portion of the plunger head moving through the **transition zone** in the **nose** to release the needle holder by uncoupling the **retainer member** and needle holder at said **bridging portion** thereby reducing the holding force to an amount less than the retraction force on the needle holder to cause retraction of the retractable part into the retraction cavity of the plunger.

24. A method of assembling a tamperproof retractable syringe which is well suited for automated assembly;

providing a one piece hollow syringe **body** having a longitudinally extending wall with an open back end, comprising an elongated **barrel** and **nose portion** of reduced cross sectional area relative to the **barrel,** and an **inwardly facing surface** in the wall at the most constricted part of a **transition zone** between the **barrel** and **nose** where the **nose** begins;

providing a plunger assembly having a front portion and a back portion, the front portion including a head configured for sliding sealed contact with the interior of the elongated **barrel,** said head having a retraction cavity and a leading end configured to contact and remove a **retainer member** from a needle holder to be mounted in the **nose;**

providing a needle holder having an elongated **body** portion in front and a head in back with a fluid path therethrough, the head of the needle holder having a **retainer member** which can be separated from the head of the

needle holder by contact with the leading end of the plunger, the **retainer member** having an **outwardly facing surface** configured to slidingly and frictionally engage said **inwardly facing surface** in the **nose** and hold the needle holder against a retraction force provided by the spring when the spring is compressed within the **nose;**

loading the spring followed by the needle holder into the back opening in the **barrel** part of the syringe **body** and positioning at least the forward portion of the spring and a portion of the elongated body of the needle holder within the **nose;**

moving the head end of the needle holder and the **retainer member** into the most constricted part of the transition zone where the **nose** begins; and

installing the needle holder and **retainer member** in the **nose** by sliding engagement of the **outwardly facing surface** of the **retainer member** with the **inwardly facing surface** in the wall while compressing the spring within the **nose.**

'733, 14:65-15:49, 16:64-17:37 (emphasis added).

B. Claim Construction

1. "body"

a. Parties' Positions

The parties propose the following constructions for "body," which is present in each of the asserted claims as well as the two other patents-in-suit. Dkt. No. 114. The primary dispute between the parties is whether the syringe body must be limited to a one-piece structure.

RTI	BD
A hollow outer structure that houses the syringe's components	A one-piece hollow outer structure that houses the syringe's components

RTI contends this term should not contain a one-piece limitation because many of the claims in the '733 Patent already contain such a limitation. Dkt. No. 111 at 22. To add this limitation to the definition of body itself would render the additional claim language meaningless. *Id.* RTI also contends the patentee expressly used a one-piece limitation in the '733 Patent while no such limitation is generally present in the '077 or '224 Patents. Id. at 23. In fact, the patentee in the '224 patent used the limitation to differentiate between certain claims. *Compare* '224, 22:38-40 (claim 43), *with* 24:23-25 (claim 57-"The syringe assembly of claim 43 wherein the body comprises a one-piece barrel.").

Judge Davis previously construed this term in connection with the '011 and ' 077 Patents. *See RTI v. New Medical Techs.*, Civil Action No. 4:02-CV-34, Dkt. No. 110 at 6-9 (E.D.Tex. March 8, 2008). Judge Davis, like RTI, found significant the fact that the patentee in this family of patents included the phrase "one piece" in some claims, but not in others. *Id.* at 7. As such, Judge Davis found it improper to limit the term to a preferred embodiment containing only a one-piece body. *Id.* at 8-9.

b. Court's Construction

At the outset, this Court notes that certain terms, such as barrel, pervade all of the patents-in-suit. Because all of these patents are related-the latter patents being continuations-in-part of earlier patents and patent applications-this Court finds that terms should be construed consistently throughout absent some evidence to the contrary. In addition, the specifications and claims of each patent within this family may provide guidance when construing such pervasive terms.

Regardless of whether collateral estoppels applies to the construction of this term, the Court finds no reason to deviate from Judge Davis' previous construction. *See Id.* at 6-9. Accordingly, this Court finds that "body" means "a hollow outer structure that houses the syringe's components."

2. "barrel"

a. Parties' Positions

The parties propose the following constructions for "barrel," which is present in each of the asserted claims as well as the other two patents-in-suit. Dkt. No. 114. The primary dispute between the parties is whether the syringe barrel must be cylindrical in shape.

RTI	BD
The elongated part of the syringe body including a portion within which the plunger moves during	The elongated cylindrical portion of the syringe body through which the plunger moves during

RTI contends the claimed barrel could take a number of conceivable shapes and should not be limited to a cylindrical form. Dkt. No. 111 at 26-27. RTI further argues that the '224 specification specifically contemplates a non-cylindrical barrel. *Id.* (citing '224, 10:47-50). Moreover, the principle of claim differentiation supports RTI's broad construction as certain claims specifically contain a cylindrical limitation while others do not. *Id.* at 27 (citing '224, 20:22-23 (claim 25)). Finally, RTI contends that it is improper to limit the claimed barrel to the portion of the syringe through which the plunger moves. *Id.* Instead, some claims within the '224 and ' 077 Patent suggest that the term may encompass other structures through which the plunger does not move; specifically, the term may also define the front end portion of the syringe, including the nose portion and retraction mechanism. Id. at 27-28 (citing *inter alia* '224, 22:37-40 (claim 43) & '077, 22:13-15).

In response, BD relies on numerous dictionaries, which suggest that a barrel is limited to a cylindrical shape. Dkt. No. 112 at 30-31. BD also maintains that every figure in this family of patents shows a cylindrical barrel and expressly labels the non-cylindrical parts of the syringe as a 'nose' or 'transition zone'. *Id.* Thus, BD argues that the patent figures make clear that the term is limited to a cylindrical shape and does not include narrow parts in the front end of the syringe. *Id.* In addition, BD contends that the terms barrel, nose, and transition zone should each be given distinct meanings because they are given different names and labels throughout the patent-to do otherwise would render the different labels superfluous. *Id.*

b. Court's Construction

The Federal Circuit has made it clear that when the specification discloses only a single preferred embodiment, limitations from that embodiment generally should not be imported into the claim language. Phillips v. AWH Corp., 415 F.3d at 1323 (rejecting the contention that "if a patent describes only a single embodiment, the claims of the patent must be construed as being limited to that embodiment"). Limitations from the specification may be imported into the claims where it is clear that the patentee intended for the "claims and embodiments in the specification to be strictly coextensive." *Id.* (citing SciMed Life Sys., Inc. v. Advanced Cardiovascular Sys., Inc., 242 F.3d 1337, 1341 (Fed.Cir.2001)). Such intention is evidenced by the manner in which the patentee uses a term within the specification and the claims. *Id.* (citing Snow v. Lake Shore & M.S. Ry. Co., 121 U.S. 617, 630 (1887) (it was clear from the specification that there was "nothing in the context to indicate that the patentee contemplated any alternative" embodiment to the one presented)).

RTI is correct that all figures in the patents-in-suit generally depict syringes having a cylindrical barrel. The specification of the '224 Patent, however, makes it clear that the patentee contemplated alternative shapes. Specifically, the patent states that the "head of the needle holder is preferably circular but could conceivably be another shape with the retainer member correspondingly configured to conform to it." '224, 10:47-50. As the ' 224 Patent generally depicts a syringe having a barrel and needle holder having similar shape, such a statement evidences the patentee's belief that both the needle holder and related barrel could have a non-circular shape. Thus, the patentee may have contemplated a non-cylindrical barrel.

Moreover, claim 25 of the '224 Patent specifically recites a "substantially cylindrical barrel," which strongly suggests that the term is not inherently cylindrical. Furthermore, the absence of this "substantially cylindrical" limitation in other claims suggests that it should not be read into claims in which it is not present. *See* Amgen Inc. v. Hoechst Marion Roussel, Inc., 314 F.3d 1313, 1326 (Fed.Cir.2003) ("when a patent claim does not contain a certain limitation and another claim does, that limitation cannot be read into the former claim"). The Court therefore finds that the term barrel should not be limited to a cylindrical shape.

Finally, although this Court believes that the terms barrel, nose, and transition zone are generally distinct

components within the patents-in-suit, the patents also suggest that the barrel may encompass some portion of the syringe through which the plunger does not move. Specifically, claim 25 of the '077 Patent recites a "barrel having a front end portion containing a retraction mechanism." If this front end portion of the claimed barrel contains the retraction mechanism, then it cannot logically also be a portion through which the plunger moves. Although the plunger will assuredly move through some portion of the barrel, this Court finds that it would be improper to limit the barrel to that portion.

Accordingly, this Court finds that "barrel means "the elongated part of the syringe body including a portion through which the plunger moves during injection."

3. "nose"/"nose portion"

The parties have agreed on a meaning for the term "nose," which appears in each asserted claim. The proposed construction is "the portion of the syringe at the injection end that has a reduced diameter relative to the barrel." Dkt. No. 110 at 1. The parties have further agreed that these claims require the "nose" to be distinct from the barrel and transition zone.

The parties have also agreed on a meaning for the term "nose portion," which appears in claims 24 and 36. The proposed construction is "section of the syringe body that has a reduced diameter relative to the barrel portion of the body." *Id.*

The Court has no reason to disagree and therefore adopts the parties' constructions.

4. "transition zone"

a. Parties' Positions

The parties propose the following constructions for "transition zone," which is present in each asserted claim. Dkt. No. 114.

RTI	BD
Portion of the syringe located between the barrel and the nose	Portion of the syringe with varied inner diameter located between the barrel and the nose

RTI contends this term should not be limited to the preferred embodiment, which identifies a transition zone with a sloping inner wall. Dkt. No. 111 at 21. While RTI concedes that the transition zone has a "constricted portion," it believes that the patent does not require that the transition zone have a varied inner diameter. *Id.* BD counters by arguing that the phrase "most constricted part of the transition zone" pertains to the whole invention and requires a varied inner diameter. Dkt. No. 112 at 28 (citing '733, 14:8-10).

Judge Davis previously construed this term in connection with the '011 and ' 077 Patents. *See RTI v. New Medical Techs.*, Civil Action No. 4:02-CV-34, Dkt. No. 110 at 15 (E.D.Tex. March 8, 2008). Judge Davis did not limit the term to a varied inner diameter. *Id.*

b. Court's Construction

Once again, the Court finds no reason to deviate from Judge Davis' previous construction. *See RTI v. New Medical Techs.*, Civil Action No. 4:02-CV-34, Dkt. No. 110 at 13-14 (E.D.Tex. March 8, 2008). In addition, the Court finds no reason to limit the term to the preferred embodiment. Accordingly, this Court finds that term "transition zone" means "portion of the syringe located between the barrel and the nose."

5. "inwardly facing surface"

a. Parties' Positions

The parties propose the following constructions for "inwardly facing surface," which is present in each asserted claim. Dkt. No. 114.

RTI	BD
A surface that faces the inside of the syringe	A surface in the wall that faces toward the center of the syringe and is parallel to the direction of the plunger motion

RTI contends this term should not be restricted to a surface that is parallel to the motion of the plunger, as such would improperly restrict the term to a preferred embodiment. Dkt. No. 111 at 29. RTI contends that the '733 specification attaches no significance to the fact that the preferred embodiment's surfaces happen to be parallel to the plunger's motion. *Id*. Additionally, RTI contends that claim differentiation precludes such a limitation, as the patentee chose to specifically align these surfaces in certain claims of the '011 Patent. Id. (citing '011, 13:40-43 (claim 3)).

In response, BD contends that every embodiment described or depicted in the ' 733 Patent demonstrates surfaces that are parallel to the vertical direction of the plunger motion. Dkt. No. 112 at 23-24. In addition, the Summary of the Invention within the '733 Patent also aligns these surfaces with the plunger motion. Id. (citing '733, 2:64-65 (inwardly and outwardly facing surfaces meet "along an interface oriented in the direction of retraction")). Alternatively, BD argues that during prosecution RTI took a narrower view of the scope of this term to overcome prior art. Id. As such, BD argues that RTI has surrendered broader, non-parallel coverage. Id.

b. Court's Construction

As discussed above, limitations from the preferred embodiment generally should not be imported into the claim language, unless the claims and the embodiments in the specification were meant to be strictly coextensive. Phillips, 415 F.3d at 1323. While the descriptions and depictions of the invention in the '733 Patent generally show an inwardly facing surface that is parallel to the plunger motion, this Court finds no evidence that such embodiments are strictly coextensive with the claimed invention. Indeed, the ' 011 Patent, from which the '733 Patent is a continuation-in-part, expressly claims such an orientation. '011, 13:40-43 (claim 3: "The tamperproof retractable syringe of claim 2 wherein said frictional holding [inwardly and outwardly facing] surfaces comprise a linear interface aligned in the direction of retraction."). Thus, when the patentee wished to limit the alignment of surfaces, he expressly claimed such. Accordingly, this Court finds that it would be improper to import an alignment limitation into claims where such is not expressly present.

Accordingly, this Court finds that the term "inwardly facing surface" means "a surface that faces toward the center of the syringe."

6. "retraction mechanism sealingly disposed in the nose"

The parties have agreed on a meaning for the term "retraction mechanism sealingly disposed in the nose," which appears in claim 1. The proposed construction is "a retraction mechanism sealed in the nose." Dkt. No. 110 at 1. The Court has no reason to disagree and therefore adopts the parties' construction.

7. "retainer member"

a. Parties' Positions

The parties propose the following constructions for "retainer member," which is present in each asserted claim and the '224 Patent. Dkt. No. 114. The primary dispute between the parties is whether the retainer

member must operate by means of a frictional force.

RTI	BD
A nonretractable part of the retraction mechanism that retains the retraction mechanism	A nonretractable part of the retraction mechanism, separate from the needle holder, that retains the retraction mechanism by frictional force with the wall of the syringe

RTI contends that BD's construction would not only limit the patent to a preferred embodiment, but would also limit the patent to RTI's particular commercial product, the VanishPoint(R)-syringe. Dkt. No. 111 at 8-10. The construction proposed by BD would read a frictional holding force limitation into the term. RTI believes this improper because some claims do not require any engagement or holding force, much less some kind of frictional force. *Id.* at 10 (citing '224, 20:46-54 (claim 43)). Moreover, RTI contends that the patentee explicitly stated in some claims that frictional forces were required, raising the implication that claims without such explicit statements are not limited to friction. *Id.* (comparing '733, 14:32-37 (claim 1) with 17:18-21 (claim 24) and 18:38-41 (claim 36)). RTI also contends that the specification expressly contemplates embodiments that operate using something other than friction to hold the retainer member in place. *Id.* at 11-13. Specifically, the patents teach that the holding force used in the invention, while preferably frictional, may instead rely on tack welding, sonic welding, adhesive, or clamping forces. *Id.* at 12-13 (citing '733, 9:50-53, 10:4-8, 6:47-55, and 11:49-52).

RTI also believes that BD's proposed construction is improper in another regard, it requires that the retainer member and needle holder be separate parts. *Id.* at 16-18. While one preferred embodiment teaches that the two components are separate parts, RTI argues that there is nothing in either the claims or the specification that requires such. *Id.* To the contrary, an alternative embodiment suggests that the two are welded together to form a single structure. *Id.* at 17 (citing '733, 9:7-27). Therefore, RTI contends that-despite being two components-the patents contemplate that the retainer member and needle holder may be formed into a single structure. *Id.*

In response, BD contends that the specification repeatedly describes the invention as a retracting syringe in which the needle holder is engaged and released by sliding surfaces, and therefore, friction. Dkt. No. 112 at 17. BD identifies numerous points in the specification where the holding force used in the invention is identified as a frictional force. *Id.* at 17-18 (citing ' 733, 2:67-3:6, 3:11-13, and 3:61). BD also contends that the specification uses the terms 'holding force' and 'frictional holding force' interchangeably, thus demonstrating that they are intended to have the same meaning. *Id.* (citing Tate Access Floors, Inc. v.. Maxcess Techs., Inc., 222 F.3d 958, 968 (Fed.Cir.2000)). Moreover, BD argues that the specification criticizes syringes in the prior art that operate without friction and rely instead on flexing, breaking, or penetration. *Id.* at 18 (citing '733, 1:48-54, 2:18-35). Specifically, BD contends the specification asserts that the invention was new and different because it "relies entirely on clamping force or friction...." *Id.* (quoting '733, 2:20-21).

In connection with the second issue regarding this term, that is whether the needle holder and retainer member must be separate parts, BD argues that the ' 733 claims suggest that the two components are inherently separate parts. *Id.* at 25. BD argues that a single, unitary structure cannot couple with itself or surround itself. *Id.* In addition, BD contends that the patent specification, specifically the Summary of the Invention, explains that the retraction mechanism has a "two part head." *Id.* (citing '733, 3:25-26). Finally, BD argues that melting or tacking two parts together do not make them a single part; instead, such coupling is further evidence that they are indeed two separate parts. *Id.* at 25-26.

b. Court's Construction

First, this Court finds that nothing in the specification requires the needle holder and retainer member be two separate parts. The specification states that in " *one embodiment,* the head of the holder is a two part head

comprising an inner head surrounded by a separable retainer ...." '733, 3:19-22 (emphasis added). This statement is explicitly limited to a single, preferred embodiment, thus suggesting that other embodiments of the invention may utilize a unitary structure. Such a structure is contemplated in an alternative embodiment in which the two components are initially welded together and later "ruptured or separated." *Id* . at 9:7-13.

Second, this Court finds that the invention operates through the use of a frictional or clamping force, and that the retainer member must utilize these forces. Although the claims by themselves may seem broad enough to encompass other methods of operation, the patent as a whole disavows such methods and limits itself to frictional or clamping forces. The Federal Circuit has stated that where "the general summary or description of the invention describes a feature of the invention ... and criticizes other products ... that lack the same feature, this operates as a clear disavowal of these other products...." Astrazeneca AB v. Mutual Pharm. Co., 384 F.3d 1333, 1340 (Fed.Cir.2004), *see also* SciMed Life Sys., Inc. v. Advanced Cardiovascular Sys., Inc., 242 F.3d 1337, 1341 (Fed.Cir.2001) ("Where the specification makes clear that the invention does not include a particular feature, that feature is deemed to be outside the reach of the claims ... even though the language of the claims, read without reference to the specification, might be considered broad enough to encompass the feature in question.").

RTI is correct in asserting that some claims of the '733 Patent are explicitly limited to a frictional force while others do not. Claim differentiation would ordinarily require that all claims not be so limited. The specification, however, makes clear that the invention does not include the use flexing, breaking, or penetration as methods of operation. It does so by expressly criticizing other methods used in retractable syringes:

Other problems with the prior art are dependence on flexing or breaking of internal parts by the plunger in order to release the retraction mechanism and use of a diaphragm at the end of the plunger which must be penetrated by a needle holding member and spring. These structures present serious quality control and assembly problems.

'733, 1:48-54. In contrast to these less preferable methods, the specification asserts that the present invention is superior because it relies entirely on clamping or frictional forces: "The prior art has not recognized a retraction mechanism with separable parts that *relies entirely* on clamping force or friction...." '733, 2:18-20. By distinguishing itself from the prior art in such absolute terms, the patent has limited itself to a certain type of holding force-clamping or friction.

Finally, the varied embodiments in the invention demonstrate that this holding force may be utilized in different manners within the syringe. In one embodiment, a pair of frictional holding forces function to retain the needle in the projecting position: a frictional force between the wall of the syringe and the retainer member, and another between the retainer member and the needle holder. *See* '733, 6:56-67, 3:8-24. In another embodiment, the needle holder and retainer member are welded or tack molded together as discussed above. *See* ' 733, 9:50-53, 10:4-8, and 11:49-52. Although this weld or tack mold holds the needle holder and retainer member together, there is still a clamping or frictional force between the wall of the syringe and the retainer member. Without this force between the wall of the syringe and the retainer member, the syringe would be inoperable-it would be unable to retain the needle in a projecting position. Thus, the retainer member can only function through the use of a frictional or clamping force.

Accordingly, this Court finds that the term "retainer member" means "a non-retractable part of the retraction mechanism that uses some clamping or frictional force to keep the needle in the projecting position until released."

8. "bridging portion"

a. Parties' Positions

The parties propose the following constructions for "bridging portion," which is present in claim 1 and in the '224 Patent. Dkt. No. 114. The primary dispute between the parties is whether the bridging portion must be limited to a ridge-like structure.

RTI	BD
The structure that joins the retainer member and the head of the needle holder	A ridge on one of the facing surfaces that joins the retainer member and the head of the needle holder

RTI contends that BD's construction improperly limits the invention to a preferred embodiment. Dkt. No. 111 at 28. While the embodiment in Figure 8 admittedly depicts a raised ridge between facing surfaces, RTI argues that nothing in the specification limits the bridging portion to such a structure. *Id.* Instead, the specification states that the bridging portion may be joined to needle holder by a tack weld, or "by providing any other form of frangible bridging portion that holds the separable ring member and needle holder together." *Id.* at 28-29 (citing '733, 9:37-40).

In response, BD argues that the specification defines the bridging portion as a "small ridge" or "raised portion" joining facing surfaces. Dkt. No. 112 at 27 (citing '733, 3:43 and '077, 10:38-39). While the bridging portion may admittedly be made of various materials, BD contends that it must have some definable structure, which the patent identifies as a ridge on one of the facing surfaces. *Id.*

b. Court's Construction

The specification describes the bridging portion as a ridge-like structure that may take the form of a single "very small raised portion" or a "series of horizontally spaced apart raised portions ." While the preferred embodiment describes the bridging portion as such ridge-like structures, the Court finds no evidence that the patentee intended to limit the term to that structure. *See* Phillips, 415 F.3d at 1323 (claims should not be limited to particular embodiments unless the inventor has indicated such a narrow construction). Additionally, the bridging portion is part of an embodiment depicted in Figure 8, which the specification distinguishes from those embodiments depicted in Figures 1-3. *See* '733, 9:7-17. It is thus apparent that Figures 1-3 do not contain the claimed bridging portion, as the adjoining surfaces of the retainer member and needle holder in those embodiments are flush with one another. Thus, if two surfaces are completely flush with one another they cannot logically be joined by a bridging portion. As such, the claimed bridging portion, whatever the form it takes, must be a distinguishable structure that both joins the two components and provides some separation between them. The separation may take the form of a "small gap between them all around" ('733, 9:30-31) as depicted in Figure 8. Conversely, the bridging portion could take the form of a "frangible web" (Dkt. No 111 at 29), the gaps of which separate the two surfaces.

Accordingly, as the Court previously ruled, the term "bridging portion" means "a structure that spans the gap between and connects the retainer member and needle holder."

9. "releaseably installed by sliding engagement of said retainer member and said inwardly facing surface"

a. Parties' Positions

The parties propose the following constructions for "releaseably installed by sliding engagement of said retainer member and said inwardly facing surface," which is present in claim 1. Dkt. No. 114.

RTI	BD
Releaseably installed by sliding the retainer member along the inwardly facing surface to engage it with the wall of the syringe	Installed and released by sliding the retainer member along the inwardly facing surface to create and the release a frictional force with the wall of the syringe

As above, this term concerns the nature of the force involved in the invention. In addition, however, the parties also dispute the meaning of the words "releaseably installed" in this term. BD contends that "releaseably installed by sliding engagement" has two functional meanings. Dkt. No. 112 at 20. First, the phrase refers to the creation of a frictional force. *Id.* Second, the word "releaseably" requires that the retainer member be releaseable in the same way that it was installed. *Id.* at 20-21. BD contends that if the retraction mechanism is "installed by sliding engagement," then it must be released in the same manner-by sliding the retainer member away from the inwardly facing surface. *Id.* at 21.

RTI disagrees and contends that the term is not so limited. Dkt. No. 111 at 14. Instead, RTI argues that one of the alternate methods of release taught by the patent could achieve the release-namely by spreading the syringe wall and allowing a one-piece needle holder to retract. *Id.* at 14-15 (citing '733, 11:49-52).

b. Court's Construction

For the reasons stated above, this Court finds that the invention operates through the use of a clamping or fictional force. This Court, however, is not persuaded that the claimed release must be accomplished in the same manner as the installation. The patent teaches alternative methods for providing release of the holding force. Specifically, the patent allows the holding force to be released by spreading the barrel apart slightly, thus releasing the retraction mechanism. *See* '733, 11:49-52 ("The barrel is flexible and is spread outwardly a slight among to the position of FIG. 6 just prior to retraction. Here the mating surfaces are separated an amount which reduces the clamping force on the needle holder."). Therefore, although the holding force is created by sliding engagement in this claim, the Patent contemplates another method of its release.

Accordingly, the Court finds that the term "releaseably installed by sliding engagement of said retainer member and said inwardly facing surface" means "installed by sliding the retainer member along the inwardly facing surface to engage it with the wall of the syringe, which creates a clamping or frictional force that can be released at a later time."

10. "sliding engagement producing a holding force"

The parties propose the following constructions for "sliding engagement producing a holding force," which is present in claim 1. Dkt. No. 114.

RTI	BD
Sliding the retainer member along the inwardly facing surface of the body to produce a force that maintains the needle holder in the projected position	Sliding the retainer member along the inwardly facing surface of the body produces a frictional force that maintains the needle holder in the projected position

Once again, the dispute between the parties center on whether the holding force must be a frictional force. RTI and BD proffer the same arguments as those discussed above in connection with the term "retainer member." Dkt. Nos. 111 at 18 & 112 at 16-20.

For the reasons stated above, this Court finds that the invention operates through the use of a clamping or fictional force. Accordingly, the Court finds that the term "continuous retainer member surrounding the inner head" means "sliding the retainer member along the inwardly facing surface of the body produces a clamping or frictional force that maintains the needle holder in the projected position."

11. "outwardly facing surface"

The parties propose the following constructions for "outwardly facing surface," which is present in claims

24 and 36. Dkt. No. 114.

RTI	BD
A surface that faces toward the outside of the syringe	A surface that faces away from the center of the syringe and is parallel to the direction of the plunger motion

The parties present arguments similar to those presented in connection to the term "inwardly facing surface." For the same reasons as stated above in connection with inwardly facing surfaces, the Court finds that the claimed outwardly facing surfaces should not be limited to a direction parallel to the plunger motion.

Accordingly, this Court finds that the term "outwardly facing surface" means "a surface that faces away from the center of the syringe."

V. U.S. PATENT NO. 6,090,077

A. Overview

RTI has asserted claims 10 and 25 of the '077 Patent against BD in this lawsuit. Dkt. No. 114. For reference, the asserted claims are reproduced below (terms to be construed emphasized):

10. A syringe plunger handle assembly and syringe barrel combination for use in a retractable syringe for injecting fluids, comprising:

a hollow syringe **body** having an elongated tubular wall comprising an elongated **barrel** portion having an open back end;

an elongated plunger disposed for reciprocation in sliding sealed contact with the **barrel** portion of the **body,** the plunger having a tubular wall defining a head portion in front, a back end portion carrying a thumb cap and hollow interior comprising a retraction cavity located between the head portion and thumb cap;

the thumb cap having an outer side adapted to reside in close association with the open back end of the plunger **barrel** when the plunger is nearly fully depressed; and

the plunger having a **vent** in fluid communication with the retraction cavity, to allow airflow from the retraction cavity.

25. A tamperproof retractable syringe structure designed for one use, comprising:

a hollow syringe **body** comprising a syringe **barrel** having an open back end, **the barrel having a front end portion containing a retraction mechanism configured for operation by a plunger;**

a plunger reciprocatably mounted in sliding sealed contact with the **barrel,** the plunger having a thumb cap at its back end for working the plunger relative to the **barrel** and **a front end configured to operate the retraction mechanism;**

the plunger having a tactile first position felt by a user pressing the thumb cap at the end of free travel of the plunger in the **barrel** when the plunger is moved forward to a stop, the plunger having a length relative to the length of the **barrel** whereby in the tactile first position of the plunger a portion of the plunger and the thumb cap extend behind the **barrel** for grasping in order to draw fluid into the **barrel** by partially withdrawing the plunger from the **barrel;**

the plunger having a retraction position obtained by pressing the thumb cap to move the plunger forward beyond the tactile first position and thereby operating the retraction mechanism and simultaneously lodging the thumb cap in the open back end of the **barrel** thereby rendering the thumb cap inaccessible for grasping.

'007 Patent, 19:33-50, 20:48-21:7 (emphasis added).

B. Claim Construction

1. "body"/"barrel"

The Court construed these terms as part of its analysis of the '733 Patent, of which the '077 Patent is a continuation-in-part. The Court finds no reason to deviate from its prior constructions.

2. "vent"

The parties have agreed on a meaning for the term "vent," which appears in claim 10. The proposed construction is "an aperture that provides an opportunity or means of escape, passage, or release ." Dkt. No. 110 at 1-2. While the Court has does not disagree with the overall construction, it does believe that the word "aperture" would be unnecessarily confusing to the jury. Thus, the Court finds that the term "vent" should be construed as "an opening that provides an opportunity or means of escape, passage, or release."

3. "the barrel having a front end portion containing a retraction mechanism configured for operation by a plunger"

The parties have agreed on a meaning for the term "the barrel having a front end portion containing a retraction mechanism configured for operation by a plunger," which appears in claim 25. The proposed construction is "the section of the barrel at the injection end has a retraction mechanism that is configured to be operated by a plunger." Dkt. No. 110 at 1-2. The Court has no reason to disagree and therefore adopts the parties' construction.

4. "a front end configured to operate the retraction mechanism"

The parties have agreed on a meaning for the term "a front end configured to operate the retraction mechanism," which appears in claim 25. The proposed construction is "portion of the plunger closer to the injection end of the syringe that operates the retraction mechanism." Dkt. No. 110 at 1. The Court has no reason to disagree and therefore adopts the parties' construction.

VI. U.S. PATENT NO. 7,351,224

A. Overview

RTI has asserted claims 43, 47, 55, 60, and 61 of the '224 Patent against BD in this lawsuit. Dkt. No. 114. Claim 43 is an independent claim, upon which claims 47, 55, 60, and 61 depend. For reference, the asserted claims are reproduced below (terms to be construed emphasized):

43. A syringe assembly having a retractable needle that is rendered unusable after a single injection of fluid into a patient, the assembly comprising:

a hollow syringe **body** comprising a **barrel** and having a front end portion and a back end portion, the back end portion further comprising at least one radially extending member providing finger grips for the syringe **body;**

a retraction mechanism disposed in the front end portion, the retraction mechanism further comprising a

needle holder having a head portion, an elongated needle holding portion, and a longitudinally extending fluid passageway through the head portion and the elongated needle holding portion, the head portion further comprising an inner head, **a continuous retainer member surrounding the inner head,** and a **bridging portion** disposed between the continuous **retainer member** and the inner head, wherein said **bridging portion** couples the continuous **retainer member** and the inner head to form a fluid seal between the fluid passageway and the **barrel** prior to retraction, and a compressed retraction spring surrounding at least part of the elongated needle holding portion and biasing the inner head toward the back end portion prior to retraction;

a retractable needle extending into the front end portion of the **body** through an opening in the front end portion of the **body,** the retractable needle being held in fixed relation to the elongated needle holding portion of the needle holder and in fluid communication with the longitudinally extending fluid passageway through the head portion and the needle holding portion;

a plunger reciprocally disposed inside the **barrel** and forming a variable chamber between the plunger and the needle holder prior to and during injection, the plunger being receivable into the **barrel** through the back end portion of the **body** and comprising an outer wall, a retraction cavity disposed inwardly of the outer wall, a plunger seal element providing sliding, sealed engagement between the plunger and the **barrel** and preventing fluid leakage between the plunger and the **barrel,** the plunger seal element being restrained from sliding longitudinally along the outer wall of the plunger, and a back end with an **end cap** having an outer periphery; and

a barrier disposed in the front end portion of the **body** that limits forward motion of the needle holding portion and the retractable needle relative to the **body** as the plunger is depressed inside the barrel during injection and retraction;

wherein the continuous retainer member is releasable from the inner head of the needle holder when the plunger is further depressed inside the barrel following injection.

47. The syringe assembly of claim 43 wherein the **body** further comprises a collar having an open back end, the collar extending rearwardly behind the at least one radially extending member and longitudinally separating the at least one radially extending member from the open back end, and wherein the outer periphery of the **end cap** is in close proximity to the back end of the collar following injection and during retraction.

55. The syringe assembly of claim 43 wherein the retraction cavity is **vented** behind the plunger seal element.

60. The syringe assembly claim 43 wherein the continuous retaining member has an outside mating surface making a fluid seal with the **barrel.**

The syringe assembly of claim 43 wherein the **body** and the elongated needle holder cooperate as a spring guide during compression of the retraction spring.

'224 Patent, 22:35-23:19, 23:32-39, 24:18-19, 24:33-35, 24:36-38 (emphasis added).

B. Claim Construction

1. "body"/"barrel"/"bridging portion"/"retainer member"

The Court construed these terms as part of its analysis of the '733 Patent, of which the '224 Patent is a continuation-in-part. The Court finds no reason to deviate from its prior constructions.

2. "continuous retainer member surrounding the inner head"

The parties propose the following constructions for "continuous retainer member surrounding the inner head," which is present in claim 43. Dkt. No. 114.

RTI	BD
A nonretractable part of the retraction mechanism that encircles the inner head of the needle holder, and retains the retraction mechanism	A nonretractable part of the retraction mechanism, separate from the needle holder, that encircles the inner head of the needle holder, and retains the retraction mechanism by frictional force with the wall of the syringe

RTI and BD proffer the same arguments as those discussed above in connection with the term "retainer member." Dkt. Nos. 111 at 13-14. Once again, the dispute between the parties is two-fold: (1) whether the holding force must be a frictional force, and (2) whether the needle holder and retainer member must be separate parts.

For the reasons stated above, this Court finds that the invention operates through the use of a clamping or fictional force and that there is no requirement that two components be separate parts. Accordingly, the Court finds that the term "continuous retainer member surrounding the inner head" means "a non-retractable part of the retraction mechanism that encircles the inner head of the needle holder and uses some clamping or frictional force to keep the needle in the projecting position until released."

3. "end cap"

a. Parties' Positions

The parties offer the following constructions for "end cap," which is present in claims 43 and 47. Dkt. No. 114.

RTI	BD
Back end of the plunger	A separate piece that caps the open end of the plunger

RTI contends that BD's proposed construction improperly limits this term. Dkt. No. 111 at 30-31. RTI believes that nothing in the specification requires the end cap be a separate piece or that it cap the open end of the plunger. *Id*. Instead, RTI contends that the "force fit plug" is the separate piece that caps the end of the plunger, while the end cap is a part of the plunger itself. *Id* . (citing '224, 7:22-24 & Figs. 1-7). In addition, one claim specifically recites that "the end cap has an opening and a closure is installed in the opening." *Id*. (citing '224, 24:16-17 (claim 54)).

In response, BD contends that RTI's proposed construction does not make sense in light of the claim language. Dkt. No. 112 at 32. Specifically, the claims require a "back end with an end cap," and BD believes that RTI's construction would make this requirement nonsensical-a back end with a back end. *Id*. (citing '224, 22:65-23:9 (claim 43)).

b. Court's Construction

The Patent figures depict the end cap as a part of the plunger rather than a separate piece. *See* '224, Figs. 1-7. The Federal Circuit has held that an interpretation of a claim, which would not include a preferred embodiment disclosed in the specification, is "rarely, if ever, correct." Vitronics, 90 F.3d at 1583. This Court finds no reason to require the end cap to be a separate piece, as such a construction would not include the

embodiments depicted in Figures 1-7. This Court, however, also finds no reason to limit the term to these embodiments, in which the end cap is a part of the plunger. The Patent could conceivably cover an alternative embodiment in which the end cap was a separate piece.

In addition, the Patent states that it is the "force fit plug" rather than the end cap that closes the retraction cavity-the open end-at the back of the plunger. '224, 7:33-36. The end cap itself has a "central opening for permanently receiving [the] force fit plug." *Id.* As such, the end cap, in contradiction with the plain meaning of the word "cap," does not necessarily close the open end of the plunger. Instead, it allows the force fit plug to accomplish that function once it is permanently installed within the end cap's opening. This Court, however, also finds no reason to limit the term to this one preferred embodiment-it is possible that the Patent could cover a syringe in which the end cap and force fit plug were a single piece, rather than two separate parts.

Finally, because it is located at the back of the plunger, the Patent describes the end cap as a portion of the plunger with which the thumb contacts during depression. *Id.* ("Plunger has an end cap for depression of the plunger by the thumb.").

Accordingly, the Court finds that the term "end cap" means "a component at the back of the plunger, which may be contacted by the thumb during depression."

4. "wherein the continuous retainer member is releasable from the inner head"

a. Parties' Positions

The parties offer the following constructions for the term "wherein the continuous retainer member is releasable from the inner head," which appears in claim 43. Dkt. No. 114.

RTI	BD
The plunger releases the continuous retainer member from the inner head as the plunger is further depressed in the barrel	The plunger releases the continuous retainer member from the inner head by pushing the continuous retainer member off of the inner head as the plunger is depressed in the barrel to reduce the frictional force with the wall of the syringe

The parties' arguments in connection with this term closely mirror those proffered in connection with the term "releaseably installed by sliding engagement of said retainer member and said inwardly facing surface" construed above. *See* Dkt. Nos. 111 at 19-20 & 112 at 26-27.

b. Court's Construction

For the reasons stated above, this Court finds that the invention operates through the use of a clamping or fictional force. However, since the clamping or frictional forces are already part of this Court's construction of "continuous retainer member," this Court finds that it would be unnecessarily confusing and duplicative to include a reference to those forces in this term's construction. As also discussed above, this Court finds that that the holding force may be released by some other manner than that with which it was installed.

Accordingly, the Court finds that the term "wherein the continuous retainer member is releasable from the inner head" means "the plunger releases the continuous retainer member from the inner head as the plunger is further depressed in the barrel."

VII. CONCLUSION

The Court hereby **ORDERS** the claim terms addressed herein construed as indicated. The table below summarizes the Court's constructions:

Term	Court's Construction
	'773 Patent
body	"a hollow outer structure that houses the syringe's components." A hollow outer structure that houses the syringe's components
barrel	The elongated part of the syringe body including a portion through which the plunger moves during injection
nose	The portion of the syringe at the injection end that has a reduced diameter relative to the barrel.
nose portion	Section of the syringe body that has a reduced diameter relative to the barrel portion of the body.
transition zone	Portion of the syringe located between the barrel and the nose
inwardly facing surface	A surface that faces toward the center of the syringe
retraction mechanism sealingly disposed in the nose	A retraction mechanism sealed in the nose.
retainer member	A non-retractable part of the retraction mechanism that uses some clamping or frictional force to keep the needle in the projecting position until released
bridging portion	A structure that spans the gap between and connects the retainer member and needle holder
releaseably installed by sliding engagement of said retainer member and said inwardly facing surface	Installed by sliding the retainer member along the inwardly facing surface to engage it with the wall of the syringe, which creates a clamping or frictional force that can be released at a later time
sliding engagement producing a holding force	Sliding the retainer member along the inwardly facing surface of the body produces a clamping or frictional force that maintains the needle holder in the projected position
outwardly facing surface	A surface that faces away from the center of the syringe
	'077 Patent
body	Same as above
barrel	Same as above
vent	An opening that provides an opportunity or means of escape, passage, or release
the barrel having a front end portion containing a retraction mechanism configured for operation by a plunger	The section of the barrel at the injection end has a retraction mechanism that is configured to be operated by a plunger.
a front end configured to operate the retraction mechanism	Portion of the plunger closer to the injection end of the syringe that operates the retraction mechanism.
	'224 Patent
body	Same as above
barrel	Same as above
retainer member	Same as above
bridging portion	Same as above
continuous retainer member surrounding the inner head	A non-retractable part of the retraction mechanism that encircles the inner head of the needle holder and uses some clamping or frictional force to keep the needle in the projecting position until released
end cap	A component at the back of the plunger, which may be contacted by the thumb during depression
wherein the continuous retainer member is releasable from the inner head	The plunger releases the continuous retainer member from the inner head as the plunger is further depressed in the barrel

IT IS SO ORDERED.

E.D.Tex.,2009.
Retractable Technologies, Inc. v. Becton Dickinson & Co.

Produced by Sans Paper, LLC.

CARTRIDGE AND TEST INFORMATION

i-STAT® sensors are available in a variety of panel configurations. Sensors are contained in cartridges with microfluidic components and, in some cartridges, calibration solution. i-STAT cartridges are used with the i-STAT 1 Analyzer* for the simultaneous quantitative determination of specific analytes and coagulation parameters in whole blood.

CARTRIDGE SPECIFICATIONS

Shelf Life:

Refrigerated at 2 to 8 °C (35 to 46 °F) until expiration date.

Refer to the cartridge box for room temperature storage requirements.

Preparation for Use:

Individual cartridges may be used after standing five minutes at room temperature. An entire box of cartridges should stand at room temperature for one hour.

All cartridges should be used immediately after opening pouch. If the pouch has been punctured, the cartridge should not be used.

Sample Type:

Fresh whole blood from arterial, venous, or skin punctures.

(Note: Skin puncture is NOT a recommended sample type for ACT, cTnI, CK-MB, ß-hCG or BNP testing.)

cTnI, ß-hCG and CK-MB cartridges require the use of heparinized whole blood or plasma, or non-heparinized whole blood tested within one minute of patient draw.

BNP cartridges require the use of EDTA whole blood or plasma samples.

Sample Volume:

17 µL, 20 µL, 40 µL, 65 µL, or 95 µL depending on cartridge type.

Test Timing:

Immediately after collection

- Samples for the measurement of ACT, PT/INR and Lactate

Within 3 minutes after collection

- Samples collected in capillary tubes with balanced heparin anticoagulant
- Samples collected in evacuated or non-evacuated tubes and syringes without anticoagulant

Within 10 minutes after collection

- Samples collected with anticoagulant for the measurement of pH, PCO_2, PO_2 and iCa. Maintain anaerobic conditions. Remix before filling cartridge.

Within 30 minutes after collection

- Sodium, potassium, chloride, glucose, BUN/urea, creatinine, hematocrit, troponin I, CK-MB, ß-hCG and BNP. Remix thoroughly before testing.

Abbott Point of Care

Art: 714258-01O Rev. Date: 15-Aug-16

* The cTnI, CK-MB, ß-hCG and BNP cartridges can only be used with the i-STAT 1 analyzer bearing the  symbol.

Analysis Time:

- ACT cartridge: to detection of end point - up to 1000 sec (16.7 min)
- PT/INR cartridge: to detection of end point – up to 300 sec (5 min)
- cTnI, ß-hCG and BNP cartridges: 600 sec (10 min)
- CK-MB cartridge: 300 sec (5 min)
- Other cartridges: typically 130 to 200 sec

Cartridges	Collection Options			
	Syringes	**Evacuated Tubes**	**Capillary Tubes**	**Directly from Skin Puncture**
Cartridges which measure ionized calcium	• Without anticoagulant • With balanced heparin anticoagulant (syringe must be filled to labeled capacity)	• Without anticoagulant • With lithium heparin anticoagulant (tubes must be filled to capacity)	• With balanced heparin anticoagulant	• Not recommended • Not recommended for blood gas analysis; arterial specimens are preferred
Cartridges which perform ACT	• Without anticoagulant ONLY • Syringes must be plastic	• Without anticoagulant, clot activators, or serum separators ONLY • Tubes must be plastic • Devices used to transfer sample to cartridge must be plastic	• Not recommended	• Not recommended
Cartridges which perform PT/INR	• Without anticoagulant ONLY • Syringes must be plastic	• Without anticoagulant, clot activators, or serum separators ONLY • Tubes must be plastic • Devices used to transfer sample to cartridge must be plastic	• Not recommended	• Recommended
Cartridges which measure Troponin I or CK-MB	• With sodium or lithium heparin anticoagulant (syringe must be filled to labeled capacity) • Without anticoagulant if tested within one minute of patient draw	• With sodium or lithium heparin anticoagulant (tubes must be filled to capacity) • Without anticoagulant if tested within one minute of patient draw	• Not recommended	• Not recommended

Cartridges	Collection Options			
	Syringes	Evacuated Tubes	Capillary Tubes	Directly from Skin Puncture
Cartridges which measure Total ß-hCG	• With sodium or lithium anticoagulant (syringe must be filled to labeled capacity) • Without anticoagulant if tested within one minute of patient draw • Syringes must be plastic	• With sodium or lithium heparin anticoagulant (tubes must be filled to capacity)	• Not recommended	• Not recommended
Cartridges which measure BNP	• With EDTA anticoagulant (syringe must be filled to labeled capacity) • Syringes must be plastic	• With EDTA anticoagulant (tubes must be filled to capacity) • Tubes must be plastic	• Not recommended	• Not recommended
All other cartridges	• Without anticoagulant • With lithium or balanced heparin anticoagulant (syringe must be filled to labeled capacity)	• Without anticoagulant • With lithium heparin anticoagulant (tubes must be filled to capacity)	• With balanced heparin anticoagulant • With lithium heparin if labeled for the measurement of electrolytes	• While a sample can be transferred directly from a skin puncture to a cartridge, a capillary tube is preferred • Not recommended for blood gas analysis; arterial specimens are preferred

Note Regarding System Reliability

The i-STAT System automatically runs a comprehensive set of quality checks of analyzer and cartridge performance each time a sample is tested. This internal quality system will suppress results if the analyzer or cartridge does not meet certain internal specifications (see Quality Control section in System Manual for detailed information). To minimize the probability of delivering a result with medically significant error the internal specifications are very stringent. It is typical for the system to suppress a very small percentage of results in normal operation given the stringency of these specifications. If however the analyzer or cartridges have been compromised, results may be persistently suppressed, and one or the other must be replaced to restore normal operating conditions. **Where unavailability of results while awaiting replacement of analyzers or cartridges is unacceptable, APOC recommends maintaining both a backup i-STAT System analyzer and cartridges from an alternate lot number.**

EXPECTED VALUES

Measured:

TEST	UNITS	REPORTABLE RANGE	REFERENCE RANGE (arterial)	REFERENCE RANGE (venous)
Sodium/Na	mmol/L (mEq/L)	100 – 180	138 – 146	138 – 146
Potassium/K	mmol/L (mEq/L)	2.0 – 9.0	3.5 – 4.9	3.5 – 4.9
Chloride/Cl	mmol/L (mEq/L)	65 – 140	98 – 109	98 – 109
Glucose/Glu	mmol/L mg/dL g/L	1.1 – 38.9 20 – 700 0.20 – 7.00	3.9 – 5.8 70 – 105 0.70 – 1.05	3.9 – 5.8 70 – 105 0.70 – 1.05
Lactate/Lac	mmol/L mg/dL	0.30 – 20.00 2.7 – 180.2	0.36 – 1.25 3.2 – 11.3	0.90 – 1.70 8.1 – 15.3
Creatinine/Crea	mg/dL µmol/L	0.2 – 20.0 18 – 1768	0.6 – 1.3 53 – 115	0.6 – 1.3 53 – 115
pH		6.5 – 8.2	7.35 – 7.45	7.31 – 7.41
***P*CO$_2$**	mmHg kPa	5 – 130 0.67 – 17.33	35 – 45 4.67 – 6.00	41 – 51 5.47 – 6.80
TCO$_2$ (on the CHEM8+ cartridge only)	mmol/L (mEq/L)	5 – 50	23 – 27	24 – 29
***P*O$_2$**	mmHg kPa	5 – 800 0.7 – 106.6	80 – 105 10.7 – 14.0	
Ionized Calcium/iCa	mmol/L mg/dL	0.25 – 2.50 1.0 – 10.0	1.12 – 1.32 4.5 – 5.3	1.12 – 1.32 4.5 – 5.3
Urea Nitrogen/BUN **Urea**	mg/dL mmol/L mg/dL g/L	3 – 140 1 – 50 6 – 300 0.06 – 3.00	8 – 26 2.9 – 9.4 17 – 56 0.17 – 0.56	8 – 26 2.9 – 9.4 17 – 56 0.17 – 0.56
Hematocrit/Hct	%PCV Fraction	15 – 75 0.15 – 0.75	38 – 51 0.38 – 0.51	38 – 51 0.38 – 0.51
Celite Activated Clotting Time / ^{Celite}ACT *The range from 80 - 1000 seconds has been verified through method comparison studies.*	seconds	50 – 1000	74 – 125 (Prewarm) 84 – 139 (Nonwarm)	74 – 125 (Prewarm) 84 – 139 (Nonwarm)
Kaolin Activated Clotting Time / ^{Kaolin}ACT *The range from 77 - 1000 seconds has been verified through method comparison studies.*	seconds	50 – 1000	74 – 137 (Prewarm) 82 – 152 (Nonwarm)	74 – 137 (Prewarm) 82 – 152 (Nonwarm)
Prothrombin Time / PT *Performance characteristics have not been established for INRs above 6.0.*	INR	0.9 – 8.0		
Troponin I / cTnI	ng/mL (µg/L)	0.00 – 50.00		0.00 – 0.03* 0.00 – 0.08**
Performance characteristics have not been established for cTnI values above 35.00 ng/mL. ** Represents the 0 to 97.5% range of results.* *** Represents the 0 to 99% range of results.*				
Creatine Kinase MB / CK-MB ****Represents the 0 to 95% range of results.*	ng/mL (µg/L)	0.0 – 150.0		0.0 – 3.5***

EXPECTED VALUES (CONT.)

Measured: (CONT.)

TEST	UNITS	REPORTABLE RANGE	REFERENCE RANGE (arterial)	REFERENCE RANGE (venous)
B-Type Natriuretic Peptide / BNP	pg/mL (ng/L)	15 – 5000		<15 – 50#
# Represents the 0 to 95% range of results.				
Total Beta-Human Chorionic Gonadotropin /ß-hCG	IU/L	5.0 – 2000.0		<5.0

Calculated:

TEST	UNITS	REPORTABLE RANGE	REFERENCE RANGE (arterial)	REFERENCE RANGE (venous)
Hemoglobin/Hb	g/dL	5.1 – 25.5	12 – 17	12 – 17
	g/L	51 – 255	120 – 170	120 – 170
	mmol/L	3.2 – 15.8	7 – 11	7 – 11
TCO_2 (on all cartridges but the CHEM8+)	mmol/L (mEq/L)	5 – 50	23 – 27	24 – 29
HCO_3	mmol/L (mEq/L)	1.0 – 85.0	22 – 26	23 – 28
BE	mmol/L (mEq/L)	(-30) – (+30)	(-2) – (+3)	(-2) – (+3)
Anion Gap/AnGap	mmol/L (mEq/L)	(-10) – (+99)	10 – 20	10 – 20
sO_2	%	0 – 100	95 – 98	

CARTRIDGE CONFIGURATIONS AND SAMPLE VOLUME

i-STAT $^{EC}8^{+}$ (65µL)
Sodium (Na)
Potassium (K)
Chloride (Cl)
pH
PCO_2
Urea Nitrogen (BUN)/Urea
Glucose (Glu)
Hematocrit (Hct)
TCO_2*
HCO_3*
BE*
Anion Gap* (Angap)
Hemoglobin* (Hb)

i-STAT 6^{+} (65µL)
Sodium (Na)
Potassium (K)
Chloride (Cl)
Urea Nitrogen (BUN)/Urea
Glucose (Glu)
Hematocrit (Hct)
Hemoglobin* (Hb)

i-STAT $^{EC}4^{+}$ (65µL)
Sodium (Na)
Potassium (K)
Glucose (Glu)
Hematocrit (Hct)
Hemoglobin* (Hb)

i-STAT $^{E}3^{+}$ (65µL)
Sodium (Na)
Potassium (K)
Hematocrit (Hct)
Hemoglobin* (Hb)

i-STAT *G* (65µL)
Glucose (Glu)

i-STAT *CREA* (65µL)
Creatinine (Crea)

i-STAT $^{EG}7^{+}$ (95µL)
Sodium (Na)
Potassium (K)
Ionized Calcium (iCa)
Hematocrit (Hct)
pH
PCO_2
PO_2
TCO_2*
HCO_3*
BE*
sO_2*
Hemoglobin* (Hb)

i-STAT $^{EG}6^{+}$ (95µL)
Sodium (Na)
Potassium (K)
Hematocrit (Hct)
pH
PCO_2
PO_2
TCO_2*
HCO_3*
BE*
sO_2*
Hemoglobin* (Hb)

i-STAT $^{G}3^{+}$ (95µL)
pH
PCO_2
PO_2
TCO_2*
HCO_3*
BE*
sO_2*

i-STAT $^{CG}4^{+}$ (95µL)
pH
PCO_2
PO_2
Lactate
TCO_2*
HCO_3*
BE*
sO_2*

i-STAT *TOTAL ß-hCG* (17µL)
Total Beta-Human Chorionic Gonadotropin

**Calculated*

i-STAT $^{CG}8^{+}$ (95µL)
Sodium (Na)
Potassium (K)
Ionized Calcium (iCa)
Glucose (Glu)
Hematocrit (Hct)
pH
PCO_2
PO_2
TCO_2*
HCO_3*
BE*
sO_2*
Hemoglobin* (Hb)

i-STAT ^{Celite}*ACT* (40µL)
Celite® ACT

i-STAT ^{KAOLIN}*ACT* (40µL)
Kaolin ACT

i-STAT *PT/INR* (20µL)
Prothrombin Time

i-STAT *cTnI* (17 µL)
Troponin I

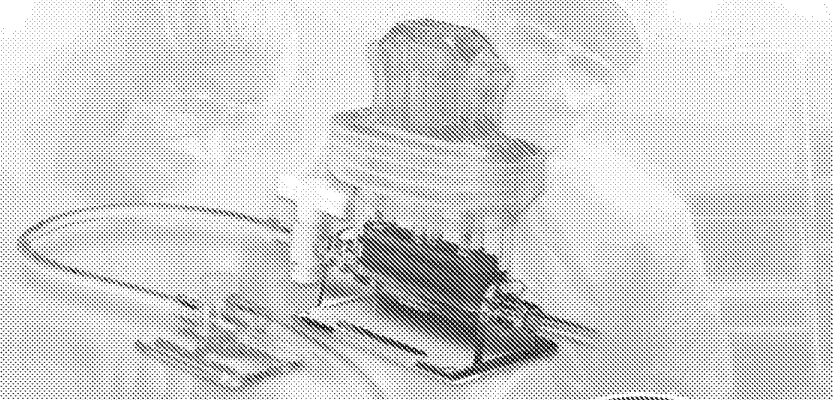
i-STAT *CK-MB* (17µL)
Creatine Kinase MB

i-STAT *BNP* (17µL)
B-type Natriuretic Peptide

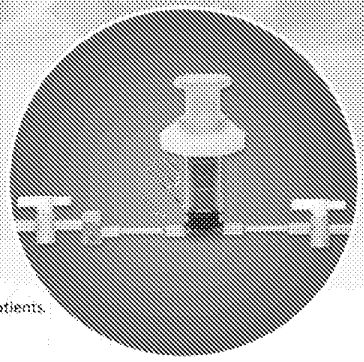
i-STAT *CHEM8+* (95µL)
Sodium (Na)
Potassium (K)
Chloride (Cl)
Urea Nitrogen (BUN)/Urea
Glucose (Glu)
Creatinine (Crea)
Ionized Calcium (iCa)
TCO_2
Hematocrit (Hct)
Anion Gap* (Angap)
Hemoglobin* (Hb)

Celite is a registered trademark of Celite Corporation, Santa Barbara, CA, for its diatomaceous earth products.

Conservation. Safety. Simplicity. Edwards VAMP and VAMP Jr. Systems.



VAMP System
Venous Arterial blood Management Protection System



VAMP Jr. System
for pediatric and neonatal patients

Edwards

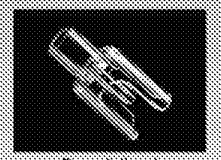


Figure 1 [illegible]

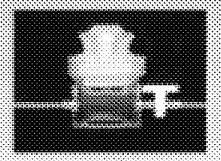


Figure 2 VAMP Reservoir

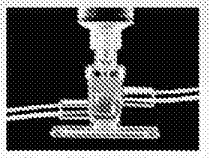


Figure 3 Z-site sampling port

VAMP Kits

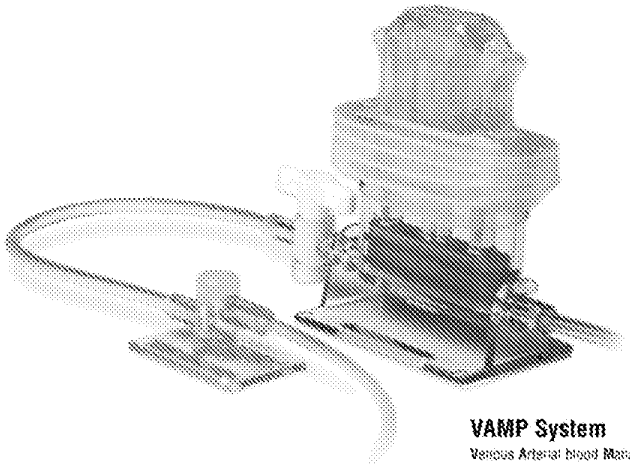
The closed blood sampling system that protects patient from the Edwards TruWave Disposable Pressure Transducer. The Edwards VAMP system provides the safest and easiest method of needleless blood sampling. The blunt cannula design (Figure 1) provides safety by eliminating the needlesticks associated with blood sampling.

It's the only system with the VAMP reservoir – a unique design that conserves blood and ensures consistent blood sampling (Figure 2).

Another unique design that enables the collection of undiluted samples while greatly reducing residual blood holding, is our Z-site sampling port (Figure 3). The VAMP system was designed with the benefits of a closed system in mind. From the self-sealing sampling port that replaces stopcocks to our patented reservoir and shut-off valve, we're dedicated to providing safe and convenient blood sampling for your patients.

The VAMP system is easy, safe, and convenient for your patient. And it works best with TruWave Disposable Pressure Transducers.

An Easy, Convenient System... An Accurate Sys



VAMP System

Venous Arterial blood Management Protection System

The safe way to perform pediatric and neonatal blood sampling.

Because it's not the right size for pediatric and neonatal care, the Edwards VAMP Jr. system makes blood sampling safer and safer for you and your special patients. Completely closed, which may provide greater protection against nosocomial infections, the VAMP Jr. system reduces the loss of patient blood while providing consistent clearing volumes, safer reinfusion and unaltered accurate blood samples. The needleless system also reduces the threat of needlesticks.

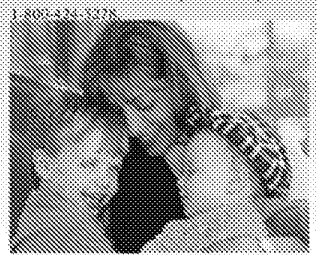
A unique in-line reservoir puts safety first.

Blood conservation and consistent sampling are critical for optimal pediatric and neonatal care. The VAMP Jr. reservoir is designed with "cc" markings to help you select the appropriate clearing volumes based on the size of your patient and the samples required. And since the volume is held in the in-line reservoir and not set aside in a syringe to be reinfused later, the potential for contamination may be reduced. After sampling, the plunger is pushed closed, wiping the walls clean and safely reinfusing all the blood to the patient. Plus, VAMP Jr.'s special contamination hood and one way in line shut-off valves may reduce the risk of sepsis from touch and/or airborne contaminants.

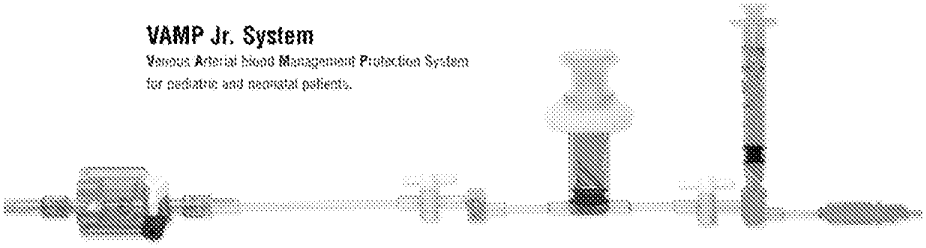
The VAMP Jr. system fits the special needs of your special patients.

The VAMP Jr. system is designed to require decreased volume over a smaller incision for more accurate sampling and flushing in pediatric and neonatal patients. For the added convenience of accurate pressure monitoring, the VAMP Jr. system is available preassembled with TruWave disposable pressure transducers (DPTs) in kit configurations to meet the specific needs of your specific patients.

To learn more about the VAMP Jr. system, contact your Edwards Lifesciences Corporation Representative at 1-800-424-3278.



Item.. And with VAMP Kits, A complete System



VAMP System Venous Arterial blood Management Protection

TruWave/VAMP Combination Kits	Case Qty.	Model No.
30" VAMP System with Arm-mount Reservoir	10	PXVMP130
60" VAMP System with Arm-mount Reservoir	10	PXVMP160
72" VAMP System with Arm-mount Reservoir	10	PXVMP172
84" VAMP System with Arm-mount Reservoir	10	PXVMP184
60" VAMP System with Pole-mount Reservoir	10	PXVMP260
72" VAMP System with Pole-mount Reservoir	10	PXVMP272
84" VAMP System with Pole-mount Reservoir	10	PXVMP284
60" VAMP System with Arm-mount Reservoir on the arterial line with: • Two TruWave Disposable Pressure Transducers with two 3 ml/hr flush devices • Bifurcated IV set (manifold) • One set of 48" and 12" pressure tubing • Three 3-way stopcocks	10	PXVMP2321
60" VAMP System with Pole-mount Reservoir on the arterial line with: • Two TruWave Disposable Pressure Transducers with two 3 ml/hr flush devices • Bifurcated IV set (manifold) • One set of 48" and 12" pressure tubing • Three 3-way stopcocks	10	PXVMP2322

Please contact your local sales representative for VAMP® combination kit information and model numbers.

VAMP Jr. System

VAMP Jr.	VAMP Jr./DPT Combo Kits
VMP306 2" proximal, 4" distal for neonatal application	VMP306PX 3cc TruWave DPT with 2" proximal, 4" distal VAMP Jr. for neonatal application
VMP408 3" proximal, 3" distal for pediatric application	VMP408PX 3cc TruWave DPT with 3" proximal, 3" distal VAMP Jr. for pediatric application
VMP428 12" proximal, 16" distal for pediatric application	VMP428PX 3cc TruWave DPT with 12" proximal, 16" distal VAMP Jr. for pediatric application
VMP448 19" proximal, 29" distal for pediatric application	VMP448PX 3cc TruWave DPT with 19" proximal, 29" distal VAMP Jr. for pediatric application

CE

Certificate number
to European MDD

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1708-1906-01

Edwards Lifesciences

Edwards Lifesciences LLC • One Edwards Way • Irvine, CA 92614 USA • 949.250.2500 • 800.424.3278 • www.edwards.com
Edwards Lifesciences (Canada) Inc. • 1290 Central Pkwy West, Suite 800 • Mississauga, Ontario • Canada L5C 4R3 • Phone 905.566.4220 • 800.268.3993
Edwards Lifesciences S.A. • Ch. du Glapin 8 • 1162 Saint-Prex • Switzerland • Phone 41.21.823.4300
Edwards Lifesciences Japan • 2-8 Nakanoshima • Kita-ku, Tokyo 102-0083 • Japan • Phone 81.3.6213.5700

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
3 June 2010 (03.06.2010)

PCT

(10) International Publication Number
WO 2010/062734 A1

(51) International Patent Classification:
A61F 13/02 (2006.01) *A61P 7/04* (2006.01)
A61L 15/44 (2006.01)

(21) International Application Number:
PCT/US2009/063049

(22) International Filing Date:
3 November 2009 (03.11.2009)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
61/110,698 3 November 2008 (03.11.2008) US
61/234,773 18 August 2009 (18.08.2009) US

(71) Applicants *(for all designated States except US)*: **UNIVERSITY OF MARYLAND, BALTIMORE** [US/US]; 520 West Lombard Street, Baltimore, Maryland 21201 (US). **UNIVERSITY OF MARYLAND, COLLEGE PARK** [US/US]; Office of Technology Commercialization, 0133 Cole Student Activities Bldg., College Park, Maryland 20742 (US).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **CASEY, Brendan, J.** [US/US]; 9540 Rhode Island Avenue, College Park, Maryland 20740 (US). **KOFINAS, Peter** [US/US]; 5809 Nicholson Lane, #610, North Bethesda, Maryland 20852 (US). **BEHRENS, Adam** [US/US]; 3608 Toddsbury Lane, Olney, Maryland 20832 (US). **SNYDER, Trevor, A.** [US/US]; c/o UNIVERSITY OF MARYLAND, BALTIMORE, 520 West Lombard Street, Baltimore, Maryland 21201 (US). **GRIFFITH, Bartley, P.** [US/US]; c/o UNIVERSITY OF MARYLAND, BALTIMORE, 520 West Lombard Street, Baltimore, Maryland 21201 (US).

(74) Agents: **IYER, Chid, S.** et al.; Sughrue Mion, PLLC, 2100 Pennsylvania Ave., N.W., Suite 800, Washington, District of Columbia 20037-3213 (US).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— *with international search report (Art. 21(3))*

— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))*

(54) Title: BLOOD COAGULATION INDUCING POLYMER HYDROGEL

(57) Abstract: The present application is drawn to a synthetic, polymer hydrogel-based material, which is able to actively induce the body's natural hemostatic coagulation process in blood or acellular plasma. The present invention provides the development of a primary amine containing polymer hydrogel capable of inducing blood coagulation and delivering therapeutics for hemostatic or wound care applications, and a method of forming such a primary amine containing polymer hydrogel capable of inducing the blood coagulation process. The primary amine containing polymer hydrogel is able to achieve the same end result as biological-based hemostatics, without the innate risk of disease transmission or immunological response, and at a fraction of the price. Furthermore, due to its inherent hydrogel-based design the material has the capability of arresting blood loss while simultaneously delivering therapeutics in a controlled manner, potentially revolutionizing the way in which wounds are treated.

WO 2010/062734 A1

BLOOD COAGULATION INDUCING POLYMER HYDROGEL

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims priority to U.S. provisional applications Serial Nos. 61/110,698, filed November 3, 2008 and 61/234,773, filed August 18, 2009, which are incorporated in their entireties by reference herein.

STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT

[0002] This invention was made with government support under CTS0640778 awarded by the National Science Foundation. The U.S. Government has certain rights in this invention.

TECHNICAL FIELD

[0003] The present invention relates to a polymer material capable of actively inducing the blood coagulation cascade while simultaneously delivering therapeutics in a controlled manner for application in the wound care field.

BACKGROUND

[0004] Technology capable of effectively controlling traumatic hemorrhaging does not exist. As a result, millions of people around the world are dying every year. Over 3,000,000 worldwide, 156,000 in the U.S. alone, die from trauma related injuries each year. Half will die before they reach the hospital, and 80% will die within 24 hours of hospital admission. Uncontrolled hemorrhaging, or blood loss, accounts for almost half of these deaths. Moreover, on the battlefield an astounding 85% of military mortalities are due to blood loss, a statistic that has remained mostly unchanged since the Vietnam War. Army medics, emergency medical technicians (E.M.T.) personnel, and other various emergency responders need a product capable of providing rapid and effective hemostasis until they can get their patients to the operating room. Once at the operating room, hemostatic products are still crucial to surgeons who must control bleeding to maintain the stability of their patient.

[0005] Current products are either exorbitantly expensive, ineffective, and/or have adverse side effects. There is a clear need for a hemostatic product which is inexpensive,

effective, with little to no adverse side effects and medics, emergency responders, and surgeons are all looking for a solution. Furthermore, there is currently no existing product or material on the market with the capability of providing rapid hemostasis along with simultaneous drug delivery. A product which could effectively stop blood loss while simultaneously delivering potentially life-saving therapeutics such as adrenaline or insulin in a regulated manner would have a multitude of applications from the battlefield to the operating room.

[0006] Death may occur in minutes after a traumatic injury due to blood loss. The body has natural mechanisms to control hemorrhaging yet these processes may be insufficient in cases of excessive hemorrhaging, defective due to medical conditions such as hemophilia, or compromised due to adverse effects of medication like Coumadin. The natural hemostatic response is not adequate to control major hemorrhaging due to traumatic injury, which is the main reason why such injuries, if gone untreated, are typically fatal. Administration of biologically derived blood products to augment the native hemostatic response and to maintain adequate oxygen delivery to the brain and vital organs, carries significant risks including disease transmission, infection, pulmonary dysfunction, and immune response. Furthermore, many people have deficiencies within their hemostatic response i.e. hemophilia, which prevent them from adequately stopping blood loss. Millions of people around the world suffer from bleeding disorders, and are unable to clot blood effetively. Current treatments are typically limited to clotting factor (Factor VIII, Factor II) replacement therapies, which are typically painful and exorbitantly expensive. There is a clear need for an inexpensive, painless alternative to current treatments. Whether the injury overwhelms the body's clotting response or the native response is deficient or compromised, an inexpensive, synthetic material which has the ability to induce clotting effectively, while simultaneously delivering therapeutics would undoubtedly revolutionize the way in which wounds are treated.

[0007] The field of hemostatic agents and materials has expanded dramatically within the last decade. This considerable expansion and evolution of the field, throughout the last decade has also been accompanied by tremendous diversification resulting in a multitude of hemostatic products now available on the market, each with their own advantages and disadvantages. The hemostatic products currently available on the market today are either biological-based or synthetic-based. Biological-based hemostatics are comprised of animal or "animal derived" substrates which are able to initiate, amplify, and/or assist the natural

coagulation response. Although they have excellent hemostatic effects and work via the promotion of the body's natural responses, they are incredibly expensive (up to $500 per application) and carry risks of disease infection and severe immunological response. Synthetic hemostatic agents are typically less expensive and immune inert yet often fail to effectively induce the coagulation cascade. Such synthetic agents are mainly designed to be mere physical obstructions to impede blood flow while providing a scaffold for the coagulation process to occur. A purely synthetic, polymer-based hydrogel material capable of effectively inducing the body's natural coagulation response has enormous potential within the field. Such a material is unique to the market in that it could be used to effectively stop bleeding while simultaneously delivering necessary therapeutics to a wound site.

SUMMARY OF THE INVENTION

[0008] The inventors of the present application have developed a purely synthetic, polymer hydrogel-based material, which is able to actively induce the body's natural hemostatic coagulation process in blood or acellular plasma. There is currently no polymer hydrogel-based, synthetic hemostatic agent with the capability of inducing the formation of a natural hemostatic matrix in the absence of platelets or blood cells. Since the material is able to induce the formation of a natural hemostatic plug in the absence of platelets or cells, it has enormous potential as a hemostatic agent in surgery, to treat trauma victims, and especially for patients with platelet disorders. The material is able to achieve the same end result as biological-based hemostatics, without the innate risk of disease transmission or immunological response, and at a fraction of the price. Furthermore, due to its inherent hydrogel-based design the material has the capability of arresting blood loss while simultaneously delivering therapeutics in a controlled manner, potentially revolutionizing the way in which wounds are treated.

[0009] The blood coagulation cascade may be activated via two distinct routes, the tissue factor pathway and the intrinsic pathway, also known as the contact activation pathway. Both pathways eventually result in the activation of a common pathway, which leads to the formation of a fibrin-based hemostatic clot Our research has shown that a material is able to induce the formation of fibrin via the tissue pathway factor Specifically, a positively charged polymer network with adequate mechanical rigidity is capable of efficiently and effectively inducing the activation of FVII, which in turn leads to the activation of the common pathway and subsequent fibrin formation. Furthermore, the material is able to induce the activation of

FVII irrespective of calcium or platelets which are typically vital cofactors of the process.

[0010] In one aspect, the present invention provides a cross-linked primary amine containing polymer hydrogel capable of inducing blood coagulation, and subsequent fibrin clot formation, while simultaneously delivering therapeutics in a controlled or regulated manner for wound care applications.

[0011] In another aspect the present invention is able to induce coagulation in Factor XII, XI, IX, VIII, and V deficient blood plasma.

[0012] In another aspect the present invention is capable of inducing the activation of FVII irrespective of calcium and platelets.

[0013] In another aspect, the present invention provides a method of forming the specific type of cross-linked primary amine containing polymer hydrogel in order to effectively induce blood coagulation: (a) adding either a primary amine containing monomer or primary amine containing polymer with a pKa greater than 7.4 thereby being positively charged within a plasma or blood environment (pH 7.4); (b) addition of additional monomers different from the initial primary amine containing monomer; (c) forming a polymer matrix by initiating polymerization of monomer units into polymer strand; (d) cross-linking the polymer strands to produce a polymeric mesh network.

[0014] In other aspects, the present invention provides various uses for a polymer hydrogel capable of inducing blood coagulation and delivering therapeutics in a controlled manner, in the health care field.

BRIEF DESCRIPTION OF THE DRAWINGS

[0015] **Figure 1: Coagulate complex formed by optimal hydrogel after immersion in citrated plasma.** Typical coagulate complex (fibrin-hydrogel complex) formed after rotating the optimal hydrogel in human plasma (4 % w/v sodium citrate) for 18 hours.

[0016] **Figure 2: Characterization images (H&E, IHC, ESEM) of coagulate complex formed by optimal hydrogel after immersion in citrated plasma.** (**A**) H&E stained micrograph image of coagulate complex. Polymer hydrogel appears as lighter, smoother material on right side of the micrograph while fibrin appears as the darker, rougher material on the left side of them micrograph. (**B**) IHC stained micrograph image of coagulate complex. (**C**) ESEM surface image of the coagulate complex.

[0017] **Figure 3: Optimization experiment.** Experiment aimed to investigate the dependence of fibrin formation on various compositional factors including total monomer

concentration (acrylamide + APM + BIS), positive electrostatic charge (APM), and cross-linker ratio (acrylamide:APM:BIS). Acrylamide concentration is located on the horizontal axis while APM concentration is on the vertical axis. BIS concentration is also indicated on the horizontal axis and is kept constant for each respective acrylamide concentration. The amount of fibrin formation induced by each composition was visually scored from 0 (no fibrin formation) to 10 (substantial fibrin formation). All samples were run in triplicate.

[0018] Figure 4. Factor deficient and factor inhibited plasma experiment. Optimal hydrogel composition tested in various factor deficient and factor inhibited plasmas. The resulting fibrin formation was visually scored from 0 (no fibrin formation) to 10 (substantial fibrin formation) and graphed accordingly. All samples were run in triplicate.

[0019] Figure 5: Kinetic biological mechanism experiments. Factor VIIa concentration (**A**), calcium concentration (**B**) , and TFPI activity (**C**) was measured in human plasma containing various hydrogel compositions at 30, 90, and 180 minutes (left axis: bar graph). The amount of fibrin formation was also rated for each composition at each time point (right axis: line graph). Data is representative of an average and corresponding standard deviation (error bar) of three (n=3) separate sample trials. Asterisk (*) indicates duplicate sample point.

[0020] Figure 6: Dynamic mechanical analysis. Dynamic mechanical analysis of three compositions used in the kinetic biological mechanism experiments (FVIIa, calcium, TFPI) ranging from high APM, low acrylamide and BIS content (composition A) to low APM, high acrylamide and BIS content (composition F). Spectra for sample compositions C and F are shifted vertically to avoid overlapping of data.

[0021] Figure 7: Fresh sheep blood experiment. 250 mg of our hydrogel material (**A**) compared to a control (**B**). Clotting time of blood with material was dramatically decreased (~45 seconds) compared to control (~10 minutes).

[0022] Figure 8: Prototype images. (**A**) Computer generated graphic of prototype used in animal experiment. (**B**) Actual prototype used in animal trial.

[0023] Figure 9: Animal trial. (**A**) Image of lung at time of incision, before hydrogel was applied. (**B**) Image of the incision site after the hydrogel prototype bandage was applied for approximately 2 minutes.

[0024] Figure 10: Stained lung section of incision site. Micrograph of hematoxylin and eosin (H&E) stained section of incision site after hydrogel material was applied for two minutes.

DETAILED DESCRIPTION OF THE INVENTION

[0025] A reference to an element by the indefinite article "a" or "an" does not exclude the possibility that more than one of the element is present. Rather, the article "a" or "an" is intended to mean one or more (or at least one) unless the text expressly indicates otherwise. The terms "first," "second," and so on, when referring to an element, are not intended to suggest a location or ordering of the elements. Rather, the terms are used as labels to facilitate discussion and distinguish elements from one another.

[0026] The foregoing description and examples have been set forth merely to illustrate the invention and are not intended to be limiting. Each of the disclosed aspects and embodiments of the present invention may be considered individually or in combination with other aspects, embodiments, and variations of the invention. Modifications of the disclosed embodiments incorporating the spirit and substance of the invention may occur to persons skilled in the art and such modifications are within the scope of the present invention.

[0027] The present invention provides the development of a primary amine containing polymer hydrogel capable of inducing blood coagulation and delivering therapeutics for hemostatic or wound care applications. Various therapeutics intended to be delivered include but are not limited to ester or amide based anesthetics such as Novocain or Lidocain, antibiotics such as erythromycin or bacitracin, vasoconstrictors such as adrenaline, and pain relievers or anti-inflammatory medicines such as topricin, acetaminophen, or ibuprofen. The hydrogel may be designed in order to deliver the drugs in various ways including based on a swelling change, a change in pH, or via the introduction of a magnetic or electric field.

[0028] The present invention provides the development of a primary amine containing polymer hydrogel capable of inducing blood coagulation and delivering other hemostatic agents for hemostatic or wound care applications, including biological-based hemostatic agents and non biological-based hemostatic agents.

[0029] Biological-based hemostatics contain, incorporate, or are derived from biological substrates, i.e. proteins, or cells. They can further be subdivided into the type of biological substrates incorporated into the system including collagen, thrombin, fibrin, albumin, and/or platelets.

[0030] Collagen is the main protein of connective tissue in mammals, including the skin, bones, ligaments, and tendons making up about 30% of the total protein in the body. In addition to providing structural integrity for the animal body, including all organs, collagen also activates the contact activation pathway of the coagulation cascade. Due to collagen's

ability to induce coagulation, along with the fact that is it naturally occurring, makes it an ideal choice for a hemostatic agent. Collagen is typically incorporated into the products via gelatin or microfibrillar form. Gelatin is an irreversibly hydrolyzed form of collagen and may be prepared as a powder, sponge, sheet, film or foam. Gelatin products are typically pliable, easy to handle, and relatively inert. When placed in soft tissue gelatin products typically absorb in 4 to 6 weeks, yet when applied to bleeding nasal, rectal or vaginal mucosa, will liquefy in approximately 2 to 5 days. The product Gelfoam (Pfizer, New York, NY), first introduced in 1945, is produced from purified pork skin gelatin granules. The foam swells up to 45 times its original dry weight and 200% of its initial volume.

[0031] Microfibrillar collagen is the predominant form used in modern hemostatic products. The collagen network acts as a framework which aggregates clotting factors, platelets, along with various coagulative and adhesive proteins to facilitate clot formation. Furthermore, the collagen fibrils are able to efficiently activate the contact activation coagulation pathway. The product is typically formed into various products including powder (shredded fibrils), sheets, and sponges. Market examples include Ultrafoam and Avitene (Davol Inc., Cranston, RI), Instat (Johnson & Johnson, Langhorne, PA), Helistat and Helitene (Integra LifeSciences, Plainsboro, NJ), Collatape/CollaCote/CollaPlug (Integra Lifesciences Corporation, Plainsboro, NJ), Collastat and Collatene (Xemax, Napa, CA).

[0032] Collagen-based hemostatic products are easily removable, cause little aggravation to the wound site, and can be very effective hemostats (especially relative to cellulose or gelatin hemostats). Disadvantages of collagen products include their prohibitive high price (around $150 per dressing), poor biodegradability, inherent risk of antigenicity, low solubility (difficult to make concentrated solutions), and handling difficulties since the products will irreversibly adhere to any hydrated surface.

[0033] Thrombin is the central activating enzyme of the common coagulation pathway. Thrombin circulates within the blood in its precursor, or zymogen form, prothrombin. Prothrombin is specifically cleaved to produce the enzyme thrombin. The main role of thrombin in the coagulation pathway is to convert fibrinogen into fibrin, which in turn is covalently cross-linked to produce a hemostatic plug. Thrombin-based products are typically sold in liquid or powder form and include Thrombostat (ParkeDavis, Ann Arbor, MI), Thrombin-JMI (King Pharmaceuticals, Briston, TN), and Quixil (Omrix Biopharmaceuticals Ltd, Tel Hashomer, Israel). There are also several combination products which include Evicel

(Johnson & Johnson, Langhorne, PA) which is a combination of thrombin and fibrin used mainly as a tissue sealant, along with FloSeal (Baxter Healthcare Corporation, Westlake Village, CA) and SurgiFlow which are both hybrid products composed of bovine or porcine gelatin and thrombin.

[0034] Thrombin-based products take advantage of the natural physiologic coagulation response by augmenting, amplifying, and assisting the process. Advantages of these products include low risk of foreign body or inflammatory reactions, firm attachment to wound bed, and its excellent hemostatic effect, specifically with patients that have platelet dysfunctions. Another advantage of thrombin is the versatility that the product may be applied, in powder or liquid (spray on) form. Disadvantages of these products include their often prohibitive high price ($75-$300 per application), difficulty of use including the inconvenience of premixing preparation, along with the risk of intravenous introduction which may result in intravascular clotting.

[0035] Fibrin is a fibrillar protein which is polymerized and cross-linked to form a mesh network, typically at the site of an injury after the induction of the coagulation cascade. The mesh network, incorporative of other various proteins and platelets, forms a hemostatic plug to prevent continuous or further blood loss. Fibrin is activated from its inert zymogen, fibrinogen, by thrombin. Fibrin is in turn polymerized and covalently cross-linked by another coagulation factor, known as Factor XIIIa. Due to its natural mechanical hemostatic role fibrin has been commercially used to control blood flow since the early 1900s. Most fibrin glues or fibrin sealants are derived from human and bovine proteins. The product is typically sold in the form of a dual syringe. The first syringe compartment contains the matrix and matrix stabilizing components including fibrinogen, factor XIII, fibronectin, and fibrinolysis inhibitors. The second syringe compartment contains the activating agent, typically thrombin and calcium chloride. At the time of application, the contents of both syringes are ejected, combining to activate fibrin matrix formation which typically takes a matter of seconds to set and approximately 5 to 10 days to degrade or absorb into the body. Various fibrin sealants on the market include Tiseel (Baxter HealthCare Corporation, Westlake Village, CA), FibRx (CryoLife Inc., Kennesaw, GA), Crosseel (Johnson & Johnson, Langhorne, PA), Hemaseel (Haemacure Corporation, Montreal, Quebec), Beriplast P (Aventis Behring, King of Prussia, PA), and Bolheal (Kaketsuken, Kumamoto, Japan).

[0036] Fibrin-based hemostatics or tissue sealants are fast-acting, composed of native coagulative factors, are biodegradable, do not promote inflammation or tissue necrosis, have diverse applications, and are particularly useful in patients with coagulation deficiencies such as hemophilia or von Willebrand's disease. Major disadvantages of fibrin-based hemostatics include their often prohibitive price ($100- $300/mL), their fragile nature, and difficulty of handling and application.

[0037] Other prominent biological-based hemostatic products include those composed of covalently cross-linked protein networks such as BioGlue (Cryolife, Kennewsaw, GA), along with products which incorporate platelets such as Costasis, marketed as Vitagel (Orthovita, Malvern, PA). BioGlue is comprised of bovine serum albumin, and various other proteins, cross-linked with glutaraldehyde to form a rigid, insoluble matrix. The reaction occurs spontaneously upon the introduction of glutaraldehyde to the protein mixture, and requires no external factors such as coagulation factors. Disadvantages of the product include the high price ($300-$425/5 ml application), mediocre hemostatic effect, necessity of a dry environment for application, the toxic effects associated with tissue exposure to glutaraldehyde, and risk of immune reactions associated with glutaraldehyde-based products.

[0038] Costasis is a combination product combining bovine collagen and the patient's own platelets. The collagen within the product promotes the initiation of the contact activation pathway of the coagulation cascade. The presence of platelets in such a product improves overall clot strength and supplies various growth factors which facilitate tissue regeneration. Disadvantages include high price ($100- $150/mL) and difficultly of application.

[0039] Non biological-based, or synthetic, hemostatic agents are defined as any products which do not incorporate biological materials, or more specifically animal derived components. Synthetic hemostatics are typically cheaper, easier to use, and easier to apply relative to their biological counterparts. Furthermore, synthetic hemostatics have no innate antigenicity, rarely induce immune responses or inflammatory reactions, and are inherently free of disease vectors." The main classes of synthetic hemostatics include cyanoacrylates, polysaccharides (e.g. oxidized cellulose, N-acetyl glucosamine), synthetic polymers, and mineral/metal based.

[0040] Cyanoacrylates are liquids that rapidly polymerize. These products create a tight seal between tissues, obstructing blood flow. Cyanoacrylates are categorized upon their

length. Shorter chain cyanoacrylates (ethyl cyanoacrylates) are typically quicker to absorb yet more toxic relative to intermediate (butyl cyanoacrylates) or longer chain cyanoacrylates (octyl cyanoacrylates). Due to their inherent high toxicity few hemostatic products composed of short chain cyanoacrylates have reached the market. There is however some research supporting the efficacy of Krazy Glue (ethyl-2-cyanoacrylate, Elmer's, Columbus, OH) for cutaneous wound closure. Cohera Medical Corporation is currently in the process of developing a butyl cyanoacrylate (isobutyl-2-cyanoacrylate), marketed as TissuGlu (Cohera Medical Inc., Pittsburgh, PA). Furthermore, there are currently several octyl acrylate-based hemostatic products that are FDA-approved for skin closure which include Dermabond (Ethicon, Somerville, NJ) and Band-Aid Liquid Bandage (Johnson & Johnson, Langhore, PA).

[0041] Cyanoacrylates are typically nonreactive, do not promote infection, are rapidly curing, and are only moderately expensive. Disadvantages of cyanoacrylates and cyanoacrylate-based hemostatics include difficulty of application due to their highly adhesive nature, and risk of tissue neurotoxicity, fibrosis and inflammatory reactions.

[0042] The two main polysaccharides used as hemostatics today are oxidized cellulose and poly-N-acetyl glucosamine. The hemostatic effects of certain polysaccharides, specifically oxidized cellulose and N-acetyl glucosamine, have been known since the early twentieth century. Oxidized cellulose is derived from plant fiber, which is in turn oxidized in the presence of nitrogen dioxide to form cellulosic acid. Oxidized cellulose activates the coagulation cascade (contact activation pathway) and accelerates thrombin generation within the body. Furthermore, the polysaccharide meshwork serves as a physical framework for coagulation to occur, with moderate absorbent properties. Oxidized cellulose products on the market today include Oxycel (Becton Dickinson, Franklin Lakes, NJ), Celox (Medtrade Products Ltd., Crewe, England), Surgicel (Ethicon Incorporation), and BloodStop (LifeScience PLUS, Inc., Santa Clara, CA).

[0043] Cellulose-based hemostatics are relatively easy to handle, fully absorbable and biodegradable (over 1 to 6 weeks), relatively inexpensive, and have antibacterial properties. The major drawback of these products is the risk of foreign body reactions. Furthermore, these products have only moderate coagulation-inducing capability and therefore are reserved as an adjunct to the natural response rather than a synthetic replacement.

[0044] Poly-N-acetyl glucosamine, also known as chitin or chitosan, is a complex polysaccharide produced by fermenting microalgal cultures. The hemostatic effects of poly-N-acetyl glucosamine are believed to be a result of the attraction and binding of circulating blood cells. The positive charges on the polymer attract the negatively charged erythrocytes, to help seal the clot. Poly-N-acetyl glucosamine also has vasospasm effects. Poly-N-acetyl glucosamine products include HemCon (HemCon Inc., Portland, OR), TraumaDex (Medafor, Minneapolis, MN), SyvekPatch (Marine Polymer Technologies Inc., Danvers, MA), Clo-Sur P.A.D. (Scion Cardio-Vascular, Miami, FL), and Chito-Seal (Abbott Vascular Devices, Redwood, City, CA).1

[0045] Advantages of poly-N-acetyl glucosamine dressings include their ease of application, robustness, and lack of toxicity. Disadvantages include the high cost ($100 per unit), and variability of efficacy between batches.

[0046] Most polymer-based hemostatics are designed to provide a mechanical tissue sealant. The majority of products on the market today are composed of polyethylene glycol (PEG) which are applied and polymerized at the wound site. The polymer is typically cross-linked with itself or with a primer to yield a robust framework stopping blow flow and sealing tissue. Most PEG products undergo biodegradation in approximately 30 days. PEG products include Coseal (Baxter Healthcare Corporation, Westlake Village, CA) and AdvaSeal-S (Genzyme Corporation, Cambridge, MA). PEG-based hemostatics or tissue sealants are typically non inflammatory, do not induce immune response, and are biodegradable. Drawbacks include difficulty of application and high price ($400/application).

[0047] Pro QR Powder (Biolife, Sarasota, FL) is another polymer-based hemostatic on the market today. Pro QR is a combination product of a hydrophilic polymer and a potassium iron oxyacid salt. The polymer is absorptive of blood flow, promoting the formation of a natural blood clot while the potassium salt component releases iron which complexes with proteins and activates hemostatic channels. The product is inexpensive, nontoxic, easily stored, flexible, stops bleeding rapidly, and is available over the counter. The main drawback of the product is its awkward application.

[0048] The final class of non-biological, or synthetic, hemostatics includes those which incorporate metal salts or minerals such as zinc, iron, silver nitrate, or aluminum chloride. Although this class of hemostatics are typically easy to use, cost-effective, and provide adequate hemostatic effects their toxic side effects limit their appeal.

[0049] Zinc paste was first used to fix tissue after surgery in the early 1940s. Zinc paste solutions have impressive hemostatic abilities but are rarely used do to their harmful side effects including pain and toxicity of the site. Monsel's solution is a 20% ferric subsulfate solution, which is believed to occlude vessels via protein precipitation. Monsel's solution is easy to obtain, cost-effective, and resistant to bacterial contamination. Major disadvantages include its caustic and toxic nature which may promote melanocyte activity, increased erythema, dermal fibrosis, and reepithelialization. Silver nitrate is typically used as a 10% solution and coagulates blood through protein precipitation. Silver nitrate is cost-effective, easy to use, and has potent antibacterial properties. Disadvantages include its severe tissue toxicity, risk of permanent skin discoloration, and the painful burning sensation experienced upon application. Aluminum chloride has modest hemostatic properties and is prepared in concentrations of 20% to 40% in water, alcohol, ether, or glycerol. Its mechanism of action is thought to be caused by the hydrolysis of the salt, resulting in the generation of hydrogen chloride which causes vasoconstriction, and can assist in the activation of the extrinsic coagulation pathway. Aluminum chloride is cost effective, easy to use, and may be stored at room temperature. Side effects of its use include painful paresthesias, tissue irritation, and reepithelialization. Aluminum chloride solutions are marketed as Drysol and Xerac AC (person-Covey, Dallas, TX).I

[0050] A small subclass of hemostatics is based upon various mixtures of minerals. Zeolite is a granular mixture of silicon, aluminum, sodium, and magnesium derived from lava rock. When coming into contact with blood the mixture absorbs water, concentrating platelets and coagulation factors within the wound, accelerating the clotting process. QuikClot (Z-Medica, Wallingford, CT) and WoundStat (TraumaCure, Bethesda, MD) are two main products based upon a zeolite mixture. Zeolite is inexpensive, easy to manufacture, clots fairly quickly, robust under various conditions, and is fairly immunological inert. The main drawback of the formulation is the risk of thermal injury associated with use.

[0051] A hydrogel is generically defined as an insoluble, cross-linked network of polymer chains which swells in an aqueous environment. A hydrogel may be chemically cross-linked through covalent bonds or physically cross-linked through entanglements or non-covalent interactions. Due to their unique properties hydrogels have been used in various pharmaceutical and biomedical applications. Since it is possible to create hydrogel constructs with specific degradative and swelling characteristics their potential for tissue engineering

and artificial implantation is immense. Furthermore, because hydrogels can be engineered with "smart" swelling behavior based on time, pH, ionic concentration, electrical, or magnetic stimuli they have been used with incredible success as drug delivery systems.

[0052] A cationic, acrylamide-based hydrogel has been developed which exhibits unique and potent coagulation-inducing effects upon the interaction with blood or acellular plasma. The hydrogel is composed of acrylamide, N-(3-Aminopropy)methacrylamide hydrochloride, and cross-linked with N-N'- methylenebisacrylamide. Upon interaction with acellular plasma the hydrogel initiates the coagulation cascade which results in the formation of a natural, fibrin-based hemostatic matrix (Figure 1). The stained microscopic images clearly show two distinct materials; the polymer hydrogel, which appears smooth and glassy on the right side of each image and a fibrin layer, which surrounds the polymer hydrogel located on the left side of each image.

[0053] In one aspect, the present invention provides a specific method of forming such a primary amine containing polymer hydrogel capable of inducing the blood coagulation process. In one embodiment, the primary amine monomer may be a strong base (wherein its ability to exhibit a positive charge is largely pH independent). In another embodiment, the primary amine monomer may be a weak base (wherein its ability to exhibit a positive charge is largely pH dependent). In yet another embodiment, the primary amine monomer is a weak base with a pKa above 7.4 and is able to exhibit a strong positive charge at the pH of blood and plasma (~7.4).

[0054] The method involves mixing at least one monomer with a primary amine group, along with desired other monomers, different from the initial primary amine containing monomer in a solvent, specifically an aqueous solvent. The polymer hydrogel is formed by polymerizing the monomers and cross-linking either after or during the polymerization process. Preferably, the polymer hydrogel is cross-linked in such a way so as to ensure the creation of pockets within the hydrogel which are incredibly dense with primary amine functionality. These dense pockets of positive electrostatic charge are able to induce coagulation through a Factor VII dependent mechanism. Without being bound to any specific theory, it is believed that that hydrogel acts as a catalyst activating and enhancing the functioning of Factor VII along with the Factor VII-tissue factor complex. Research has shown that this phenomenon is dependent on positive electrostatic charge and the mechanical rigidity of the hydrogel formed. That is to say, the primary amine monomer, within the hydrogel, should be positively charged at the pH of blood and/or plasma, 7.4. Therefore, if

the monomer is a weak base it preferably has a pKa of at least 7.4, more preferably at least 8, and even more preferably, at least 8.5, to ensure the predominant majority of the monomers are hydrogenated bearing a positive charge. Furthermore, as stated previously the amine monomer containing polymer strand must be sufficiently cross-linked to create an appropriately rigid material.

[0055] In certain embodiments, the monomer units are capable of exhibiting an electrostatic charge in an aqueous solution. In particular the primary amine containing monomer is able to exhibit a positive electrostatic in a salt buffered, aqueous environment of pH 7.4 (blood/plasma). In some cases, the contributing monomer units may be acidic or basic, which under the appropriate pH conditions, exhibit a negative or positive electrostatic charge, respectively. The acid/base monomer units may have varying levels of acidity/basicity, which will determine the extent to which the monomer units will be present in the anionic/cationic form at the pH level of the aqueous solution. With respect to acidic monomer units, the monomer unit may be a strong acid (in which its ability to exhibit a negative charge is largely pH independent) or a weak acid (in which its ability to exhibit a negative charge is pH dependent respect to basic monomer units), the monomer unit may be a strong base (in which its ability to exhibit a positive charge is largely pH independent) or a weak base (in which its ability to exhibit a positive charge is pH dependent).

[0056] In certain embodiments, the monomer units used are able to exhibit marked morphological or structural changes based on certain stimuli such as pH, electric field, magnetic field, or temperature for regulated drug delivery applications. In some cases the contributing monomer units may be basic, which under the appropriate pH conditions, exhibit a positive electrostatic charge. The base monomer units may have varying levels of basicity, which will determine the extent to which the monomer units will be present in the cationic form at the pH level of the aqueous solution. The monomer unit may be a strong base (in which its ability to exhibit a positive charge is largely pH independent) or a weak base (in which its ability to exhibit a positive charge is pH dependent).

[0057] In some cases the contributing monomers may be electrically sensitive, that is, the monomer is able to exhibit a structural phase change upon introduction to an electrical field. Examples of such monomers include vinyl alcohol, diallyldimethylammonium chloride, and acrylic acid.

[0058] In some cases the contributing monomers may able to exhibit a marked morphological or structural change based upon temperature. An example of such a

temperature sensitive monomer is N-isopropylacrylamide. The monomer may be used to produce a temperature-sensitive hydrogel for regulated release or rather for a hydrogel capable of inducing coagulation in a temperature dependent manner.

[0059] Examples of primary amine containing monomers include but are not limited to allylamine, N-3-aminopropyl methacrylamide (APM), and N-2-aminoethyl methacrylamide (AEMA). Examples of monomer units that are strong bases include those having ammonium groups, such as 3-acrylamidopropyl trimethylammonium chloride (AMPTAC). The monomer units may also be neutral monomers exhibiting no electrostatic charge in the solution. Examples of such monomers include acrylamide (Am), N-tertbutylacrylamide (NTBAAm), N-isopropylacrylamide (NIPAAm), and N,N'-dimethylacrylamide (DMAAm).

[0060] Polymerization of the monomer units can be achieved using any of various techniques known in the art, including chemical processes (e.g., using free-radical initiators and/or catalysts), photochemical processes (e.g., exposure to UV-irradiation), or electrochemical processes. Likewise, cross-linking can be achieved using any of various techniques known in the art, including the addition of a cross-linking agent to the solution. In some cases, polymerization may be effected by the addition of ammonium persulfate (APS) as the polymerization initiator and N,N,N',N'-tetramethylethylenediamene (TEMED) as the catalyst. In some cases, the cross-linking agent is a difunctional monomer, N,N'-methylenebisacrylamide (BIS), epichlorohydrin (EPI), genipin, glutaraldehyde, or ethylene glycol diglycidyl ether (EDGE). Biodegradable cross-linkers such as ethylene glycol dimethacrylate and ethylene glycol diacrylate may also be used as the cross-linking agent. The biodegradable polymers are capable of undergoing hydrolytic cleavage in vivo. Polymerization and cross-linking may take place simultaneously or sequentially in any order. As such, the polymerization initiator, catalyst, and/or cross-linking agent may be added to the solution simultaneously or sequentially in any order.

[0061] Upon polymerization (and cross-linking, in some cases) of the monomer units, a polymer matrix is formed. The amount of cross-linker used (ratio of cross-linker monomer:total remaining functional monomers) determines the mesh size of the gel network. If a polymer hydrogel composed of a primary amine containing monomer is cross-linked appropriately the material, is capable of inducing the blood coagulation pathway, in a factor VII-tissue factor dependent manner. The ability of the polymer hydrogel to induce coagulation is dependent mainly on mechanical rigidity, i.e. cross-link density, and the primary amine functionality on the main chain polymer backbone. It should be noted that

experiments were conducted using the non-cross-linked amine containing polymers, and they were unable to induce coagulation.

[0062] In certain embodiments, the polymer hydrogel is able to induce clotting in platelet deficient plasma. In other embodiments, the polymer hydrogel is able to induce clotting in Factor XII, XI, Factor IX, or Factor VIII-deficient plasma.

[0063] In a specific aspect the invention details the production of a multi-component material consisting of two different compositions of polymeric hydrogels – one for use in any internal hemostatic application, and one for use in any external hemostatic application.

[0064] In another aspect, an embodiment of the present invention provides a polymeric material comprising a cross-linked polymer matrix having a cavity, highly dense in primary amine functionality capable of inducing the blood coagulation pathway. This polymeric hydrogel may be synthesized using any of various techniques, including those described above.

[0065] The cavity may have a geometry (including its size and shape) which is capable of aiding in the activation process. Geometry of the cavity, along with density of electrostatic functional groups within the cavity, is determined, in part, by the amount of cross-linker used in the process.

[0066] The created polymeric hydrogel, depending on the specific concentration of primary amine monomers and corresponding cross-link density may have varying degrees of inducing the blood coagulation cascade, as shown in Figure 6 herein. In a specific embodiment, the optimum concentration for the APM, acrylamide, BIS hydrogel is between 1.5-2 M of APM and 1.5-2 M of acrylamide cross-linked at between 5:1 and 7:1 (acrylamide:BIS). In another specific embodiment (blood optimization) the optimum composition is approximately 2.73 M of APM, .27 M of acrylamide, and .056 M BIS.

[0067] The ability of the hydrogel to initiate blood coagulation in the absence of cells offers a potentially substantial advantage over other hemostatic approaches. In particular these polymers may offer treatment alternatives for patients experiencing platelet-related disorders for which there are no accepted treatment methods available. Another desirable characteristic of the materials, depicted in Figure 1 herein, is their ability to swell in plasma. In practice this would allow the polymers to apply pressure (tamponade) at the site of action, which also aids in reducing blood loss. Furthermore, because of this characteristic swelling in plasma, the hydrogel may be designed in order to administer therapeutics in a controlled and regulated manner.

EXAMPLES

[0068] In one experiment, a randomized copolymer composed of acrylamide and APM, initiated with a 7.5% weight percent solution of TEMED (20 μL/1 mL) and a 15% weight percent solution of APS (20 μL/1 mL), and cross-linked with BIS, was produced. Figure 3 depicts an optimization chart where 156 different polymer compositions, each cross-linked at three different ratios, were tested in citrated human plasma, and rated accordingly their ability to produce a clot. As shown the optimal concentration for inducing coagulation lies between 1.5-2 M of acrylamide and 1.5-2 M of APM, each at its highest cross-link density (maximal amount soluble). The primary amine-containing hydrogel is able to induce the blood coagulation cascade resulting in the formation of a fibrin clot. Figure 1 depicts the ability of the material to induce a fibrin based clot in human plasma (4% sodium citrate). The hydrogel shown is composed of 1.5 M acrylamide 1.5 M APM and cross-linked with .3 M BIS (acrylamide:BIS ratio = 5:1).

[0069] Figure 2 shows micrographs of the coagulate complex (fibrin-hydrogel complex) after hematoxlyin and eosin (H&E) staining, immunohistochemical (IHC) staining, along with an image of the complex obtained using an environmental scanning electron microscope.

[0070] Figure 4 shows the ability of the optimized hydrogel (1.5 M acrylamide, 1.5 M APM< and .3 M BIS) to induce fibrin formation in a variety of factor deficient and factor inhibited plasmas.

[0071] Figure 5 shows the ability of the optimized hydrogel to induce the activation of FVII (5C).

[0072] Figure 6 shows that the optimized hydrogel is not in fact a homogenous network but rather is made up of several mechanically distinct regions.

[0073] Experimentation in human and sheep blood produced an optimum composition consisting of .27 M of acrylamide and 2.73 M of APM and .056 M (acrylamide:BIS ratio= 5:1). [Composition 2]

[0074] The effectiveness of the primary amine-containing hydrogel in hemostatic clot formation was assessed. Blood was drawn from a live adult sheep and added immediately to a vial containing a small amount of the primary amine-containing hydrogel (Figure 7A) and an empty vial (Figure 7B), used as a control. The material was able to induce the formation of a robust clot within seconds of blood contact, compared to the control which took

approximately 10 minutes. Furthermore, the mechanical integrity of the clot produced was dramatically superior to that of the control.

[0075] The primary amine-containing hydrogel was also effective in inducing hemostatic clot formation in vivo. A primary amine-containing hydrogel, consisting of 0.27 M acrylamide, 2.73 M N-3-aminopropyl methacrylamide (APM), and 0.054 M N-N'-methylene bisacrylamide (BIS), placed on a 4x4 inch gauze bandage (a prototype of the presently claimed invention, shown in Figure 8), was administered to inhibit bleeding from an incision introduced into a live sheep lung. The hydrogel was able to successfully stop bleeding from the induced lung incision in approximately 2 minutes. Figure 9 shows an image of the site immediately after the surgeon made the incision (Figure 9A) along with an image of the incision site after the hydrogel based prototype was applied for 2 minutes (Figure 9B). Initial post operative analysis showed that the material was able to induce fibrin formation at the incision causing a natural suturing process, and thus sealing the tissue preventing blood loss. Hematoxylin and eosin stained sections of the incision site confirmed that the material was able to induce the rapid formation of a natural, fibrous-based hemostatic suture, as shown in Figure 10.

INDUSTRIAL APPLICABILITY

[0076] The polymer hydrogel created of the present invention may have various uses. Such uses include a bandage for trauma related injuries or a surgical gauze for use in the operating rooms. In terms of the bandage the hydrogel would be incorporated into a filtered bandage, similar to that of a Band-Aid®, which would then be applied to the wound in order to prevent blood loss and deliver necessary therapeutics. In terms of the surgical gauze the hydrogel would be incorporated into a filtered gauze-like material for use by surgeons to control blood loss during surgery.

[0077] Notably, the bandage application of the hydrogel is novel in the sense that there is no other synthetic polymer, hydrogel material capable of inducing blood clotting while simultaneously delivering therapeutics. Furthermore, the hydrogel functions in Factor VIII and Factor IX deficient plasma, a functionality which should revolutionize wound care for people suffering from hemophilia.

CLAIMS

We claim:

1. A cross-linked polymer, comprising cross-links between at least two monomer backbones, wherein at least one monomer comprises a primary, secondary, tertiary or quaternary amine with a pKa of at least 7.4, and capable of displaying a positive electrostatic charge at the pH of blood or plasma (7.4), and wherein the polymer is capable of activating the blood coagulation cascade by inducing fibrin formation.

2. The polymer of claim 1, wherein said at least one monomer is selected from the group consisting of N-3-aminopropyl methacrylamide, allylamine, and a primary-amine containing monomer capable of displaying a positive electrostatic charge at the pH of blood or plasma (7.4).

3. The polymer of claim 1, wherein at least one of the monomer backbones is acrylamide, or a derivative thereof.

4. A hydrogel comprising the polymer of claim 1, wherein the monomer backbones are cross-linked with cross-linkers selected from the group consisting of N-N'-methylene bisacrylamide, N-N'-bisacrylylcystamine, bisacrylyl piperazine, ethylene glycol diglycidyl ether, epichlorohydrin, N-N'-diallyltartardiamide, ethylene glycol dimethacrylate and ethylene glycol diacrylate.

5. The hydrogel of claim 4, wherein the primary amine is allylamine and the cross-linker is either ethylene glycol diglycidyl ether or epichlorohydrin.

6. The hydrogel of claim 4, therein the monomer backbones are cross-linked with cross-linkers selected from the group consisting of ethylene glycol dimethacrylate and ethylene glycol diacrylate.

7. The polymer of claim 1, wherein the primary amine containing monomer is N-3-aminopropyl methacrylamide (APM), the co-monomer is acrylamide, and the cross-linker is N-N'-methylene bisacrylamide (BIS).

8. The hydrogel of claim 4, wherein said hydrogel consists of 1.5 M acrylamide, 1.5 M N-3-aminopropyl methacrylamide (APM), and 0.3 M N-N'-methylene bisacrylamide (BIS).

9. The polymer of claim 7, wherein said hydrogel consists of 0.27 M acrylamide, 2.73 M N-3-aminopropyl methacrylamide (APM), and 0.054 M N-N'-methylene bisacrylamide (BIS).

10. The hydrogel of claim 4, wherein said hydrogel consists of 1.5 M acrylamide, 1.5 M N-3-aminopropyl methacrylamide (APM), and 0.3 M N-N'-methylene bisacrylamide (BIS).

11. The hydrogel of claim 4, further comprising one or more pharmaceutical active ingredients selected from the group consisting of Novocain, Lidocain, erythromycin, bacitracin, adrenaline, topricin, acetaminophen, ibuprofen, and a hemostatic agent.

12. A method of forming the hydrogel of claim 4, comprising:

adding the monomer backbone comprising a primary amine to the aqueous solution, wherein the first monomer unit exhibits an electrostatic positive charge in the aqueous solution at pH of 7.4 (pH of blood or plasma);

adding a second monomer backbone to the aqueous solution, wherein the second monomer backbone is different from the first monomer unit;

forming the cross-linked polymer using a cross-linking agent, wherein the step of forming polymer comprises polymerizing the monomer backbone.

13. The method of claim 12, wherein the second monomer backbone is neutral or exhibits an electrostatic charge opposite to that of the first monomer backbone.

14. The method of claim 12, wherein the first monomer backbone is added before the second monomer backbone is added.

15. The method of claim 12, wherein the second monomer backbone is added before the first monomer backbone.

16. The method of claim 12, wherein the first and second monomer backbone are added simultaneously to the aqueous solution.

17. A kit for inducing hemostatic clot formation, comprising the polymeric hydrogel of claim 4.

18. A kit for inducing hemostatic clot formation, comprising the polymeric hydrogel of claim 5.

19. A kit for inducing hemostatic clot formation, comprising the polymeric hydrogel of claim 6.

20. A kit for inducing hemostatic clot formation, comprising the polymeric hydrogel of claim 8.

21. A kit for inducing hemostatic clot formation, comprising the polymeric hydrogel of claim 10.

22. A method of treating trauma-induced hemorrhage, comprising administering the hydrogel of any of Claims 4-6, 8, 10 and 11 to a subject in need thereof.

23. A method of treating internal hemorrhaging, comprising administering the hydrogel of any of Claims 4-6, 8, 10 and 11 to a subject in need thereof.

24. A method of treating hemorrhaging during surgical operations, comprising administering the hydrogel of any of Claims 4-6, 8, 10 and 11 to a subject in need thereof.

25. The method of any one of Claims 22-24, wherein said hydrogel is administered on a material selected from the group consisting of a bandage, gauze, tape and adhesive wound dressing.

FIG. 1

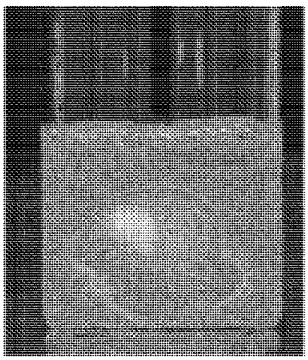
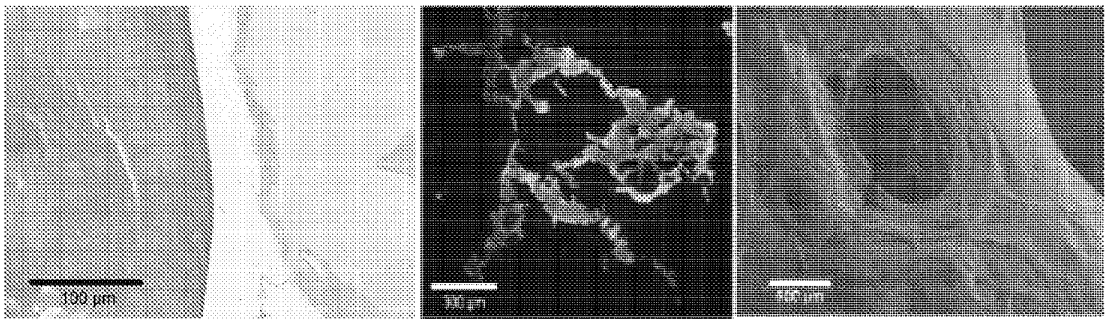


FIG. 2



a b c

FIG. 3

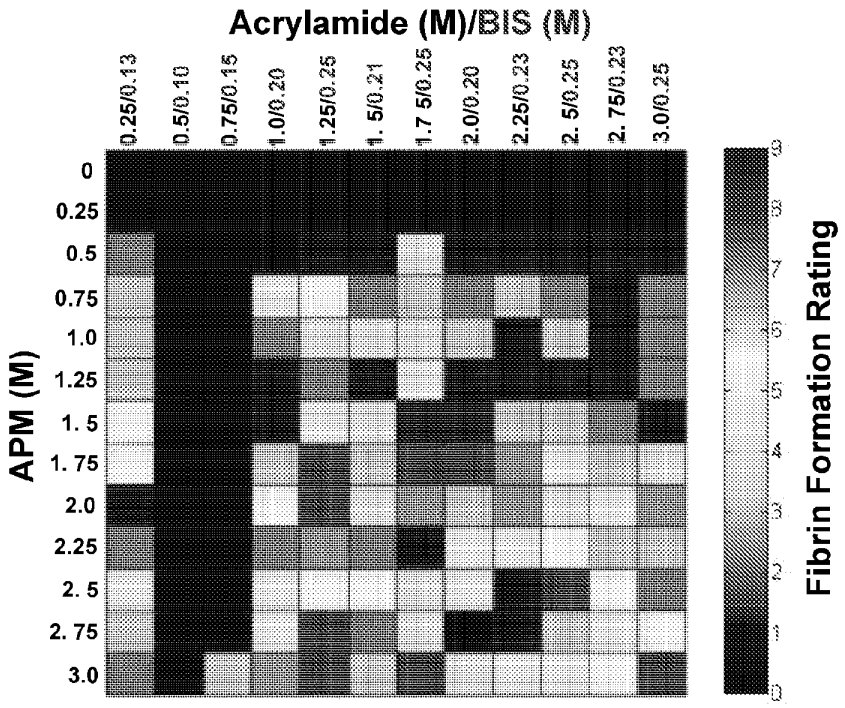

Acrylamide (M)/BIS (M)
0.25/0.13
0.5/0.10
0.75/0.15
1.0/0.20
1.25/0.25
1. 5/0.21
1.7 5/0.25
2.0/0.20
2.25/0.23
2. 5/0.25
2. 75/0.23
3.0/0.25
APM (M)
0
0.25
0.5
0.75
1.0
1.25
1. 5
1. 75
2.0
2.25
2. 5
2. 75
3.0
Fibrin Formation Rating

FIG. 4

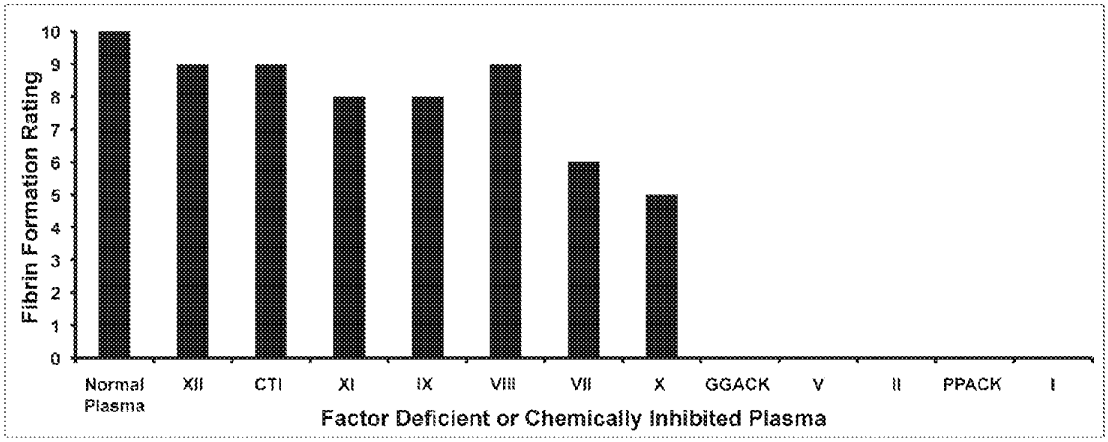

Fibrin Formation Rating
10
9
8
7
6
5
4
3
2
1
0
Normal Plasma
XII
CTI
XI
IX
VIII
VII
X
GGACK
V
II
PPACK
I
Factor Deficient or Chemically Inhibited Plasma

FIG. 5

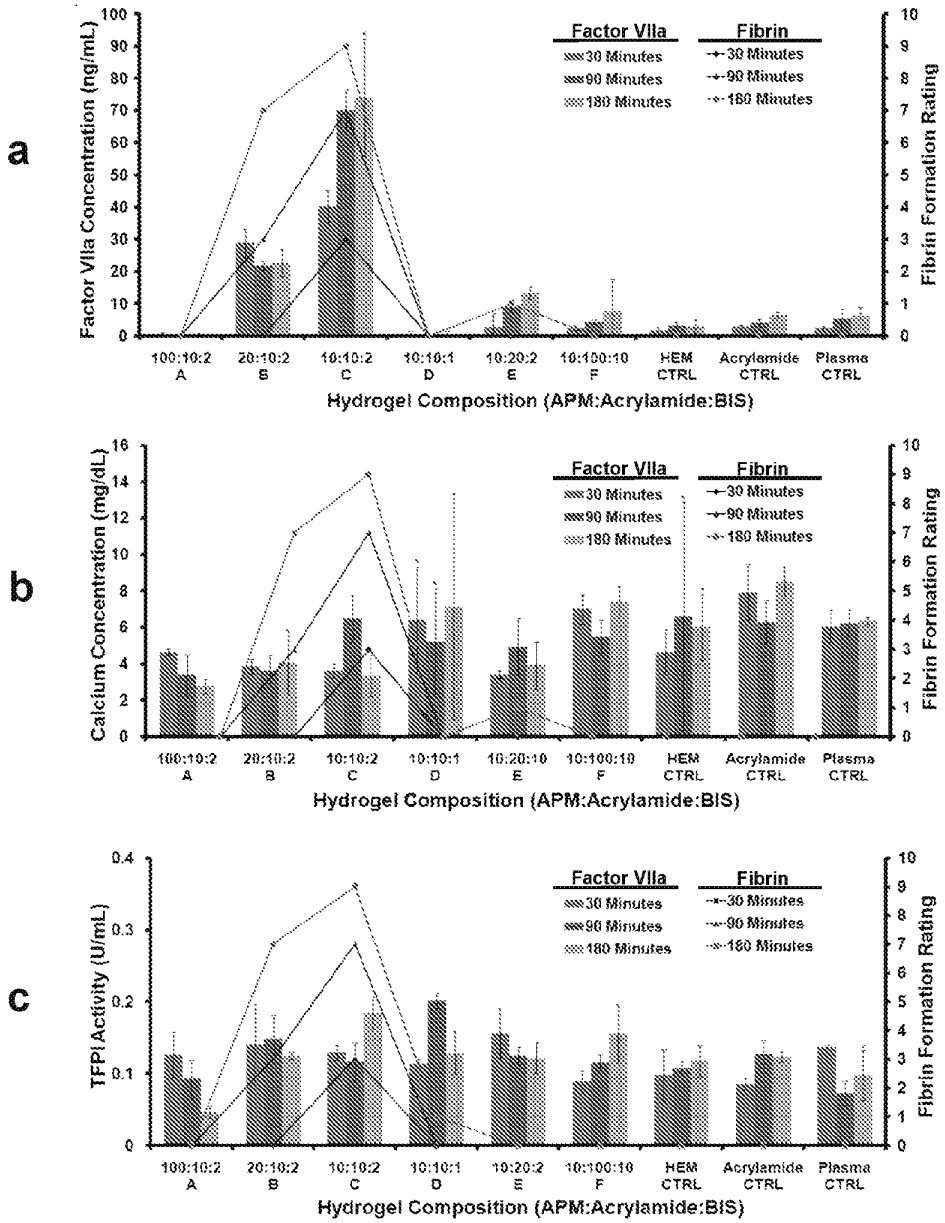

a
Factor VIIa Concentration (ng/mL)
Fibrin Formation Rating
Factor VIIa
30 Minutes
90 Minutes
180 Minutes
Fibrin
30 Minutes
90 Minutes
180 Minutes
100:10:2 A
20:10:2 B
10:10:2 C
10:10:1 D
10:20:2 E
10:100:10 F
HEM CTRL
Acrylamide CTRL
Plasma CTRL
Hydrogel Composition (APM:Acrylamide:BIS)
b
Calcium Concentration (mg/dL)
Fibrin Formation Rating
Factor VIIa
30 Minutes
90 Minutes
180 Minutes
Fibrin
30 Minutes
90 Minutes
180 Minutes
100:10:2 A
20:10:2 B
10:10:2 C
10:10:1 D
10:20:10 E
10:100:10 F
HEM CTRL
Acrylamide CTRL
Plasma CTRL
Hydrogel Composition (APM:Acrylamide:BIS)
c
TFPI Activity (U/mL)
Fibrin Formation Rating
Factor VIIa
30 Minutes
90 Minutes
180 Minutes
Fibrin
30 Minutes
90 Minutes
180 Minutes
100:10:2 A
20:10:2 B
10:10:2 C
10:10:1 D
10:20:2 E
10:100:10 F
HEM CTRL
Acrylamide CTRL
Plasma CTRL
Hydrogel Composition (APM:Acrylamide:BIS)

FIG. 6

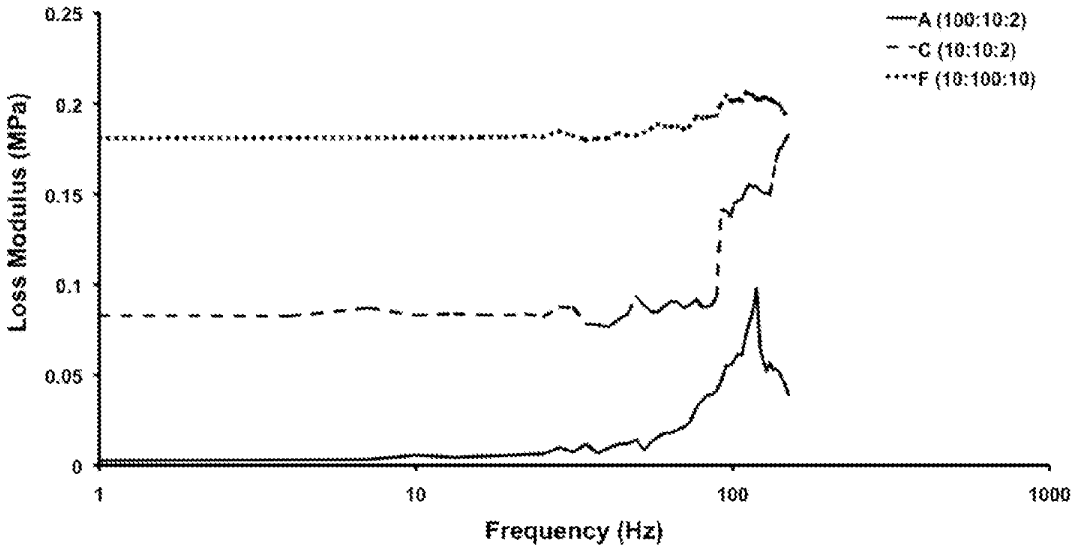

A (100:10:2)
C (10:10:2)
F (10:100:10)
Loss Modulus (MPa)
0.25
0.2
0.15
0.1
0.05
0
1
10
100
1000
Frequency (Hz)

FIG. 7

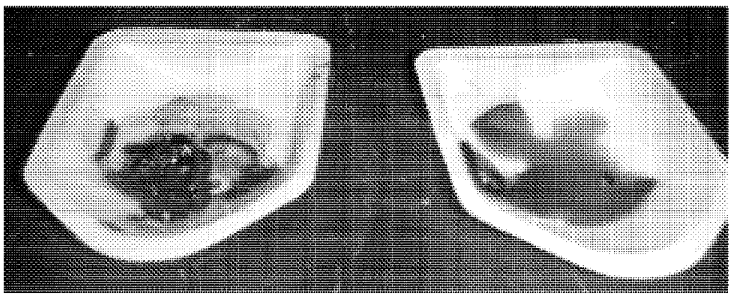
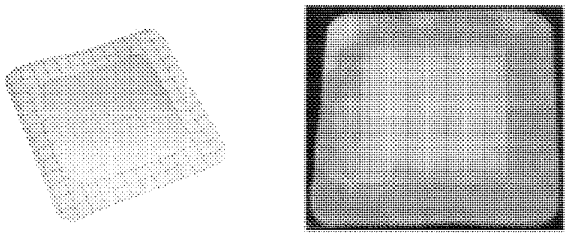
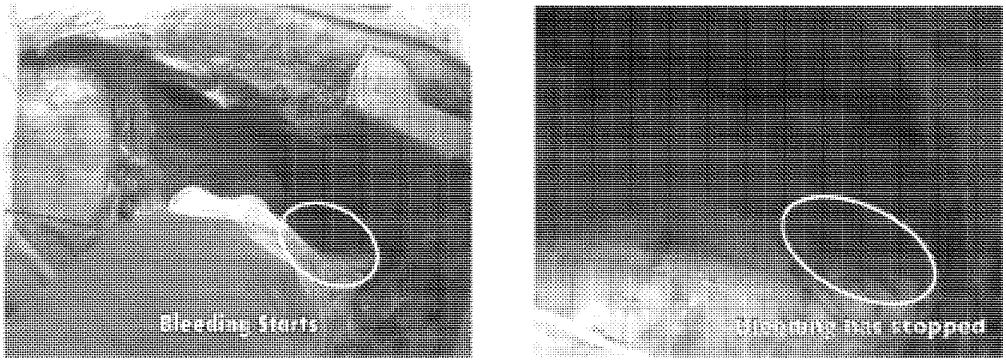

A
B

FIG. 8



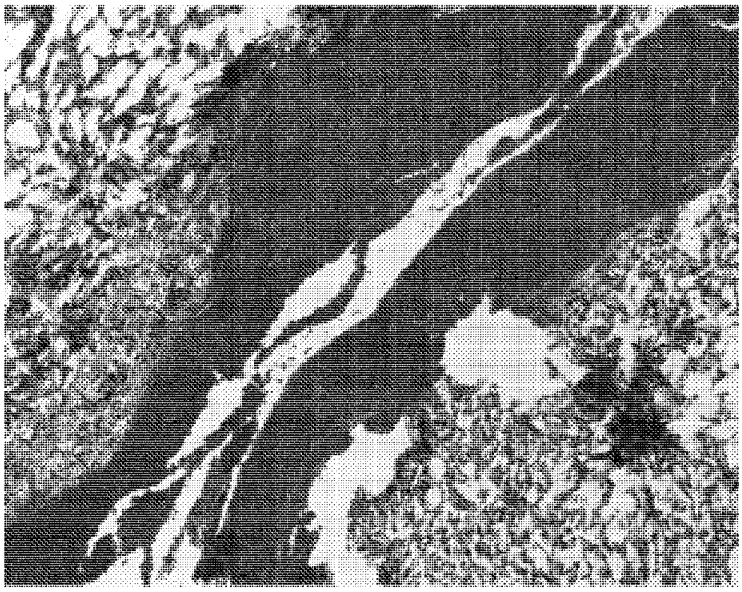
A B

FIG. 9



A B

FIG. 10



INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2009/063049

A. CLASSIFICATION OF SUBJECT MATTER

A61F 13/02(2006.01)i, A61L 15/44(2006.01)i, A61P 7/04(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)
A61F 13/02; A61K 31/785; A61K 9/14; A61K 9/16; A61K 9/50; B01D 21/26

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
(Chinese Patents and application for patent)

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
eKOMPASS(KIPO internal) & Keywords: coagulation, polymer, crosslink, hydrogel

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2007-0237742 A1 (GARRET FIGULY et al.) 11 October 2007 See whole pages.	1-21
A	US 2003-0215519 A1 (ALEXANDER SCHWARZ et al.) 20 November 2003 See whole pages.	1-21
A	US 5648100 A1 (BOSCHETTI; EGISTO et al.) 15 July 1997 See whole pages.	1-21
A	US 4994192 A1 (CORIN; ALAN F. et al.) 19 February 1991 See whole pages.	1-21

☐ Further documents are listed in the continuation of Box C.

☒ 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
"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 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
31 MARCH 2010 (31.03.2010)	**01 APRIL 2010 (01.04.2010)**

Name and mailing address of the ISA/KR
Korean Intellectual Property Office
Government Complex-Daejeon, 139 Seonsa-ro, Seo-gu, Daejeon 302-701, Republic of Korea
Facsimile No. 82-42-472-7140

Authorized officer
LEE, Dong Won
Telephone No. 82-42-481-5549

Form PCT/ISA/210 (second sheet) (July 2009)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2009/063049

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.: 22-25
because they relate to subject matter not required to be searched by this Authority, namely:
Claims 22-25 pertain to methods for treatment of the human body by therapy, and thus relate to a subject matter which this International Searching Authority is not required, under Article 17(2)(a)(i) of the PCT and Rule 39.1(iv) of the Regulations under the PCT, to search.

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:

1. ☐ As all required addtional 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 an additional fee, this Authority did not invite payment of any additional fee.

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.:

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

Information on patent family members

International application No.
PCT/US2009/063049

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2007-0237742 A1	11.10.2007	None	
US 2003-0215519 A1	20.11.2003	AU 2003-239374 A1	11.11.2003
		WO 03-094930 A1	20.11.2003
US 5648100 A1	15.07.1997	CA 2110290 C	05.02.2002
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		JP 06-249849 A	09.09.1994
		KR 10-1991-0014707 A	31.08.1991

Form PCT/ISA/210 (patent family annex) (July 2009)

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Literature display help

1 / 1 display

Patent 5643474

publication Document unit PDF progress information OPD search key URLs

Display format of the document display screen:
text display PDF display

primary literature

bibliography close

(19) [Country of issue] Japan Patent Office (JP)
(12) [Type of publication] Patent publication (B2)
(11) [Patent number] Patent No. 5643474 (P5643474)
(24) [Registration date] 2014 November 7 (2014.11.7)
(45) [Date of Issue] December 17, 2014 (2014.12.17)
(54) [Title of Invention] Multiphase Mixing Process Using Microchannel Process Technology
(51) [International Patent Classification]
B01F 3/04 (2006.01)
B01F 1/00 (2006.01)
B01F 5/06 (2006.01)
B01F 15/06 (2006.01)
[FI]
B01F 3/04 A
B01F 1/00 A
B01F 1/00 B
B01F 1/00 G

B01F 5/06

B01F 15/06 Z

[Number of claims] 35

[Total number of pages] 47

(21) [Application number] Patent application 2007-534825 (P2007-534825)

(86) (22) [Application date] September 30, 2005 (2005.9.30)

(65) [Publication number] Special table 2008-514428 (P2008-514428A)

(43) [Publication date] May 8, 2008 (2008.5.8)

(86) [International application number] PCT/US2005/035330

(87) [International publication number] WO2006/039568 (87)) [International publication date] April 13, 2006 (2006.4.13) [Examination request date] September 29, 2008 (2008.9.29) [Trial number] Appeal 2012-12061 (P2012-12061/J1) [Date of appeal] June 27, 2012 (2012.6.27) (31) [Priority claim number] 60/615,509 (32) [Priority date] October 1, 2004 (2004.10.1) (33)) [Country claiming priority] United States (US) (73) [Patent holder] [Identification number] 505056694 [Name] Verosys, Inc. (74) [Agent] [Identification number] 110000062 [Name] Daiichi International Patent Office (72) [Inventor] [Name] Tonkovic, Anna Lee (72) [Inventor] [Name: Silva, Laura, Jay. (72) [Inventor] [Name] Hesse, David John (72) [Inventor] [Name] Marchiando, Michael Allan

(72) [Inventor]
[Name] Lamont, Michael Jay
(72) [Inventor]
[Name] Qiu, Dong Min
(72) [Inventor] [
Name] Dritz, Terrence Andrew
(72) [Inventor]
[Name]] Pugnot, Christina, Em.
(72) [Inventor]
[Name] Stevenson, Rick
(72) [Inventor]
[Name] Perry, Stephen, Tee.
(72) [Inventor]
[Name] Fanelli, Madalena
(72) [Inventor]
[Name] Arora, Ravi
(72) [Inventor] [
Name] Yang, Bing
(72) [Inventor]
[Name] Fitz Gerald, Sean
(72) [Inventor]
[Name] Sullivan, Tim
(72) [Inventor]
[Name] Jarosh, Kai Todd Paul
(72) [Inventor]
[Name] Yushak, Thomas
[Panel]
[Chief Judge: Shigeju Chiba
Judge: Toyohide Watanabe
Judge: Tsuyoshi Kumakura
(56) References: References
: Japanese Unexamined Patent Publication No. 2003-210957 (JP, A)
[Document] Japanese Unexamined Patent Publication No. 2003-1076 (JP, A) [Document] National Publication of International Patent Application No. 2000-509330 (JP, A) [Document] Japanese Unexamined Patent Publication No. 10-146523 (JP, A) (58) [Investigated field] (Int.Cl., DB name)B01F3/04

The scope of the claims open —

(57) [Claim]

[Claim 1]

A process for making a multiphase mixture, comprising

the step of flowing a first fluid stream through a process microchannel, wherein the first fluid stream is a liquid stream comprising , said process microchannel having an open section com prising a plurality of openings , said open section flowing through said process microchannel; a second fluid stream having a length along the flow path of a fluid stream and a thickness di mension perpendicular to the flow path of said first fluid stream flowing in said process microc hannel

; into the process microchannel and in contact with the first fluid stream to form the multiph ase mixture, wherein the second fluid stream is a gas stream comprising wherein the first flui d stream forms a continuous phase within the multiphase mixture and the second fluid stream forms a dispersed discontinuous phase within the continuous

phase ,

said second fluid stream flows through said open section from a second fluid stream channel adjacent said process microchannel, said heat exchange

channel being said process microchannel, said second fluid stream channel, or adjacent to b oth the process microchannel and the second fluid stream channel, between the process micr ochannel and the heat exchange channel, between the second fluid stream channel and the h eat exchange channel, or a process microchannel and said second fluid flow channel

A process in which heat is exchanged between both a cell and a heat exchange channel, and a heat exchange liquid is in the heat exchange channel.

2. The process of claim 1,

wherein said first fluid stream and said second fluid stream contact each other in a mixing zo ne within said process microchannel.

3.

The process of claim 1 or 2, wherein said process microchannel has a mixing zone with a nar rowed cross-section.

4.

The process microchannel has spaced apart walls and open sections in each of the spaced ap art walls, wherein the second fluid stream passes through each of the open sections to the pr ocess microchannel. 4. The process according to any one of claims 1 to 3, flowing into the

5. Said

process microchannel is a first process microchannel and is in a multiphase mixture forming unit, said multiphase mixture forming unit comprising a second process microchannel and sai d first process microchannel. a second fluid stream channel located between a process microc hannel and said second process microchannel, each process microchannel having a wall with a n open section, said first fluid stream comprising said flowing through a first process microcha nnel and said second process microchannel, said second fluid stream passing from said secon d fluid stream channel through said open section into said first process microchannel; 5. Any of claims 1-4, wherein the microchannel flows in and into contact with the first fluid stream an d through the open section into the second process microchannel and in contact with the first fluid stream. The process of paragraph 1.

6.

A process for making a multiphase mixture comprising:

flowing a first fluid stream through a process microchannel, said first fluid stream being a liq uid stream comprising ; a step having an open section , said open section being a length alon g a flow path of said first fluid stream flowing within said process microchannel and a flow pat h of said first fluid stream flowing within said process microchannel; and flowing a second flui d stream through a second fluid stream channel ,

said second fluid stream being a liquid stream comprising

at least one liquid. wherein said process microchannel has an apertured section comprising a plurality of apertures allowing said second fluid stream to enter said process microchannel, sai d apertured section receiving said second fluid stream having a length along the flow path of s aid second fluid stream flowing within said channel and a thickness dimension perpendicular t o the flow path of said second fluid stream flowing within said second fluid stream

channel ; flowing a fluid stream through a third fluid stream channel, said third fluid stream being a gas stream comprising third fluid stream to a second fluid stream; having another ope n section comprising a plurality of openings to allow flow into two fluid flow channels, said sep arate open section flowing through said third fluid flow channel; having a length along a fluid f low path and a thickness dimension perpendicular to the flow path of said third fluid stream fl owing within said third fluid flow channel ;

The third fluid stream flows from the third fluid stream channel through the another open se ction having the thickness into the second fluid stream channel to contact the second fluid str eam and form another forming a multi-phase mixture, flowing said another multi-phase mixtu re through said open section having said thickness into said process microchannel and contact ing said first fluid stream to form said multi-phase

mixture , a

heat exchange channel is adjacent to said process microchannel and/or either said second fl uid stream channel or said third fluid stream channel, wherein heat is transferred between sai d process channel and said heat exchange channel; exchanged and the heat exchange liquid i s in the heat exchange channel;

process including.

7.

The process of any one of claims 1 to 6, wherein the process microchannels are formed from parallel spaced sheets and/or plates.

8.

The process of claim 7, wherein the second fluid flow channel is formed from parallel spaced sheets and/or plates.

9.

The process of claim 8, wherein said heat exchange channels are formed from parallel space d sheets and/or plates.

10.

The process is performed in a microchannel mixer, the microchannel mixer including a plurali ty of the process microchannels and a second fluid flow channel, each process microchannel h aving an open section. a wall and an adjacent second fluid stream channel, wherein the secon d fluid stream flows from the second fluid stream channel through the open section into the pr ocess microchannel to form the first fluid stream; wherein said process microchannel and seco nd fluid flow channel are formed from parallel spaced apart sheets and/or plates, said process microchannel and second fluid flow channel being adjacent to each other and side by side 10. A process according to any one of claims 1 to 9 arranged in alternating planes stacked on top of each other or alternating planes stacked one above the other.

11.

The microchannel mixer further comprises a plurality of heat exchange channels formed fro m parallel spaced apart sheets and/or plates, said heat exchange channels being connected to said process microchannels, said second fluid stream, and said heat exchange channels. 11. T he process of claim 10 adjacent to a channel, or both the process microchannel and the secon d fluid stream channel.

12.

The process of any one of claims 1 to 6, wherein said process microchannel and said second fluid flow channel comprise concentrically arranged circular tubes.

13.

The process is carried out in a microchannel mixer, the microchannel mixer comprising a plur ality of the process microchannels, wherein a separate multiphase mixture is formed within ea ch of the process microchannels. 13. The process of any one of claims 1 to 12, wherein the m ultiphase mixtures formed in at least two of the process microchannels are different from eac h other.

14.

A process according to any one of claims 1 to 13, wherein said apertured section comprises a sheet and/or plate and a plurality of apertures in said sheet and/or plate.

15.

having a coating over at least a portion of said sheet and/or plate and filling a portion of said openings; or said sheet and/or plate is heat treated; 15. The process of claim 14.

16. Clause 1,

wherein said apertured section is made of a porous material, said porous material being met allic, non-metallic, oxidized, or coated with alumina, nickel or combinations thereof. 16. The p rocess according to any one of paragraphs 1 to 15.

17. Said

first fluid stream comprises water or an organic liquid, said second fluid stream comprises at least one gas, or said second fluid stream comprises air, hydrogen, nitrogen 17. A process acc ording to any one of the preceding claims, comprising a gas selected from , carbon dioxide or mixtures of two or more thereof.

18.

The process microchannel of any one of claims 1 to 17, wherein the process microchannel ha s an internal dimension of 10 millimeters or less perpendicular to the flow of the first fluid stre am through the process microchannel. Described process.

19.

Said second fluid flow flows through said open section from a second fluid flow channel, said second fluid flow channel passing said second fluid flow channel through said second fluid flow channel. 19. A process according to any one of the preceding claims, having internal dimensio ns of 100 centimeters or less perpendicular to said flow of fluid stream.

20.

A process according to any one of claims 1 to 19, wherein said heat exchange channels have internal dimensions of 50 millimeters or less perpendicular to said flow of heat exchange fluid through said heat exchange channels.

21. The process

microchannels, second fluid flow channels and heat exchange channels are made of steel, m onel, inconel, aluminum, titanium, nickel, copper, brass, alloys of any of these metals, polyme rs, ceramics. 21. The process of any one of claims 1 to 20, made of a material comprising: , g lass, a composite comprising polymer and glass fibers, quartz, silicon, or a combination of two or more thereof.

22.

A process according to any one of claims 1 to 21, wherein said heat exchange fluid undergoe s a phase change within said heat exchange channels.

23.

A process according to any one of claims 1 to 21, wherein endothermic or exothermic proces ses are carried out in said heat exchange channels.

[Claim 24]

the heat exchange fluid is air, water vapor, liquid water, carbon monoxide, carbon dioxide, ga seous nitrogen, liquid nitrogen, at least one gaseous hydrocarbon, at least one liquid hydrocar

bon, or a combination of two or more thereof; 24. The process of any one of claims 1-23, com prising the first fluid stream, the second fluid stream, or a mixture of the first and second fluid streams.

25.

The process of any one of claims 1 to 24, wherein said multiphase mixture comprises foam.

26. The

multiphase mixture comprises emulsifiers, surfactants, UV protection agents, waxes, consist ency agents, thickeners, superfatting agents, stabilizers, cationic, anionic, zwitterionic, ampho teric or Nonionic polymers, silicone compounds, fats, waxes, lecithins, phospholipids, biophar maceuticals, antioxidants, deodorants, antiperspirants, antidandruff agents, swelling agents, a nthelmintics, self-tanning agents, tyrosine inhibitors, 26. A process according to any precedin g claim, comprising one or more of solubilizers, preservatives, perfume oils or pigments, or mi xtures of two or more thereof.

27.

The process of any one of claims 1 to 26, wherein solids are dispersed in said multiphase mi xture. 28. A process according to any one of claims 1 to 27, wherein said first fluid stream c omprises a reaction medium for conducting a hydrogenation reaction and said second fluid str eam comprises hydrogen

. 29. The first fluid stream comprises a liquid stream, and the second fluid stream comprises one or more of air, oxygen, nitrogen, carbon dioxide, hydrogen, ammonia, chlorine gas, ozon e, and one or more of one or more. gaseous hydrocarbons, or a combination of two or more t hereof, or said first fluid stream comprises a liquid waste stream of

said second fluid stream comprises air; or said first fluid stream comprises a liquid hazardous waste stream; said second fluid stream comprises air; or said first fluid stream comprises liqui d salad dressing or mustard, said second fluid stream comprises nitrogen, or said first fluid str eam comprises liquid beverage or beer, said second fluid stream comprises carbon dioxide, or said first fluid stream comprises the fluid stream comprises liquid bleached pulp, said second f luid stream comprises chlorine, or said first fluid stream comprises coal dispersed in water, sai d second fluid stream comprises air, or said The first fluid stream comprises motor oil with ent rained water, the second fluid stream comprises nitrogen, or the first fluid stream comprises li quid-containing cells for a culture reaction, the second comprises oxygen or air, or said first fl uid stream comprises a liquid reaction medium and said second fluid stream comprises air or oxygen, or said first fluid stream comprises a mixture of oil and water said second fluid strea m comprising air or natural gas, or said first fluid stream comprising liquid bleached pulp, said second fluid stream comprising oxygen, or said first fluid the streams comprise edible oil, win e or juice, the second fluid stream comprises nitrogen, or the first fluid stream comprises wat

er used in fish farming, the second fluid stream comprises oxygen, or said first fluid stream co mprises water and said second fluid stream comprises ozone; or said first fluid stream compri ses a liquid waste or process stream and said second fluid stream comprises carbon dioxide or ammonia, or wherein the first fluid stream comprises a liquid waste stream comprising volatil e organic compounds and the second fluid stream comprises air. process.

30.

A process according to any one of claims 1 to 29, wherein the process produces at least 1 lit er of multiphase mixture per minute.

[Claim 31]

31. The process of any one of claims 1-30, wherein the process is performed in a microchan nel mixer, the microchannel mixer comprising at least two process microchannels.

32.

Said process is carried out in a microchannel mixer, said microchannel mixer comprising a pl urality of process microchannels and a plurality of second fluid flow channels, said process mic rochannels comprising at least one first fluid stream channel. connected to one fluid flow mani fold, wherein the first fluid flow flows through the at least one first fluid flow manifold to the p rocess microchannel; the second fluid flow channel is connected to the process microchannel; Adjacent to the microchannel, at least one second fluid flow manifold connects to said second fluid flow channel, said second fluid flow passing through said at least one second fluid flow m anifold to said first fluid flow manifold. 32. The process of any one of claims 1-31, wherein the process flows into two fluid flow channels.

33.

The microchannel mixer further comprises at least one heat exchange manifold connected to the heat exchange channels, wherein heat exchange fluid flows through the at least one heat exchange manifold into the heat exchange channels. 33. The process of claim 32.

34.

The process microchannel of claims 1 to 33, wherein the process microchannel includes surf ace features formed in and/or on one or more inner walls for altering flow within the process microchannel. A process according to any one of paragraphs.

[Claim 35]

The surface features are depressions in one or more of the inner microchannel walls oriented at an oblique angle to the direction of fluid flow through the process microchannel and/or the i nner microchannel walls. or said surface features are in the shape of at least two surface feat ure regions, and said mixing of said first and second fluids is in the form of a first carried out i n a flow through a surface feature region followed by a second surface feature region, said flo w pattern in said second surface feature region being formed by said first surface feature regi on; different from said flow pattern in the region or said opening

A section includes an interior portion forming one or more portions of the inner wall of the pro cess microchannel and a surface feature sheet overlying the interior portion of the open sectio

n, wherein the surface feature sheet includes: or the multiphase mixture comprises solid particles dispersed in the first and/or second fluid streams and is in the form of the fluidized bed; includes surface features formed in and/or on one or more of the inner walls thereof to alter flow within said process microchannel; or said surface features are stacked on top of each other; and or comprising two or more layers intertwined in a three-dimensional pattern, or wherein said surface features are circular, elliptical, square, rectangular, checkerboard, V-shaped, corrugated or combinations thereof; Alternatively, the surface features include sub-elements, and the main wall of the surface features is notched, corrugated, jagged, perforated, burr-shaped, checkered, fan-shaped, or a combination thereof. 35. The process of Claim 34, further comprising small surface features.

detailed description open —

Description: BACKGROUND OF THE INVENTION 1.

Field of the Invention The present invention relates to multiphase mixing processes using microchannel process technology. BACKGROUND OF THE INVENTION The dispersion of air bubbles in liquids, with or without chemical reaction, is useful for gas-liquid contact to promote absorption or stripping or for foam product production . can be Examples of these are air injection to meet the BOD (Biological Oxygen Demand) requirements of waste streams, air injection to mix liquids in baths, stimulation of bacterial growth for hazardous waste treatment. Nitrogen blowing to extend salad dressings or mustards, CO2 blowing for carbonated drinks and beer, Chlorine blowing for bleaching pulp in the manufacture of paper, Coal flotation and other solids Blowing air for separation, blowing nitrogen to remove entrained water from motor oil, blowing oxygen or air to enhance cell growth in culture reactions, reacting air, oxygen or other gases for improved performance hydrogen blowing for various types of chemical hydrogenation reactions, air or natural gas blowing for oil removal from well spring water, for bleaching pulp in the manufacture of paper Oxygen blowing, Nitrogen blowing to remove oxygen from edible oils, wine and juices, Oxygen blowing to stimulate fish growth in fish farming, Ozone blowing to sterilize ultrapure water systems in pharmaceutical plants, waste or process streams CO2 or NH 3 to adjust the pH in

Blowing, efficient heating, and direct steam injection to quell steam hammering, air blowing for removal of VOCs (volatile organic compounds) from waste streams, and similar operations.

One problem with many of these operations is the inefficiency of gas distribution. SUMMARY OF THE INVENTION The present invention provides a solution to this problem. In one embodiment, the present invention provides dispersion of relatively small gas bubbles having a relatively large surface area into a liquid. As a result, a relatively large gas/liquid contact area is obtained. The bubbles are small and have a large surface area, so the gas can be efficiently dissolved in the liquid. This results in a reduced gas consumption. It also reduces the time required to dissolve the gas into the liquid, resulting in faster processing and higher productivity. The present invention is a process for making a multiphase mixture comprising flowing a first fluid stream through a process microchannel, the first fluid stream comprising at least one liquid and a /or a step comprising at least one gas and the process microchannel having an open section, flowing a second fluid stream into the process microchannel through the open section;

contacting the streams to form a multi-phase mixture, the second fluid stream comprising at least one gas and/or at least one microbody-forming material, and the first fluid stream comprising a multi-phase mixture; Forming a continuous phase in the phase mixture, the second fluid stream comprising forming a discontinuous phase dispersed within the continuous phase.

[0005]

In one embodiment, the second fluid dissolves in the first fluid. This may occur within the process microchannels or after the multiphase mixture exits the process microchannels. One advantage of the process of the present invention is that, in at least one embodiment, the second fluid in the multiphase mixture has a higher density than the larger bubbles formed by conventional techniques that do not employ microchannel processing technology. The advantage is that it can contain relatively small air bubbles that dissolve more efficiently into the fluid.

[0006]

In one embodiment, the multiphase mixture further comprises solid particles dispersed in the first fluid stream.

[0007]

In one embodiment, heat is exchanged between the process microchannel and the heat source and/or heat sink. In one embodiment, the heat source and/or heat sink comprises at least one heat exchange channel.

[0008]

In one embodiment, the open section extends along at least part of the axial length of the process microchannel. In one embodiment, the open section is at least about 10% of the axial length of the process microchannel, in one embodiment at least about 20% of the axial length of the process microchannel, and in one embodiment at least about 20% of the axial length of

the process microchannel. At least about 35% of the directional length, in one embodiment at least about 50% of the axial length of the process microchannel, in one embodiment at least about 65% of the axial length of the process microchannel, in one embodiment the process It extends along at least about 80% of the axial length of the microchannel, and in one embodi ment at least about 95% of the axial length of the process microchannel.

In one

embodiment, the second fluid stream flows from the second fluid stream channel through th e open section.

[0010]

In one embodiment, between a process microchannel and a heat source and/or heat sink, be tween a second fluid stream channel and a heat source and/or heat sink, or between a proces s microchannel and a second fluid stream channel. and heat sources and/or heat sinks. Heat s ources and/or heat sinks may be used for heating, cooling, or both cooling and heating. The h eat source may include heat exchange channels and/or heating elements. The heat sink may i nclude heat exchange channels and/or cooling elements. In one embodiment, the heat source and/or heat sink can be adjacent to the process microchannel, the second fluid stream channe l, or both the process microchannel and the second fluid stream channel. In one embodiment, the heat source and/or heat sink may be remote from the process microchannel and/or the se cond fluid stream channel, but not into the process microchannel and/or the second fluid strea m channel or into the process microchannel. It should be sufficiently close to the process micr ochannel and/or the second fluid stream channel to transfer heat from the channel and/or the second fluid stream channel.

[0011]

In one embodiment, the process is performed in a polyphase mixer. Within the multi-phase mixer, one or more headers or manifolds are used to provide fluid flow into the process microc hannels, the second fluid stream channels and the heat exchange channels, the process micro channels and the heat exchange channels. One or more footers or manifolds are used to provi de fluid flow out of the exchange channels

.

In one embodiment, the first fluid stream and the second fluid stream contact each other in a mixing zone within the process microchannel. In one embodiment, heat is exchanged betwe en heat sources and/or heat sinks and at least a portion of the process microchannels in the mixing zone. In one embodiment, heat is exchanged between the heat source and/or heat sin k and at least a portion of the process microchannel upstream of the mixing zone. In one emb odiment, heat is exchanged between the heat source and/or heat sink and at least a portion o f the process microchannel downstream of the mixing zone. In one embodiment, the process microchannel has a restricted cross-section within the mixing zone

. In one embodiment, the process microchannel has spaced apart walls and open sections in each of the spaced apart walls, and the second liquid passes through each of the open section

s into the process microchannel. flow into. In one embodiment, the aperture section in each o f the spaced apart walls includes a plurality of apertures, the apertures in the aperture section of one wall being located directly across from the apertures in the aperture section of the opp osite wall. be done. In one embodiment, the opening section in each of the spaced apart walls includes a plurality of openings, and at least some of the openings in the opening section of o ne wall are the openings in the opening section of the other wall. They are staggered so that t hey are not directly opposite each other. [0015]

In one embodiment, the process microchannel is in the multiphase mixture forming unit. The multiphase mixture forming unit includes a first process microchannel, a second process micro channel, and a second fluid channel located between the first and second process microchann els, each The process microchannel has a wall with an open section, a first fluid stream flows t hrough the first process microchannel and a second process microchannel, and a second fluid stream flows through the second process microchannel. From the fluid stream channel, flow t hrough an open section in the first process microchannel to contact the first fluid stream, and flow through an open section in the second process microchannel to allow the first fluid to flo w. come into contact with the current.

[0016]

In one embodiment, a third fluid stream flows in a third fluid stream channel, the third fluid stream channel having another wall with another open section, the process comprising: flowin g a second fluid stream through another open section and contacting the third fluid stream to form another multiphase mixture; and flowing the other multiphase mixture through the open section into the process microchannel; Further comprising contacting with the first fluid strea m. In one embodiment, the process microchannels are formed from parallel spaced sheets a nd/or plates

.

In one embodiment, the second fluid flow channel is formed from parallel spaced apart sheets and/or plates, the second fluid flow channel adjoining the process microchannel. In one embo diment, the heat exchange channels are formed from parallel spaced apart sheets and/or plat es, and the heat exchange channels are process microchannels, second fluid stream channels, or process microchannels and second fluid stream channels. and adjacent to both.

[0018]

In one embodiment, the process is carried out in a microchannel mixer, the microchannel mi xer comprising a plurality of process microchannels and a second fluid flow channel, each proc ess microchannel having a wall with an open section. and an adjacent second fluid stream cha nnel, the second fluid stream flowing from the second fluid stream channel through the open

section into the process microchannel to contact the first fluid stream; The process microchan nels and the second fluid stream channels are formed from parallel spaced apart sheets and/o r plates, the process microchannels and the second fluid stream channels being adjacent to ea ch other and alternating side by side. Arranged in the form of planes or alternating planes sta cked on top of each other.

In one

embodiment, the process microchannel includes two or more open sections through each of which a separate second fluid stream flows. In one embodiment, separate second fluid stream s flowing through each of the open sections have different compositions. In one embodiment, separate second fluid streams flowing through each of the open sections have different proper ties.

In one embodiment

, the process is carried out in a microchannel mixer, the microchannel mixer comprising at le ast two process microchannels, in one embodiment at least about ten process microchannels, in one embodiment at least It contains about 100 process microchannels, and in one embodi ment at least about 1000 process microchannels.

[0021]

In one embodiment, the process is carried out in a microchannel mixer, the microchannel mi xer comprising a plurality of process microchannels connected to at least one first fluid flow m anifold, the first Fluid streams flow through at least one first fluid stream manifold to the proc ess microchannels. In one embodiment, the process microchannel is adjacent to a second flui d flow channel, the microchannel mixer further comprising at least one second fluid flow manif old connected to the second fluid flow channel, the second Fluid flows through at least one sec ond fluid flow manifold to the second fluid flow channels. In one embodiment, the process mic rochannels and/or liquid channels are adjacent to heat exchange channels, and the microchan nel mixer further comprises at least one heat exchange manifold connected to the heat excha nge channels, wherein the at least one heat exchange manifold is A heat exchange fluid flows through the heat exchange channels.

[0022]

In one embodiment, the second fluid stream flows from the second fluid stream channel thro ugh an open section into the process microchannel, the process microchannel and liquid chan nel comprising concentric annular tubes.

[0023]

In one embodiment, the process is carried out in a microchannel mixer, the microchannel mi xer comprising a plurality of process microchannels, with separate multiphase mixtures forme d in each of the process microchannels. , the multiphase mixtures formed in at least two of th e process microchannels are different from each other. These multiphase mixtures may have different compositions and/or different properties. This microchannel mixer can be referred to as a combinatorial synthesis and screening device. One advantage of this embodiment of the

present invention is that it provides for the formation and evaluation of multiple multiphase m ixture products simultaneously using the same equipment. This can be an advantage when it i s desired to screen multiple formulations as new product candidates.

[0024]

In one embodiment, the process is carried out in a microchannel mixer, the microchannel mi xer comprising a plurality of multiphase mixture forming units, either side by side or stacked on top of each other, each multiphase mixture The forming unit includes a process microchann el and an adjacent second fluid flow channel, the process microchannel and the adjacent seco nd fluid flow channel having a common wall and an open section within the common wall. , th e open section is adapted to channel a second fluid stream from the second fluid stream chan nel through the open section into the process microchannel, each process microchannel and t he second fluid stream channel being parallel spaced apart. Formed from a sheet, plate, or co mbination of such sheets and plates, the process comprises the steps of: flowing a first fluid s tream through a process microchannel; from a second fluid stream channel through an open s ection of the process microchannel; and mixing the first and second fluid streams in the proce ss microchannel to form a multiphase mixture.

In one embodiment, the process of the present invention can be operated with a relatively lo w flow pressure drop of the first fluid stream through the process microchannel . In one embo diment, the process of the present invention can be operated with a relatively low pressure dr op in the flow of the second fluid stream through the open section into the process microchan nel.

[0026]

In one embodiment, mixing within a process microchannel can be improved through the use of surface features formed on one or more inner walls of the process microchannel. In one em bodiment, the second fluid contacts the first fluid within the process microchannel and then su rface features are formed on one, two or more inner walls of the process microchannel. may fl ow through regions within the processed process microchannel. The surface features are depr essions in one or more of the inner microchannel walls and/or protrusions from the inner micr ochannel walls oriented at an oblique angle to the direction of fluid flow through the process microchannel. It is preferable that it has a shape. The angled component may be oriented wit h the direction of flow or against the direction of flow. The surface features may be placed at an angle (eg, from about 1° to about 89°, in one embodiment from about 30° to about 75°) with respect to the direction of flow. Fluid flow in contact with the surface features forces a po rtion of the fluid flow to flow into the depressions or surface features, while a portion of the fl uid flow continues to flow over the surface features. The flow within the surface feature confor ms to the surface feature and forms an angle to the bulk flow. As the fluid exits the surface fe ature, it can exert momentum in the x and y directions in an x, y, z coordinate system in whic h the bulk fluid flows in the z direction. This effect can stir or rotate the fluid stream. This patt

ern is particularly useful for mixing two-phase flows because the imparted velocity gradient pr oduces fluid shear and breaks up the second fluid into small, well-dispersed bubbles or particu lates. can be done.

[0027]

In one embodiment, mixing of the first and second fluids is achieved using a first surface fea ture area followed by at least one second feature area that creates another flow pattern. As pr acticable, surface feature regions within a process microchannel may be arranged in series. A second flow pattern may be used to separate or separate the first and second fluids. This step may be used to assist in gas or liquid recovery. This embodiment of the present invention pro vides that after the gas is introduced into the liquid, the resulting mixture is passed through a first surface feature region containing a heterogeneous catalyst, a homogeneous catalyst, or n o catalyst. can be particularly useful in the case of gas-liquid reactions that flow through the T he mixture is then subjected to a second surface feature region, where the flow pattern option ally generates centrifugal force, forcing the liquid in an annular flow pattern toward the inner wall of the process microchannel while the gas remains within the fluid core. may flow throug h This latter profile may help separate or draw away unreacted gases from the reactant mixtu re. One pattern of surface features that can create a strong central vortex in the fluid is a pair of angled slots at the top and bottom of the process microchannel. A central vortex flow patte rn can be created. In one embodiment, the foamy mixture may drive liquids toward the walls of the process microchannels and forces gases toward the center of the process microchannel s.

[0028]

In one embodiment, the open section may include interior portions that form part of one or more of the interior walls of the process microchannel. There may be a surface feature sheet over this interior portion of the open section. Surface features may be formed in and/or on th e surface feature sheet. A second fluid may flow through the apertured section and the surfac e component sheet. A flux of fluid entering through the open section can be directed away fro m the surface of the surface feature sheet while within the surface features of the surface feat ure sheet. A surface feature sheet may include angled features having a relatively small width or span compared to the overall flow length. The surface component sheet may provide mech anical support to the apertured section. In addition, the surface composition

The flow vortices or angled flow created by the element further impart shear to the second flu id flowing through the open section, thus reducing the size of particles or bubbles of the secon d fluid in the bulk flow path. can be preferred above. In one embodiment, the multiphase mi xture may comprise a liquid-solids flow or a gas-liquid-solids flow

.

The second fluid stream may comprise a dispersion of solids in either gas or liquid. The first fl uid stream may comprise a gas, a liquid, or solids dispersed in a gas or liquid. Flow of a multi phase mixture through a surface feature section in a process microchannel can act to keep th

e mixture well-mixed or dispersed with momentum different from the direction of imparted flo w. so it can be an advantage. This utilization can be useful for dispersion of solid catalysts in li quid reactants.

[0030]

In one embodiment, the multiphase mixture may comprise solid particles dispersed in the fir st and/or second fluid streams, is in the form of a fluidized bed, and the process microchannel s are process microchannels. It includes surface features formed in and/or on one or more of i ts inner walls to alter the flow therein. This may involve mixing a gas stream into the solid par ticle-containing fluid stream. Solids may be blown into the carrier fluid or entrained by the car rier fluid. Surface constituents may facilitate mixing of multiphase mixtures. In one embodi ment, solids may form in the multiphase mixture as a result of chemical reactions and/or prec ipitation

. [0032]

In one embodiment, the multiphase mixture is in foam form. In one embodiment, the multip hase mixture may optionally contain one or more surfactants. Some foams do not require the presence of surfactants, although they may be included to facilitate foam formation.

[0033]

In the accompanying drawings, similar parts and components have similar reference numera ls. BEST

MODE FOR CARRYING OUT THE INVENTION

The term "microchannel" means a channel within at least one of a height or width of up to a bout 10 millimeters (mm), in one embodiment up to about 5 mm, in one embodiment up to a bout 2 mm, and in one embodiment up to about 1 mm. Refers to a channel with dimensions. Fluid flow through a microchannel can proceed along the length of the microchannel perpendic ular to the height and width of the microchannel. An example of a process microchannel, opti onally a microchannel that can be used as a second fluid stream channel, a third fluid stream channel and/or a heat exchange channel in the process of the present invention is shown in FI G. A microchannel 10, an example of which is shown in FIG. 1, has a height (h), a width (w) a nd an axial length (l). Fluid flows through microchannel 10 along the length of the microchann el in the directions indicated by arrows 12 and 14 . The height (h) or width (w) of the microch annel is about 0.05 to about 10 mm, in one embodiment about 0.05 to about 5 mm, in one e mbodiment about 0.05 to about 2 mm, in one embodiment from about 0.05 to about 1.5 mm, in one embodiment from about 0.05 to about 1 mm, in one embodiment from about 0.05 to a bout 0.75 mm, in one embodiment from about 0.05 to about 0.5 mm should be in the range o f The other dimension of height or width is any dimension, such as up to about 3 meters, in o ne embodiment from about 0.01 to about 3 meters, in one embodiment from about 0.1 to abo

ut 3 meters. good. The axial length (l) of the microchannel can be any dimension, such as up to about 10 meters, in one embodiment from about 0.1 to about 10 meters, in one embodiment from about 0.2 to about 6 meters, in one embodiment Embodiments may be from about 0.2 to about 3 meters. Although the microchannel 10 illustrated in FIG. 1 has a rectangular cross-section, it should be understood that the microchannel may have a cross-section of any shape, such as square, circular, semi-circular, trapezoidal, etc. be. The cross-sectional shape and/or size of a microchannel
can change. For example, the height or width may taper from a relatively large dimension to a relatively small dimension or vice versa over the length of the microchannel.

[0035]

The term "adjacent", when referring to the relative position of one channel to another, means directly adjacent such that a single wall separates these two channels. . This wall may vary in thickness. However, "adjacent" channels are not separated by intervening channels that interfere with heat transfer between the channels.

The
term "surface feature" refers to depressions in and/or protrusions from the microchannel wall that alter flow within the microchannel. Surface features may be circular, oval, square, rectangular, checkered, V-shaped, wavy and similar shapes. A surface component may include sub-components. In this case, the main wall of the surface features further comprises smaller surface features, these surface features being notched, corrugated, jagged, perforated, burred, checked, fan-shaped and similar. There may be. A surface feature has a depth, a width, and a length if it is a non-circular surface feature. Examples are shown in FIGS. Surface features can be formed on or in one or more of the interior sidewalls of the process microchannels used in the processes of the present invention. Surface features can be formed on or in one or more of the interior sidewalls of the second fluid flow channels and/or heat exchange channels used in the process of the present invention. Surface constituents can be referred to as passive surface constituents or passive mixing constituents.

[0037]

The terms "upstream" and "downstream" refer to positions within channels used in the processes of the invention, including microchannels, relative to the direction of fluid flow through the channel. For example, a position within a channel that has not yet been reached by a portion of the fluid flowing through the channel toward that position is downstream of that portion of the fluid. A position within the channel already passed by a portion of the fluid flowing through the channel away from that position is upstream of that portion of the fluid. The terms "upstream" and "downstream" do not necessarily refer to vertical positions, as the process channels used in the process of the invention may be oriented horizontally, vertically, or at an angle.

[0038]

The term "microbody" refers to up to about 200 microns, in one embodiment about 0.01 to

about 200 microns, in one embodiment about 0.01 to about 100 microns, in one embodiment about 0.01 to about 50 microns. , in one embodiment from about 0.01 to about 25 microns, i n one embodiment from about 0.01 to about 10 microns, in one embodiment from about 0.01 to about 5 microns, in one embodiment from about 0.01 to about 2 microns, in one embodim ent from about 0.01 to about 1 micron, in one embodiment from about 0.01 to about 0.5 micr ons, in one embodiment from about 0.01 to about 0.2 microns, in one embodiment about 0.0 1 to about 0.1 microns, in one embodiment about 0.01 to about 0.08 microns, in one embodi ment about 0.01 to about 0.05 microns, in one embodiment about 0.01 to about Refers to a t hree-dimensional body having average dimensions (eg, diameter, height, width, length) in the range of about 0.03 microns. These microbodies include bodies with circular and/or elliptical s haped cross-sections. Microbodies may be spherical, spheroidal, ovoid and similar shapes. The microbodies may have a needle-like shape. Microbodies may be hollow or solid. A microbody may be a microsphere. A microbody may have a major dimension (eg, diameter, length) and a minor dimension (eg, diameter, height, width), wherein the ratio of the major dimension to t he minor dimension is from about 10:1 to about 1:1. 1, in one embodiment from about 5:1 to about 1:1, and in one embodiment from about 2:1 to about 1:1.

The term " fluid

" means a gas, a liquid, a gas or liquid containing dispersed solids, a gas containing droplets, a liquid containing bubbles, a gas containing droplets and dispersed solids, or a liquid containi ng bubbles and dispersed solids,

and analogues.

[0040]

The term "heat source" refers to an object or device that emits heat and can be used to heat another object or device. The heat source may be in the form of a heat exchange channel hav ing a heat exchange fluid therein and transferring heat to another object or device, the other object or device being, for example, adjacent to the heat exchange channel, or Or a channel c lose enough to receive the heat transferred from the heat exchange channel. A heat exchange fluid may be contained within and/or flow through the heat exchange channels. The heat sour ce may be in the form of a heating element, such as an electric heating element or a resistanc e heater. The term "heat sink" refers to an object or device that absorbs heat and can be used to cool another object or device. A heat sink may be in the form of a heat exchange channel h aving a heat exchange fluid therein that receives heat transferred from another object or devi ce. Another object or device is, for example, a channel adjacent to or sufficiently close to the heat exchange channel to conduct heat to the heat exchange channel. A heat exchange fluid may be contained within and/or flow through the heat exchange channels. The heat sink may be in the form of a cooling element, eg, a non-fluid cooling element.

[0041]

The term "heat source and/or heat sink" refers to an object or device that can emit heat or a bsorb heat. A heat source and/or heat sink has a heat exchange fluid therein that transfers he

at to another object or device adjacent to or near the heat exchange channel when the other object or device is heated. even in the form of a heat exchange channel that conducts or recei ves heat transferred from another object or device adjacent to or near the heat exchange cha nnel when the other object or device is cooled good. A heat exchange channel that functions a s a heat source and/or a heat sink may function as a heating channel at some times and a co oling channel at other times. A portion(s) of the heat exchange channels may function as heat ing channels, while another portion(s) of the heat exchange channels may function as cooling channels.

The term "heat exchange channel" refers to a channel having a

heat exchange fluid therein and capable of releasing heat and/or absorbing heat.

[0043]

The term "heat exchange fluid" refers to a fluid capable of producing and/or absorbing heat.

[0044]

Referring to FIG. 2, the process can be performed using a microchannel mixer 100, which in cludes a microchannel mixer core 102, a process fluid header 104, a product footer 106 and a heat exchange manifold 108. include. Microchannel mixer core 102 includes a plurality of proc ess microchannels, adjacent second fluid flow channels and heat exchange channels. The seco nd fluid flow channels and/or heat exchange channels may be microchannels. The process mic rochannels, second fluid stream channels and heat exchange channels may be arranged in lay ers, one above the other or side by side. The process header 104 allows a first fluid stream to flow into the process microchannels and a second fluid flow to flow into the second fluid flow c hannels to provide a uniform or substantially uniform flow distribution in these channels. provi de an aisle for The product footer 106 provides a passageway for the multiphase mixture prod uct to flow rapidly from the process microchannels and have a relatively high flow rate. A first fluid stream enters microchannel mixer 100 through header 104 , as indicated by arrow 110 . A second fluid stream enters microchannel mixer 100 through header 104 , as indicated by ar row 112 . The first fluid stream and the second fluid stream enter the microchannel mixer cor e 102 and mix to form a multiphase mixture. The multiphase mixture flows from the microcha nnel mixing core 102 to the product fluoride.

through footer 106 and out of product footer 106 as indicated by arrow 114 . In one embodim ent, the multiphase mixture may be recycled back through the microchannel mixer core 102 a ny number of times, eg, 1, 2, 3, 4, etc. times. Heat exchange fluid flows into heat exchange manifold 108 as indicated by arrow 116, from heat exchange manifold 108, through heat exch ange channels in microchannel mixer core 102, and back to heat exchange manifold 108, whe re arrow It exits the heat exchange manifold 108 as indicated at 118 . Microchannel mixer 10 0 may be used with reservoirs, pumps, valves, flow control devices and similar devices. These are not shown in the drawings but are obvious to those skilled in the art.

[0045]

The microchannel mixer core may contain multiple multiphase mixture forming units. Figure

s 3-9 and 12 show examples of useful embodiments of multiphase mixture forming units. Ref erring to FIG. 3, the process of the present invention can be carried out using a multiphase mi xture forming unit 200 that includes a process microchannel 210 having opposing sidewalls 21 2 and 214 and an open section 240 in sidewall 212. can. The open section 240 may be referre d to as a porous section or porous substrate. Aperture section 240 may include a sheet or plat e 242 having an array of apertures 244 extending throughout the aperture section. Adjacent s idewall 212 is a second fluid stream 270 that opens into process microchannel 210 through op ening 244 in open section 240 . Process microchannel 210 has non-open or non-porous region s 211 and 217 and mixing zone 213 . A non-apertured region 211 extends from the entrance to the process microchannel to the entrance to the mixing zone 313 . A non-apertured region 211 is upstream of the mixing zone 213 . Mixing section 213 is adjacent to aperture section 2 40 . A non-apertured region 217 extends from the end of the mixing zone 213 to the exit of t he process microchannel 210 . A non-apertured region 217 is downstream of the mixing zone 213 . Adjacent to sidewall 214 are heat exchange channels 290 . In operation, a first fluid stre am enters process microchannel 210 , through non-apertured region 211 and into mixing zon e 213 , as indicated by arrow 216 . A second fluid stream enters second fluid stream channel 270 , as indicated by arrow 272 , and then through open section 240 and into mixing zone 21 3 , as indicated by arrow 274 . Within the mixing zone 213, the second fluid stream contacts and mixes with the first fluid stream to form a multiphase mixture. The second fluid stream m ay form a discontinuous phase within the first fluid stream. The first fluid stream may form a continuous phase. The multiphase mixture passes from mixing zone 213 through non-apertur ed region 217 and into the process as indicated by arrow 218. out of the microchannel 210 . Heating or cooling can be an option. When heating or cooling is desired, a heat exchange fluid flows through heat exchange channels 290, as indicated by arrows 292, to heat or cool the flu id in process microchannels 210 and second fluid flow channels 270. . The degree of heating o r cooling may vary over the length of process microchannel 210 and second fluid stream chan nel 270 . Heating or cooling may be negligible or non-existent in some sections of the process microchannels and liquid channels, and may be moderate or relatively large in other sections. Alternatively, heating or cooling may be accomplished using other than heat exchange channe ls. For example, heating may be accomplished using electrical heating elements or resistance heaters. Electrical heating elements or resistive heaters may be used to form one or more wal ls of process microchannel 210 and/or second fluid flow channel 270 . Electric heating elemen ts or resistive heaters may be in one or more walls of process microchannel 210 and/or secon d fluid flow channel 270 . Cooling may be accomplished using non-fluid cooling elements. Mult iple heating or cooling zones may be used along the length of the process microchannel 210 . Similarly, varying temperatures of heat exchange fluid may be used in one or more heat exch ange channels along the length of process microchannel 210 and/or second fluid stream chan nel 270 . Some sections of the liquid channel may be negligible or non-existent, while others may be moderate or relatively large. Alternatively, heating or cooling may be accomplished us

ing other than heat exchange channels. For example, heating may be accomplished using elec trical heating elements or resistance heaters. Electrical heating elements or resistive heaters may be used to form one or more walls of process microchannel 210 and/or second fluid flow channel 270 . Electric heating elements or resistive heaters may be in one or more walls of pr ocess microchannel 210 and/or second fluid flow channel 270 . Cooling may be accomplished using non-fluid cooling elements. Multiple heating or cooling zones may be used along the len gth of the process microchannel 210 . Similarly, varying temperatures of heat exchange fluid may be used in one or more heat exchange channels along the length of process microchanne l 210 and/or second fluid stream channel 270 . Some sections of the liquid channel may be ne gligible or non-existent, while others may be moderate or relatively large. Alternatively, heatin g or cooling may be accomplished using other than heat exchange channels. For example, hea ting may be accomplished using electrical heating elements or resistance heaters. Electrical h eating elements or resistive heaters may be used to form one or more walls of process microc hannel 210 and/or second fluid flow channel 270 . Electric heating elements or resistive heate rs may be in one or more walls of process microchannel 210 and/or second fluid flow channel 270 . Cooling may be accomplished using non-fluid cooling elements. Multiple heating or cooli ng zones may be used along the length of the process microchannel 210 . Similarly, varying t emperatures of heat exchange fluid may be used in one or more heat exchange channels alon g the length of process microchannel 210 and/or second fluid stream channel 270 .

Multiphase mixture forming unit 200A, an example of which is shown in FIG .
It is identical to the multi-phase mixture forming unit 200 illustrated in FIG. The tapered secti on 220 reduces the width or height of the process microchannel 210 in the mixing zone 213, t hus providing a narrower cross-section for the process microchannel 210 in the mixing zone 2 13. FIG. This width or height may range from about 0.001 to about 5 mm, and in one embodi ment from about 0.01 to about 2 mm. The presence of the tapered section 220 results in an i ncrease in the velocity of the fluid flowing through the mixing section 213 . As the velocity of t he liquid flowing through mixing zone 213 increases, the shear force acting on the second flui d entering mixing zone 213 through openings 244 increases. This facilitates flow of the secon d fluid stream through opening 244 . The velocity through the mixing zone 213 of the fluid flo wing through the narrowed cross-section of the process microchannel 210 is from about 0.00 5 to about 100 meters per second (m/s), in one embodiment from about 0.01 to about It sho uld be in the range of 50 m/s.

[0047]

Multiphase mixture forming unit 200B illustrated in FIG. 5 is similar to the multiphase mixtur e illustrated in FIG. 3, except that multiphase mixture forming unit 200B also includes second fluid flow channel 270a and open section 240a. Similar to forming unit 200 . A second fluid flo w channel 270 a is located between the process microchannel 210 and the heat exchange cha nnel 290 . An open section 240a is formed in sidewall 214 . A second fluid flow channel 270a

opens into the process microchannel 210 through the open section 240a. Aperture section 24 0a may include a sheet or plate 242a having an array of apertures 244a extending therethrou gh. Process microchannel 210 has non-open or non-porous regions 211 and 217 and mixing z one 213 . Non-apertured region 211 extends from the entrance to the process microchannel t o the entrance to mixing zone 213 and is upstream of mixing zone 213 . Mixing section 213 is located between aperture sections 240 and 240a. A non-apertured region 217 extends from t he end of mixing zone 213 to the exit of process microchannel 210 . A non-apertured region 2 17 is downstream of the mixing zone 213 . In operation, a first liquid stream enters process m icrochannel 210 , as indicated by arrow 216 , through non-opened region 211 and into mixing zone 213 . A second fluid stream flows into second fluid stream channels 270 and 270a, as in dicated by arrows 272 and 272a, respectively. A second fluid stream enters mixing section 21 3 through open sections 240 and 240a, as indicated by arrows 274 and 274a, respectively. Wi thin the mixing zone 213, the second fluid stream contacts and mixes with the first fluid strea m to form a multiphase mixture. The second fluid stream may form a discontinuous phase wit hin the first liquid. The first fluid stream may form a continuous phase. The multiphase mixtur e exits process microchannel 210 through non-opened region 217 as indicated by arrow 218 . Heating or cooling may be an option. addition When heat or cooling is desired, heat exchange fluid flows through heat exchange channels 290, as indicated by directional arrows 292, to he at or cool the fluid in process microchannels 210 and second fluid flow channels 270. do. The degree of heating or cooling may vary over the length of the process microchannel and the se cond fluid stream channel. Heating or cooling may be negligible or non-existent in some sectio ns within the process microchannels and liquid channels, and may be moderate or relatively la rge in other sections.

The multiphase mixture forming unit 200C illustrated in FIG. 6 had openings 244 and 244a il lustrated in FIG . 244 and 244a are identical to the multi-phase mixture forming unit 200B illu strated in FIG. 5, except that 244 and 244a are offset from such direct orientation. In FIG. 5, streams of the second fluid stream flowing through openings 244 and 244a collide directly wit h each other, thereby promoting diffusion of the second fluid stream into the first fluid stream. . 6, the streams of the second fluid stream flowing through openings 244 and 244a are offset from each other, thereby promoting diffusion by providing a swirling effect within mixing zone 213. In FIG.

[0049]

Multiphase mixture forming unit 200D, an example of which is shown in FIG. An open sectio n 240 is formed in sidewall 212 and an open section 240a is formed in sidewall 212a. Apertur e sections 240 and 240a may be referred to as porous compartments or porous substrates. Th rough open sections 240 and 240a, a second fluid flow channel 270 opens to process microch annels 210 and 210a, respectively. Aperture section 240 may include a sheet or plate 242 hav ing an array of apertures 244 extending therethrough. Similarly, apertured section 240a may i

nclude a sheet or plate 242a having an array of apertures 244a extending therethrough. Proc ess microchannels 210 and 210a have non-open or non-porous regions 211 and 217, and 211 a and 217a, and mixing zones 213 and 213a, respectively. Non-apertured regions 211 and 21 1a extend from the inlets to process microchannels 210 and 210a to the inlets to mixing zone s 213 and 213a, respectively. Non-apertured regions 211 and 211a are upstream of mixing zo nes 213 and 213a, respectively. Mixing zones 213 and 213a adjoin open sections 240 and 240 a, respectively. Non-apertured regions 217 and 217a extend from the ends of mixing zones 2 13 and 213a to the exits of process microchannels 210 and 210a, respectively. Non-apertured regions 217 and 217a are downstream of mixing zones 213 and 213a, respectively. Adjacent t o process microchannel 210 are heat exchange channels 290 . In operation, a first fluid strea m flows through process microchannels 210 and 210a, respectively, as indicated by arrows 21 6 and 216a, through unopened regions 211 and 211a and into mixing zones 213 and 213a. As indicated by arrow 272, the second A second fluid stream enters two fluid stream channels 27 0 and then through open sections 240 and 240a into mixing zones 213 and 213a, respectivel y, as indicated by arrows 274 and 274a. Within mixing zones 213 and 213a, the second fluid s tream contacts and mixes with the first fluid stream to form a multiphase mixture. The second fluid stream may form a discontinuous phase within the first fluid stream. The first fluid strea m may form a continuous phase. The multiphase mixture flows through non-opened compart ments 217 and 217a and out of process microchannels 210 and 210a, respectively, as indicat ed by arrows 218 and 218a. Heating or cooling can be an option. When heating or cooling is d esired, heat exchange fluid flows through heat exchange channel 290 , as indicated by arrows 292 , to heat or cool the fluid in channels 210 , 210 a and 270 . The degree of heating or cooli ng may vary over the length of the channel. Heating or cooling may be negligible or nonexiste nt in some sections of process microchannels 210 and 210a and second fluid stream channel 270, and may be moderate or relatively large in other sections. Heats or cools the fluid in the cells 210, 210a and 270. The degree of heating or cooling may vary over the length of the cha nnel. Heating or cooling may be negligible or nonexistent in some sections of process microch annels 210 and 210a and second fluid stream channel 270, and may be moderate or relatively large in other sections. Heats or cools the fluid in the cells 210, 210a and 270. The degree of heating or cooling may vary over the length of the channel. Heating or cooling may be negligi ble or nonexistent in some sections of process microchannels 210 and 210a and second fluid s tream channel 270, and may be moderate or relatively large in other sections.

In one embodiment, multiple multiphase mixing

formulations and/or sets of processing conditions can be used to generate separate multipha se mixtures within a single microchannel mixer. For example, a single microchannel mixer use s two or more process microchannels, associated second fluid stream channels, and heat exch ange channels to achieve 2, 3, 4 , 5, 6, 7, 8, 9, 10, tens, hundreds, thousands, tens of thousa nds, hundreds of thousands, etc. distinct multiphase mixtures can be made. Mixers of this typ e may be referred to as combinatorial synthesis devices. This is illustrated in Figure 8, where

an example of a multi-phase mixture forming unit 300 is shown. The multiphase mixture form ing unit 300 uses four process microchannels so that up to four separate multiphase mixtures can be generated. The multiphase mixture forming unit 300 can be operated any desired num ber of times, such as 2, 3, 4, 5, 6, 7, 8, 9, 10, 10, 100, Thousands, tens of thousands, etc. of repetitions can provide the possibility of multiple distinct multiphase mixtures as indicated abo ve. The multiphase mixture forming unit 300 includes process microchannels 310, 320, 330 a nd 340, the

It includes two fluid flow channels 350 and 360 and heat exchange channels 370 and 380 . An open section 311 is formed in the sidewall 312 . An open section 321 is formed in the sidewall 322 . An open section 331 is formed in sidewall 332 . An open section 341 is formed in sidewa ll 342 . Apertures 313, 323, 333 and 343 are located in and extend through aperture sections 311, 321, 331 and 341, respectively. Process microchannels 310, 320, 330 and 340 include cl osed compartments 314, 324, 334 and 344 located upstream of mixing zones 315, 325, 335 and 345, respectively. Mixing zones 315, 325, 335 and 345 are located adjacent to aperture z ones 311, 321, 331 and 341, respectively. Process microchannels 310, 320, 330 and 340 also include closed compartments 316, 326, 336 and 346 located downstream of mixing zones 31 5, 325, 335 and 345, respectively. In operation, a first fluid stream flows into process microch annels 310, 320, 330 and 340, as indicated by arrows 317, 327, 337 and 347, respectively. T he first fluid streams entering process microchannels 310, 320, 330 and 340 may have the sa me composition as each other or may have different compositions. The first fluid stream enter s mixing zones 315, 325, 335 and 345 through non-open compartments 314, 324, 334 and 3 44, respectively. A second fluid stream enters second fluid stream channels 350 and 360 as in dicated by arrows 351 and 361 . The second fluid flow entering second fluid flow channel 350 may be the same as or different from the second fluid flow entering second fluid flow channel 360 . The difference between the second fluid stream entering the second fluid stream channe l 350 and the second liquid entering the liquid channel 360 may be due to composition, proces sing conditions, physical properties (e.g., viscosity, density, surface tension, etc.).) and/or m ay be based on operating parameters. A second fluid stream entering second fluid stream cha nnel 350, as indicated by arrow 351, flows through open sections 311 and 321 and into mixin g sections 315 and 325, as indicated by arrows 352 and 353. flow into each. Within mixing zo nes 315 and 325, the second fluid stream contacts and mixes with the first fluid stream to for m a multiphase mixture. Similarly, a second fluid stream flows into second fluid stream chann el 360, as indicated by arrow 361, and then through open sections 331 and 341, as indicated by arrows 362 and 363, into the mixing zone. 335 and 345 respectively. Within mixing zones 315, 325, 335 and 345, the second fluid stream contacts and mixes with the first fluid stream to form a multiphase mixture. The multiphase mixtures formed in mixing zones 315, 325, 335 and 345 may be the same or different. When different, multiphase mixtures may vary in com position and/or physical properties or operational parameters (e.g., dispersed and/or continuo us phase composition, particle size, particle size distribution, viscosity, density, surface tensio

n, temperature, pressure, flow rate, etc.). etc.) may be different from each other. The multiph ase mixture passes from mixing zones 315, 325, 335 and 345 through non-apertured zones 3 16, 326, 336 and 346 to process microchannels 310, 320, 320, 348, respectively, as indicated by arrows 318, 328, 338 and 348, respectively. It flows out from 330 and 340. Heating or coo ling using heat exchange channels 370 and 380 may be an option. When heating or cooling is desired, heat exchange fluid flows through heat exchange channels 370 and 380, as indicated by arrows 371 and 372, and 381 and 382, and channels 310, 320, 330, 340, 360 and 360 he ats or cools the fluid in The degree of heating or cooling may vary over the length of each of t he channels. In sections with process channels and/or liquid channels may have negligible or no heating or cooling, and may be moderate or relatively large in other intervals. One advanta ge of this embodiment of the present invention is that the same equipment can be used to pr ovide for the formation and evaluation of multiple multiphase mixture products at the same ti me. This can be an advantage when it is desired to screen multiple formulations as new produ ct candidates.

In one embodiment, the process of the invention is suitable for making dual multiphase mixt ures . These dual multiphase mixtures are made using multiphase mixture forming unit 400, a n example of which is shown in FIG.
can be done. In FIG. 9, multiphase mixture forming unit 400 is positioned between centerlines 402 and 404 . Multiphase mixture forming unit 400 includes process microchannel 410 and liq uid channels 420 , 430 , 440 and 450 . Fluid flow channels 420 and 430 adjoin process microc hannel 410 . Fluid flow channel 440 is adjacent to fluid flow channel 420 and fluid flow channe l 450 is adjacent to fluid flow channel 430 . A common wall 412 containing a coarsely open se ction 415 separates the process microchannel 410 and the fluidic channel 420 . A common wa ll 422 containing a coarsely open section 425 separates the process microchannel 410 and the fluidic channel 430 . Aperture sections 415 and 425 include apertures 416 and 426, respective ly. Located between fluid flow channel 440 and fluid flow channel 420 is a micro-aperture secti on 435 including opening 436 to separate fluid flow channel 440 and fluid flow channel 420 . Between fluid flow channel 450 and fluid flow channel 430 is a micro-aperture section 445 incl uding opening 446 to separate fluid flow channel 450 and fluid flow channel 430 . Apertures 4 16 and 426 in coarsely apertured sections 415 and 425 are larger than apertures 436 and 446 in finely apertured sections 435 and 445 . Process microchannel 410 has a non-open or non-p orous region 411 and a mixing zone 413 . Non-apertured region 411 extends from the inlet to the process to the inlet to mixing zone 413 . Mixing section 413 is adjacent to open sections 4 15 and 425 . Optionally, heat exchange channels may be inserted at locations indicated by ce nterlines 402 and/or 404 to provide the desired heating or cooling to the fluid.
[0052]

Below centerline 402 lies a portion of adjacent multi-phase mixture forming unit 400a, an ex ample of which is also shown in FIG. Multiphase mixture forming unit 400a includes process m

icrochannel 410a, coarsely open sections 415a and 425a, fluid flow channel 430a and finely o pen section 445a. These are the same as the process microchannel 410, coarsely apertured s ections 415 and 425, fluid flow channel 430 and finely apertured section 445 discussed above. Also located above centerline 404 in FIG. 9 is a portion of another adjacent multiphase mixtur e forming unit 400b. Multiphase mixture formation 400b includes micro-opened section 435b and fluid flow channel 420b. These are the same as the micro-aperture section 435 and fluid f low channel 420 discussed above. The inclusion of portions of multiphase mixture forming uni ts 400a and 400b in FIG. 9 illustrates the repetitive nature of multiphase mixture forming unit 400 when used in a microchannel mixer for the process of the present invention. An example i s given.

[0053]

In operation, referring to FIG. 9, a first fluid stream enters the process microchannel 410 an d flows through the non-apertured region 411 into the mixing zone 413 as indicated by arrow 414 . A second fluid flow enters fluid flow channels 420 and 430, as indicated by arrows 423 a nd 433, respectively. A third fluid stream enters liquid channels 440 and 450, as indicated by arrows 442 and 452, respectively. A third fluid stream flows from fluid stream channel 440 thr ough open section 435 into fluid stream channel 420 and mixes with the second fluid stream t o form another multiphase mixture. A third fluid stream also enters fluid stream channel 430 f rom fluid stream channel 450 through open section 445 and mixes with the second fluid strea m to form another multiphase mixture. The third fluid stream forms the discontinuous phase and the second fluid stream forms the continuous phase in another multiphase mixture forme d in fluid flow channels 420 and 430 . Another multiphase mixture formed in fluid stream cha nnels 420 and 430 enters mixing zone 413 through open sections 415 and 425, respectively, and is mixed with the first fluid stream. Within the mixing zone 413, the additional multiphase mixture is dispersed as a discontinuous phase into the first fluid stream, and the first fluid str eam is brought into continuous phase form. The multiphase mixture formed in mixing zone 41 3 may be referred to as a dual multiphase mixture. Within the dual multiphase mixture, at lea st a portion of the third fluid stream can be encapsulated within the bubbles or microbodies (e g, microspheres) of the second fluid stream. Encapsulated bubbles or microbodies can be disp ersed as a discontinuous phase within the first fluid stream, which can be in the form of a con tinuous phase. A dual multiphase mixture is shown by arrow 418
, exit the process microchannel 410 . A dual multiphase mixture, which in one embodiment m ay be in the form schematically shown in FIG. It includes a third fluid stream 492 (ie, gas) enc apsulated within a fluid stream 494 (eg, liquid or microbody).

[0054]

In one embodiment, the process of the present invention can be used in an air blowing proce ss. An example of this is shown in FIGS. In this embodiment, the process is performed using an air-blown tank 500 containing a microchannel mixer 502 . In operation, air-blown fluid is c ontained within tank 500 and enters microchannel mixer 502 as a first fluid stream, as indicat

ed by arrow 504 . An example of a fluid that can be aerated is cell culture medium. A second f luid stream enters microchannel mixer 502 , as indicated by arrow 506 . The second fluid stre am may contain air or oxygen. A first fluid stream (e.g., cell culture medium) is mixed with a second fluid stream (e.g., air or oxygen) in the microchannel mixer, resulting in a multiphase mixture (e.g., air-blown cell culture medium). is formed. Microchannel mixer 502 may include multiple multiphase mixture forming units. The multiphase mixture forming unit 510 may be i n the form of a process microchannel 520, secondary fluid stream channels 530 and 540, ope n sections 550 and 560 which may be in the form of fine ceramic membranes, macroporous s upports. Includes open sections 570 and 580 and heat exchange channel 590 . In operation, a first fluid stream enters process microchannel 520 as indicated by arrow 522 . A second fluid stream enters second fluid stream channels 530 and 540, as indicated by arrows 532 and 54 2, respectively. The second fluid stream flows from second fluid stream channel 532 through o pen section 570 and then into process microchannel 520 through open section 550 . Similarly, another second fluid stream enters second fluid stream channel 540 , through open section 58 0 , and then through open section 560 and into process microchannel 520 , as indicated by ar row 542 . do. The first fluid stream and the second fluid stream are mixed in the process micr ochannel 520 to form a multiphase mixture. Polyphase The mixture exits process microchann el 520 as indicated by arrow 524 . Within the multiphase mixture, the first fluid stream may f orm the continuous phase and the second fluid stream may form the discontinuous phase. In one embodiment, the multiphasic mixture can comprise a cell culture medium having elevated levels of oxygen or air dispersed throughout the cell culture medium. The fluid can be heated or cooled by flowing the heat exchange fluid through the microchannel mixer 502, through th e heat exchange channels 590, and out of the microchannel mixer 502, as indicated by arrows 507. .

Although only one multiphase mixture forming unit is fully illustrated in each of FIGS. 3-9 an d 12, it may be used in a microchannel mixer to carry out the process of the present invention . There is virtually no upper limit to the number of multiphase mixture forming units. For exa mple, 1, 2, 3, 4, 5, 6, 8, 10, 20, 50, 100, hundreds, 1000, 1000, 10,000, tens of thousands, 100,000, 100,000, 1 million A multi-phase mixture forming unit as described above may also be used. In one embodiment, each multiphase mixture forming unit may be manifolded. Manif old connections may be accomplished by connecting macro-, pipe-, or duct-lines to each unit. Alternatively, multiple multiphase mixture forming units may be internally manifolded within a microchannel mixer containing the multiphase mixture forming units by creating relatively eq ual pressure drop circuits between each unit. On the other hand, the pressure drop need not be equal between each unit, as some flow imbalance may not affect product quality. In one e mbodiment, flow imbalances of up to about 50% are acceptable in forming multiphase mixtur es using the process of the present invention. The process microchannels, associated second and third fluid flow channels, and heat exchange channels may be arranged side-by-side or on

e above the other. For example, in multiphase mixture forming units 200 and 200A, process microchannels 210 may be arranged in a plane and parallel, and the second fluid
The flow channels 270 may be arranged parallel in adjacent planes on one side of the process microchannels 210 and the heat exchange channels 290 may be arranged parallel in another plane on the opposite side of the process microchannels 210 . For example, in multi-phase mi xture forming units 200B and 200C, process microchannels 210 may be arranged in one plane and parallel, and second fluid flow channels 270 and 270a are adjacent planes on each side of process microchannel 210. The heat exchange channels 290 may be arranged parallel in a pla ne adjacent to the second fluid flow channel 270a. In the multi-phase mixture forming unit 20 0D, the second fluid flow channels 270 may be arranged parallel in one plane and the process microchannels 210 and 210a are arranged parallel in adjacent planes on each side of the liqui d channel 270. The heat exchange channels 290 may be arranged parallel and in a plane adja cent to the process microchannels 210 . These multi-phase mixture forming units are not sho wn in FIGS. 3-9 and 12, but can be provided by those skilled in the art, with suitable headers, It may have footers, manifolds, valves, conduits, piping, control mechanisms, and the like. Fo r example, using slanted headers and footers to connect conduits or tubing at the inlets and o utlets to microchannel mixers containing multiphase mixture forming units to reduce unneces sary pressure drops associated with the size of the process microchannels. You can avoid it.
[0056]

In one embodiment, multiple multi-phase mixture forming units (200, 200A, 200B, 200C, 20 0D, 300, 400, 510) are stacked on top of each other to form the core of a scaled-up unit for la rge on-demand production capacity. may be formed. A scaled-up unit may have slanted head ers and footers not only for the multiphase mixture product, but also as manifolds for the liqui ds used to form the multiphase mixture. A more uniform flow distribution may be facilitated b y the addition of orifice plates or other open sections at the inlets of process channels, dispers ed phase channels or heat exchange channels. A frame section may be used to hold and seal t he multiphase mixture forming unit.
[0057]

Each of the process microchannels (210, 210a, 310, 320, 330, 340, 410, 520) may have any configuration, e.g., square, rectangular, circular, annular, elliptical, trapezoidal, etc. cross-secti on. . A process microchannel may be tubular. Process microchannels may be formed from par allel spaced apart sheets and/or plates that are placed side by side or stacked one on top of t he other. The term "sheet" refers to wall thicknesses up to about 5 mm. The term "plate" refe rs to a wall thickness of about 5 mm or greater. Sheets may be supplied to the user in the for m of rolls, while plates may be supplied to the user in the form of flat strips of material. Each of the process microchannels has internal dimensions (e.g., height, width or diameter). This di mension is about 0.05 to about 50 mm, in one embodiment about 0.05 to about 10 mm, in on e embodiment about 0.05 to about 5 mm, in one embodiment about 0.05 to about 2 mm, in o ne embodiment Embodiments may range from about 0.05 to about 1.5 mm, in one embodime

nt from about 0.05 to about 1 mm, and in one embodiment from about 0.05 to about 0.5 m m. Another internal dimension (e.g. height or width) perpendicular to the flow of liquid throug h the process microchannel may be any value, e.g. 01 cm to about 75 cm, in one embodiment from about 0.1 cm to about 50 cm, and in one embodiment from about 0.2 cm to about 25 c m.

[0058]

In one embodiment, the process microchannels (210, 210a, 310, 320, 330, 340, 410, 520) are mixed to provide uniform distribution of the first liquid flow within the process microchann els. non-open or non-porous regions (211, 211) in the inlet upstream of the zones (213, 213 a, 315, 325, 335, 345, 413)
a, 314, 324, 334, 344, 411). This can be useful when multiple process microchannels are arra nged side by side and/or on top of each other and the first liquid flow into the multiple proces s microchannels is not uniform. be. Providing these non-open areas may stabilize the flow of t he first fluid stream prior to reaching the mixing zone. The use of non-opened or non-porous r egions can be advantageous when the process microchannel has a circular cross-section (ie tu bular geometry). In one embodiment, the ratio of the length of the non-open area from the e ntrance to the process microchannel to the entrance to the mixing zone to the minimum inter nal dimension of the process microchannel within the non-open area or non-porous area is ab out It may range from 0.0001 to about 10000, in one embodiment from about 0.001 to about 1000.

[0059]

One or more of the interior walls of the process microchannels (210, 210a, 310, 320, 330, 3 40, 410, 520) may have surface features for altering flow within the process microchannels. . Examples of these surface features are shown in Figures 22-26. A surface feature may have t wo or more layers that are overlaid or intertwined with each other in a three-dimensional patt ern. The patterns in each separate layer may be the same or different. The flow may rotate or translate within each layer or within only one layer. Additional surface area may be created usi ng sublayers that may not be adjacent to the bulk flow channel. For example, these may be u sed to deposit a catalyst. The flow may rotate within the first level of surface features and mol ecularly diffuse into the second sublayer and beyond to facilitate reactions. Three-dimensional components may be made by metal casting or other processes. These methods also do not re quire the varying patterns to be decomposed into separate planes as if they were layered on t op of each other. A three-dimensionally varying surface feature can be placed adjacent to the bulk flow channel. These components have varying depths, shapes and locations, with sub-co mponents having patterns of varying depths, shapes and locations. Surface structures can be advantageous for chemical reactions that require additional surface area for catalyst depositio n, or for chemical separations such as distillation.

[0060]

FIG. 23 is a schematic plan view of a three-dimensional surface component structure. FIG. 2

4 shows an example of a back view of a three-dimensional surface element structure, with a r ecessed V at the adjacent interfaces of the bulk flow microchannels, and below the V is a bulk flow microchannel. There is a series of three-dimensional structures made up of structures of varying shapes, depths and locations that are connected to the passageway adjacent compon ents. It is further advantageous to create sub-layer passages that are not directly beneath op en surface features, but adjacent to bulk flow microchannels, but connected by one or more t ortuous two-dimensional or three-dimensional passages. Sometimes. This approach can be ad vantageous for creating a tailored residence time distribution in a reactor where it is desirable to have a broad residence time distribution rather than a narrow residence time distribution. FIG.

25 shows a three-dimensional surface feature in which a recessed V borders the bulk flow mi crochannel, behind the V is additional features of various shapes at varying depths and locatio ns. is a front view of the. The surface features may have a depth of less than about 2 mm, i n one embodiment less than about 1 mm, and in one embodiment in the range of about 0.01 mm to about 0.5 mm

.

The lateral width of the surface features should be sufficient to nearly reach the microchannel width (as shown in a fishbone design), but in one embodiment (such as fill features) is about 60% or less of the microchannel width. , in one embodiment about 40% or less, in one embo diment from about 0.1% to about 60%, and in one embodiment from about 0.1% to about 5 0%.

[0063]

The lateral width of the surface features ranges from about 0.05 mm to about 100 cm, and i n one embodiment is about 0 cm.

. It may range from 5 mm to about 5 cm, and in one embodiment from about 1 to about 2 c m.

[0064]

The length and width of the surface features may be defined similarly to the length and widt h of the microchannel. Depth may be the distance that a surface feature sinks into the microc hannel surface, in which case it is in the same direction as the microchannel height or the mic rochannel gap. This may correspond to the direction of stacking the laminated and bonded mi crochannel devices with surface features formed on or in the sheet surface. These dimensions of the surface feature refer to the maximum dimension of the surface feature. For example, th e depth of a groove with rounded corners may refer to the maximum depth, ie, the depth at t he bottom of the groove.

A microchannel

may contain multiple surface features or regions of surface features, including features that are recessed into one or more microchannel walls at varying depths. The spacing between the indentations may range from about 0.01 to about 10 mm, and in one embodiment from about

0.1 to about 1 mm. Surface features may be present throughout the length of the microchannel or may be present in portions or regions of the microchannel. Portions or regions having surface features may be intermittent so as to facilitate desired reactions or unit operations within specially tailored areas. For example, a 1 inch section of microchannel may have an array of dense surface features, followed by a 4 inch flat channel with no features, and a subsequent 2 inch section of sparse surface features. Sparsely spaced surface features refer to surface features having a pitch or inter-feature distance greater than five times the length of the surface features.

[0066]

In one embodiment, the surface features may extend substantially the entire axial length of the microchannel. In one embodiment, a microchannel may have surface features over about 50% or less of its axial length, and in one embodiment over about 20% or less of its axial length. In one embodiment, the surface features may extend over about 10% to about 100% of the axial length of the microchannel.

FIG.

26 shows several different patterns that can be used for surface features. These patterns are not meant to limit the invention, but merely to give examples of the possibilities. As with any surface feature, the pattern may be used in various axial or lateral sections of the microchannel.

[0068]

The second fluid flow channels (270, 270a, 350, 360, 420, 430, 530, 540) and the third fluid flow channels (440, 450) have dimensions too large to be characterized as microchannels. However, it is preferable that it is a microchannel. Each of these channels may have any configuration, eg, square, rectangular, circular, annular, elliptical, trapezoidal, etc. cross-section. These channels may include surface features, as described above. The second and third fluid flow channels may be tubular. The second and third fluid flow channels may be formed from parallel spaced apart sheets and/or plates arranged side-by-side or one above the other. Each second and third fluid flow channel ranges up to about 100 cm, in one embodiment from about 0.05 mm to about 100 cm, in one embodiment from about 0.05 mm to about 50 cm, in one embodiment about 0 cm. 0.05 mm to about 10 cm, in one embodiment about 0.05 mm to about 5 cm, in one embodiment about 0.05 mm to about 10 mm, in one embodiment about 0.05 mm to about 5 mm, in one embodiment about 0.05 mm to about 2 mm, and in one embodiment about 0.05 mm to about 1 mm, perpendicular to the fluid flow through the second and third fluid flow channels (eg, height, width or diameter). Another internal dimension (e.g., height or width) perpendicular to fluid flow through the second and third fluid flow channels is from about 0.01 cm to about 100 cm, in one embodiment from about 0.01 cm to about 75 cm. In embodiments it may range from about 0.1 cm to about 50 cm, and in one embodiment from about 0.2 cm to about 25 cm. The lengths of the second and third fluid flow channels are
Any value, such as from about 0.1 cm to about 500 cm, in one embodiment from about 0.1 c

m to about 250 cm, in one embodiment from about 1 cm to about 100 cm, in one embodimen t from about 1 cm to about 50 cm, in one embodiment It may range from about 2 cm to abou t 25 cm. The distance between each process microchannel and the next adjacent second fluid flow channel or adjacent second and third fluid flow channels is from about 0.05 mm to about 50 mm, in one embodiment about 0.1 to about 10 mm, and in one embodiment from about 0. 2 mm to about 2 mm.

[0069]

Heat sources and/or heat sinks may be used for cooling, heating, or both cooling and heatin g. A heat source and/or heat sink may include one or more heat exchange channels. The heat source may include one or more electrical heating elements or resistance heaters. The heat si nk may include one or more non-fluid cooling elements. These may be adjacent to process mi crochannels and/or second or third fluid flow channels. In one embodiment, the heat source a nd/or heat sink are not in contact with or adjacent to the process microchannels and/or the se cond and third fluid stream channels, and the process microchannels and/or the second and t hird fluid stream channels are away from either or both of the channels, but to transfer heat b etween the heat source and/or heat sink and the process microchannel and/or the second and third fluid stream channels. /or sufficiently close to the second and third fluid flow channels. p rocess microchannels (210, 310a, 310, 320, 330, 340, 410, 520), second fluid flow channels (270, 270a, 350, 360, 420, 430, 530, 540) and/or one or more walls of the third fluid flow ch annel (440, 450). Electric heating elements, resistive heaters and/or non-fluid cooling elemen ts may be constructed in one or more walls of the process microchannels, the second fluid flo w channels and/or the third fluid flow channels. The electric heating elements and/or resistive heaters may be thin sheets, rods, wires, discs or other shaped structures embedded within th e walls of the process microchannels and/or liquid channels. Electric heating elements and/or resistive heaters may be in the form of foils or wires adhered to the process microchannel wall s and/or liquid channel walls. Heating and/or cooling may be provided by Peltier-type thermoe lectric cooling and/or heating elements. It can also be implemented using a child. Multiple hea ting and/or cooling zones may be used along the length of the process microchannel, second f luid stream channel and/or third fluid stream channel. Similarly, along the length of the proce ss microchannel, the second fluid stream channel and/or the third fluid stream channel, using a heat transfer fluid of varying temperature in one or more heat exchange channels. good too. Heat sources and/or heat sinks may be used to provide precise temperature control within the process microchannels, second fluid stream channels and/or third fluid stream channels.

The heat exchange channels (290, 370 , 380, 590

) may be microchannels, but may have dimensions so large that they are not typically micro channels. Each of these channels may have any configuration, eg, square, rectangular, circula r, annular, elliptical, trapezoidal, etc. cross-section. The heat exchange channels may be tubul ar. The heat exchange channels are formed together with adjacent process microchannels or s econd and third fluid flow channels from parallel spaced apart sheets and/or plates arranged s

ide by side or one above the other. You may These channels may include the surface features described above. Each of the heat exchange channels has an internal dimension perpendicular to the heat exchange fluid flow through the heat exchange channels, such as a height, width o r diameter. This dimension is about 0.05 to about 50 mm, in one embodiment about 0.05 to a bout 10 mm, in one embodiment about 0.05 to about 5 mm, in one embodiment about 0.05 t o about 2 mm, in one embodiment Aspects may range from about 0.5 to about 1 mm. Anothe r internal dimension, such as height or width, perpendicular to the heat exchange fluid flow th rough the heat exchange chamber may be any value, such as from about 0.01 cm to about 10 0 cm, in one embodiment

may range from about 0.01 cm to about 75 cm, in one embodiment from about 0.1 cm to abo ut 50 cm, and in one embodiment from about 0.2 cm to about 25 cm. The length of the heat exchange channel is, for example, from about 0.1 cm to about 500 cm, in one embodiment fr om about 0.1 cm to about 250 cm, in one embodiment from about 1 cm to about 100 cm, in one embodiment from about 1 cm to about 50 cm. In embodiments, it may be any value in th e range of about 0.2 cm to about 25 cm. The distance between each process microchannel or second or third fluid stream channel and the next adjacent heat exchange channel is from abo ut 0.05 mm to about 50 mm, in one embodiment from about 0.1 to about 10 mm; Embodime nts may range from about 0.2 mm to about 2 mm. The heat exchange channels (290, 370, 380, 590) are arranged in a co-current direction parallel to the flow of fluid through the chann els through adjacent process microchannels or through the second and third fluid flow channel s

.

A heat exchange fluid may flow. Alternatively, the heat exchange fluid may flow through the h eat exchange channels in a direction countercurrent to fluid flow through the process microch annels or the second and third fluid flow channels. Alternatively, the heat exchange channel is in the process microchannel or the second and third fluid flow channels so as to provide heat exchange fluid flow in a cross-flow direction with respect to fluid flow through the process mic rochannel or the second and third fluid flow channels. It may be oriented with respect to the t hird fluid flow channel. The heat exchange channels may have a serpentine configuration to pr ovide a combination of cross-flow and co-flow or counter-flow.

[0072]

In one embodiment, a process microchannel (210, 210a, 310, 320, 330, 340, 410, 520), a s econd fluid flow channel (270, 270a, 350, 360, 420, 430, 530, 540), The third fluid flow chan nels (440, 450) and/or heat exchange channels (290, 370, 380, 590) have a square or rectan gular cross section and are formed from parallel spaced sheets or plates. The channels may b e arranged in vertically oriented alternating planes side by side or horizontally oriented altern ating planes stacked one above the other. These configurations, which may be referred to as p arallel plate configurations, have several advantages. For example, compared to a circular tub e, a parallel plate configuration experiences less pressure drop while achieving the same shea

r force for height, width or diameter at the same continuous phase material flux. For example, as the aspect ratio of a rectangular channel approaches about 10, i.e. approaching a parallel s heet or plate configuration, its pressure drop can be only about 50% of the pressure drop in a circular channel under the same conditions. . A process microchannel with a parallel plate conf iguration, a second fluid stream channel, a third fluid stream channel and a heat transfer chan nel can be easily arranged in a miniature device for scale-up. Higher throughput per unit volu me of the multiphase mixture formation process can also be achieved by using a parallel plate configuration as compared to circular tubes. An advantage of using parallel plate configuratio ns is that these configurations have a higher fluid/wall material ratio compared to circular tub es and are therefore more compact and have greater manufacturability or output potential

.

It is a point.

[0074]

In one embodiment, a process microchannel (210, 210a, 310, 320, 330, 340, 410, 520), a s econd fluid flow channel (270, 270a, 350, 360, 420, 430, 530, 540), The third fluid flow chan nels (440, 450) and/or heat exchange channels (290, 370, 380, 590) may be in the form of c oncentrically arranged circular tubes. The process microchannel and the second fluid stream c hannel may be adjacent to each other, one channel in the annular space and the other channe l in the central space or the adjacent annular space. In one embodiment, a microchannel mixe r useful in the process of the present invention comprises a plurality of interleaved concentric tube process microchannels, a second fluid flow channel, and optionally a third fluid flow chan nel. , the microchannel mixer may be cylindrical in shape.

The apertures (244, 244a, 313, 323, 333 , 343, 416, 426, 436, 446

) may be of sufficient size to permit the indicated fluid flow through the apertured section. A pertures may be referred to as pores. The opening section (240, 240a, 311, 321, 331, 341, 4 15, 425, 435, 445, 550, 560, 570, 580) is about 0.01 to about 50 mm, in one embodiment ab out 0.05 to It may have a thickness in the range of about 10 mm, and in one embodiment ab out 0.1 to about 2 mm. Apertures range up to about 50 microns, in one embodiment from ab out 0.001 to about 50 microns, in one embodiment from about 0.05 to about 50 microns, in o ne embodiment from about 0.1 to about 50 microns. should have an average diameter of In o ne embodiment, the apertures may have an average diameter ranging from about 0.5 to abou t 10 nanometers (nm), in one embodiment from about 1 to about 10 nm, and in one embodi ment from about 5 to about 10 nm. The number of openings in the aperture section is from a bout 10 to about 5×10^{8} openings per square centimeter, in one embodiment from about 1 to about 1×10^{6} openings per square centimeter. It should be within the range of the opening. The openi ngs may or may not be isolated from each other. Some or all of the apertures may be in fluid communication with other apertures within the aperture section. The ratio of the thickness of the open section to the length of the open section along the flow path of the fluid flowing thro

ugh the process microchannel (210, 210a, 310, 320, 330, 340, 410, 520) is about 0 .001 to a bout 100, in one embodiment about 0.01 to about 50, in one embodiment about 0.03 to abou t 25, in one embodiment about 0.05 to about 10, in one embodiment about 0.08 to about 5, a nd in one embodiment from about 0.1 to about 1. The open section may be constructed of an y material that provides sufficient strength and dimensional stability to allow operation of the process of the present invention. These materials include steel (e.g. stainless steel, carbon ste el and the like), monel, inconel, aluminum, titanium, nickel, platinum, rhodium, copper, chrom ium, brass, alloys of any of the above metals, polymers (e.g. thermosets), ceramics, glasses, composites containing one or more polymers (e.g. thermosets) and glass fibers, quartz, silico n, microporous carbon containing carbon nanotubes or carbon molecular sieves, zeolites or th eir Including combinations of two or more. Apertures may be made using known techniques s uch as laser drilling, microelectromachining systems (MEMS), lithographic electrodeposition an d molding (LIGA), electrosparkling or electrochemical etching. The apertures may be made usi ng techniques used to make structured plastics, such as extrusion, or techniques used to mak e films, such as aligned carbon nanotube (CNT) films. Apertures may be made using techniqu es such as sintering or compacting metal powders or particles to form tortuous and interconne cted capillary channels, and techniques of membrane fabrication. Apertures may vary from th e size provided by any of these methods to the inner sidewalls of the aperture that partially fil l the aperture. The size may be reduced by the application of ting. Selective coatings may for m a thin layer on the outside of the porous body and provide minimal pore sizes adjacent to t he continuous flow paths. The minimum average pore opening may range from about 1 nano meter to about several hundred microns, depending on the desired droplet size for the multip hase mixture. Apertures may be reduced in size by heat treatment and by methods that caus e an oxide scale or coating to form on the inner sidewalls of the aperture. These techniques m ay be used to partially occlude the apertures to reduce the size of the apertures exposed to fl ow. Figures 13 and 14 show a comparison of the SEM surface structure of the stainless steel p orous substrate at the same position at the same magnification before and after heat treatme nt. FIG. 13 shows the surface before heat treatment and FIG. 14 shows the surface after heat treatment. The surface of the porous material after heat treatment has significantly smaller g aps and opening sizes. Correspondingly, the average distance between apertures increases.

The open section (240, 240a, 311, 321, 331, 341, 415, 425, 435, 445, 550, 560, 570, 580) has average pores ranging from about 0.01 to about 200 microns . It may be made from a m etallic or non-metallic porous material with sized interconnecting channels or pores. These por es have openings (244, 244a, 313, 323, 3
33, 343, 416, 426, 436, 446). Porous materials may be made from powders or particulates su ch that the average interpore distance is similar to the average pore diameter. When very sma ll pore sizes are used, the pore-to-pore distance can also be very small, and the droplets are e ither in the process microchannels (210, 210a, 310, 320, 330, 410, 520) or in the second Und

esirably large droplets may coalesce at the surfaces on the sides of the fluid flow channels (420, 430). The porous material is formed by oxidation at elevated temperatures in the range of about 300° C. to about 1000° C. for a length of about 1 hour to about 20 days, or by sol coating alumina or another material such as nickel using chemical vapor deposition. A thin layer may be coated on the surface and inside the pores to close the small pores and reduce the pore size of the large pores, thus increasing the interpore distance. . As such, droplet coalescence may be reduced or eliminated, allowing the production of smaller droplets. An SEM image of the conditioned substrate or aperture section is shown in FIG.

[0077]

The openings (244, 244a, 313, 323, 333, 343, 416, 426, 436, 446) are regularly spaced throughout the mixing zone (213, 213a, 315, 325, 335, 345, 413). good. The openings may be preferentially spaced so that smaller openings or larger openings are used closer to either the front or back of the mixing zone. Together, the openings may be closer together at the beginning of the mixing zone and farther apart near the end of the mixing zone to help suppress droplet coalescence. Microscale openings or pores (244, 244a, 313, 323, 333, 343, 416, 426, 436, 446) small enough to provide multiphase mixtures with bubble or microsphere sizes smaller than about 1 micron Fabrication of substrates used as open sections (240, 240a, 311, 321, 331, 341, 415, 425, 435, 445, 550, 560, 570, 580) with One of the reasons for this lies in the fact that untreated ordinary porous materials, such as metallic porous substrates made from powders/particles by compaction and/or sintering, produce a relatively large surface roughness. . In general, these metallic porous substrates do not have the required pore size in the surface region when a given nominal pore size is below a certain value. Although the bulk of the porous material has a specified nominal pore size, the surface region is often characterized by much larger sized fused pores and cavities. This problem can be overcome by tailoring these substrates to provide the desired pore size and interpore distance in the surface area. This may be done by removing a surface layer from the porous substrate to expose or add a smooth new surface with smaller openings. The bubble or microsphere size in multiphase mixtures formed using these tailored substrates can be reduced without increasing the pressure drop across the substrate. Direct polishing or machining of porous surfaces results in smearing of the surface structure and removal of pores. Filling the porous structure with a liquid filler may be followed by solidification and mechanical grinding/polishing, as this may cause clogging. The filler is then removed to regain the porous structure of the material. The filler may be a metal with a low melting point such as zinc or tin or a precursor of a polymer such as an epoxy. Liquid filling and removal processes may be assisted by the use of vacuum. Grinding/polishing may be performed using a grinder and grinding powder. Metal filler removal may be accomplished by fusing and vacuuming or by acid etching. Epoxies or other polymers may be removed by solvent dissolution or by burning off in air.

Referring to FIGS. 16-19, in one embodiment the apertured sections (240, 240a, 311, 321,

331, 341, 415, 425, 435, 445, 550, 560, 570, 580) are It may be constructed of a relatively t hin sheet 600 containing relatively small openings 602 and a relatively thick sheet or plate 61 0 containing an array of relatively large openings 612 coaxially arranged or connected to the o penings 600 . A relatively thin sheet 600 is bonded over a relatively thick sheet 610, and the r elatively thin sheet 600 is bonded to the process microchannels (210, 210a, 310, 320, 330, 3 40, 410) or the second

The relatively thick sheet 610 faces the interior of the fluid flow channels (420, 430) of the se cond fluid flow channel (270, 270a, 350, 360, 420, 430, 530, 540) or the third fluid flow chan nel (270, 270a, 350, 360, 420, 430, 530, 540). Facing the interior of the flow channels (440, 450). The relatively thin sheet 600 can be bonded to the relatively thick sheet 610 using any suitable procedure (eg, diffusion bonding) to provide a composite structure 620 with increase d mechanical strength. A relatively thin sheet 600 may have a thickness in the range of about 0.001 to about 0.5 mm, and in one embodiment about 0.05 to about 0.2 mm. Relatively small openings 602 may have any shape, such as circular, triangular, or rectangular. Relatively small openings 602 may have an average diameter in the range of about 0.05 to about 50 microns, and in one embodiment about 0.05 to about 20 microns. A relatively thick sheet or plate 610 may have a thickness in the range of about 0.1 to about 5 mm, and in one embodiment about 0.1 to about 2 mm. Relatively large opening 612 may have any shape, such as circular, triang ular, or rectangular. The relatively large openings 612 may have an average diameter ranging from about 0.1 to about 4000 microns, in one embodiment from about 1 to about 2000 micro ns, and in one embodiment from about 10 to about 1000 microns. The number of openings 60 2 in sheet 600 and the number of openings 612 in sheet or plate 610 are each in the range of about 2 to about 10,000 openings per square centimeter, and in one embodiment about 2 to a bout 1,000 openings per square centimeter. good. Sheet 600 and sheet or plate 610 are descr ibed above as being useful for constructing apertured sections (240, 240a, 311, 321, 331, 34 1, 415, 425, 435, 445, 550, 560, 570, 580). may be constructed from any of the materials de scribed in . Apertures 602 and 612 are coaxial such that liquid flowing through the apertured section first flows through aperture 612 and then through aperture 602 . may be arranged or connected. The relatively short path for liquid to flow through the relatively small opening 602 is the pressure drop that would occur if the path through the opening had a length equal to th e length of the openings 602 and 612 combined. allows liquid to flow through opening 602 wit h a relatively low pressure drop compared to .

In the embodiment illustrated in FIG. 19, composite structure 620a is similar to that illustrate d in FIG .

18, except that convex portion 604 of relatively thin sheet 600 covering opening 612 is provi ded. have the same design as Convex portions 604 provide increased local shear forces in adj acent channels. Directional arrows 630 in FIG. 19 indicate fluid flow in channels adjacent to o penings 602 . Due to the greater shear forces, fluid flowing through openings 602 has a small er bubble or microsphere size. In the embodiment illustrated in FIG. 20, a surface coating 64

2 is deposited over the surface of sheet or plate 640 and interior sidewalls 644 of opening 646 .

This coating provides an easier way to reduce the diameter of the apertures (244, 244a, 313, 323, 333, 343, 416, 426, 436, 446). Coating materials used to form coating 642 may include alumina, nickel, gold, or polymeric materials (eg, Teflon®). Coating 642 may be applied to sh eet or plate 640 using known techniques including chemical vapor deposition, metal sputterin g, metal plating, sintering, sol coating, polymer coating and similar methods. The diameter of the opening may be controlled by adjusting the thickness of coating 642 .

[0081]

In one embodiment, the open section (240, 240a, 311, 321, 331, 341, 415, 425, 435, 445, 550, 560, 570, 580) is an asymmetric porous material, such as a plurality of sintered particle s. It may be formed of a porous material having a layer of The number of layers may be 2, 3 or 4 or more. The advantage of these multilayer substrates is that they provide increased dur ability and bond strength. Examples include sintered ceramics with relatively large pores on o ne side and relatively small pores on the other side. Relatively small pores range from about 2 to about 10 nm.

diameter. Relatively small pores may be located in relatively thin layers of the multilayer subst rate. A relatively thin layer may have a thickness in the range of about 1 to about 10 microns. The side with the smaller pores faces the interior of the process microchannel (210, 210a, 31 0, 320, 330, 340, 410, 520) or the second fluid flow channel (420, 430). , relatively high shea r forces may be used to remove relatively small multiphase mixture bubbles or microspheres as they form. Process microchannels (210, 210a, 310, 320, 330, 340, 410, 520), second flui d flow channels (270, 270a, 350, 360, 420, 430, 530, 540),

third

The fluid flow channels (440, 450) and heat exchange channels (290, 370, 380, 590) of, alon g with associated headers, footers, manifolds, etc., are of sufficient strength to enable operati on of the process of the present invention, It may be made of any material that provides dime nsional stability, corrosion resistance and heat transfer properties. These materials include ste el (e.g. stainless steel, carbon steel and the like), monel, inconel, aluminum, titanium, nickel, platinum, rhodium, copper, chromium, brass, alloys of any of the aforementioned metals, poly mers (thermosets), ceramics, glasses, composites comprising one or more polymers (eg, the rmosets) and glass fibers, quartz, silicon, or combinations of two or more thereof.

[0083]

The first fluid stream may comprise a gas or a liquid. The second fluid stream may contain a gas or microbody-forming material. The third fluid stream may contain gas.

[0084]

Gases may include any gas. In one embodiment, the gas may include one or more of air, oxy gen, nitrogen, carbon dioxide, water vapor, ammonia, ozone, chlorine gas, hydrogen and the l ike. The gas may include one or more gaseous hydrocarbons, such as hydrocarbons containin

g from 1 to about 5 carbon atoms. These include saturated and unsaturated hydrocarbons. Hydrocarbons include methane, ethane, ethylene, propane, isopropane, propylene, butanes, butylenes, pentanes, cyclopentane, pentylenes, cyclopentylene and the like.

[0085]

The liquid may include any liquid. Liquids may include water, organic liquids, or combinations thereof. The liquid may contain one or more liquid hydrocarbons. They have from 1 to about 24 carbon atoms, in one embodiment from about 5 to about 24 carbon atoms, in one embodiment from about 6 to about 18 carbon atoms, in one embodiment about 6 to about 12 carbon atoms. The term "hydrocarbon" denotes a compound having a hydrocarbon or predominantly hydrocarbon character. These hydrocarbon compounds include:

(1) Pure hydrocarbon compounds, i.e. aliphatic compounds (e.g. alkanes or alkylenes), cycloaliphatic compounds (e.g. cycloalkanes, cycloalkylenes), aromatic compounds, aliphatic and alicyclic substituted aromatic compounds, aromatics Substituted Aliphatic Compounds and Aromatically Substituted Alicyclic Compounds and the like. Examples include hexane, 1-hexene, dodecane, cyclohexene, cyclohexane, ethylcyclohexane, benzene, toluene, xylenes, ethylbenzene, styrene, and the like.

(2) Substituted hydrocarbon compounds, i.e., hydrocarbon compounds containing non-hydrocarbon substituents that do not alter the predominantly hydrocarbon character of the compound. Examples of non-hydrocarbon substituents include hydroxy, acyl, nitro, halo, and the like.

(3) Heterosubstituted hydrocarbon compounds, i.e., hydrocarbon compounds that are predominantly hydrocarbon in nature but contain atoms other than carbon in chains or rings that are normally composed of carbon atoms. For example, heteroatoms include nitrogen, oxygen and sulfur. The liquid may contain natural oils, synthetic oils or mixtures thereof

.

Natural oils include animal and vegetable oils (eg castor oil, lard oil) and liquid petroleum oils. and mineral oils such as solvent-treated or acid-treated mineral oils of the paraffinic, naphthenic or mixed paraffinic-naphthenic type. Natural oils include oils derived from coal or shale. The oil may be a saponifiable oil from the triglyceride family, such as soybean oil, sesame seed oil, cottonseed oil, safflower oil and the like. The oil may be a silicone oil (eg, cyclomethicone, silicone methicones, etc.). The oil may be an aliphatic or naphthenic hydrocarbon such as petrolatum, squalane, squalene or one or more dialkylcyclohexanes, or mixtures of two or more thereof. Synthetic oils include polymerized and intermolecularly reacted olefins (e.g. polybutylenes, polypropylenes, propylene isobutylene copolymers, etc.), poly(1-hexenes), poly(1-octenes), poly(1-decenes).) and mixtures thereof, alkylbenzenes (e.g. dodecylbenzenes, tetradecylbenzenes, dinonylbenzenes, di-(2-ethylhexyl)benzenes, etc.), polyphenyls (e.g. biphenyls, terphenyls, alkylated polyphenyls, etc.), alkylated diphenyl ethers and alkylated diphenyl sulfides and their derivatives, analogs and homologues and likes. Alkylene oxide polymers and copolymers and derivatives thereof in which the terminal hydroxyl groups have been modified by esterification, etherification, etc. are synthetic oils that can be used. Synthetic oils may include p

oly-alpha-olefins or Fischer-Tropsch synthetic hydrocarbons.

The liquid

may comprise a normally liquid hydrocarbon fuel, for example a distillate fuel such as motor gasoline as defined in ASTM standard D439, or a diesel fuel or heavy oil as defined in ASTM st andard D396.

[0088]

The liquid may comprise fatty alcohols, fatty acid esters or mixtures thereof. The fatty alcoh ol may be Guerbet alcohol. The fatty alcohol may contain from about 6 to about 22 carbon ato ms, in one embodiment from about 6 to about 18 carbon atoms, and in one embodiment from about 8 to about 12 carbon atoms. Fatty acid esters are esters of straight chain fatty acids of about 6 to about 22 carbon atoms with straight or branched chain fatty alcohols of about 6 to about 22 carbon atoms; It can also be an ester of a branched carboxylic acid of 1 atom with a straight or branched chain fatty alcohol of from about 6 to about 22 carbon atoms, or mixture s thereof. Examples are myristyl myristate, myristyl palmitate, myristyl stearate, myristyl isos tearate, myristyl oleate, myristyl behenate, myristyl erucate, cetyl myristate, cetyl palmitate, cetyl stearate, cetyl isostearate, cetyl oleate. , cetyl behenate, cetyl erucate, stearyl myristat e, stearyl palmitate, stearyl stearate, stearyl isostearate, stearyl oleate, stearyl behenate, ste aryl erucinate, isostearyl myristate, isostearyl palmitate, iso-stearate Stearyl, isostearyl isoste arate, isostearyl oleate, isostearyl behenate, isostearyl oleate, oleyl myristate, oleyl palmitate, oleyl stearate, oleyl isostearate, oleyl oleate, oleyl behenate, oleyl erucate, behenyl myristate, behenyl palmitate, behenyl stearate, behenyl isostearate, behenyl oleate, behenyl behenate, behenyl erucate, erucyl myristate, erucyl palmitate, erucyl stearate, erucyl isostearate, erucyl oleate, behenic acid Includes erucyl and erucyl erucate. fatty acid
mixtures of mono-, di-, and/or triglycerides made up of one or more fatty acids of about 18 c arbon atoms; one with one or more fatty alcohols and/or Guerbet alcohols of about 6 to about 22 carbon atoms; esters with one or more aromatic carboxylic acids (e.g., benzoic acid); one or more dicarboxylic acids of 2 to about 12 carbon atoms and one or more linear chains of 1 t o about 22 carbon atoms; or esters with branched alcohols, one or more polyols containing 2 to about 10 carbon atoms and 2 to about 6 hydroxyl groups, or mixtures of such alcohols and polyols, 2 to about 12 esters of one or more dicarboxylic acids (e.g. phthalic acid) of 1 to 22 c arbon atoms with one or more alcohols (e.g. butyl alcohol, hexyl alcohol) of 1 to 22 carbon at oms, benzoic acid and from about 6 It may also include esters with linear and/or branched alc ohols of about 22 carbon atoms, or mixtures of two or more thereof. The liquid is one or mor e branched primary alcohols of about 6 to about 22 carbon atoms, one or more linear and/or branched aliphatic alcohols of about 6 to about 22 carbon atoms

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carbonates, one or more Guerbet carbonates made from one or more aliphatic alcohols of fro m about 6 to about 22 carbon atoms, one or more of which each alkyl group contains from 1 t o about 12 carbon atoms; dialkyl (e.g. diethylhexyl) naphthalate, one or more linear or branc

hed, symmetrical or asymmetrical dialkyl ethers containing from about 6 to about 22 carbon a toms per alkyl group, from about 6 to about 22 carbon atoms Epoxidized fatty acid esters and one or more ring-opening products of polyols containing 2 to 10 carbon atoms and 2 to 6 hydr oxyl groups, or mixtures of two or more thereof. good.

[0090]

Water may be obtained from any convenient source. Water may be deionized or purified usin g osmotic or distillation methods. The microbody-forming material may include any microbod y-forming material

.

The microbody-forming material may be in the form of a liquid or solid melt. Microbody-formi ng materials may include glass, eg, glass microbody (eg, microsphere)-forming materials, pol ymeric, eg, polymeric microbody (eg, polymeric microsphere)-forming materials. The polymer ic microbody-forming material is one or more of acrylic resins, silicone resins, urethane resin s, vinyl acetate resins, Teflon resins, polyamide resins, vinyl chloride resins, styrene-based res ins, phenolic resins, epoxy resins, styrene resins. -butadiene-styrene block copolymer resin, s tyrene-ethylene-butylene-styrene block copolymer resin, styrene-isoprene-styrene block copol ymer resin, n-butyl rubber, chloroprene rubber, natural rubber or two or more thereof It may also include combinations. In one embodiment, the polymeric microbody-forming material ma y comprise (meth)acrylic acid esters of alcohols of 1 to about 14 carbon atoms. In one embod iment, the polymeric microbody-forming material may comprise at least one alkyl (meth)acryl ate.

[0092]

In one or more embodiments of the present invention, emulsifiers and/or surfactants are not required, although one or more emulsifiers and/or surfactants may be used in forming the mu ltiphase mixture prepared by the process of the present invention. may be used. Emulsifiers a nd/or surfactants may be premixed with the liquid. The emulsifiers and/or surfactants are ioni c or non-ionic with a Hydrophilic-Lipophilic Balance (HLB) in the Griffin system ranging from 0 to about 18, in one embodiment from about 0.01 to about 18. may contain a chemical compo und. Ionic compounds may be cationic or amphoteric compounds. Examples include those disc losed in "McCutcheons Surfactants and Detergents", 1998 Edition, North American and Intern ational Editions. Pages 1-235 of the North American version and pages 1-199 of the Internatio nal version are hereby incorporated by reference in part for their disclosure of such emulsifier s. Emulsifiers and/or surfactants that can be used are

, alkylene oxide repeat units, carboxylated alcohol ethoxylates, ethoxylated alcohols, ethoxyla ted alkylphenols, ethoxylated amines and amides, ethoxylated fatty acids, ethoxylated fatty a cid esters and oils, fatty acid esters, fatty acid amides, glycerol esters , glycol esters, sorbitan esters, imidazoline derivatives, lecithin and derivatives, lignin and derivatives, monoglycerides and derivatives, olefin sulfonate esters, phosphate esters and derivatives, propoxylated and et hoxylated fatty acids or alcohols or alkylphenols, sorbitan derivatives, Sucrose esters and deri

vatives, sulfates or alcohols or ethoxylated alcohols or fatty acid esters, dodecylbenzenes and tridecylbenzenes or condensed naphthalenes or petroleum sulfonates, sulfosuccinates and der ivatives, tridecylbenzene and dodecyl Contains benzenesulfonic acid. Emulsifiers and/or surfac tants include one or more polyalkylene glycols, glycerol or sorbitan and one or more partial es ters of fatty acids containing from about 12 to about 22 carbon atoms, or mixtures thereof. m ay contain. Emulsifying agents and/or surfactants may include pharmaceutically acceptable m aterials such as lecithin. The concentration of these emulsifiers and/or surfactants in the multi phasic mixture made by the process of the present invention is up to about 20% by weight of the multiphasic mixture, and in one embodiment from about 0.01 to about 5% by weight. It may be in the range, in one embodiment from about 0.01 to about 2% by weight. In one emb odiment, this concentration may be up to about 2% by weight, in one embodiment up to abou t 1% by weight, and in one embodiment up to about 0.5% by weight.

[0093]

In one embodiment, the first fluid stream comprises a liquid stream and the second fluid str eam comprises air.

[0094]

In one embodiment, the first fluid stream comprises a liquid waste stream and the second fl uid stream comprises air. In one embodiment, the first fluid stream contains the hazardous li quid waste stream and the second fluid stream contains air

. In one embodiment, the first fluid stream contains salad dressing or mustard and the seco nd fluid stream contains nitrogen . [0097] In one embodiment, the first fluid stream compris es a liquid beverage or beer and the second fluid stream comprises carbon dioxide. In one e mbodiment, the first fluid stream contains bleached pulp used in paper manufacture and the s econd fluid stream contains chlorine . [0099] In one embodiment, the first fluid stream com prises a dispersion of coal in water and the second fluid stream comprises air. In one embodi ment, the first fluid stream comprises motor oil with entrained water and the second fluid stre am comprises nitrogen . [0101] In one embodiment, the first fluid stream contains the cells for the culture reaction and the second fluid stream contains oxygen or air. In one embodime nt, the first fluid stream contains the liquid reaction medium and the second fluid stream cont ains air or oxygen . In one embodiment, the first fluid stream contains the reaction medium for carrying out the hydrogenation reaction and the second fluid stream contains hydrogen . [0104]

In one embodiment, the first fluid stream comprises a mixture of oil and water and the seco nd fluid stream comprises air or natural gas. In one embodiment, the first fluid stream conta ins bleached pulp used in paper manufacture and the second fluid stream contains oxygen . In one embodiment, the first fluid stream contains edible oil, wine or juice and the second f luid stream contains nitrogen . In one embodiment, the first fluid stream contains water use d in fish farming and the second fluid stream contains oxygen . In one embodiment, the first fluid stream contains water and the second fluid stream contains ozone . [0109] In one emb odiment, the first fluid stream comprises a waste or process stream and the second fluid strea m comprises carbon dioxide or ammonia. In one embodiment, the first fluid stream contains air and the second fluid stream contains water vapor . In one embodiment, the first fluid stre am comprises a waste or process stream containing volatile organic compounds and the secon d fluid stream comprises air . [0112] In one embodiment, the first fluid stream comprises a gas or liquid and the second fluid stream comprises the microbody-forming material. In one embodiment, the first fluid stream contains the water-based composition and the second fluid stream contains hydrogen and/or oxygen . This may be used for direct combination for hydrog en peroxide production. [0114]

In one embodiment, the first fluid stream contains the 2-alkylanthraquinone and the second stream contains hydrogen. It may be used to generate hydrogen peroxide. The first fluid str eam material comprises about 0.1 to about 80 weight percent, in one embodiment about 1 to about 50 weight percent, in one embodiment about 0.1 to about 80 weight percent, in the mu ltiphase mixture made by the process of the present invention

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may be present in concentrations ranging from about 1 to about 20% by weight. The second f luid stream material comprises from about 1 to about 95 weight percent, in one embodiment f rom about 10 to about 50 weight percent, in one embodiment from about 10 to about It may be present at a concentration in the range of 25% by weight. The third fluid stream material c omprises up to about 0.01% to about 50% by weight, in one embodiment about 1 to about 1 5% by weight, in one embodiment It may be present in concentrations ranging from about 0. 1 to about 1% by weight.

[0116]

In one embodiment, the second fluid may dissolve in the first fluid. This may occur within th e process microchannel or after the multiphase mixture exits the process microchannel. In on e embodiment, the second fluid is mixed with the first fluid within a period of up to about 10 h ours, in one embodiment up to about 1 hour, into the first fluid. It should dissolve.

[0117]

The multiphase mixture of the present invention may contain more than one type of solid pa rticles. These may be premixed with the first, second and/or third liquid. Solid particles may b e organic, inorganic, or a combination thereof. The solid particles are catalysts (e.g. CeO2 / Ba Al12O19 , Pt / Al Combustion catalysts such as 2O3 , polymerization catalysts and the like) , pigments (e. g.

TiO 2 , carbon black, iron oxide, etc.), fillers (eg, mica, silica, talc, barium sulfate, polyethylen es, polytetrafluoroethylene, nylon powder, methyl methacrylate powder) and the like. Solid pa rticles may include nano-sized particles. The solid particles may have an average particle diam eter ranging from about 0.001 to about 10 microns, and in one embodiment from about 0.01 to about 1 micron. The concentration of solid particles in the multiphase mixture may range u p to about 70% by weight, and in one embodiment from about 0.1 to about 30% by weight, b ased on the weight of the multiphase mixture.

[0118]

In one embodiment, the multiphase mixture made by the process of the present invention c

omprises a discontinuous phase dispersed within a continuous phase. The discontinuous phas e is up to about 200 microns, in one embodiment about 0.01 to about 200 microns, in one em bodiment about 0.01 to about 100 microns, in one embodiment about 0.01 to about 50 micro ns, one In embodiments from about 0.01 to about 25 microns, in one embodiment from about 0.01 to about 10 microns, in one embodiment from about 0.01 to about 5 microns, in one em bodiment from about 0.01 to about 2 microns. , in one embodiment about 0.01 to about 1 mi cron, in one embodiment about 0.01 to about 0.5 micron, in one embodiment about 0.01 to a bout 0.2 micron, in one embodiment about 0 .01 to about 0.1 microns, in one embodiment ab out 0.01 to about 0.08 microns, in one embodiment about 0.01 to about 0.05 microns, in one embodiment about 0.01 to about 0 It may contain bubbles or microbodies having volume-bas ed average dimensions (eg, diameter, height, width, length) in the range of 0.03 microns. On e advantage of the process of the present invention is that, in at least one embodiment, the b ubbles or microbodies are characterized by having a relatively narrow average diameter (or h eight, width or length) distribution.

[0119]

A "relative span" is often referred to as a "span". Relative span is a dimensionless parameter calculated from the volume distribution. As with the volume median foam or microbody size (VMD), D[v, 0.1] and D[v, 0.9] correspond to 10% and 90% of the dispersed foam or microbo dy volume, respectively. A diameter (or height, width or length) representing a point within a smaller diameter bubble or microbody. The span may be defined as the quotient of D[v,0.9] m inus D[v,0.1] divided by VMD(D[v,0.5]). In one embodiment, the span of bubbles or microbod ies in the multiphase mixture made by the process of the present invention ranges from about 1.3 to about 5, in one embodiment from about 1.8 to about 2.5. Good to have. In one embodi ment, the process of the invention is carried out in a single process microchannel and the spa n may range from about 1.3 to about 2.5. In one embodiment, the process of the present inv ention is carried out in a scaled-up multiphase mixing process using multiple process microch annels and spans may range from about 1.3 to about 5. In one embodiment, the volume-ba sed average diameter (or height, width or length) of the bubbles or microbodies in the multip hase mixture made by the process of the present invention is from about 0.1 to about
100
It may be in the micron range and the span may be in the range of about 1 to about 25. In on e embodiment, the volumetric average diameter (or height, width or length) may range from about 1 to about 10 microns and the span may range from about 1.8 to about 2.5. Good to ha ve.

[0121]

In one embodiment, cells are formed, the cells having a volume-based average diameter in t he range of up to about 25 microns and a span in the range of about 1.9 to about 2.5.

[0122]

In one embodiment, microbodies are formed having a volumetric average diameter (or heigh

t, width or length) in the range of up to about 5 microns and a diameter in the range of about 1.8 to about 2.5. span. Microbodies formed by the process of the invention have numerous u ses

.

these

includes glass microspheres for density-reducing cast filings, glass microspheres for selective species immobilization in fluid bed reactors, and the like. Other examples include microsphere polymer, gel or colloidal suspension generation used for immunoassays and treatments. Micro bodies (e.g. microspheres) are processed in secondary processes to form aggregates, catalyti c fluidized or packed beds, drug delivery systems (e.g. protein-enzymatic reactions), and mod ern separation and fluidized bed applications (e.g. magnetic vibration Encapsulated solids may be formed for some applications, including coated magnetic carriers that can be advantageous ly separated or excited by In at least one embodiment, one advantage of the process of the present invention is that whether the process is for laboratory, pilot plant scale, or commercial scale, the process microchannel,

first

The gap distance between the two fluid flow channels, optionally the third fluid flow channel, and/or the heat exchange channel may be the same. As a result, whether the microchannel m ixer is built at laboratory or pilot plant scale, or as a commercial scale plant unit, the particle s ize distribution of the multiphase mixture produced by the microchannel mixer used in the pro cess of the present invention is , can be substantially the same. The shear force in the direct ion of velocity u for a fluid control element (discrete) is given by the formula F

$X = mu^{*}$

It can be calculated by du/dy. where mu is the viscosity and du/dy is the velocity gradient of the liquid flow perpendicular to the aperture section. However, as with liquid position (represe nted by a control element), velocity generally has three components, and shear force also has three components. For near-surface and surface-channel flow, one-dimensional assumptions c an be made and the net shear force of the liquid at the element surface can be approximated by Fx . Computational fluid dynamics, including commercially available software packages such as Fluent or FEMLAB, can be used to solve the necessary transport equations and consequentl y to calculate surface shear forces. Surface shear forces parallel to the direction of flow along the channel length can be calculated. Shear forces between parallel channels can also be calc ulated, incorporating flow distribution effects to determine the mass flux into each parallel cha nnel as a function of detailed channel and manifold geometry. For example, "Fundamentals of Fluid Mechanics", 3rd Edition, BR Munson, D.F. Young and T.H. Okiishi (T. H. Okiishi), John Wil ey & Sons, Inc., Weinheim, 1998, for more detailed calculations.

In one embodiment, the shear force deviation

factor (SFDF) for a process using a single process microchannel is within about 50% of the S FDF for a scaled-up process containing multiple process microchannels. can do. The SFDF is c

alculated by the formula

$SFDF=(F_{max}-F_{min})/(2F_{mean})$

. where F_{max} is the maximum shear force in the process microchannel for a particular liquid, F_{min} is the minimum shear force in the process microchannel for the same liquid, F_{mean} is th e open section in the process microchannel (240, 240a, 311, 321, 331, 341, 415, 425, 435, 4 45, 550, 560, 570, 580) are the arithmetic mean shear forces for the same liquid at the surfa ce. Within a single process microchannel operated by the process of the present invention, the SFDF is less than about 2, in one embodiment less than about 1, in one embodiment less than about 0.5, in one embodiment about 0.5. Should be less than 2. In one embodiment, the pr ocess of the present invention can provide relatively uniform shear forces while using multiple process microchannels

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of multiple process microchannels

To measure the inter-channel shear force uniformity, the average shear force for each channel is calculated and compared. F_{max} is the maximum average channel shear force and F_{min} is t he minimum average shear force. F_{mean} is the mean value of the mean shear force of all cha nnels. SFDF can be calculated from these values. Among the plurality of process microchannel s, in at least one embodiment of the process of the invention, the SFDF is less than about 2, i n one embodiment less than about 1, in one embodiment less than about 0.5, in one embodi ment In embodiments it can be less than about 0.2.

[0128]

The heat exchange fluid may comprise any fluid. These include air, steam, liquid water, gase ous nitrogen, liquid nitrogen, other gases including inert gases, carbon monoxide, carbon diox ide, molten salts, oils such as mineral oil, gaseous hydrocarbons, liquid hydrocarbons and Do w. - including heat exchange fluids such as Dowtherm A and Therminol available from Dow-Un ion Carbide.

Heat

exchange fluids may include first, second and/or third fluids used to create a multiphase mix ture. This can provide process preheating or precooling to increase the overall thermal efficien cy of the process.

[0130]

In one embodiment, the heat exchange channels include process channels in which endother mic or exothermic processes are performed. These heat exchange process channels may be m icrochannels. Examples of endothermic processes that can be carried out in heat exchange ch annels include steam reforming and dehydrogenation reactions. In one embodiment, the incor poration of simultaneous endothermic reactions that provide heat sink enhancement typically allows for heat fluxes approximately an order of magnitude greater than convective cooling he at fluxes. Examples of exothermic processes that can be carried out in heat exchange channel s include water gas shift reactions, methanol synthesis reactions and ammonia synthesis react

ions.

In one embodiment

, the heat exchange fluid undergoes a phase change within the heat exchange channels. This phase change provides additional heating or removal of heat from the process microchannels or liquid channels beyond the heat supplied by convective heating or cooling. In the case of a n evaporating liquid heat exchange fluid, this additional heat transferred from the process mic rochannels can come from the latent heat of vaporization required by the heat exchange fluid. Examples of such phase changes are nucleate boiling oil or water. In one embodiment, the va por mass fraction quality of boiling of the phase change fluid can be up to about 100%, in one embodiment up to about 75%, and in one embodiment up to about 50%. The use of phase c hange or chemical reaction enhancement heat transfer can be made even more advantageous when multiphase mixture generation occurs in concert with the chemical reaction in the proce ss channel

.

In one embodiment, for example, the multiphase mixture may require reactive monomers or other additional heat exchange for the polymerization reaction.

[0133]

The heat flux of convective heating or cooling in the microchannel mixer is about 0.01 to abo ut 125 watts per square centimeter of surface area of the process microchannel in the microc hannel mixer (W/cm 2), in one embodiment about ^{0} . .1 to about 50 W/cm ^{2} , in one embodi ment about 1 to about 25 W/cm ^{2} , in one embodiment about 1 to about 10 W/cm ^{2} . The he at flux of the heating or cooling phase is in the range of about 1 to about 250 W/cm ^{2} , in one embodiment about 1 to about 100 W/cm ^{2} , in one embodiment about 1 to about 50 W/cm ^{2} , in one embodiment Embodiments may range from about 1 to about 25 W/cm ^{2} , and in one embodiment from about 1 to about 10 W/cm ^{2} .

Heat

exchange channels can be used to provide aseptic conditions during the preparation of multi phase mixtures using the process of the present invention. Unlike batch mixers, the process o f the present invention is closed to the environment.

and does not need to be blanketed with an inert gas to isolate it from the environment. Since the heat exchange channels are adjacent to the process microchannels or liquid channels, the y provide relatively short heat transport and diffusion distances to rapidly heat and cool the liq uid in the microchannel mixer and reduce temperature gradients. can be done. As a result, th e process of the present invention can be used to prepare multiphase mixtures that are unsuit able for prolonged heating or that may degrade under large temperature gradients. In one em bodiment, the temperature gradient between the process microchannel wall at the same axial location within the process microchannel and the bulk flow within the process microchannel is

less than about 5°C, and in one embodiment about 2°C. It can be less, and in one embodiment less than about 1°C. Process microchannels with controlled heating and/or cooling and/or heat exchange channels in intimate contact with the second or third fluid stream channels provide a uniform temperature profile among the plurality of process microchannels

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can provide. This allows for uniform heating and cooling at faster rates than can be obtained using conventional processing equipment such as mixing tanks. a temperature difference between the process microchannels of less than about 5°C, in one embodiment less than about 2°C, at least in some axial locations along the length of the process stream in the multichannel microchannel mixer; In one embodiment, it can be less than about 1°C.

[0136]

Heat exchange channels adjacent to either the process microchannels and/or the second or third fluid stream liquid channels can employ temperature zones along the length of such channels. In one embodiment, the temperature in the first zone near the entrance to the process microchannel is maintained at a higher temperature than the second temperature in the second zone near the end of the process microchannel. A cooling or quench zone may be incorporated into the process microchannels to rapidly cool and stabilize the multiphase mixture. Optimal along the length of the process microchannel, including the possibility of sections both before and/or after the mixing zone within the process microchannel that heat and/or cool the feedstock and/or the multiphase mixture product A large number of combinations of heat profiles are possible that allow for a wide range of heat profiles.

Fluid flow rates through the process microchannels (210, 210a, 310, 320, 330 , 340,

410, 520) are from about 0.01 to about 50 lpm, in one embodiment from about 0.01 to about 10 lpm. should be in range. The velocity of fluid flowing through the process microchannels may range from about 0.1 to about 100 m/s, and in one embodiment from about 0.1 to about 10 m/s. The Reynolds number of the fluid flowing through the process microchannels may range from about 25 to about 10,000, and in one embodiment from about 250 to about 5000. The temperature of the fluid entering the process microchannels may range from about 10°C to about 550°C, and in one embodiment from about 25°C to about 400°C. The absolute pressure within the process microchannels may range from about 1 to about 20 atmospheres, and in one embodiment from about 1 to about 5 atmospheres.

[0138]

of the second fluid flow through the second fluid flow channels (270, 270a, 350, 360, 420, 430, 530, 540) and the third fluid flow through the third fluid flow channels (440, 450) Flow rates may range from about 0.01 to about 10 ml/s, in one embodiment from about 0.1 to about 2 ml/s. The velocities of the second and third fluid streams may range from about 0.1 to about 100 m/s, and in one embodiment from about 0.1 m/s to about 10 m/s. The Reynolds number of the second and third fluid streams may range from about 50 to about 5000, and in one embodiment from about 50 to about 500. The temperature of the second fluid stream entering

the second fluid stream channel and the third fluid stream entering the third fluid stream chan nel are from about -10°C to about 650°C, in one embodiment from about 25°C to about 450° C. °C. The absolute pressure within the second and third fluid flow channels may range from a bout 1 to about 25 atmospheres, and in one embodiment from about 1 to about 5 atmosphere s. Apertures (244, 244a, 313, 323, 333, 34
3, 416, 426, 436, 446) is in the range of about 0.005 to about 0.5 atmospheres, and in one e mbodiment about 0.05 to about 0.1 atmospheres. good. A schematic of the formation of bub bles or microbodies by the process of the present invention is shown in FIG
.
Referring to FIG. 21, gas bubbles or microbodies 650 emerge from openings 652 in microchan nels 654 and disperse into first fluid stream 656 . The bubble or microbody may grow in size while attached to the gas or microbody-forming material base 658 within the opening 652, for example, about ten times the size of the opening or more. Ultimately, shear forces at the bas e of the gas or microbody-forming material base 658 separate the bubbles or microbodies fro m the openings, dispersing the bubbles or microbodies into the first fluid stream 656 . In one embodiment, a relatively high open section pressure drop or, correspondingly, a high flow velo city of the second fluid stream through the second fluid stream channel results in a second flui d stream within the first fluid stream. may not be necessary to achieve the distribution of The lower pressure drop or lower flow velocity results in a lower inertia of the second fluid stream flowing through the apertured section, reducing bubble or microbody growth before the bubbl e or microbody separates from the aperture. can give rise to smaller bubbles or microbodies.
The multiphase mixture exiting the process microchannels (210, 210a, 310, 320, 330, 340, 410, 520) has a temperature of about 10°C to about 600°C, in one embodiment about 25°C t o about 450°C
.
It should be within the temperature range.
[0141]
The heat exchange fluid entering the heat exchange channels (290, 370, 380, 590) may be at a temperature ranging from about -40°C to about 300°C, and in one embodiment from abo ut 25°C to about 100°C. The heat exchange fluid exiting the heat transfer channels may have a temperature in the range of about -30°C to about 550°C, and in one embodiment about 30° C to about 200°C. The pressure drop of the heat exchange fluid as it flows through the heat e xchange channels may range from about 0.005 to about 5 atmospheres, and in one embodim ent from about 0.05 to about 1 atmosphere. The Reynolds number of the heat exchange fluid stream flowing through the heat exchange channels is up to about 10,000, in one embodimen t up to about 5000, in one embodiment in the range of about 100 to about 5000, in one embo diment from about 500 to about It should be in the range of 2000. The fluid stream may be preheated in the microchannel mixer or prior to entering the microchannel mixer using any ty pe of heat transfer device including microchannel heaters or heat pipes

.

In one embodiment, the first fluid stream may be preheated in a non-apertured region of the process microchannel upstream of the mixing zone. The multiphase mixture produced in the microchannel mixer is cooled in the microchannel mixer or after exiting the microchannel mix er using any type of heat exchange device including a microchannel heat exchanger. good too. In one embodiment, the multiphase mixture may be quenched to stabilize or remain stable. I n one embodiment, the multiphase mixture may be quenched in non-apertured regions of the process microchannel downstream of the mixing zone. In one embodiment, the multiphase mi xture may be cooled to room temperature or quenched within a time period ranging from abo ut 0.01 to about 100 seconds, in one embodiment from about 0.01 to about 10 seconds. goo d.

[0143]

Using the process of the present invention, a multiphase mixture can be produced at a rate of at least about 0.01 liter per minute, and in one embodiment at least about 1 liter per minut e. In one embodiment, the process can be used to create a multiphase mixture at a rate of at least about 10 liters per second. In one embodiment, optical or thermo-optical properties ma y be adjusted within the process microchannel

.

Examples of techniques for measuring and/or adjusting these optical or thermo-optical proper ties are in-line LSD (laser scattering diffraction) detection for multiphase mixture quality contr ol and analysis, including mean droplet size and span; Viscosity to assess product viscosity an d solids content

holographic imaging and similar methods including interferometry by modulating the propertie s of multiphase mixtures, optical measurements using photometry for bubble or microsphere size measurement.

Example 1 A multiphase microchannel containing an acrylic process microchannel having a r ectangular cross section and internal dimensions of 0.040 x 1.25 x 3 inches (1.02 x 31.75 x 7 6.2 mm)

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A mixing device is constructed. A process microchannel has an open section in one of its side walls. The open section has a nominal aperture or pore size of 0.1 microns and dimensions of 0.010 x 1 x 1.5 inches (0.254 x 25.4 x 38.1 mm). The aperture section is constructed of stain less steel 316L and is supplied by Mott Corporation of Farmington, Conn. under catalog numb er 1110-12-12-018-01-A. The open section is connected to a gas distribution plenum and tubi ng to allow gas flow through the open section and into the process microchannel. The process microchannels are connected to plumbing to allow liquid flow through the process microchann els. Gas enters the process microchannel through the open section and contacts the liquid flo wing through the process microchannel. Bubbles form in the process microchannel as the gas flows through the openings in the open section. The process is carried out using air as the gas

and deionized water as the liquid. The air flow rate varies between 2 and 20 standard cubic ce ntimeters per minute (SCCM) and the water flow rate varies between 10 and 80 milliliters per minute (ml/min). Bubbles are formed with diameters in the range of 5 to 15 microns.

Example

2

The process described in Example 1 is carried out using a gas flow rate of 2 SCCM and a liqui d flow rate of 60 ml/min.

EXAMPLE 3 The process described in Example 1 is carried out using hydrogen as the gas and 1-hexene as the liquid

. Example 4 A high velocity gas (flow rate greater than 1 SLPM) and liquid (flow rate greater than 0.1 liters per minute) are mixed near the inlet of a process microchannel and then subje cted to surface feature regions. flows through The surface feature area has features with a de pth of 0.01 inch and an angle of 45 degrees on one side of the wall. The bulk flow path within the surface features is 0.0065 inches. A foam is produced having uniform cells with an averag e diameter of less than 25 microns. The stream length is 1.5 inches and the channel width or span is 0.5 inches. The process microchannels are near room temperature and ambient press ure. Very small bubbles are observed on and throughout the surface feature area. Example 5

The addition of surface features to the two sides of a microchannel that induces a change fro m laminar flow in the channel to strongly mixed flow in the channel was performed using Flue nt™ . studied by dynamics (CFD) simulations. For the simulation, the properties of the fluid w ere assumed constant, with a density of 5.067 kg/m ^{3} and a viscosity of 3.62e $^{-5}$

kg/m-sec. Boundary conditions were a uniform inlet velocity of 12.13 m/sec and no slip flow on all walls. A grid size of 315,174 cells is used. The geometry assumed is 4.06 mm wide, 0. 318 mm high and 63.5

mm

Rectangular cross-section of a continuous channel with a length of . The section 0 to 3.5 mm downstream of the inlet and the section 0 to 5.0 mm upstream of the outlet contain no mixing surface features (simple rectangular microchannels). Mixing surface features (or grooves) are cut into two opposing walls, each feature being generally rectangular in cross section. The mid dle section of the microchannel (3.5 mm to 58.5 mm downstream of the inlet) contains a mixi ng surface feature. A surface feature diagonally spans one of the channel walls at an angle of 63° from the direction of the mean bulk laminar flow, as shown in FIGS. Each surface feature

is approximately 0.25 mm deep, 0.48 mm wide and 9 mm long. The surface features are arra nged parallel to each other with a spacing of 0.48 mm between the features. The surface feat ures on the opposite wall are the same as the surface features on the first wall, rotated 180° around the channel centerline (the channel geometry is the center point of the inlet face is sy mmetrical about the axis of flow extending from to the center point of the exit face).

[0151]

FIG. 27 shows a plan view of the geometry of surface features simulated by CFD. Both the t op wall and bottom wall mixing components are superimposed. FIG. 28 is an isometric view of a microchannel with mixing components simulated by CFD, showing the direction of flow enter ing the channel. FIG. 29 shows a typical flow path line initiated along the horizontal centerline of the inlet face (drawn between arrows), looking down the flow axis from the inlet face. In cl assical laminar flow, the path line runs in a straight line between the inlet and outlet planes (i n the diagram shown in FIG. 29, the classical laminar flow path line deviates from the center li ne between the arrows). considered not to). In FIG. 30 a side view of the same path line of fl ow initiated along the horizontal centerline of the inlet face is shown (arrows indicate direction of flow). In FIG. 30, the divergence of the flow path lines from the centerline and swirling mot ion among the surface features show improved mixing and reduced heat and mass transport r esistance compared to laminar flow. FIG. 31 shows the flow path line initiated along the vertic al centerline of the inlet face (drawn between the arrows), looking down the flow axis from th e inlet face. In FIG. 31, the swirling motion of the flow suggests improved mixing and reduced heat and mass transfer resistance compared to classical laminar flow. Results from CFD simu lations show that, unlike laminar flow in microchannels, the mixing surface features twist and swirl the flow path in continuous channels, which is expected for laminar flow

.

Push outwards toward the wall faster than you can. The calculated pressure drop is 5.2 kPa.

[0153]

Addition of a gas or a second fluid stream to a microchannel containing surface features crea tes a flow pattern whereby the multiphase mixture is expected to approach laminar flow and b ubbles to be small and well dispersed. A small bubble may be defined as less than 25% of the microchannel gap. Although the invention has been described in connection with specific em bodiments, it is understood that various modifications of these embodiments will become app arent to those skilled in the art upon reading the specification

.

It is therefore intended that the invention disclosed herein encompass such modifications as f all within the scope of the appended claims.

BRIEF DESCRIPTION OF THE FIGURES

[0155]

FIG. 1 is a schematic representation of a microchannel that can be useful in the process of the invention.

FIG. 2 is a flowsheet showing an example of a particular form of the process of the invention i n which a microchannel mixer is used to form a multiphase mixture;

FIG. 3 is a flowsheet showing an example of a multi-phase mixture forming unit used in the p rocess of the invention; A first fluid stream flows through the process microchannel and from an adjacent second fluid stream channel through an open section in the process microchannel to the process microchannel.

It mixes with the second fluid stream entering the channel.

FIG. 4 is a flowsheet showing an example of a multi-phase mixture forming unit used in the p rocess of the invention;

FIG. 5 is a flowsheet showing an example of a multi-phase mixture forming unit used in the p rocess of the invention;

FIG. 6 is a flowsheet showing an example of a multi-phase mixture forming unit used in the p rocess of the invention;

FIG. 7 is a flowsheet showing an example of a multi-phase mixture forming unit used in the p rocess of the invention;

FIG. 8 is a flowsheet showing an example of a multi-phase mixture forming unit used in the p rocess of the invention;

FIG. 9 is a flowsheet showing an example of a multi-phase mixture forming unit used in the p rocess of the invention;

FIG. 10 is a schematic representation of a dual multiphase mixture;

FIG. 11 is a schematic diagram of a microchannel air blowing unit that can be used in accorda nce with the process of the present invention;

12 is a schematic diagram of a microchannel multiphase mixture forming unit that can be use d in the air blowing unit illustrated in FIG. 11; FIG.

FIG. 13 is an SEM image of a porous stainless steel substrate before heat treatment;

14 is a SEM image of the substrate shown in FIG. 8 after being heat treated; FIG.

FIG. 15 is an SEM image of a specialized porous substrate useful in the process of the inventio n;

FIG. 16 is a plan view of an apertured sheet useful in making the apertured sections of proces s microchannels used in the process of the present invention;

FIG. 17 is a plan view of an apertured sheet or plate useful in making the apertured section of the process microchannels used in the process of the invention;

FIG. 18 is an illustration of a relatively thin apertured sheet overlying a relatively thick apertur ed sheet or plate useful in creating the apertured section of the process microchannels used in the process of the present invention;

FIG. 19 shows an example of a relatively thin apertured sheet overlying a relatively thick aper tured sheet or plate useful in creating the apertured sections of process microchannels used in the process of the present invention.

FIG. 20 shows examples of alternative embodiments of apertures that can be used in the aper

tured section of process microchannels used in the process of the present invention; The aperture has a coating partially filling the aperture and overlying the sidewalls of the aperture.

FIG. 21 is a schematic diagram showing the formation of gas bubbles or microbodies during operation of the process of the invention;

FIG. 22 is a schematic representation of surface features that can be provided within a microchannel used in the process of the invention;

FIG. 23 is a schematic representation of surface features that can be provided within a microchannel used in the process of the invention;

FIG. 24 is a schematic representation of surface features that can be provided within a microchannel used in the process of the invention;

FIG. 25 is a schematic representation of surface features that can be provided within a microchannel used in the process of the invention;

FIG. 26 is a schematic representation of surface features that can be provided within a microchannel used in the process of the invention;

FIG. 27 is a plan view of the surface feature geometry simulated by computational fluid dynamics (CFD) as described in Example 5; The surface elements above the upper and lower walls are visible.

FIG. 28 shows surface elements simulated by CFD as described in Example 5;

1 is an isometric view of a microchannel with

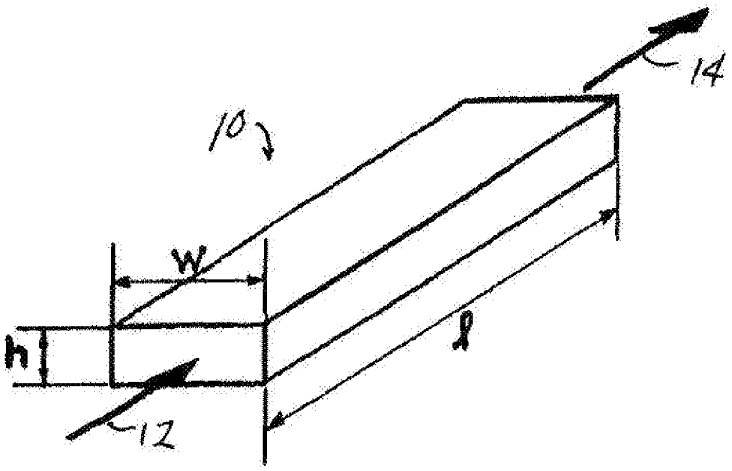
FIG. 29 shows examples of flow pathlines in microchannels initiated along the horizontal centerline of the inlet face (drawn between arrows). Looking down the flow axis from the inlet face as described in Example 5.

FIG. 30 shows flow pathlines (arrows indicate direction of flow) in microchannels initiated along the horizontal centerline of the inlet face. Viewed from the side, as described in Example 5.

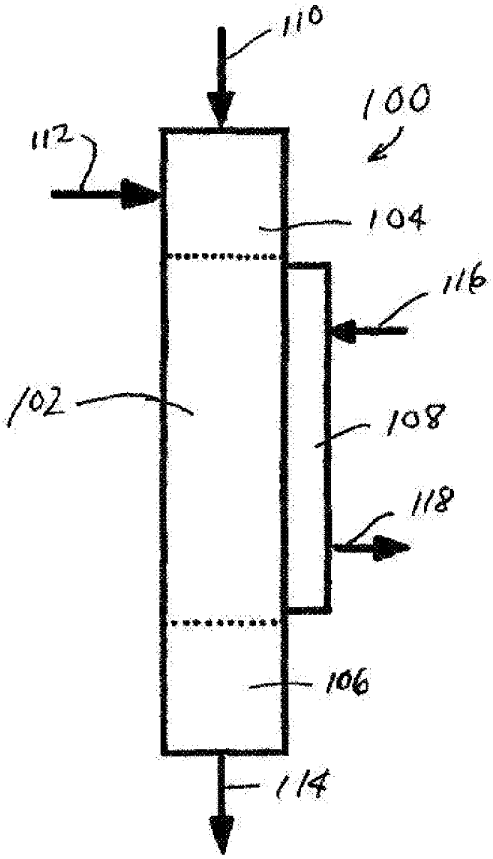
Figure 31 shows flow pathlines in the microchannel initiated along the vertical centerline of the inlet face (drawn between arrows). Looking down the flow axis from the inlet face as described in Example 5.

drawing open —

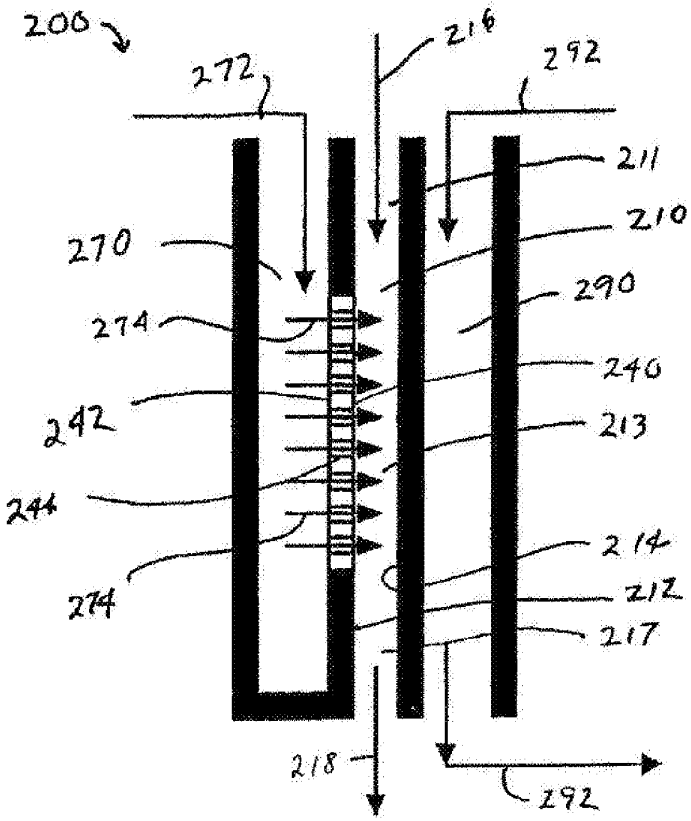
[Fig. 1]



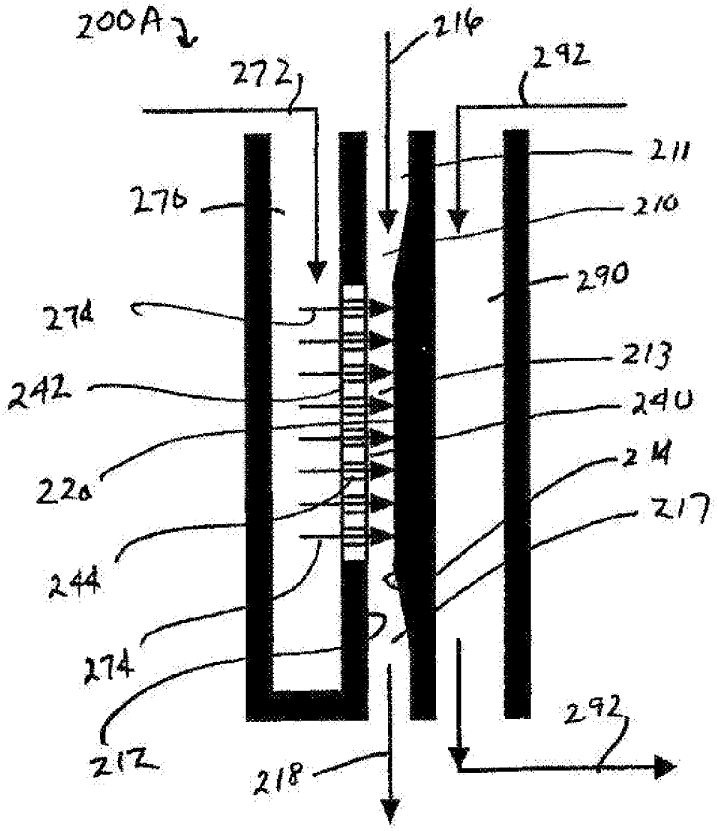
[Figure 2]



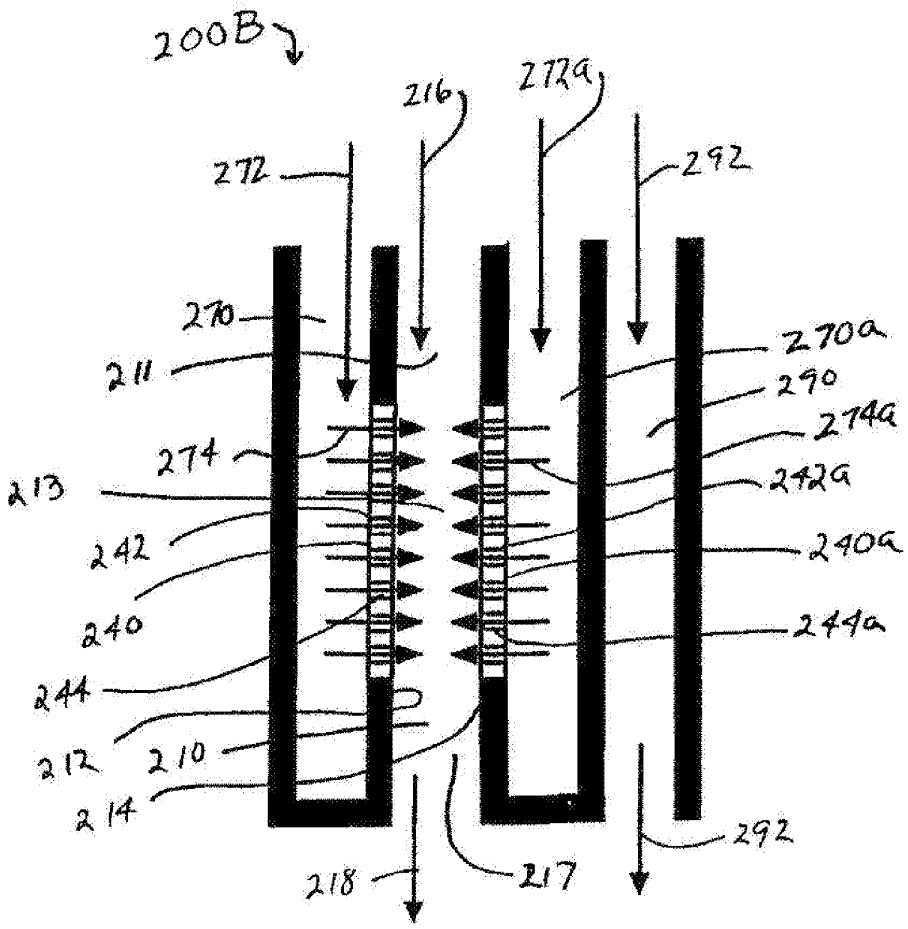
[Figure 3]


200
272
216
292
211
210
270
290
274
240
242
213
244
214
274
212
217
218
292

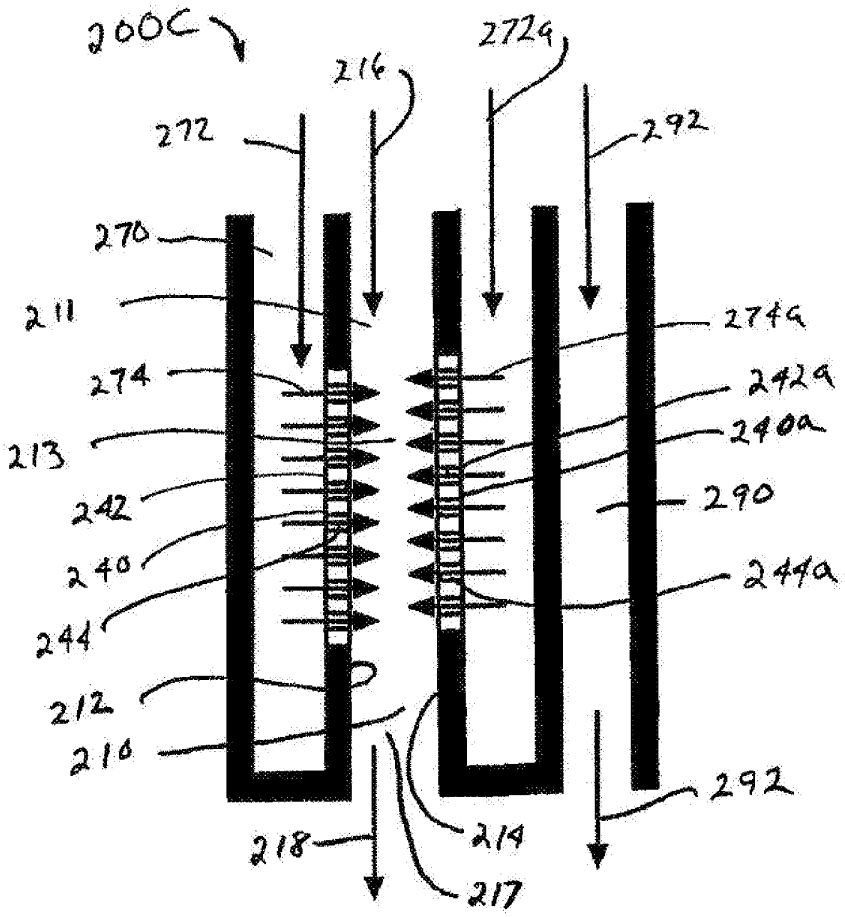
[Figure 4]


200A
272
216
292
211
276
210
290
274
213
242
240
220
214
244
217
274
212
218
292

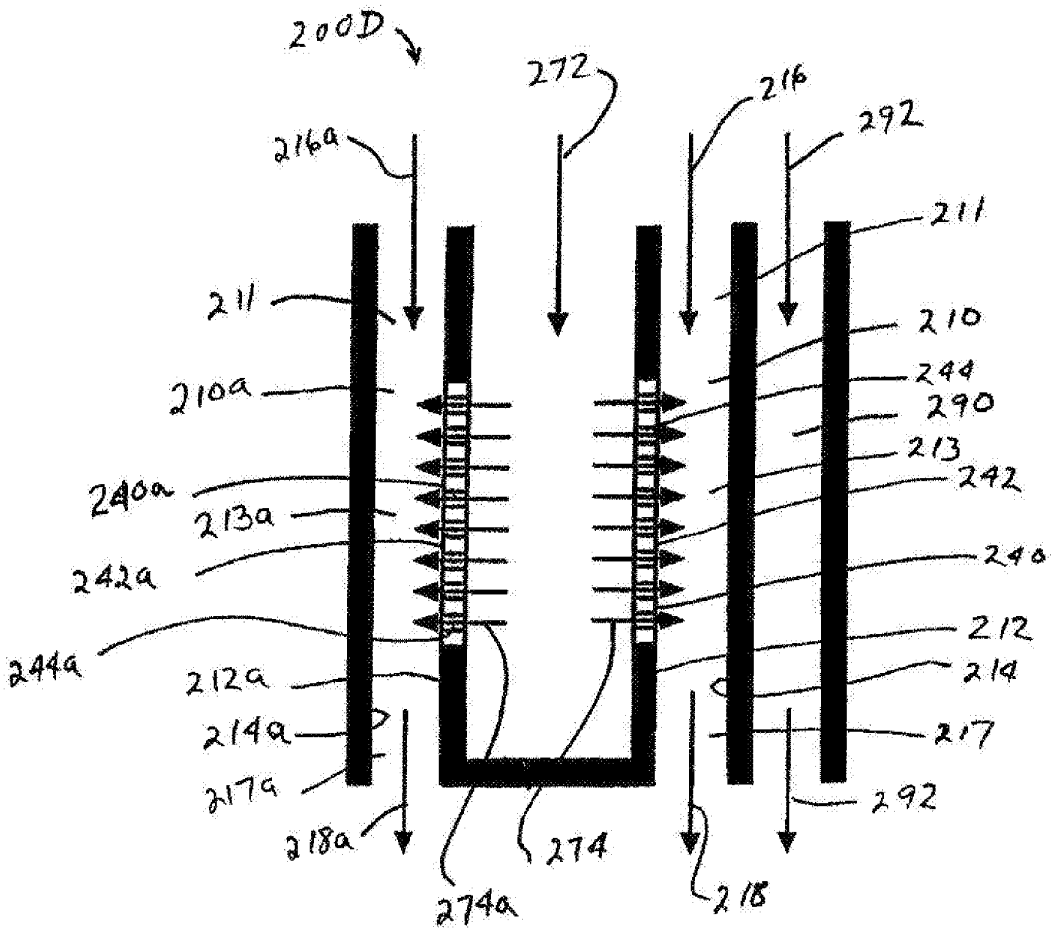
[Figure 5]


200B
216
272a
272
292
270
211
270a
290
274a
274
213
242a
242
240a
240
244a
244
212
210
214
292
218
217

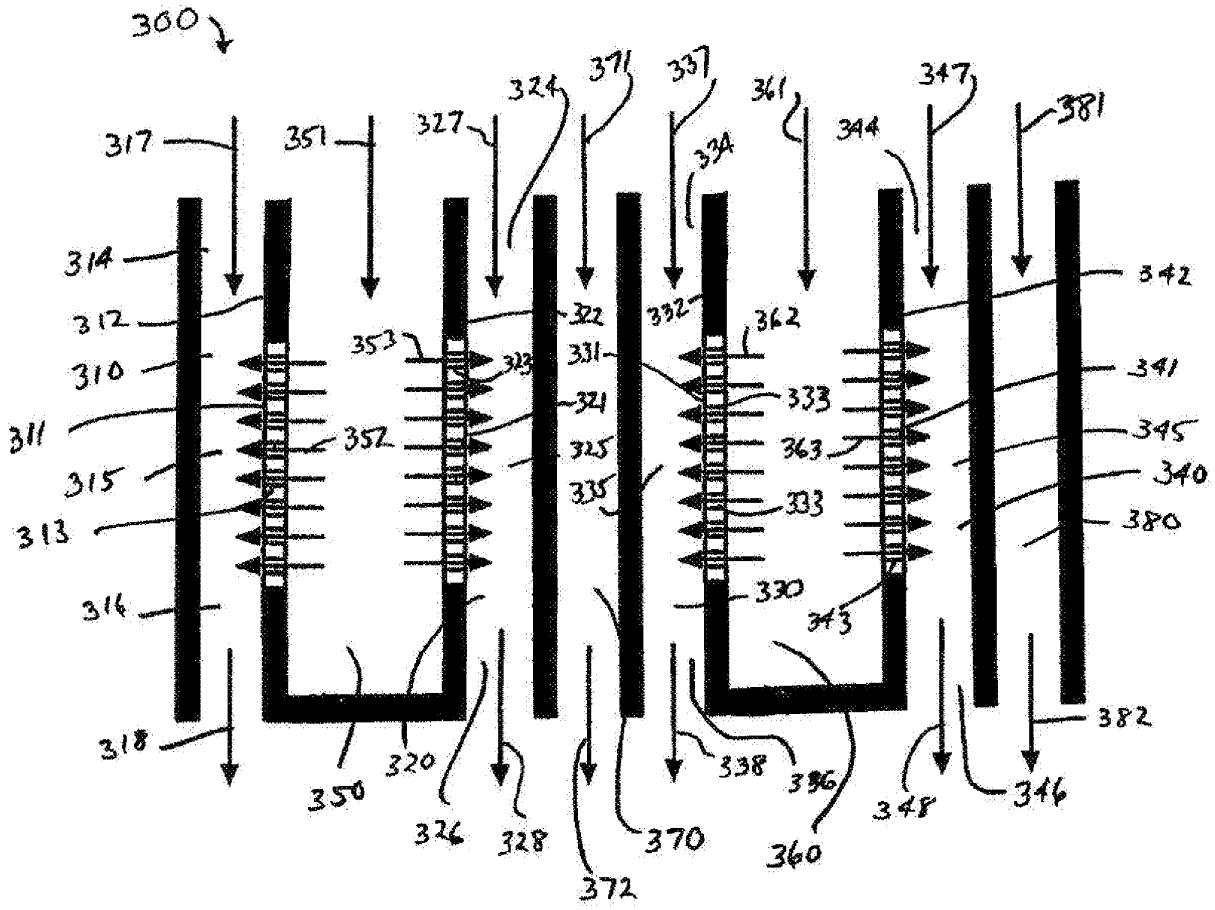
[Fig. 6]


200C
216
272a
292
272
270
211
274a
274
242a
213
240a
242
290
240
244a
244
212
210
292
218
214
217

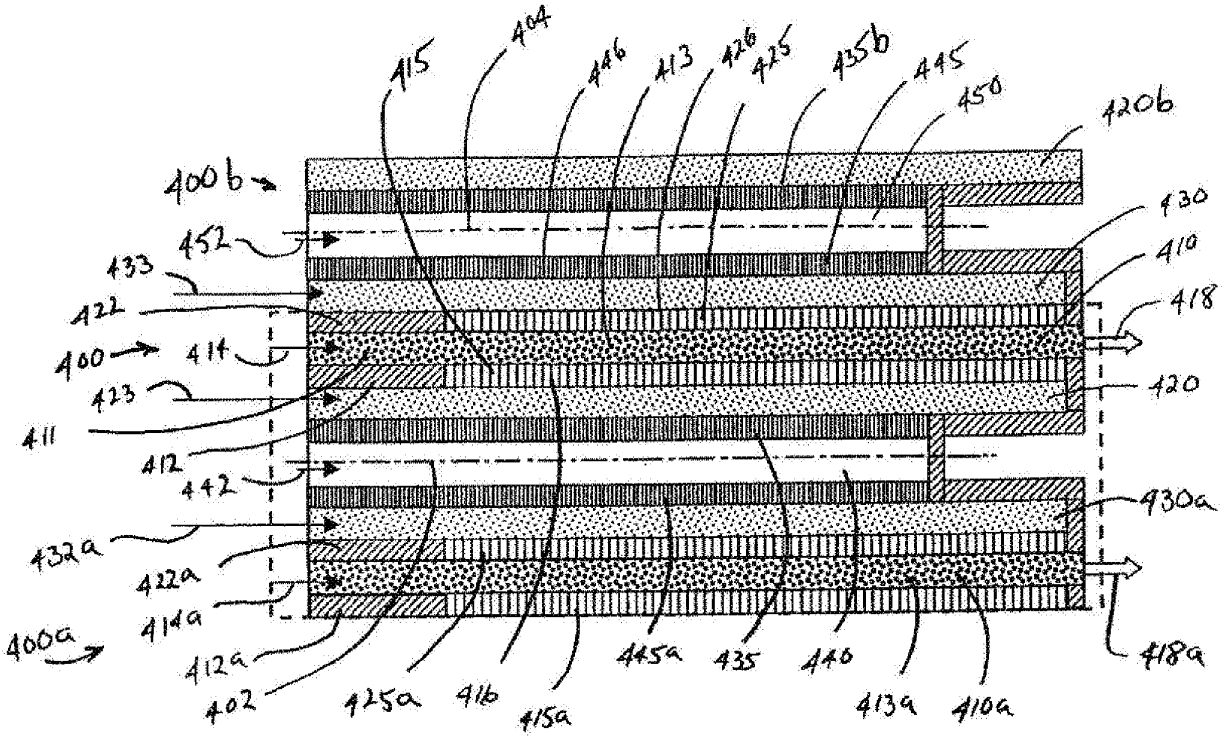
[Fig. 7]


200D
272
216
292
216a
211
211
210
210a
244
290
240a
213
213a
242
242a
240
244a
212
212a
214
214a
217
217a
292
218a
274
274a
218

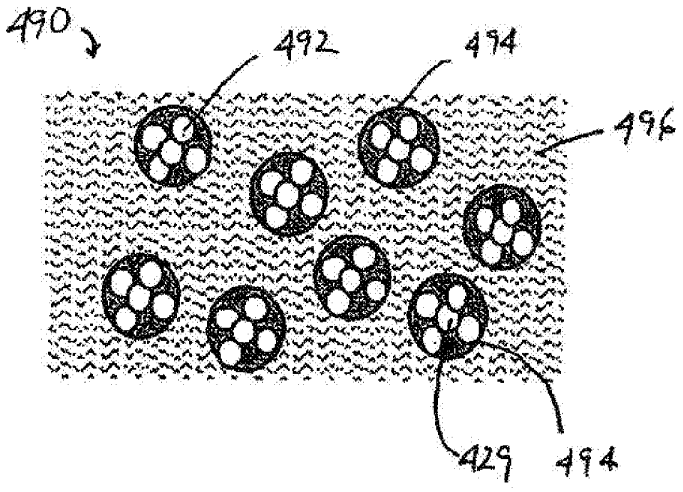
[Fig. 8]


300
317
351
327
324
371
337
361
347
381
344
334
314
312
310
311
315
313
316
318
353
352
322
331
321
325
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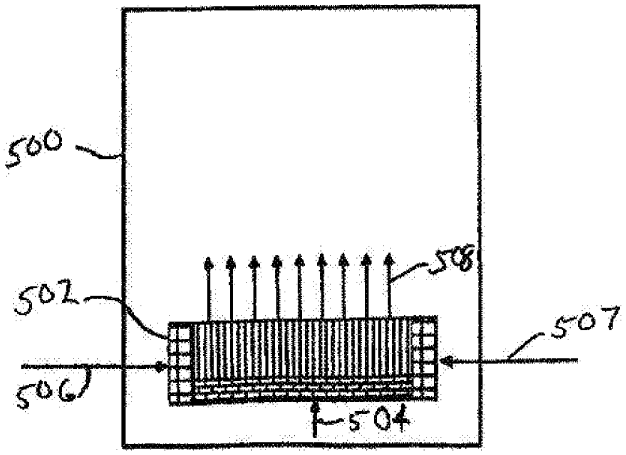
[Fig. 9]


415
404
446
413
426
425
435b
445
450
420b
400b
452
430
433
410
422
418
400
414
420
423
411
412
442
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435
440
413a
410a
418a

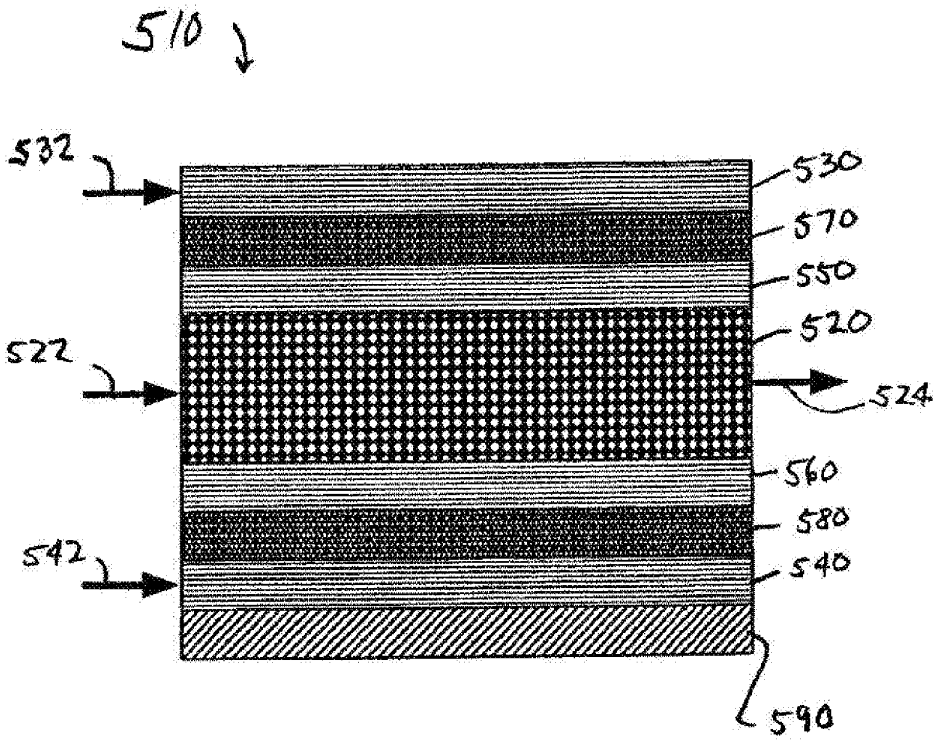
[Fig. 10]



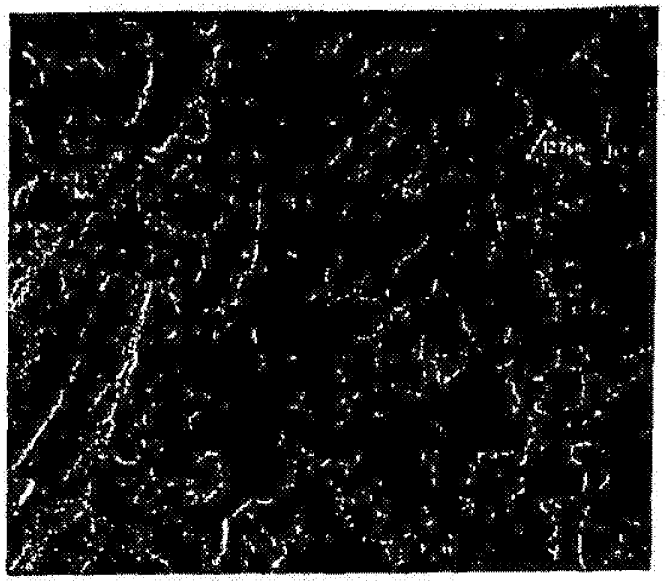
[Fig. 11]



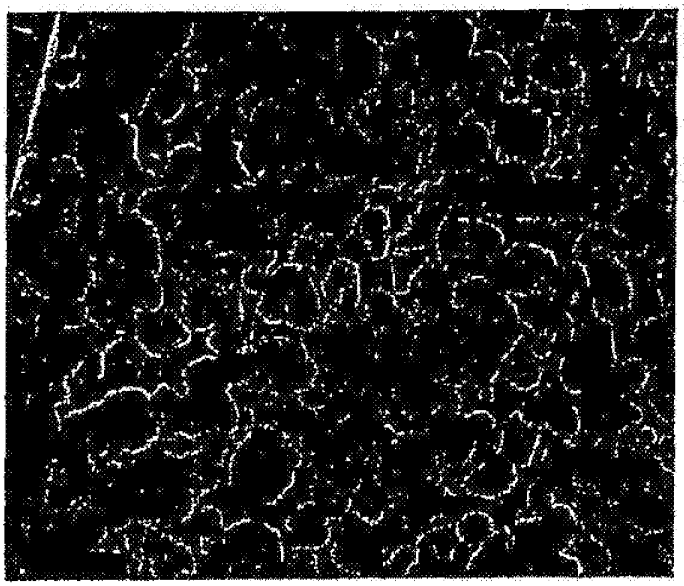
[Fig. 12]



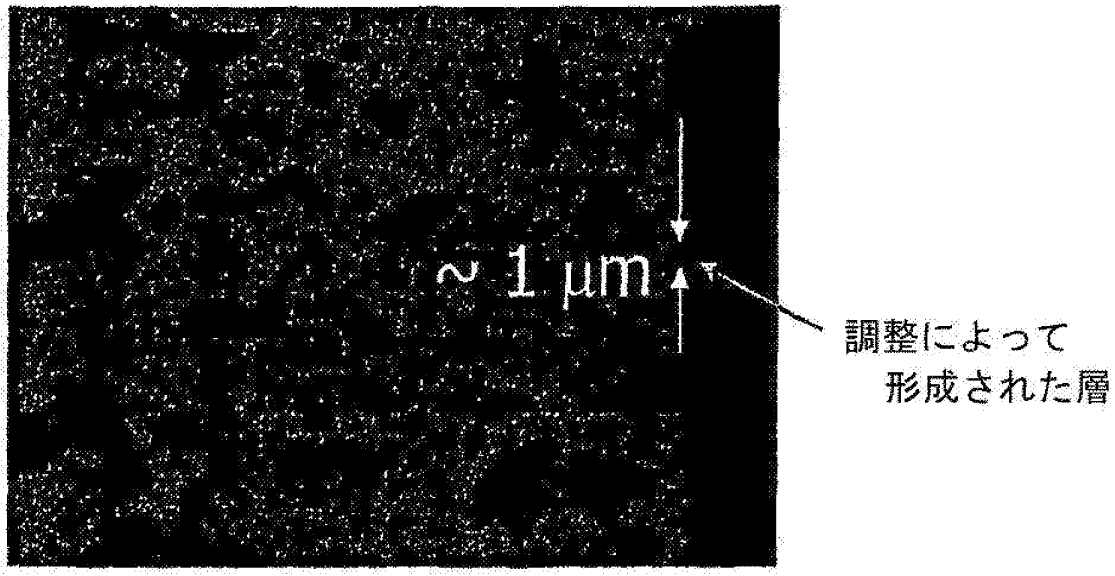
[Fig. 13]



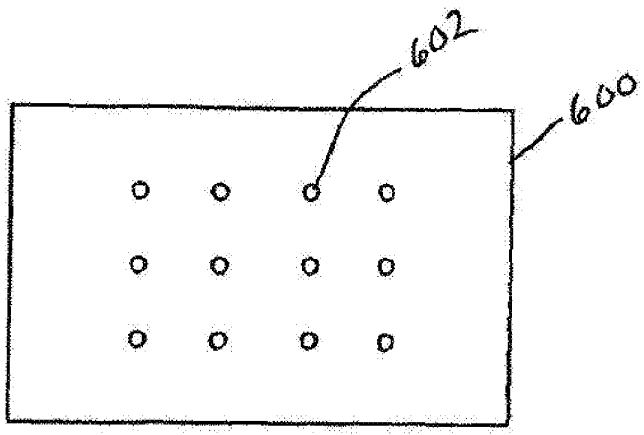
[Fig. 14]



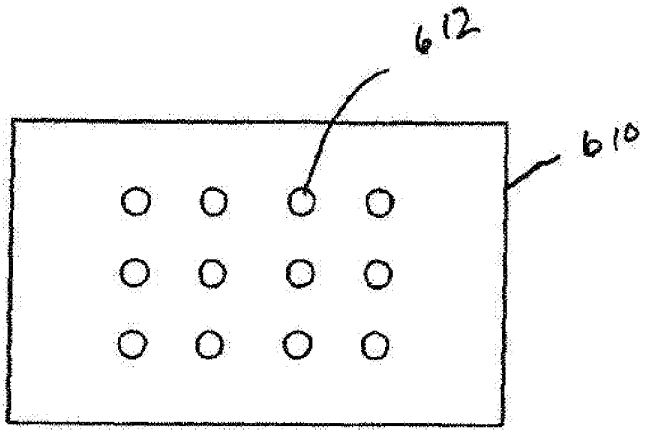
[Fig. 15]



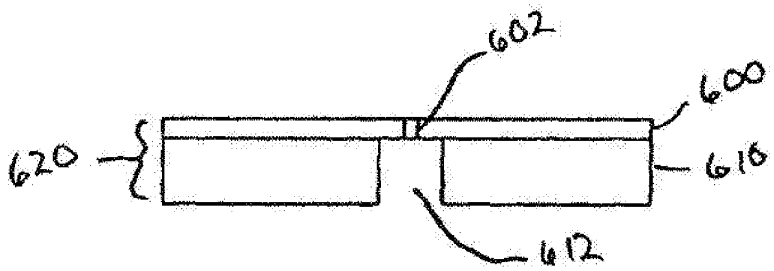
[Fig. 16]



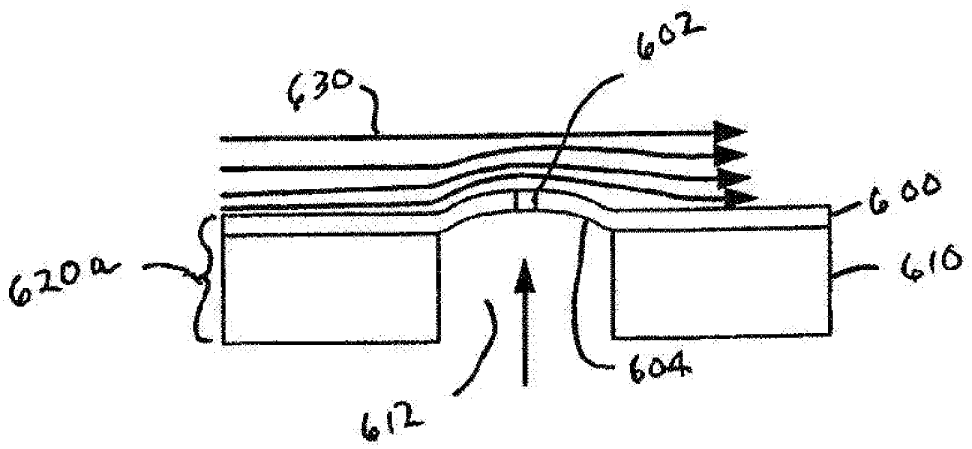
[Fig. 17]



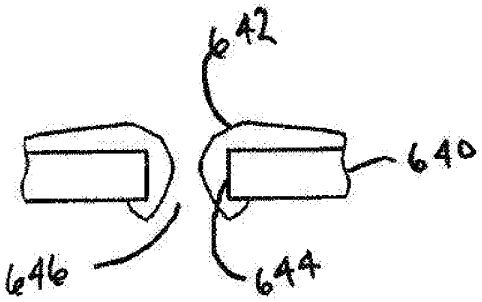
[Fig. 18]



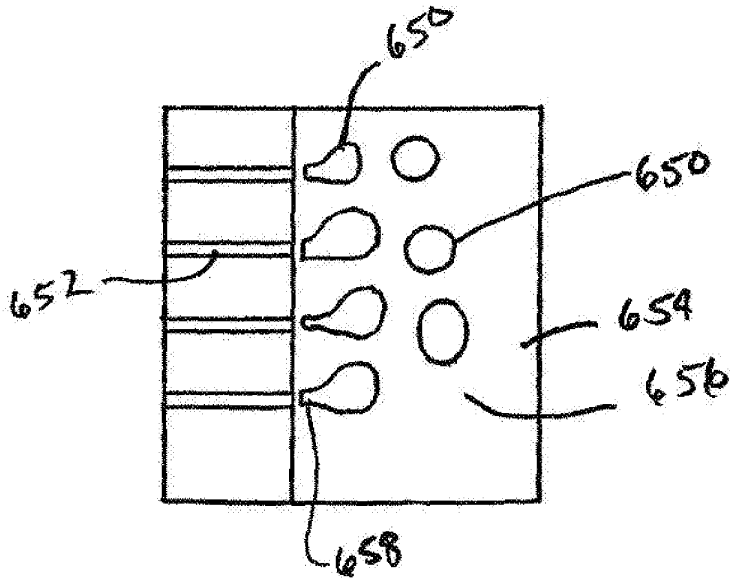
[Fig. 19]



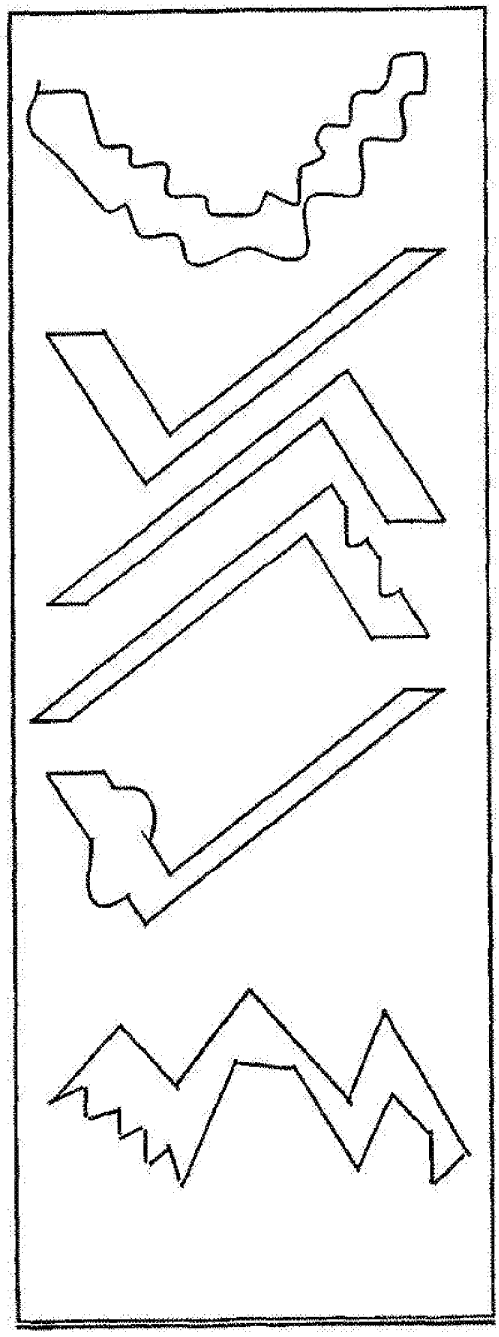
[Fig. 20]



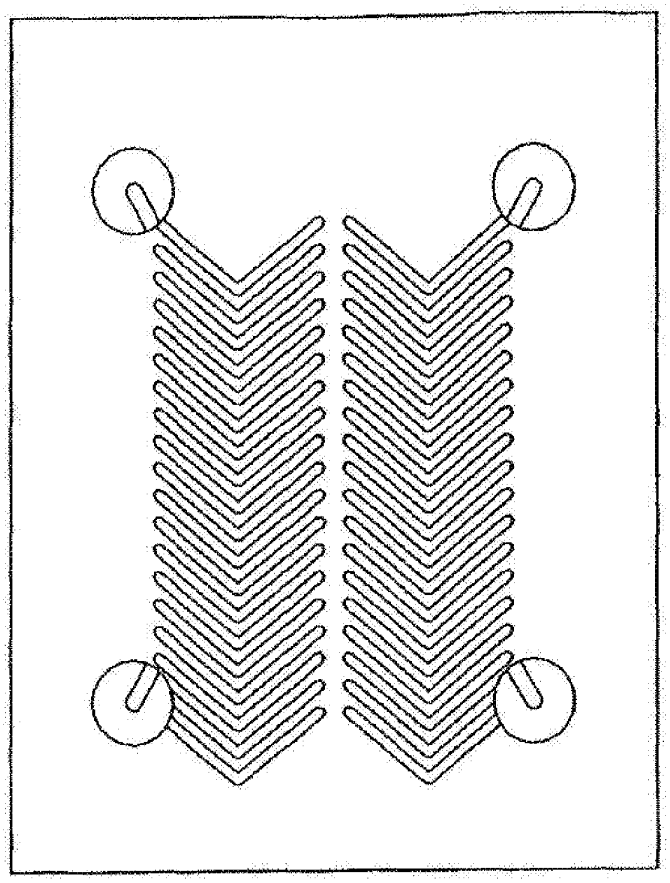
[Fig. 21]



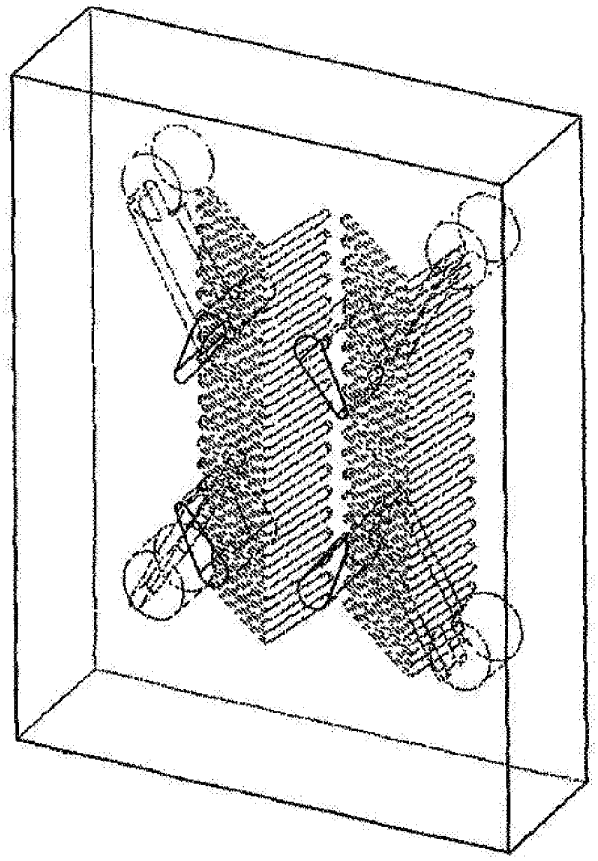
[Fig. 22]



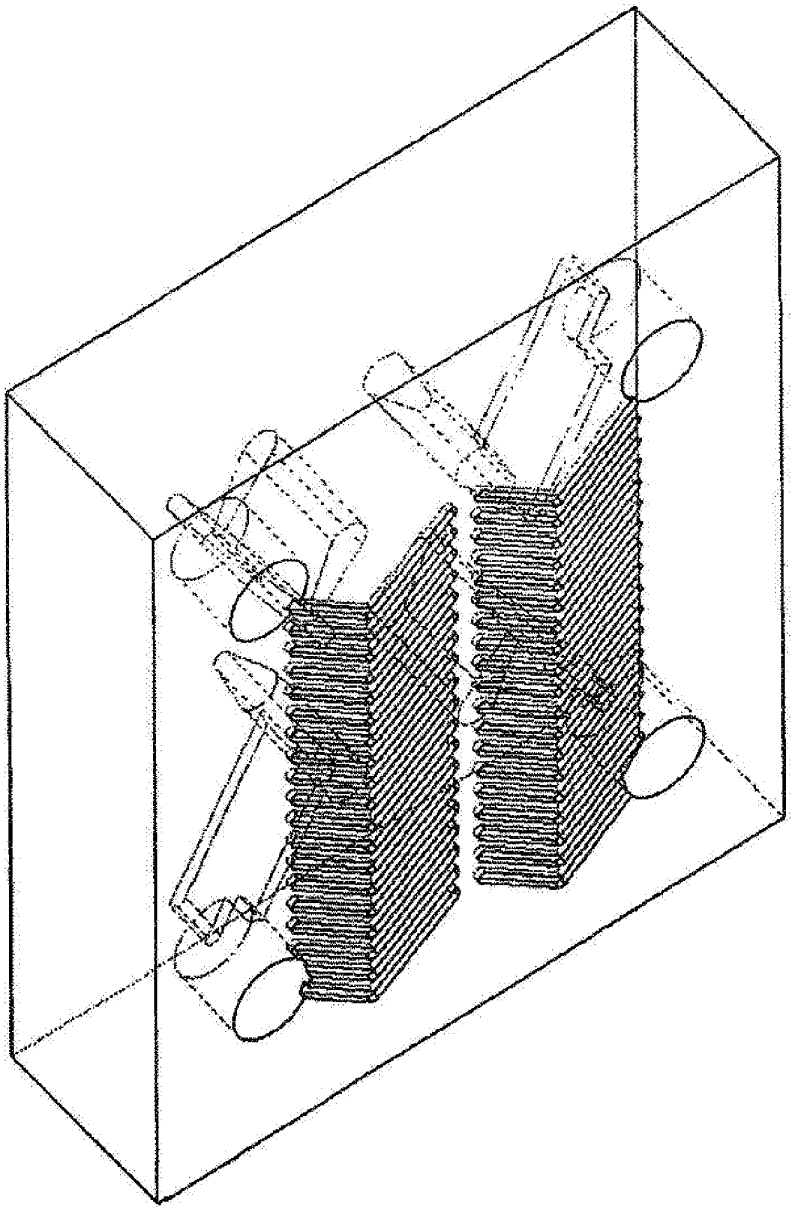
[Fig.23]



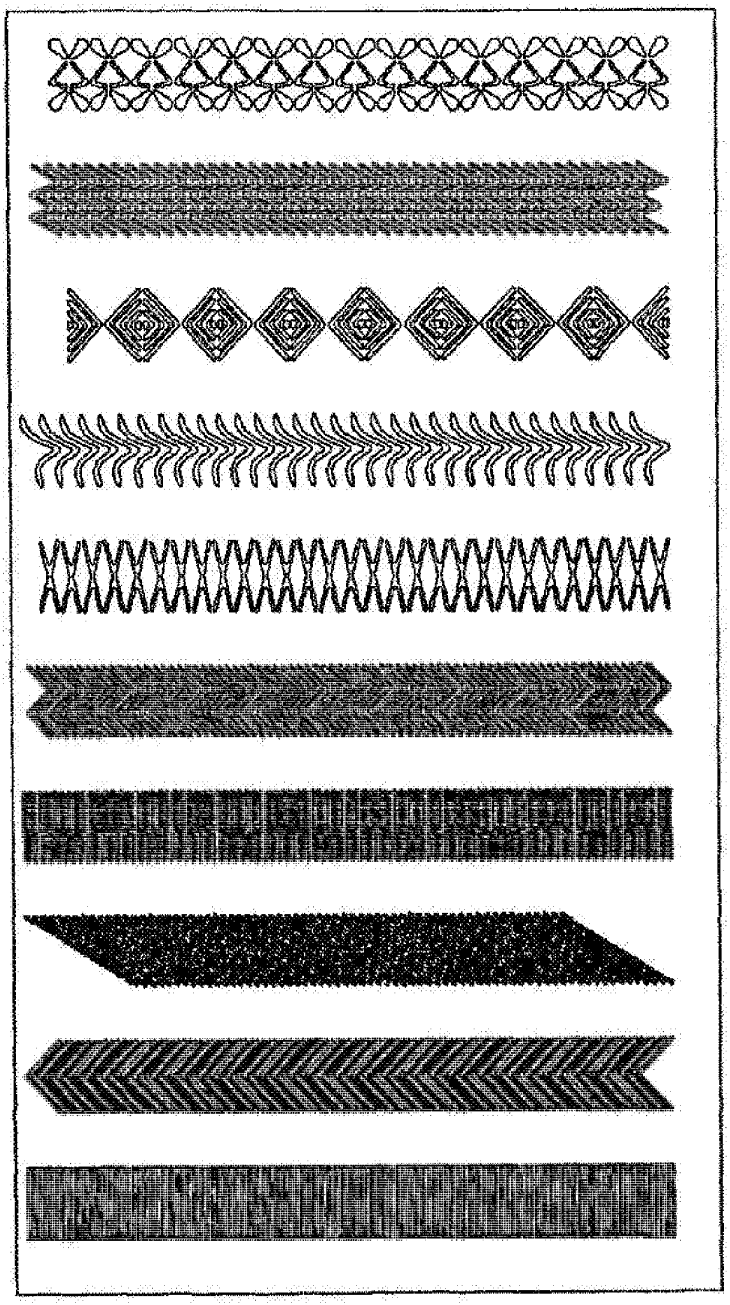
[Fig.24]



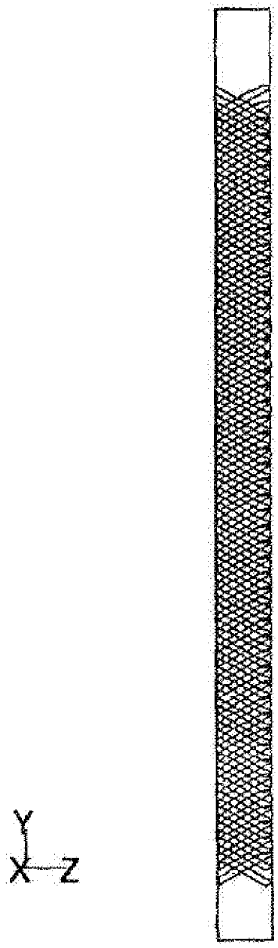
[Fig.25]



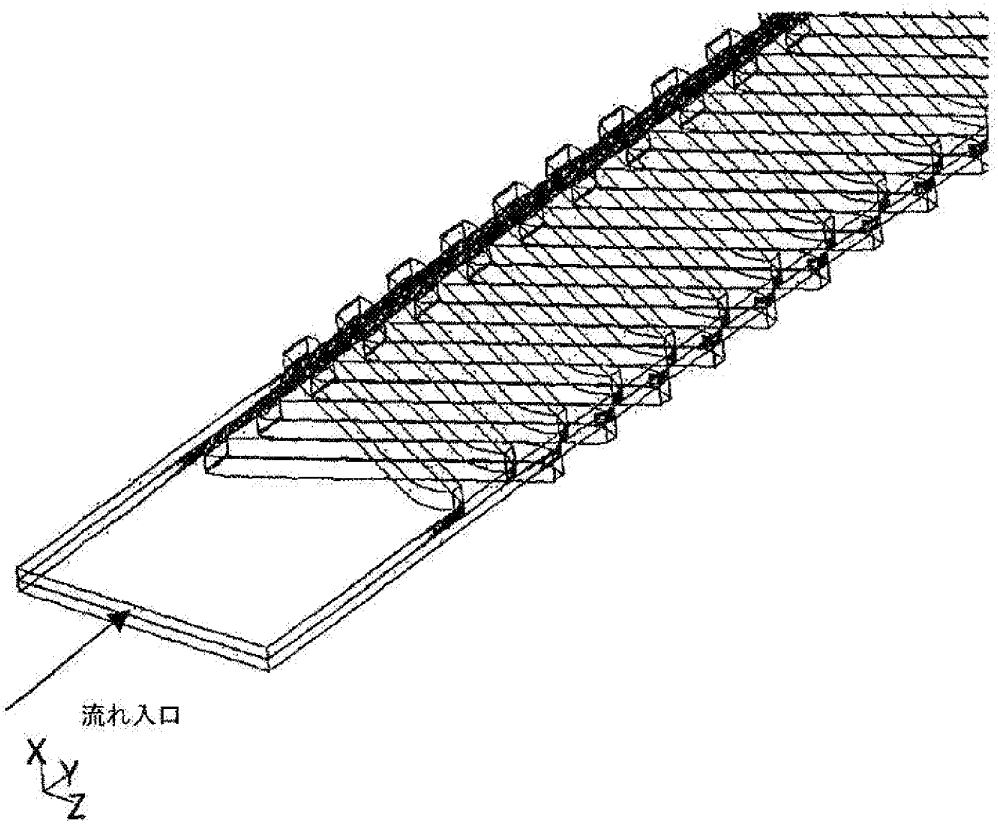
[Fig.26]



[Fig.27]



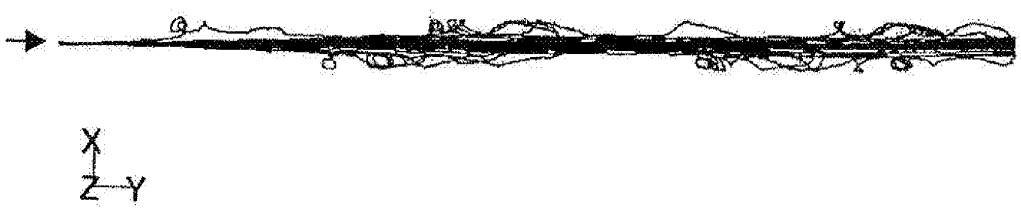
[Fig.28]



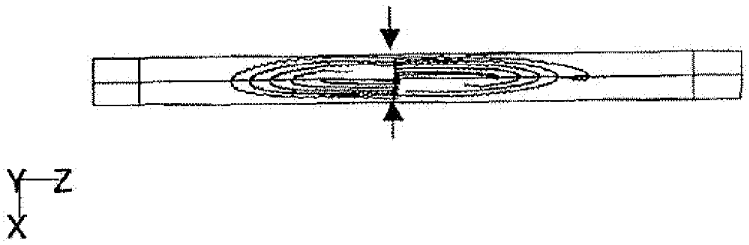
[Fig.29]



[Fig. 30]



[Fig. 31]



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1 2 3 Four Five 6 7 8 9 Ten ...

Magnify and Rotate

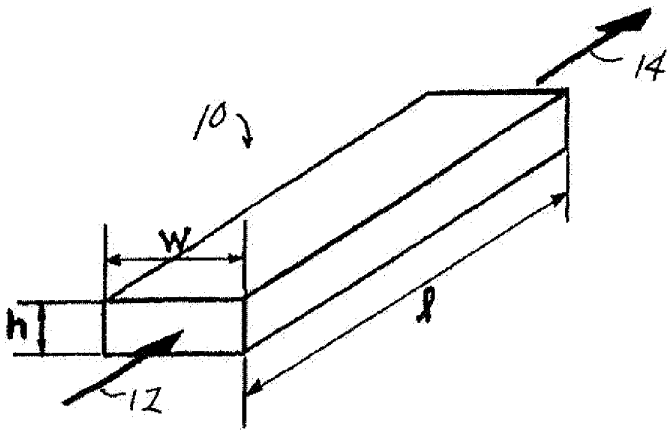


Figure 1

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Bibliographic data: JP5643474 (B2) — 2014-12-17

MULTIPHASE MIXING PROCESS USING MICROCHANNEL PROCESS TECHNOLOGY

Inventor(s): トンコヴィッチ， アンナ ， リー, ; シルヴァ ， ローラ ， ジェー . , ; ヘッセ ， デイヴィッド ジョン, ; マルキアンド ， マイケル アラン, ; ラモント ， マイケル ジェイ, ; キウ ， ドンミン, ; ドリッツ ， テレンス アンドリュー , ; パグノット ， クリスティーナ ， エム . , ; スティーブンソン ， リック, ; ペリー ， スティーブン ， ティー . , ; ファネッリ ， マダレナ, ; アローラ ， ラヴィ, ; ヤン ， ビン, ; フィッツジェラルド ， ショーン, ; サリバン ， ティム, ; ジャロッシュ ， カイ トッド ポール, ; ユシャック ， トーマス

Applicant(s): ヴェロシス，インク ．

Classification: - international: ***A23L27/18; A23L27/60; A23L29/00; B01F23/30; C09K23/00***

- cooperative: **B01F23/232 (EP, US); B01F23/41 (EP, US); B01F23/4144 (EP); B01F23/4145 (EP); B01F25/3142 (EP, US); B01F25/31421 (EP, US); B01F25/31424 (EP, US); B01F33/30 (EP, US); B01F35/92 (EP, US); B01J19/0093 (EP, US); F28F3/12 (EP, US);** B01F2215/0431 (EP, US); B01F2215/045 (EP, US); B01F2215/0472 (EP, US); B01F23/4144 (US); B01F23/4145 (US); B01J2219/00783 (EP, US); B01J2219/00788 (EP, US); B01J2219/00822 (EP, US); B01J2219/00826 (EP, US); B01J2219/00828 (EP, US); B01J2219/00831 (EP, US); B01J2219/00833 (EP, US); B01J2219/00835 (EP, US); B01J2219/0086 (EP, US); B01J2219/00873 (EP, US); B01J2219/00889 (EP, US); F28D2021/0052 (EP, US); F28F2260/02 (EP, US); Y10S516/928 (EP, US); Y10S516/929 (EP, US); Y10T436/2575 (EP, US)

Application number: JP20070534825 20050930 Global Dossier

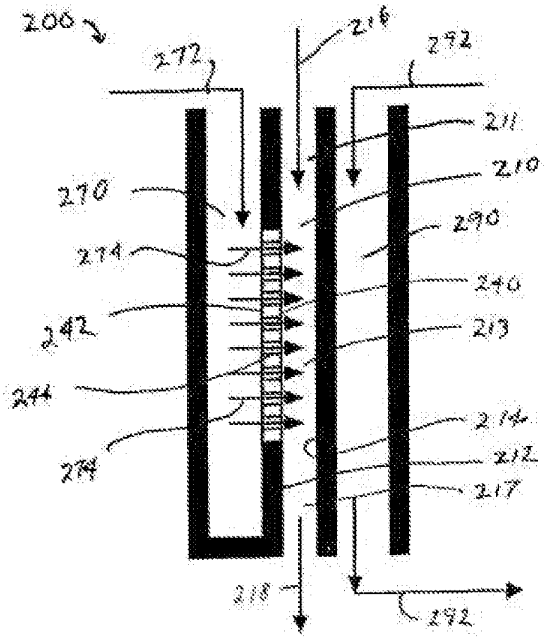
Priority number(s): US20040615509P 20041001 ; WO2005US35330 20050930

Also published as: CA2582378 (A1) CA2582378 (C) CN101084061 (A) CN101084061 (B) EP1804964 (A1) more

Abstract not available for JP5643474 (B2)
Abstract of corresponding document: WO2006039568 (A1)

The disclosed invention relates to a process for making a multiphase mixture, comprising: flowing a first fluid stream (216) through a process microchannel (210), the first fluid stream (216) comprising at least one liquid and/or at least one gas, the process microchannel (210) having an apertured section (244); flowing a second fluid

stream (272) through the apertured section (244) into the process microchannel (210) in contact with the first fluid stream (216) to form the multiphase mixture (218), the second fluid stream (272) comprising at least one gas and/or at least one microbody-forming material, the first fluid stream (272) forming a discontinuous phase dispersed in the continuous phase. Heat exchange may also take place between the process microchannel (210) and a heat source or heat sink (290).



(19)日本国特許庁(JP)　(12)特　許　公　報(B2)　(11)特許番号
特許第5643474号
(P5643474)
(45)発行日　平成26年12月17日(2014.12.17)　(24)登録日　平成26年11月7日(2014.11.7)

(51)Int.Cl.		F I		
B01F 3/04	(2006.01)	B01F	3/04	A
B01F 1/00	(2006.01)	B01F	1/00	A
B01F 5/06	(2006.01)	B01F	1/00	B
B01F 15/06	(2006.01)	B01F	1/00	G
		B01F	5/06	

請求項の数 35　(全 47 頁)　最終頁に続く

(21)出願番号　特願2007-534825 (P2007-534825)
(86)(22)出願日　平成17年9月30日 (2005.9.30)
(65)公表番号　特表2008-514428 (P2008-514428A)
(43)公表日　平成20年5月8日 (2008.5.8)
(86)国際出願番号　PCT/US2005/035330
(87)国際公開番号　WO2006/039568
(87)国際公開日　平成18年4月13日 (2006.4.13)
審査請求日　平成20年9月29日 (2008.9.29)
審判番号　不服2012-12061 (P2012-12061/J1)
審判請求日　平成24年6月27日 (2012.6.27)
(31)優先権主張番号　60/615,509
(32)優先日　平成16年10月1日 (2004.10.1)
(33)優先権主張国　米国(US)

(73)特許権者　505056694
ヴェロシス，インク．
アメリカ合衆国　オハイオ州　４３０６４　プレイン　シティ，コーポレイト　プルバード　７９５０
(74)代理人　110000062
特許業務法人第一国際特許事務所
(72)発明者　トンコヴィッチ，　アンナ，　リー
アメリカ合衆国　オハイオ州　４３０１６　ダブリン，　バラントレー　プレイス　６４９３
(72)発明者　シルヴァ，　ローラ，　ジェー．
アメリカ合衆国　オハイオ州　４３０１７　ダブリン，　ダンフリーズ　コート　ウエスト　５５８３
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(54)【発明の名称】マイクロチャネルプロセス技術を用いる多相混合プロセス

(57)【特許請求の範囲】
【請求項１】
多相混合物を作るためのプロセスであって、
第一の流体流をプロセスマイクロチャネルの中に流す工程であって、前記第一の流体流は、少なくとも一種類の液体を含む液体流であり、前記プロセスマイクロチャネルは、複数の開口を含む開口区間を有する工程であって、前記開口区間は前記プロセスマイクロチャネル内を流れる前記第一の流体流の流路に沿った長さと前記プロセスマイクロチャネル内を流れる前記第一の流体流の流路に垂直な厚さ寸法を有し、
前記厚さを有する前記開口区間を通して第二の流体流を前記プロセスマイクロチャネルの中に流し、前記第一の流体流と接触させて前記多相混合物を形成させる工程であって、前記第二の流体流は、少なくとも一種類の気体を含む気体流であり、前記第一の流体流は、前記多相混合物の中の連続相を形成し、前記第二の流体流は、前記連続相の中の分散した不連続相を形成する工程、
を含み、
前記第二の流体流は、前記プロセスマイクロチャネルに隣接する第二の流体流チャネルから前記開口区間を通って流れ、
熱交換チャネルは、前記プロセスマイクロチャネル、前記第二の流体流チャネル、または前記プロセスマイクロチャネルと前記第二の流体流チャネルとの両方に隣接して、前記プロセスマイクロチャネルと前記熱交換チャネルとの間、前記第二の流体流チャネルと熱交換チャネルとの間、あるいは前記プロセスマイクロチャネルと前記第二の流体流チャネ

ルとの両方と熱交換チャネルとの間で熱が交換され、熱交換液体が熱交換チャネル内にある、プロセス。

【請求項２】

前記第一の流体流と前記第二の流体流とは、前記プロセスマイクロチャネルの中の混合ゾーンの中で互いに接触する、請求項１に記載のプロセス。

【請求項３】

前記プロセスマイクロチャネルは、狭くなった断面を有する混合ゾーンを有する、請求項１または２に記載のプロセス。

【請求項４】

前記プロセスマイクロチャネルは、離間した壁と、前記離間した壁のそれぞれの中に開口区間を有し、前記第二の流体流は、開口区間のそれぞれを通って前記プロセスマイクロチャネルに流入する、請求項１から３のいずれか一項に記載のプロセス。

【請求項５】

前記プロセスマイクロチャネルは、第一のプロセスマイクロチャネルであり、多相混合物形成ユニットの中にあり、該多相混合物形成ユニットは、第二のプロセスマイクロチャネル、および前記第一のプロセスマイクロチャネルと前記第二のプロセスマイクロチャネルとの間に位置する第二の流体流チャネルを含み、各プロセスマイクロチャネルは、開口区間を有する壁を有し、前記第一の流体流は、前記第一のプロセスマイクロチャネルおよび前記第二のプロセスマイクロチャネルを通って流れ、前記第二の流体流は、前記第二の流体流チャネルから、前記開口区間を通って前記第一のプロセスマイクロチャネルの中に流れて前記第一の流体流と接触し、前記開口区間を通って前記第二のプロセスマイクロチャネルの中に流れて前記第一の流体流と接触する、請求項１から４のいずれか一項に記載のプロセス。

【請求項６】

多相混合物を作るためのプロセスであって、

第一の流体流をプロセスマイクロチャネルの中に流す工程であって、前記第一の流体流は、少なくとも一種類の液体を含む液体流であり、前記プロセスマイクロチャネルは、複数の開口を含む開口区間を有する工程であって、前記開口区間は前記プロセスマイクロチャネル内を流れる前記第一の流体流の流路に沿った長さと前記プロセスマイクロチャネル内を流れる前記第一の流体流の流路に垂直な厚さ寸法を有し、

第二の流体流を第二の流体流チャネルの中に流す工程であって、前記第二の流体流は、少なくとも一種類の液体を含む液体流であり、前記プロセスマイクロチャネルは、前記第二の流体流をプロセスマイクロチャネルに流入させることができるようにする複数の開口を含む開口区間を有する工程であって、前記開口区間は第二の流体流チャネル内を流れる前記第二の流体流の流路に沿った長さと前記第二の流体流チャネル内を流れる前記第二の流体流の流路に垂直な厚さ寸法を有し、

第三の流体流を第三の流体流チャネルの中に流す工程であって、前記第三の流体流は気体を含む気体流であり、第二の流体流チャネルは、前記第三の流体流を第二の流体流チャネルに流入させることができるようにする複数の開口を含む別の開口区間を有する工程であって、前記別の開口区間は前記第三の流体流チャネル内を流れる前記第三の流体流の流路に沿った長さと前記第三の流体流チャネル内を流れる前記第三の流体流の流路に垂直な厚さ寸法を有し、

前記第三の流体流を前記第三の流体流チャネルから前記厚さを有する前記別の開口区間を通して前記第二の流体流チャネルに流入させて、前記第二の流体流と接触させて別の多相混合物を形成させる工程、

前記別の多相混合物を前記厚さを有する前記開口区間を通して前記プロセスマイクロチャネルに流入させて、前記第一の流体流と接触させて前記多相混合物を形成させる工程、

熱交換チャネルは、前記プロセスマイクロチャネルおよび／または前記第二の流体流チャネルまたは前記第三の流体流チャネルのどちらかに隣接し、前記プロセスチャネルと前記熱交換チャネルとの間で熱が交換され、熱交換液体が熱交換チャネル内にある工程、

を含むプロセス。
【請求項７】
前記プロセスマイクロチャネルは、平行な離間したシートおよび／またはプレートから形成される、請求項１から６のいずれか一項に記載のプロセス。
【請求項８】
第二の流体流チャネルは、平行な離間したシートおよび／またはプレートから形成される請求項７に記載のプロセス。
【請求項９】
前記熱交換チャネルは、平行な離間したシートおよび／またはプレートから形成される請求項８に記載のプロセス。
【請求項１０】
前記プロセスは、マイクロチャネルミキサの中で実行され、前記マイクロチャネルミキサは、複数の前記プロセスマイクロチャネルおよび第二の流体流チャネルを含み、各プロセスマイクロチャネルは、開口区間を有する壁および隣接する第二の流体流チャネルを有し、前記第二の流体流は、前記第二の流体流チャネルから前記開口区間を通って前記プロセスマイクロチャネルに流入して前記第一の流体流と接触し、前記プロセスマイクロチャネルおよび第二の流体流チャネルは、平行な離間したシートおよび／またはプレートから形成され、前記プロセスマイクロチャネルおよび第二の流体流チャネルは、互いに隣接し、横に並べられた交互平面、または上下に積み重ねられた交互平面の中に配置される、請求項１から９のいずれか一項に記載のプロセス。
【請求項１１】
前記マイクロチャネルミキサは、平行な離間したシートおよび／またはプレートから形成される複数の熱交換チャネルをさらに備え、前記熱交換チャネルは、前記プロセスマイクロチャネル、前記第二の流体流チャネル、または前記プロセスマイクロチャネルと前記第二の流体流チャネルとの両方に隣接する、請求項１０に記載のプロセス。
【請求項１２】
前記プロセスマイクロチャネルおよび前記第二の流体流チャネルは、同心状に配置された円形の管を含む、請求項１から６のいずれか一項に記載のプロセス。
【請求項１３】
前記プロセスは、マイクロチャネルミキサの中で実行され、前記マイクロチャネルミキサは、複数の前記プロセスマイクロチャネルを含み、前記プロセスマイクロチャネルのそれぞれの中で別個の多相混合物が形成され、前記プロセスマイクロチャネルの少なくとも二つの中で形成された前記多相混合物は互いに異なる、請求項１から１２のいずれか一項に記載のプロセス。
【請求項１４】
前記開口区間は、シートおよび／またはプレートと、前記シートおよび／またはプレートの中にある複数の開口とを含む、請求項１から１３のいずれか一項に記載のプロセス。
【請求項１５】
前記シートおよび／またはプレートの少なくとも一部の上を覆っており、前記開口の一部に充填される、コーティングを有し、または、前記シートおよび／またはプレートは熱処理される、請求項１４に記載のプロセス。
【請求項１６】
前記開口区間は、多孔質材料から作られ、前記多孔質材料は、金属、非金属、酸化されている、またはアルミナ、ニッケルまたはそれらの組み合わせでコーティングされている、請求項１から１５のいずれか一項に記載のプロセス。
【請求項１７】
前記第一の流体流は、水または有機液体を含み、前記第二の流体流は、少なくとも一種類の気体を含み、または前記第二の流体流は、空気、水素、窒素、二酸化炭素またはそれらの二種類以上の混合物から選択される気体を含む、請求項１から１６のいずれか一項に記載のプロセス。

【請求項１８】
前記プロセスマイクロチャネルは、前記プロセスマイクロチャネルを通る前記第一の流体流の前記流れに垂直な、１０ミリメートル以下の内部寸法を有する、請求項１から１７のいずれか一項に記載のプロセス。
【請求項１９】
前記第二の流体流は、第二の流体流チャネルから前記開口区間を通って流れ、前記第二の流体流チャネルは、前記第二の流体流チャネルを通る前記第二の流体流の前記流れに垂直な、１００センチメートル以下の内部寸法を有する、請求項１から１８のいずれか一項に記載のプロセス。
【請求項２０】
前記熱交換チャネルは、前記熱交換チャネルを通る熱交換流体の前記流れに垂直な５０ミリメートル以下の内部寸法を有する、請求項１から１９のいずれか一項に記載のプロセス。
【請求項２１】
前記プロセスマイクロチャネル、第二の流体流チャネルおよび熱交換チャネルは、鋼、モネル、インコネル、アルミニウム、チタン、ニッケル、銅、真鍮、これら金属の任意のものの合金、重合体、セラミック、ガラス、重合体とガラス繊維とを含むコンポジット、石英、ケイ素、またはそれらの二種類以上の組み合わせを含む材料で作られている、請求項１から２０のいずれか一項に記載のプロセス。
【請求項２２】
前記熱交換流体は、前記熱交換チャネル内で相変化を行う、請求項１から２１のいずれか一項に記載のプロセス。
【請求項２３】
前記熱交換チャネル中で吸熱プロセスまたは発熱プロセスが実行される、請求項１から２１のいずれか一項に記載のプロセス。
【請求項２４】
前記熱交換流体は、空気、水蒸気、液体水、一酸化炭素、二酸化炭素、気体窒素、液体窒素、少なくとも一種類の気体炭化水素、少なくとも一種類の液体炭化水素またはそれらの二つ以上の組み合わせ、前記第一の流体流、前記第二の流体流、または前記第一の流体流と前記第二の流体流との混合物を含む、請求項１から２３のいずれか一項に記載のプロセス。
【請求項２５】
前記多相混合物は、泡を含む、請求項１から２４のいずれか一項に記載のプロセス。
【請求項２６】
前記多相混合物は、乳化剤、界面活性剤、紫外線保護因子、ワックス、ちょう度因子、増粘剤、過脂肪剤、安定剤、カチオン性、アニオン性、双性イオン、両性または非イオン性重合体、シリコン化合物、脂肪、ワックス、レシチン、リン脂質、生体薬剤、酸化防止剤、脱臭剤、発汗抑制剤、フケ防止剤、膨潤剤、駆虫剤、自己なめし剤、チロシン阻害剤、可溶化剤、防腐剤、香油または色素、あるいはそれらの二種類以上の混合物、の一つ以上を含む、請求項１から２５のいずれか一項に記載のプロセス。
【請求項２７】
前記多相混合物の中に固体が分散される、請求項１から２６のいずれか一項に記載のプロセス。
【請求項２８】
前記第一の流体流は水素化反応を行うための反応媒質を含み、前記第二の流体流は水素を含む、請求項１から２７のいずれか一項に記載のプロセス。
【請求項２９】
前記第一の流体流は液体流を含み、前記第二の流体流は、空気、酸素、窒素、二酸化炭素、水素、アンモニア、塩素ガス、オゾンの一種類以上、一種類以上の気体炭化水素、またはそれらの二種類以上の組み合わせを含み、または前記第一の流体流は液体廃棄物流を

含み、前記第二の流体流は空気を含み、または前記第一の流体流は液体の有害廃棄物流を含み、前記第二の流体流は空気を含み、または前記第一の流体流は液体のサラダドレッシングまたはマスタードを含み、前記第二の流体流は窒素を含み、または前記第一の流体流は液体飲料またはビールを含み、前記第二の流体流は二酸化炭素を含み、または前記第一の流体流は液体の漂白パルプを含み、前記第二の流体流は塩素を含み、または前記第一の流体流は水中に分散した石炭を含み、前記第二の流体流は空気を含み、または前記第一の流体流は随伴水を含むモータ油を含み、前記第二の流体流は窒素を含み、または前記第一の流体流は培養反応用の、液体を含有する細胞を含み、前記第二の流体流は酸素または空気を含み、または前記第一の流体流は液体反応媒質を含み、前記第二の流体流は空気または酸素を含み、または前記第一の流体流は油と水との混合物を含み、前記第二の流体流は空気または天然ガスを含み、または前記第一の流体流は液体の漂白パルプを含み、前記第二の流体流は酸素を含み、または前記第一の流体流は食用油、ワインまたはジュースを含み、前記第二の流体流は窒素を含み、または前記第一の流体流は魚の養殖に用いられる水を含み、前記第二の流体流は酸素を含み、または前記第一の流体流は水を含み、前記第二の流体流はオゾンを含み、または前記第一の流体流は液体の廃棄物流またはプロセス流を含み、前記第二の流体流は二酸化炭素またはアンモニアを含み、または前記第一の流体流は揮発性有機化合物を含む液体の廃棄物流を含み、前記第二の流体流は空気を含む、請求項１から２７のいずれか一項に記載のプロセス。

【請求項３０】

前記プロセスは、毎分少なくとも１リットルの多相混合物を製造する、請求項１から２９のいずれか一項に記載のプロセス。

【請求項３１】

前記プロセスは、マイクロチャネルミキサの中で実行され、前記マイクロチャネルミキサは、少なくとも二つのプロセスマイクロチャネルを含む、請求項１から３０のいずれか一項に記載のプロセス。

【請求項３２】

前記プロセスは、マイクロチャネルミキサの中で実行され、前記マイクロチャネルミキサは複数のプロセスマイクロチャネルと複数の第二の流体流チャネルを含み、前記プロセスマイクロチャネルは、少なくとも一つの第一の流体流マニホルドに接続されており、前記第一の流体流は、前記少なくとも一つの第一の流体流マニホルドを通って前記プロセスマイクロチャネルへ流れ、前記第二の流体流チャネルは、前記プロセスマイクロチャネルに隣接し、少なくとも一つの第二の流体流マニホルドは前記第二の流体流チャネルに接続し、前記第二の流体流は、前記少なくとも一つの第二の流体流マニホルドを通って前記第二の流体流チャネルへ流れる、請求項１から３１のいずれか一項に記載のプロセス。

【請求項３３】

前記マイクロチャネルミキサは、前記熱交換チャネルに接続された少なくとも一つの熱交換マニホルドをさらに含み、前記少なくとも一つの熱交換マニホルドを通って前記熱交換チャネルへと熱交換流体が流れる、請求項３２に記載のプロセス。

【請求項３４】

前記プロセスマイクロチャネルは、前記プロセスマイクロチャネル内の流れを変化させるために一つ以上の内壁の中および／または上に形成された表面構成要素を含む、請求項１から３３のいずれか一項に記載のプロセス。

【請求項３５】

前記表面構成要素は、前記プロセスマイクロチャネルを通る流体の流れの前記方向に対して斜めの角度に配向された前記マイクロチャネル内壁の一つ以上の中にあるくぼみ、および／または、前記マイクロチャネル内壁の一つ以上からの突起の形状であり、または前記表面構成要素は、少なくとも二つの表面構成要素領域の形状であって、前記第一の流体と第二の流体との混合は、第一の表面構成要素領域の中とそれに続く第二の表面構成要素領域の中の流れの中で実行され、前記第二の表面構成要素領域の中の前記流れのパターンは、前記第一の表面構成要素領域の中の前記流れのパターンとは異なり、または前記開口

区間は、前記プロセスマイクロチャネルの前記内壁の一つ以上の部分を形成する内部部分と、前記開口区間の前記内部部分の上を覆う表面構成要素シートとを含み、前記表面構成要素シートの中および／または上に表面構成要素があり、または前記多相混合物は、前記第一および／または第二の流体流の中に分散した固体粒子を含み、前記流動床の形であり、前記プロセスマイクロチャネルは、前記プロセスマイクロチャネル内の流れを変えるためにその内壁の一つ以上の中および／または上に形成された表面構成要素を含み、または前記表面構成要素は、互いに重ねられて積層され、および／または、三次元パターンにからみ合った二つ以上の層を含み、または前記表面構成要素は、円形、楕円形、正方形、長方形、市松模様、Ｖ字型、波型またはそれらを組み合わせた形であり、または前記表面構成要素は、副構成要素を含み、前記表面構成要素の主壁は、ノッチ形、波形、ギザギザ形、孔形、バリ形、市松模様、扇形またはそれらを組み合わせた形のさらに小さな表面構成要素をさらに含む、請求項３４に記載のプロセス。

【発明の詳細な説明】

【技術分野】

【０００１】

本発明は、マイクロチャネルプロセス技術を用いる多相混合プロセスに関する。

【背景技術】

【０００２】

液体の中の気泡の分散は、化学反応の有無にかかわらず、気‐液接触させて吸収またはストリッピングを促進するために、あるいは泡状製品生産のために有用なものとすることができる。これらのものの例は、廃液流のＢＯＤ（生物学的酸素要求量）要件を満たすための空気吹き込み、槽の中の液体を混合するための空気噴射、有害廃棄物処理用の細菌の成長を刺激するための空気吹き込み、サラダドレッシングまたはマスタードを増量するための窒素吹き込み、炭酸飲料およびビールのためのCO_2吹き込み、紙の製造においてパルプを漂白するための塩素吹き込み、石炭浮遊選鉱およびその他の固体の分離のための空気吹き込み、モータオイルから随伴水分を除去するための窒素吹き込み、培養反応において細胞発育を増強するための酸素または空気吹き込み、性能の改善のために空気、酸素またはその他の気体を反応器の中に吹き込むこと、多様な種類の化学的水素化反応のための水素吹き込み、油井からの湧水からのオイル除去のための空気または天然ガス吹き込み、紙の製造においてパルプを漂白するための酸素吹き込み、食用油、ワインおよびジュースから酸素を除去するための窒素吹き込み、魚の養殖における魚成長の刺激のための酸素吹き込み、医薬品プラントの超純水システムを滅菌するオゾン吹き込み、廃棄物またはプロセス流の中のｐＨを調節するためのCO_2またはNH_3吹き込み、効率的加熱、および蒸気ハンマリングを鎮めるための直接水蒸気噴射、廃液流からのＶＯＣ（揮発性有機化合物）の除去のための空気吹き込み、および類似の操作を含む。これらの操作の多くに伴う一問題は、気体の分散の効率がよくないことである。

【発明の開示】

【課題を解決するための手段】

【０００３】

本発明は、この問題に解決法を提供する。一実施態様では、本発明は、比較的大きな表面積を有する比較的小さな気泡の液体への分散を提供する。その結果、比較的大きな気／液接触面積が得られる。気泡が小さく、表面積が大きいので、液体の中に気体を効率的に溶解させることができる。これによって、気体消費量の低減が得られる。また、気体を液体の中に溶解するために必要な時間も短縮し、その結果、プロセス処理が迅速化し、生産性が高くなる。

【０００４】

本発明は、多相混合物を作るためのプロセスであって、プロセスマイクロチャネルの中に第一の流体流を流す工程であって、第一の流体流は、少なくとも一種類の液体および／または少なくとも一種類の気体を含み、プロセスマイクロチャネルは開口区間を有する工程、開口区間を通して第二の流体流をプロセスマイクロチャネルの中に流し、第一の流体

流と接触させて多相混合物を形成させる工程であって、第二の流体流は、少なくとも一種類の気体および／または少なくとも一種類のマイクロボディ形成材料を含み、第一の流体流は、多相混合物の中の連続相を形成し、第二の流体流は、連続相の中に分散した不連続相を形成する工程を含む。

【０００５】

一実施態様では、第二の流体は、第一の流体の中に溶解する。これは、プロセスマイクロチャネルの中で起こることもあり、多相混合物がプロセスマイクロチャネルから出た後で起こることもある。本発明のプロセスの一利点は、少なくとも一実施態様では、多相混合物の中の第二の流体が、マイクロチャネルプロセス技術を用いない従来の技法によって形成されたより大きな気泡と比較すると、第一の流体の中により効率的に溶解する、比較的小さな気泡を含むことができる点にある。

【０００６】

一実施態様では、多相混合物は、第一の流体流の中に分散した固体粒子をさらに含む。

【０００７】

一実施態様では、プロセスマイクロチャネルと発熱源および／または吸熱源との間で熱が交換される。一実施態様では、発熱源および／または吸熱源は、少なくとも一つの熱交換チャネルを含む。

【０００８】

一実施態様では、開口区間は、プロセスマイクロチャネルの軸方向長さの少なくとも一部に沿って延在する。一実施態様では、開口区間は、プロセスマイクロチャネルの軸方向長さの少なくとも約１０％、一実施態様ではプロセスマイクロチャネルの軸方向長さの少なくとも約２０％、一実施態様ではプロセスマイクロチャネルの軸方向長さの少なくとも約３５％、一実施態様ではプロセスマイクロチャネルの軸方向長さの少なくとも約５０％、一実施態様ではプロセスマイクロチャネルの軸方向長さの少なくとも約６５％、一実施態様ではプロセスマイクロチャネルの軸方向長さの少なくとも約８０％、一実施態様ではプロセスマイクロチャネルの軸方向長さの少なくとも約９５％に沿って延在する。

【０００９】

一実施態様では、第二の流体流は、第二の流体流チャネルから開口区間を通って流れる。

【００１０】

一実施態様では、プロセスマイクロチャネルと発熱源および／または吸熱源との間、第二の流体流チャネルと発熱源および／または吸熱源との間、またはプロセスマイクロチャネルと第二の流体流チャネルとの両方と、発熱源および／または吸熱源との間で、熱が交換される。発熱源および／または吸熱源は、加熱、冷却、または冷却と加熱との両方に用いてもよい。発熱源は、熱交換チャネルおよび／または加熱素子を含んでもよい。吸熱源は、熱交換チャネルおよび／または冷却素子を含んでもよい。一実施態様では、発熱源および／または吸熱源は、プロセスマイクロチャネル、第二の流体流チャネル、またはプロセスマイクロチャネルと第二の流体流チャネルとの両方に隣接させることができる。一実施態様では、発熱源および／または吸熱源は、プロセスマイクロチャネルおよび／または第二の流体流チャネルから離してもよいが、プロセスマイクロチャネルおよび／または第二の流体流チャネルへ、またはプロセスマイクロチャネルおよび／または第二の流体流チャネルから熱を移動させるために、プロセスマイクロチャネルおよび／または第二の流体流チャネルに十分近くするとよい。

【００１１】

一実施態様では、本プロセスは、多相ミキサの中で実行される。多相ミキサの中では、プロセスマイクロチャネル、第二の流体流チャネルおよび熱交換チャネルの中への流体の流れを提供するために、一つ以上のヘッダまたはマニホルドが使用され、プロセスマイクロチャネルおよび熱交換チャネルから出る流体の流れを提供するために、一つ以上のフッタまたはマニホルドが使用される

【００１２】

一実施態様では、第一の流体流と第二の流体流とは、プロセスマイクロチャネルの中の混合区域の中で互いと接触する。一実施態様では、発熱源および／または吸熱源と、混合区域の中のプロセスマイクロチャネルの少なくとも一部との間で、熱が交換される。一実施態様では、発熱源および／または吸熱源と、混合区域の上流のプロセスマイクロチャネルの少なくとも一部との間で、熱が交換される。一実施態様では、発熱源および／または吸熱源と、混合区域の下流のプロセスマイクロチャネルの少なくとも一部との間で、熱が交換される。

【００１３】

一実施態様では、プロセスマイクロチャネルは、混合区域の中で制限された断面を有する。

【００１４】

一実施態様では、プロセスマイクロチャネルは、離間した壁と、離間した壁のそれぞれの中の開口区間とを有し、第二の液体は、開口区間のそれぞれを通って、プロセスマイクロチャネルの中に流入する。一実施態様では、離間した壁のそれぞれの中の開口区間は、複数の開口を含み、一方の壁の開口区間の中の開口は、反対側の壁の開口区間の中の開口の真向かいに配置される。一実施態様では、離間した壁のそれぞれの中の開口区間は、複数の開口を含み、一方の壁の開口区間の中の開口の少なくともいくつかは、他方の壁の開口区間の中の開口の真向かいにならないようにずらして配置される。

【００１５】

一実施態様では、プロセスマイクロチャネルは、多相混合物形成ユニットの中にある。多相混合物形成ユニットは、第一のプロセスマイクロチャネル、第二のプロセスマイクロチャネル、および第一のプロセスマイクロチャネルと第二のプロセスマイクロチャネルとの間に位置する第二の流体チャネルを含み、各プロセスマイクロチャネルは、開口区間を含む壁を有し、第一の流体流は、第一のプロセスマイクロチャネルと第二のプロセスマイクロチャネルとを通って流れ、第二の流体流は、第二の流体流チャネルから、第一のプロセスマイクロチャネルの中の開口区間を通って流れて第一の流体流と接触し、第二のプロセスマイクロチャネルの中の開口区間を通って流れて第一の流体流と接触する。

【００１６】

一実施態様では、第三の流体流チャネルの中に第三の流体流が流れ、第三の流体流チャネルは、別の開口区間を有する別の壁を有し、本プロセスは、別の開口区間を通して第二の流体流を流し、第三の流体流と接触させて別の多相混合物を形成させる工程、および開口区間を通して別の多相混合物をプロセスマイクロチャネルの中に流し、第一の流体流と接触させる工程、をさらに含む。

【００１７】

一実施態様では、プロセスマイクロチャネルは、平行な離間したシートおよび／またはプレートから形成される。一実施態様では、第二の流体流チャネルは、平行な離間したシートおよび／またはプレートから形成され、第二の流体流チャネルは、プロセスマイクロチャネルに隣接する。一実施態様では、熱交換チャネルは、平行な離間したシートおよび／またはプレートから形成され、熱交換チャネルは、プロセスマイクロチャネル、第二の流体流チャネル、またはプロセスマイクロチャネルと第二の流体流チャネルとの両方に隣接する。

【００１８】

一実施態様では、本プロセスは、マイクロチャネルミキサの中で実行され、マイクロチャネルミキサは、複数のプロセスマイクロチャネルと第二の流体流チャネルとを含み、各プロセスマイクロチャネルは、開口区間を有する壁と隣接する第二の流体流チャネルとを有し、第二の流体流は、第二の流体流チャネルから開口区間を通ってプロセスマイクロチャネルの中に流れて第一の流体流と接触し、プロセスマイクロチャネルと第二の流体流チャネルとは、平行な離間したシートおよび／またはプレートから形成され、プロセスマイクロチャネルと第二の流体流チャネルとは、互いに隣接し、交互に横に並べられた面または交互に上下に重ねられた面の形で配置される。

【００１９】
一実施態様では、プロセスマイクロチャネルは、二つ以上の開口区間を含み、開口区間のそれぞれを通って、別々の第二の流体流が流れる。一実施態様では、開口区間のそれぞれを通って流れる別々の第二の流体流は、異なる組成を有する。一実施態様では、開口区間のそれぞれを通って流れる別々の第二の流体流は、異なる性質を有する。
【００２０】
一実施態様では、本プロセスは、マイクロチャネルミキサの中で実行され、マイクロチャネルミキサは、少なくとも二つのプロセスマイクロチャネル、一実施態様では少なくとも約１０のプロセスマイクロチャネル、一実施態様では少なくとも約１００のプロセスマイクロチャネル、一実施態様では少なくとも約１０００のプロセスマイクロチャネルを含む。
【００２１】
一実施態様では、本プロセスは、マイクロチャネルミキサの中で実行され、マイクロチャネルミキサは、少なくとも一つの第一の流体流マニホルドに接続された複数のプロセスマイクロチャネルを含み、第一の流体流は、少なくとも一つの第一の流体流マニホルドを通ってプロセスマイクロチャネルへ流れる。一実施態様では、プロセスマイクロチャネルに第二の流体流チャネルが隣接し、マイクロチャネルミキサは、第二の流体流チャネルに接続された少なくとも一つの第二の流体流マニホルドをさらに含み、第二の流体流は、少なくとも一つの第二の流体流マニホルドを通って第二の流体流チャネルへ流れる。一実施態様では、プロセスマイクロチャネルおよび／または液体チャネルに熱交換チャネルが隣接し、マイクロチャネルミキサは、熱交換チャネルに接続された少なくとも一つの熱交換マニホルドをさらに含み、少なくとも一つの熱交換マニホルドを通って熱交換チャネルへ熱交換流体が流れる。
【００２２】
一実施態様では、第二の流体流は、第二の流体流チャネルから開口区間を通ってプロセスマイクロチャネルの中に流れ、プロセスマイクロチャネルおよび液体チャネルは、同心状の環状管を含む。
【００２３】
一実施態様では、本プロセスは、マイクロチャネルミキサの中で実行され、マイクロチャネルミキサは、複数のプロセスマイクロチャネルを含み、プロセスマイクロチャネルのそれぞれの中で別々の多相混合物が形成され、プロセスマイクロチャネルの少なくとも二つの中で形成される多相混合物は、互いに異なっている。これらの多相混合物は、異なる組成および／または異なる性質を有してもよい。このマイクロチャネルミキサは、コンビナトリアル合成およびスクリーニングデバイスと呼ぶことができる。本発明のこの実施態様の一利点は、同じ装置を用いて同時に、複数の多相混合物製品の形成および評価を提供する点である。これは、新製品の候補として、複数の製剤をスクリーニングすることが望まれるとき、利点とすることができる。
【００２４】
一実施態様では、本プロセスは、マイクロチャネルミキサの中で実行され、マイクロチャネルミキサは、横に並べられるか、または上下に重ねられた、複数の多相混合物形成ユニットを含み、各多相混合物形成ユニットは、プロセスマイクロチャネルおよび隣接する第二の流体流チャネルを含み、プロセスマイクロチャネルおよび隣接する第二の流体流チャネルは、共通の壁と、共通の壁の中の開口区間とを有し、開口区間は、第二の流体流を第二の流体流チャネルから開口区間を通してプロセスマイクロチャネルの中に流すのに適し、各プロセスマイクロチャネルと第二の流体流チャネルとは、平行な離間したシート、プレート、またはそのようなシートおよびプレートの組み合わせから形成され、本プロセスは、プロセスマイクロチャネルの中に第一の流体流を流す工程、第二の流体流チャネルから開口区間を通してプロセスマイクロチャネルの中に第二の流体流を流す工程、および第一の流体流と第二の流体流とをプロセスマイクロチャネルの中で混合して多相混合物を形成させる工程を含む。

【００２５】
一実施態様では、本発明のプロセスは、プロセスマイクロチャネルを通る第一の流体流の流れの圧力降下を比較的低くして、動作させることができる。一実施態様では、本発明のプロセスは、開口区間を通るプロセスマイクロチャネルへの第二の流体流の流れの圧力降下を比較的低くして、動作させることができる。
【００２６】
一実施態様では、プロセスマイクロチャネル内の混合は、プロセスマイクロチャネルの一つ以上の内壁の上に形成された表面構成要素の使用によって改善することができる。一実施態様では、第二の流体は、プロセスマイクロチャネル内で第一の流体と接触し、次に、プロセスマイクロチャネルの一つ、二つまたは三つ以上の内壁の上に表面構成要素が形成されたプロセスマイクロチャネル内の領域を通って流れてもよい。表面構成要素は、プロセスマイクロチャネルを通る流体の流れの方向に対して斜めの角度で配向した、マイクロチャネル内壁の一つ以上の中にあるくぼみ、および／または、マイクロチャネル内壁からの突起物の形状であるとよい。角度のある構成要素は、流れの方向と同じに、または流れの方向と逆に配置してもよい。表面構成要素は、流れの方向に対して、ある角度（例えば、約１°から約８９°、一実施態様では約３０°から約７５°）で、配置するとよい。表面構成要素と接触する流体の流れによって、流体流の一部がくぼみまたは表面構成要素の中へ流れることを強いられるが、一方、流体流の一部は表面構成要素の上をそのまま流れる。表面構成要素内の流れは、表面構成要素と同じ形になり、バルクの流れに対して角度ができる。流体は、表面構成要素から出るとき、バルク流体がｚ方向に流れるｘ、ｙ、ｚ座標系で、ｘおよびｙ方向に運動量を及ぼすことができる。この効果によって、流体流を撹拌または回転させることができる。このパターンは、付与された速度勾配が流体せん断を発生させ、第二の流体を小さな良く分散した気泡または微粒子に細分化するので、二相の流れを混合するために特に有用なものとすることができる。
【００２７】
一実施態様では、第一の表面構成要素領域とそれに続く、別の流れのパターンを作り出す少なくとも一つの第二の構成要素領域とを用いて、第一の流体と第二の流体との混合が実現できるように、プロセスマイクロチャネル内の表面構成要素領域を直列に配置してもよい。第二の流れのパターンは、第一の流体と第二の流体とを分けるか、または引き離すために用いてもよい。この工程は、気体または液体回収を支援するために用いてもよい。本発明のこの実施態様は、液体の中に気体が導入された後、その結果得られた混合物が不均一触媒または均一触媒を含むか、あるいは触媒を含まない第一の表面構成要素領域を通って流れる、気液反応の場合に特に有用なものとすることができる。混合物は、次に、オプションとして、流れパターンが遠心力を発生させ、液体を環状流れパターンでプロセスマイクロチャネルの内壁の方へ押しやる一方、気体は流体コアの中に残る第二の表面構成要素領域を通って流れてもよい。この後者のプロフィルによって、未反応気体を反応体混合物から分けるか、または引き離すのを支援してもよい。流体の中に強い中心渦を作り出すことができる表面構成要素の一パターンは、プロセスマイクロチャネルの上部と底部との角度のある一対のスロットのことがある。中心渦流れパターンを作り出すことができる。一実施態様では、泡の多い混合物によって、液体をプロセスマイクロチャネルの壁の方へ流し、気体をプロセスマイクロチャネルの中心へ押しやるとよい。
【００２８】
一実施態様では、開口区間は、プロセスマイクロチャネルの内壁の一つ以上の一部を形成する内部部分を含んでもよい。開口区間のこの内部部分の上に表面構成要素シートがあってもよい。表面構成要素シートの中および／または上に、表面構成要素を形成してもよい。第二の流体は、開口区間と表面構成要素シートとを通って流れてもよい。開口区間を通って入って来る流体の流束は、表面構成要素シートの表面構成要素の中にある間は、表面構成要素シートの表面から離すことができる。表面構成要素シートは、流れの長さ全体と比較すると、比較的小さな幅またはスパンを有する角度のある構成要素を含んでもよい。表面構成要素シートは、開口区間に機械的支持を提供してもよい。さらに、表面構成要

素によって作り出される流れの渦または角度のある流れは、開口区間を通って流れる第二の流体にせん断をさらに付与し、ひいてはバルク流路の中の第二の流体の粒子または泡のサイズを減らす上で好ましいものとすることができる。

【００２９】

一実施態様では、多相混合物は、液体－固体の流れ、または気体－液体－固体の流れを含んでもよい。第二の流体流は、気体または液体どちらかの中の固体の分散を含んでもよい。第一の流体流は、気体、液体、あるいは気体または液体の中に分散した固体を含んでもよい。プロセスマイクロチャネルの中の表面構成要素区間を通る多相混合物の流れは、付与された流れの方向と異なる運動量が混合物を良く混合された、または分散された状態に保つように作用することができるので、有利なものとすることができる。この利用は、液体反応体の中の固体触媒の分散に有用なものとすることができる。

【００３０】

一実施態様では、多相混合物は、第一および／または第二の流体流の中に分散した固体粒子を含んでもよく、流動床の形であり、プロセスマイクロチャネルは、プロセスマイクロチャネル内の流れを変更するためにその内壁の一つ以上の中および／または上に形成された表面構成要素を含む。これは、固体粒子含有流体流の中に気体流を混合することを含んでもよい。固体は、キャリア流体の中に吹き込んでもよく、またはキャリア流体によって取り込んでもよい。表面構成要素は、多相混合物の混合を促進することがある。

【００３１】

一実施態様では、化学反応および／または沈殿の結果として、多相混合物の中に固体が形成されてもよい。

【００３２】

一実施態様では、多相混合物は泡の形である。一実施態様では、多相混合物は、オプションとして、一種類以上の界面活性剤を含んでもよい。気泡によっては、界面活性剤の存在は必要ではないが、気泡を形成させるために、これらを含んでもよい。

【００３３】

添付の図面では、同様な部品および構成要素は、同様な参照符号を有する。

【発明を実施するための最良の形態】

【００３４】

用語「マイクロチャネル」は、最大約１０ミリメートル（ｍｍ）、一実施態様では最大約５ｍｍ、一実施態様では最大約２ｍｍ、一実施態様では最大約１ｍｍの高さまたは幅のうちの少なくとも一方の内部寸法を有するチャネルを指す。マイクロチャネルを通る流体の流れは、マイクロチャネルの高さおよび幅に垂直なマイクロチャネルの長さ方向に進むことができる。本発明のプロセスでプロセスマイクロチャネル、オプションとして、第二の流体流チャネル、第三の流体流チャネルおよび／または熱交換チャネルとして用いることができるマイクロチャネルの例が図１に示される。図１に例が示されるマイクロチャネル１０は、高さ（ｈ）、幅（ｗ）および軸方向長さ（ｌ）を有する。矢印１２および１４によって示される方向のマイクロチャネルの長さに沿って、マイクロチャネル１０を通って流体が流れる。マイクロチャネルの高さ（ｈ）または幅（ｗ）は、約０．０５から約１０ｍｍ、一実施態様では約０．０５から約５ｍｍ、一実施態様では約０．０５から約２ｍｍ、一実施態様では約０．０５から約１．５ｍｍ、一実施態様では約０．０５から約１ｍｍ、一実施態様では約０．０５から約０．７５ｍｍ、一実施態様では約０．０５から約０．５ｍｍの範囲にあるとよい。高さまたは幅のうち、他方の寸法は、任意の寸法、例えば最大約３メートル、一実施態様では約０．０１から約３メートル、一実施態様では約０．１から約３メートルであるとよい。マイクロチャネルの軸方向長さ（ｌ）は、任意の寸法、例えば最大約１０メートル、一実施態様では約０．１から約１０メートル、一実施態様では約０．２から約６メートル、一実施態様では約０．２から約３メートルであるとよい。図１に例が示されるマイクロチャネル１０は、長方形の断面を有するが、マイクロチャネルは、任意の形状、例えば正方形、円形、半円形、台形等の断面を有してもよいと理解すべきである。マイクロチャネルの断面の形状および／またはサイズは、その長さにわた

って変化してよい。例えば、高さまたは幅は、マイクロチャネルの長さにわたって、比較的大きな寸法から比較的小さな寸法へ、またはその逆に、テーパを有してもよい。

【００３５】

用語「隣接する」は、別のチャネルに対する一つのチャネルの相対的な位置を指すとき、直接隣接し、その結果、これらの二つのチャネルを一枚の壁が分断することを意味する。この壁は、厚さが変化してもよい。しかし、「隣接する」チャネル同士は、チャネル間の伝熱に干渉する介在チャネルで分断されることはない。

【００３６】

用語「表面構成要素」は、マイクロチャネル内の流れを変更する、マイクロチャネル壁の中のくぼみおよび／またはマイクロチャネル壁からの突起を指す。表面構成要素は、円形、楕円形、正方形、長方形、市松模様、Ｖ字形、波形および類似の形状であってもよい。表面構成要素は、副構成要素を含んでもよい。この場合、表面構成要素の主壁は、より小さな表面構成要素をさらに含み、これらの表面構成要素は、ノッチ形、波形、ギザギザ形、孔形、バリ形、チェック形、扇形および類似の形であってもよい。表面構成要素は、深さ、幅を有し、非円形表面構成要素なら長さを有する。図２２～２６に例が示される。表面構成要素は、本発明のプロセスで用いられるプロセスマイクロチャネルの内部側壁の一つ以上の上または中に形成することができる。表面構成要素は、本発明のプロセスで用いられる第二の流体流チャネルおよび／または熱交換チャネルの内部側壁の一つ以上の上または中に形成することができる。表面構成要素は、受動表面構成要素または受動混合構成要素と呼ぶことができる。

【００３７】

用語「上流」および「下流」は、マイクロチャネルを含む本発明のプロセスで用いられるチャネルの中の位置を指し、チャネルを通る流体の流れの方向に対するものである。例えば、チャネルを通って流れてその位置に向かって来る流体の一部分がまだ到着していないチャネル内の位置は、流体のその一部分の下流にある。チャネルを通って流れてその位置から遠ざかる流体の一部分が既に通り過ぎたチャネル内の位置は、流体のその一部分の上流にある。本発明のプロセスで用いられるプロセスチャネルは、水平、垂直、あるいはある角度に配向させてもよいので、用語「上流」および「下流」は、必ずしも垂直位置を指すものではない。

【００３８】

用語「マイクロボディ」は、最大約２００ミクロン、一実施態様では約０．０１から約２００ミクロン、一実施態様では約０．０１から約１００ミクロン、一実施態様では約０．０１から約５０ミクロン、一実施態様では約０．０１から約２５ミクロン、一実施態様では約０．０１から約１０ミクロン、一実施態様では約０．０１から約５ミクロン、一実施態様では約０．０１から約２ミクロン、一実施態様では約０．０１から約１ミクロン、一実施態様では約０．０１から約０．５ミクロン、一実施態様では約０．０１から約０．２ミクロン、一実施態様では約０．０１から約０．１ミクロン、一実施態様では約０．０１から約０．０８ミクロン、一実施態様では約０．０１から約０．０５ミクロン、一実施態様では約０．０１から約０．０３ミクロンの範囲の平均寸法（例えば直径、高さ、幅、長さ）を有する三次元ボディを指す。これらのマイクロボディは、円および／または楕円の形状の断面を有するボディを含む。マイクロボディは、球体、楕円球体、卵形体および類似の形であってもよい。マイクロボディは、針状の形を有してもよい。マイクロボディは、中空であってもよく、あるいは中空でなくてもよい。マイクロボディは、マイクロスフェアであってもよい。マイクロボディは、主寸法（例えば直径、長さ）と副寸法（例えば直径、高さ、幅）とを有してもよく、副寸法に対する主寸法の比は、約１０：１から約１：１、一実施態様では約５：１から約１：１、一実施態様では約２：１から約１：１の範囲にある。

【００３９】

用語「流体」は、気体、液体、分散固体を含む気体または液体、液滴を含む気体、気泡を含む液体、液滴および分散固体を含む気体、あるいは気泡および分散固体を含む液体、

および類似物を指す。

【００４０】

用語「発熱源」は、熱を放出し、別の物体またはデバイスを加熱するために用いることができる物体またはデバイスを指す。発熱源は、熱交換流体を内部に有し、別の物体またはデバイスへ熱を伝える熱交換チャネルの形であってもよく、別の物体またはデバイスは、例えば、熱交換チャネルに隣接するか、または熱交換チャネルから伝えられる熱を受け取るのに十分に近いチャネルである。熱交換流体は、熱交換チャネルの中に収容されてもよく、および／または、熱交換チャネルを通って流れてもよい。発熱源は、加熱素子、例えば、電熱素子または抵抗加熱器の形であってもよい。用語「吸熱源」は、熱を吸収し、別の物体またはデバイスを冷却するために用いることができる物体またはデバイスを指す。吸熱源は、熱交換流体を内部に有し、別の物体またはデバイスから伝えられる熱を受け取る熱交換チャネルの形であってもよい。別の物体またはデバイスは、例えば、熱交換チャネルに隣接するか、または熱交換チャネルへ熱を伝えるのに十分に近いチャネルである。熱交換流体は、熱交換チャネルの中に収容されてもよく、および／または、熱交換チャネルを通って流れてもよい。吸熱源は、冷却素子、例えば、非流体冷却素子の形であってもよい。

【００４１】

用語「発熱源および／または吸熱源」は、熱を放出するか、または熱を吸収することができる物体またはデバイスを指す。発熱源および／または吸熱源は、熱交換流体を内部に有し、熱交換チャネルに隣接するかまたは近くにある別の物体またはデバイスが加熱されるとき、それらの別の物体またはデバイスに熱を伝えるか、あるいは、熱交換チャネルに隣接するかまたは近くにある別の物体またはデバイスが冷却されるとき、それらの別の物体またはデバイスから伝えられる熱を受け取る、熱交換チャネルの形であってもよい。発熱源および／または吸熱源として機能する熱交換チャネルは、あるときは加熱チャネル、他のときは冷却チャネルとして機能してもよい。熱交換チャネルの一部分（単数または複数）が加熱チャネルとして機能し、一方、熱交換チャネルの別の一部分（単数または複数）が冷却チャネルとして機能してもよい。

【００４２】

用語「熱交換チャネル」は、熱交換流体を内部に有し、熱を放出し、および／または熱を吸収することができるチャネルを指す。

【００４３】

用語「熱交換流体」は、熱を発生し、および／または熱を吸収することができる流体を指す。

【００４４】

図２を参照すると、本プロセスは、マイクロチャネルミキサ１００を用いて実行することができ、マイクロチャネルミキサ１００は、マイクロチャネルミキサコア１０２、プロセス流体ヘッダ１０４、生成物フッタ１０６および熱交換マニホルド１０８を含む。マイクロチャネルミキサコア１０２は、複数のプロセスマイクロチャネル、隣接する第二の流体流チャネルおよび熱交換チャネルを含む。第二の流体流チャネルおよび／または熱交換チャネルは、マイクロチャネルであってもよい。プロセスマイクロチャネル、第二の流体流チャネルおよび熱交換チャネルは、上下に重ねられるか、または横に並べられて、層状に配置してもよい。プロセスヘッダ１０４は、第一の流体流がプロセスマイクロチャネルに流入し、第二の流体流が第二の流体流チャネルに流入し、これらのチャネルの流れの分布を一様にまたは実質的に一様にするための通路を提供する。生成物フッタ１０６は、多相混合物生成物がプロセスマイクロチャネルから迅速に流れ、比較的高い流速を有するための通路を提供する。第一の流体流は、矢印１１０で示されるように、ヘッダ１０４を通ってマイクロチャネルミキサ１００に流入する。第二の流体流は、矢印１１２で示されるように、ヘッダ１０４を通ってマイクロチャネルミキサ１００の中に流入する。第一の流体流と第二の流体流とは、マイクロチャネルミキサコア１０２の中に流入し、混合されて多相混合物を形成する。多相混合物は、マイクロチャネル混合コア１０２から生成物フッ

タ１０６を通り、矢印１１４で示されるように、生成物フッタ１０６から流出する。一実施態様では、多相混合物は、任意の回数、例えば、１回、２回、３回、４回等、マイクロチャネルミキサコア１０２を通って戻り、リサイクルしてもよい。矢印１１６で示されるように、熱交換マニホルド１０８の中に熱交換流体が流入し、熱交換マニホルド１０８からマイクロチャネルミキサコア１０２の中の熱交換チャネルを通ってから熱交換マニホルド１０８に戻り、矢印１１８で示されるように、熱交換マニホルド１０８から流出する。マイクロチャネルミキサ１００は、貯槽、ポンプ、バルブ、流量制御デバイスおよび類似デバイスとともに使用してもよい。これらは、図面に示していないが、当業者には自明である。

【００４５】

マイクロチャネルミキサコアは、複数の多相混合物形成ユニットを含んでもよい。図３～９および１２に、多相混合物形成ユニットの有用な実施態様の例が示される。図３を参照すると、本発明のプロセスは、対向する側壁２１２および２１４と、側壁２１２の中の開口区間２４０とを有するプロセスマイクロチャネル２１０を含む多相混合物形成ユニット２００を用いて実行することができる。開口区間２４０は、多孔質区間または多孔質基板と呼んでもよい。開口区間２４０は、開口区間全体に広がる開口のアレイ２４４を有するシートまたはプレート２４２を含んでもよい。側壁２１２に隣接して第二の流体流２７０があり、開口区間２４０の中の開口２４４を通ってプロセスマイクロチャネル２１０に開放される。プロセスマイクロチャネル２１０は、非開口領域または非多孔質領域２１１および２１７と、混合区域２１３とを有する。非開口領域２１１は、プロセスマイクロチャネルへの入口から混合区域３１３への入口へ延在する。非開口領域２１１は、混合区域２１３の上流である。混合区域２１３は、開口区間２４０に隣接する。非開口領域２１７は、混合区域２１３の終りからプロセスマイクロチャネル２１０の出口へ延在する。非開口領域２１７は、混合区域２１３の下流である。側壁２１４に隣接して、熱交換チャネル２９０がある。動作時、第一の流体流は、矢印２１６で示されるように、プロセスマイクロチャネル２１０に流入し、非開口領域２１１を通って混合区域２１３に流入する。矢印２７２で示されるように、第二の流体流が第二の流体流チャネル２７０に流入し、次に、矢印２７４で示されるように、開口区間２４０を通って混合区域２１３に流入する。混合区域２１３の中で、第二の流体流は、第一の流体流と接触し、混合されて多相混合物を形成する。第二の流体流は、第一の流体流の中の不連続相を形成してもよい。第一の流体流は、連続相を形成してもよい。多相混合物は、混合区域２１３から非開口領域２１７を通り、矢印２１８で示されるように、プロセスマイクロチャネル２１０から流出する。加熱または冷却は、選択肢とすることができる。加熱または冷却が望まれるとき、矢印２９２で示されるように、熱交換チャネル２９０を通って熱交換流体が流れ、プロセスマイクロチャネル２１０および第二の流体流チャネル２７０の中の流体を加熱または冷却する。加熱または冷却の度合いは、プロセスマイクロチャネル２１０および第二の流体流チャネル２７０の長さにわたって変化してもよい。加熱または冷却は、プロセスマイクロチャネルおよび液体チャネルのある区間では無視できるか、または存在しなくてもよく、他の区間では中程度または比較的大きくてもよい。あるいは、加熱または冷却は、熱交換チャネル以外を用いて実現してもよい。例えば、加熱は、電熱素子または抵抗加熱器を用いて実現してもよい。電熱素子または抵抗加熱器は、プロセスマイクロチャネル２１０および／または第二の流体流チャネル２７０の一つ以上の壁を形成するために用いてもよい。電熱素子または抵抗加熱器は、プロセスマイクロチャネル２１０および／または第二の流体流チャネル２７０の一つ以上の壁の中にあってもよい。冷却は、非流体冷却素子を用いて実現してもよい。プロセスマイクロチャネル２１０の長さに沿って、複数の加熱または冷却区域が使用されてもよい。同様に、プロセスマイクロチャネル２１０および／または第二の流体流チャネル２７０の長さに沿って、一つ以上の熱交換チャネルの中でさまざまな温度の熱交換流体を使用してもよい。

【００４６】

図４に例が示される多相混合物形成ユニット２００Ａは、プロセスマイクロチャネル２

１０の側壁２１０が開口区間２４０に対向して配置されたテーパを有する区間２２０を含む点を除けば、図３に例が示される多相混合物形成ユニット２００と同一である。テーパを有する区間２２０は、混合区域２１３の中のプロセスマイクロチャネル２１０の幅または高さを小さくし、従って、混合区域２１３の中のプロセスマイクロチャネル２１０に狭くなった断面を提供する。この幅または高さは、約０．００１から約５ｍｍ、一実施態様では約０．０１から約２ｍｍの範囲にあるとよい。テーパを有する区間２２０が存在すると、混合区域２１３を通って流れる流体の速度の増加がもたらされる。混合区域２１３を通って流れる液体の速度が増加すると、開口２４４を通って混合区域２１３に流入する第二の流体に作用するせん断力が増加する。これは、開口２４４を通る第二の流体流の流れを容易にする。プロセスマイクロチャネル２１０の狭くなった断面を通って流れる流体が混合区域２１３を通る速度は、１秒あたり約０．００５から約１００メートル（ｍ／ｓ）、一実施態様では約０．０１から約５０ｍ／ｓの範囲にあるとよい。

【００４７】

図５に例が示される多相混合物形成ユニット２００Ｂは、多相混合物形成ユニット２００Ｂが第二の流体流チャネル２７０ａおよび開口区間２４０ａも含む点を除けば、図３に例を示した多相混合物形成ユニット２００と類似している。第二の流体流チャネル２７０ａは、プロセスマイクロチャネル２１０と熱交換チャネル２９０との間に位置する。側壁２１４の中に開口区間２４０ａが形成される。開口区間２４０ａを通って第二の流体流チャネル２７０ａがプロセスマイクロチャネル２１０に開放される。開口区間２４０ａは、全体に広がる開口のアレイ２４４ａを有するシートまたはプレート２４２ａを含んでもよい。プロセスマイクロチャネル２１０は、非開口領域または非多孔質領域２１１および２１７と、混合区域２１３とを有する。非開口領域２１１は、プロセスマイクロチャネルへの入口から混合区域２１３への入口へ延在し、混合区域２１３の上流である。混合区域２１３は、開口区間２４０と２４０ａとの間に位置する。非開口領域２１７は、混合区域２１３の終わりからプロセスマイクロチャネル２１０の出口へ延在する。非開口領域２１７は、混合区域２１３の下流である。動作時、矢印２１６で示されるように、プロセスマイクロチャネル２１０に第一の液体流が流入し、非開口領域２１１を通って混合区域２１３に流入する。矢印２７２および２７２ａでそれぞれ示されるように、第二の流体流チャネル２７０および２７０ａの中に第二の流体流が流入する。第二の流体流は、矢印２７４および２７４ａでそれぞれ示されるように、開口区間２４０および２４０ａを通って混合区域２１３に流入する。混合区域２１３の中で、第二の流体流は、第一の流体流と接触し、混合されて多相混合物を形成する。第二の流体流は、第一の液体内の不連続相を形成してもよい。第一の流体流は、連続相を形成してもよい。多相混合物は、非開口領域２１７を通り、矢印２１８で示されるように、プロセスマイクロチャネル２１０から流出する。加熱または冷却は、選択肢としてもよい。加熱または冷却が望まれるとき、方向矢印２９２で示されるように、熱交換チャネル２９０を通って熱交換流体が流れ、プロセスマイクロチャネル２１０および第二の流体流チャネル２７０の中の流体を加熱または冷却する。加熱または冷却の度合いは、プロセスマイクロチャネルおよび第二の流体流チャネルの長さにわたって変化してもよい。加熱または冷却は、プロセスマイクロチャネルおよび液体チャネルの中のある区間では無視できるかまたは存在しなくてもよく、他の区間では中程度または比較的大きくてもよい。

【００４８】

図６に例が示される多相混合物形成ユニット２００Ｃは、図５に例が示される開口２４４と２４４ａとは互いに真向かいに配置されていたが、一方、図６に例が示される開口２４４と２４４ａとはそのような直接配置からずらされている点を除けば、図５に例が示される多相混合物形成ユニット２００Ｂと同一である。図５では、開口２４４と２４４ａとを通って流れる第二の流体流の流れは、互いと直接衝突し、それによって、第一の流体流の中への第二の流体流の拡散を促進する。一方、図６では、開口２４４と２４４ａとを通って流れる第二の流体流の流れは、互いにずらされ、それによって、混合区域２１３内の渦巻き効果を提供することによって拡散を促進する。

【００４９】
図７に例が示される多相混合物形成ユニット２００Ｄは、プロセスマイクロチャネル２１０および２１０ａ、開口区間２４０および２４０ａ、第二の流体流チャネル２７０および熱交換チャネル２９０を含む。側壁２１２の中に開口区間２４０が形成され、側壁２１２ａの中に開口区間２４０ａが形成される。開口区間２４０および２４０ａは、多孔質区画または多孔質基板と呼んでもよい。開口区間２４０および２４０ａを通って、第二の流体流チャネル２７０がプロセスマイクロチャネル２１０および２１０ａにそれぞれ開放される。開口区間２４０は、全体に広がる開口のアレイ２４４を有するシートまたはプレート２４２を含んでもよい。同様に、開口区間２４０ａは、全体に広がる開口のアレイ２４４ａを有するシートまたはプレート２４２ａを含んでもよい。プロセスマイクロチャネル２１０および２１０ａは、非開口領域または非多孔領域２１１および２１７、ならびに２１１ａおよび２１７ａ、混合区域２１３および２１３ａをそれぞれ有する。非開口領域２１１および２１１ａは、プロセスマイクロチャネル２１０および２１０ａへの入口から、混合区域２１３および２１３ａへの入口へそれぞれ延在する。非開口領域２１１および２１１ａは、混合区域２１３および２１３ａのそれぞれ上流である。混合区域２１３および２１３ａは、開口区間２４０および２４０ａにそれぞれ隣接する。非開口領域２１７および２１７ａは、混合区域２１３および２１３ａの終わりから、プロセスマイクロチャネル２１０および２１０ａの出口へそれぞれ延在する。非開口領域２１７および２１７ａは、混合区域２１３および２１３ａのそれぞれ下流である。プロセスマイクロチャネル２１０に隣接して、熱交換チャネル２９０がある。動作時、矢印２１６および２１６ａで示されるように、プロセスマイクロチャネル２１０および２１０ａの中に、それぞれ第一の流体流が流れ、非開口領域２１１および２１１ａを通って混合区域２１３および２１３ａに流入する。矢印２７２で示されるように、第二の流体流チャネル２７０に第二の流体流が流入し、次に、矢印２７４および２７４ａで示されるように、開口区間２４０および２４０ａを通って混合区域２１３および２１３ａにそれぞれ流入する。混合区域２１３および２１３ａの中で、第二の流体流は、第一の流体流と接触し、混合されて多相混合物を形成する。第二の流体流は、第一の流体流内の不連続相を形成してもよい。第一の流体流は、連続相を形成してもよい。多相混合物は、非開口区画２１７および２１７ａを通り、矢印２１８および２１８ａで示されるように、プロセスマイクロチャネル２１０および２１０ａからそれぞれ流出する。加熱または冷却は、選択肢とすることができる。加熱または冷却が望まれるとき、矢印２９２で示されるように、熱交換チャネル２９０を通って熱交換流体が流れ、チャネル２１０、２１０ａおよび２７０の中の流体を加熱または冷却する。加熱または冷却の度合いは、チャネルの長さにわたって変化してもよい。加熱または冷却は、プロセスマイクロチャネル２１０および２１０ａ、ならびに第二の流体流チャネル２７０のある区画では無視できるかまたは存在しなくてもよく、他の区画では中程度または比較的大きくてもよい。

【００５０】
一実施態様では、単一のマイクロチャネルミキサ内で、多重の多相混合調合物および／またはプロセス処理条件の組を用いて、別個の多相混合物を発生させることができる。例えば、単一のマイクロチャネルミキサが、二つ以上のプロセスマイクロチャネル、関連する第二の流体流チャネル、および熱交換チャネルを使用して、単一のマイクロチャネルミキサ内で、２、３、４、５、６、７、８、９、１０、数１０、数１００、数１０００、数万、数１０万等の別個の多相混合物を作ることができる。この種類のミキサは、コンビナトリアル合成デバイスと呼んでもよい。多相混合物形成ユニット３００の例が示される図８に、これが示される。多相混合物形成ユニット３００は、４つのプロセスマイクロチャネルを使用し、その結果、最大４つの別個の多相混合物を発生することができる。多相混合物形成ユニット３００は、任意の所望の回数、例えば２回、３回、４回、５回、６回、７回、８回、９回、１０回、数１０回、数１００回、数１０００回、数万回等繰り返し、上記で示した多重の別個の多相混合物の可能性を提供することができる。多相混合物形成ユニット３００は、プロセスマイクロチャネル３１０、３２０、３３０および３４０、第

二の流体流チャネル３５０および３６０、ならびに熱交換チャネル３７０および３８０を含む。側壁３１２の中に開口区間３１１が形成される。側壁３２２の中に開口区間３２１が形成される。側壁３３２の中に開口区間３３１が形成される。側壁３４２の中に開口区間３４１が形成される。開口３１３、３２３、３３３および３４３が開口区間３１１、３２１、３３１および３４１の中に位置し、それぞれ全体に広がる。プロセスマイクロチャネル３１０、３２０、３３０および３４０は、混合区域３１５、３２５、３３５および３４５の上流にそれぞれ位置する非開口区画３１４、３２４、３３４および３４４を含む。混合区域３１５、３２５、３３５および３４５が、開口区間３１１、３２１、３３１および３４１にそれぞれ隣接して位置する。プロセスマイクロチャネル３１０、３２０、３３０および３４０は、混合区域３１５、３２５、３３５および３４５のそれぞれ下流に位置する非開口区画３１６、３２６、３３６および３４６も含む。動作時、矢印３１７、３２７、３３７および３４７でそれぞれ示されるように、プロセスマイクロチャネル３１０、３２０、３３０および３４０の中に第一の流体流が流入する。プロセスマイクロチャネル３１０、３２０、３３０および３４０に入る第一の流体流は、互いに同じ組成を有してもよく、あるいは互いに異なる組成を有してもよい。第一の流体流は、非開口区画３１４、３２４、３３４および３４４を通って、混合区域３１５、３２５、３３５および３４５にそれぞれ流入する。第二の流体流は、矢印３５１および３６１で示されるように、第二の流体流チャネル３５０および３６０に流入する。第二の流体流チャネル３５０に入る第二の流体流は、第二の流体流チャネル３６０に入る第二の流体流と同じであってもよく、あるいは異なっていてもよい。第二の流体流チャネル３５０に入る第二の流体流と、液体チャネル３６０に入る第二の液体との間の差は、組成、プロセス処理条件、物理的性質（例えば粘度、密度、表面張力等）および／または操作パラメータにもとづくものでもよい。矢印３５１で示されるように、第二の流体流チャネル３５０に入る第二の流体流は、矢印３５２および３５３で示されるように、開口区間３１１および３２１を通って流れ、混合区域３１５および３２５にそれぞれ流入する。混合区域３１５および３２５の中で、第二の流体流は、第一の流体流と接触し、混合されて多相混合物を形成する。同様に、第二の流体流は、矢印３６１示されるように、第二の流体流チャネル３６０に流れ、次に、矢印３６２および３６３で示されるように、開口区間３３１および３４１を通って混合区域３３５および３４５それぞれ流入する。混合区域３１５、３２５、３３５および３４５の中で、第二の流体流は、第一の流体流と接触し、混合されて多相混合物を形成する。混合区域３１５、３２５、３３５および３４５の中で形成される多相混合物は、同じであってもよく、あるいは異なっていてもよい。異なる場合、多相混合物は、組成および／または物理的性質、あるいは操作パラメータ（例えば分散相および／または連続相の組成、粒子サイズ、粒子サイズ分布、粘度、密度、表面張力、温度、圧力、流量等）が互いに異なっていてもよい。多相混合物は、混合区域３１５、３２５、３３５および３４５から非開口区画３１６、３２６、３３６および３４６を通り、矢印３１８、３２８、３３８および３４８でそれぞれ示されるように、プロセスマイクロチャネル３１０、３２０、３３０および３４０から流出する。熱交換チャネル３７０および３８０を用いる加熱または冷却は、選択肢とすることができる。加熱または冷却が望まれるとき、矢印３７１および３７２、ならびに３８１および３８２で示されるように、熱交換チャネル３７０および３８０を通って熱交換流体が流れ、チャネル３１０、３２０、３３０、３４０、３６０および３６０の中の流体を加熱または冷却する。加熱または冷却の度合いは、チャネルのそれぞれの長さにわたって変化してもよい。プロセスチャネルおよび／または液体チャネルのある区間では、加熱または冷却は無視できるかまたは存在しなくてもよく、他の区間では中程度または比較的大きくもよい。本発明のこの実施態様の一利点は、同時に同じ装置を用いて、複数の多相混合物製品の形成および評価を提供できる点である。これは、新製品の候補として複数の製剤をスクリーニングすることが望まれるとき、利点とすることができる。

【００５１】

一実施態様では、本発明のプロセスは、二重多相混合物をつくるのに適する。これらの二重多相混合物は、図９に例が示される多相混合物形成ユニット４００を用いて作ること

ができる。図９では、多相混合物形成ユニット４００は、中心線４０２と４０４との間に配置される。多相混合物形成ユニット４００は、プロセスマイクロチャネル４１０と、液体チャネル４２０、４３０、４４０および４５０とを含む。流体流チャネル４２０および４３０が、プロセスマイクロチャネル４１０に隣接する。流体流チャネル４４０が、流体流チャネル４２０に隣接し、流体流チャネル４５０が流体流チャネル４３０に隣接する。粗い開口区間４１５を含む共通壁４１２が、プロセスマイクロチャネル４１０と流体チャネル４２０とを分ける。粗い開口区間４２５を含む共通壁４２２が、プロセスマイクロチャネル４１０と流体チャネル４３０とを分ける。開口区間４１５および４２５は、開口４１６および４２６をそれぞれ含む。流体流チャネル４４０と流体流チャネル４２０との間に、開口４３６を含む微開口区間４３５が位置し、流体流チャネル４４０と流体流チャネル４２０とを分ける。流体流チャネル４５０と流体流チャネル４３０との間に、開口４４６を含む微開口区間４４５が位置し、流体流チャネル４５０と流体流チャネル４３０とを分ける。粗開口区間４１５および４２５の開口４１６および４２６は、微開口区間４３５および４４５の開口４３６および４４６より大きい。プロセスマイクロチャネル４１０は、非開口領域または非多孔領域４１１および混合区域４１３を有する。非開口領域４１１は、プロセスへの入口から混合区域４１３への入口へ延在する。混合区域４１３は、開口区間４１５および４２５に隣接する。選択肢として、中心線４０２および／または４０４で示される位置に熱交換チャネルを挿入し、所望の加熱または冷却を流体に提供してもよい。

【００５２】

中心線４０２の下に、同じく図９に例が示される隣接する多相混合物形成ユニット４００ａの一部が位置する。多相混合物形成ユニット４００ａは、プロセスマイクロチャネル４１０ａ、粗開口区間４１５ａおよび４２５ａ、流体流チャネル４３０ａおよび微開口区間４４５ａを含む。これらは、上記で考察したプロセスマイクロチャネル４１０、粗開口区間４１５および４２５、流体流チャネル４３０および微開口区間４４５と同じである。図９の中心線４０４の上に、別の隣接する多相混合物形成ユニット４００ｂの一部も位置する。多相混合物形成４００ｂは、微開口区間４３５ｂおよび流体流チャネル４２０ｂを含む。これらは、上記で考察した微開口区間４３５および流体流チャネル４２０と同じである。図９に多相混合物形成ユニット４００ａと４００ｂとの一部を含むことによって、本発明のプロセスを希求してマイクロチャネルミキサの中で使用されるときの多相混合物形成ユニット４００の反復する性質の例が示される。

【００５３】

動作時、図９を参照すると、矢印４１４で示されるように、第一の流体流がプロセスマイクロチャネル４１０に入り、非開口領域４１１を通って混合区域４１３に流入する。矢印４２３および４３３で示されるように、第二の流体流が流体流チャネル４２０および４３０にそれぞれ入る。矢印４４２および４５２で示されるように、第三の流体流が液体チャネル４４０および４５０にそれぞれ入る。第三の流体流は、流体流チャネル４４０から開口区間４３５を通って流体流チャネル４２０に流入し、第二の流体流と混合されて別の多相混合物を形成する。第三の流体流は、流体流チャネル４５０から開口区間４４５を通って流体流チャネル４３０にも流入し、第二の流体流と混合されて別の多相混合物を形成する。流体流チャネル４２０および４３０の中で形成される別の多相混合物の中で、第三の流体流は不連続相を形成し、第二の流体流は連続相を形成する。流体流チャネル４２０および４３０の中で形成された別の多相混合物は、開口区間４１５および４２５をそれぞれ通って混合区域４１３に流入し、第一の流体流と混合される。混合区域４１３の中で、別の多相混合物は、第一の流体流の中に不連続相として分散し、第一の流体流は連続相の形になる。混合区域４１３の中で形成される多相混合物は、二重多相混合物と呼んでもよい。二重多相混合物の中で、第三の流体流の少なくとも一部は、第二の流体流の泡またはマイクロボディ（例えばマイクロスフェア）の中にカプセル化することができる。カプセル化された泡またはマイクロボディは、連続相の形であってもよい第一の流体流の中の不連続相として分散させることができる。二重多相混合物は、矢印４１８で示されるように

、プロセスマイクロチャネル４１０から出る。多相混合物４９０として図１０に概略が示される形であってもよい二重多相混合物は、一実施態様では、第一の流体流４９６（例えば気体または液体）の中に分散した第二の流体流４９４（例えば液体またはマイクロボディ）の中にカプセル化された第三の流体流４９２（すなわち気体）を含む。

【００５４】

一実施態様では、本発明のプロセスは空気吹き込みプロセスの中で用いることができる。図１１および１２に、これの例が示される。この実施態様では、本プロセスは、マイクロチャネルミキサ５０２を含む空気吹き込みタンク５００を用いて実行される。動作時、空気吹き込みされる流体は、タンク５００内に収容され、矢印５０４で示されるように、第一の流体流としてマイクロチャネルミキサ５０２に入る。空気吹き込みすることができる流体の例は、細胞培養液である。矢印５０６で示されるように、マイクロチャネルミキサ５０２の中に、第二の流体流が入る。第二の流体流は、空気または酸素を含んでもよい。マイクロチャネルミキサの中で、第一の流体流（例えば細胞培養液）と第二の流体流（例えば空気または酸素）と混合され、その結果、多相混合物（例えば空気吹き込みされた細胞培養液）が形成される。マイクロチャネルミキサ５０２は、複数の多相混合物形成ユニットを含んでもよい。多相混合物形成ユニット５１０は、プロセスマイクロチャネル５２０、第二の流体流チャネル５３０および５４０、微細セラミック膜の形であってもよい開口区間５５０および５６０、マクロ多孔質担体の形であってもよい開口区間５７０および５８０、ならびに熱交換チャネル５９０を含む。動作時、第一の流体流は、矢印５２２で示されるように、プロセスマイクロチャネル５２０に入る。第二の流体流は、矢印５３２および５４２でそれぞれ示されるように、第二の流体流チャネル５３０および５４０に入る。第二の流体流は、第二の流体流チャネル５３２から開口区間５７０を通った後、開口区間５５０を通ってプロセスマイクロチャネル５２０に流入する。同様に、矢印５４２で示されるように、別の第二の流体流が、第二の流体流チャネル５４０に入り、開口区間５８０を通った後、開口区間５６０を通り、プロセスマイクロチャネル５２０に流入する。第一の流体流と第二の流体流とは、プロセスマイクロチャネル５２０の中で混合され、その結果、多相混合物が形成される。多相混合物は、矢印５２４で示されるように、プロセスマイクロチャネル５２０から出る。多相混合物の中で、第一の流体流は連続相を形成してもよく、第二の流体流は不連続相を形成してもよい。一実施態様では、多相混合物は、細胞培養液全体に分散した高められたレベルの酸素または空気を有する細胞培養液を含むことができる。流体は、矢印５０７で示されるように、熱交換流体をマイクロチャネルミキサ５０２の中に流し、熱交換チャネル５９０を通した後、マイクロチャネルミキサ５０２から流出させることによって、加熱または冷却することができる。

【００５５】

図３～９および１２のそれぞれでは、一つの多相混合物形成ユニットしか完全に例が示されていないが、本発明のプロセスを実行するためにマイクロチャネルミキサの中で用いてもよい多相混合物形成ユニットの数に、事実上、上限はない。例えば、１、２、３、４、５、６、８、１０、２０、５０、１００、数１００、１０００、数１０００、一万、数万、１０万、数１０万、数１００万等の上記で説明した多相混合物形成ユニットを用いてもよい。一実施態様では、各多相混合物形成ユニットは、マニホルド接続してもよい。マニホルド接続は、各ユニットにマクロ配管、パイプ配管またはダクト配管を接続することによって実現してもよい。あるいは、各ユニットの間に比較的等しい圧力降下回路を創り出すことによって、多相混合物形成ユニットを含むマイクロチャネルミキサ内で、多相混合物形成ユニットの多数を内部マニホルド化してもよい。一方、幾分かの流れ不均衡があっても、製品の品質に影響を及ぼさないことがあるので、圧力降下は、各ユニットの間で等しくなくてもよい。一実施態様では、本発明のプロセスを用いる多相混合物を形成させるに際して、最大約５０％の流れ不均衡は許容できる。プロセスマイクロチャネル、関連する第二および第三の流体流チャネル、および熱交換チャネルは、横に並べるか、または上下に重ねて配置するとよい。例えば、多相混合物形成ユニット２００および２００Ａでは、プロセスマイクロチャネル２１０は、一平面内に平行に配置するとよく、第二の流体

流チャネル２７０は、プロセスマイクロチャネル２１０の一方の側の隣接平面内に平行に配置するとよく、熱交換チャネル２９０は、プロセスマイクロチャネル２１０の反対側の別の平面内に平行に配置するとよい。例えば、多相混合物形成ユニット２００Ｂおよび２００Ｃでは、プロセスマイクロチャネル２１０は、一平面内に平行に配置するとよく、第二の流体流チャネル２７０および２７０ａは、プロセスマイクロチャネル２１０のそれぞれの側の隣接平面内に平行に配置するとよく、熱交換チャネル２９０は、第二の流体流チャネル２７０ａに隣接する平面内に平行に配置するとよい。多相混合物形成ユニット２００Ｄでは、第二の流体流チャネル２７０は、一平面内に平行に配置するとよく、プロセスマイクロチャネル２１０および２１０ａは、液体チャネル２７０のそれぞれの側の隣接する平面内に平行に配置するとよく、熱交換チャネル２９０は、プロセスマイクロチャネル２１０に隣接する平面内に平行に配置するとよい。これらの多相混合物形成ユニットは、図３～９および１２には示していないが、当業者なら提供することができる、プロセス液体および熱交換流体の入出力を制御するために、適切なヘッダ、フッタ、マニホルド、バルブ、導路、配管、制御機構等を有してもよい。例えば、多相混合物形成ユニットを含むマイクロチャネルミキサへの入口および出口で、導路または配管を接続するために傾斜したヘッダおよびフッタを用いて、プロセスマイクロチャネルのサイズに伴う不必要な圧力降下を回避してもよい。

【００５６】

一実施態様では、複数の多相混合物形成ユニット（２００、２００Ａ、２００Ｂ、２００Ｃ、２００Ｄ、３００、４００、５１０）を上下に積み重ねて、オンデマンドの大きな生産能力用のスケールアップしたユニットのコアを形成してもよい。スケールアップしたユニットは、多相混合物製品のためだけでなく、多相混合物を形成させるために用いられる液体のためのマニホルドとしても、傾斜したヘッダおよびフッタを有してもよい。プロセスチャネル、分散相チャネルまたは熱交換チャネルの入口にオリフィスプレートまたはその他の開口区間を加えることによって、より一様な流れの分布を容易にしてもよい。フレーム区間を用いて、多相混合物形成ユニットを保持し、封止してもよい。

【００５７】

プロセスマイクロチャネル（２１０、２１０ａ、３１０、３２０、３３０、３４０、４１０、５２０）のそれぞれは、任意の構成、例えば正方形、長方形、円形、環形、楕円形、台形等の断面を有してもよい。プロセスマイクロチャネルは、管状であってもよい。プロセスマイクロチャネルは、横に並べられるか、または上下に重ねられた平行な離間したシートおよび／またはプレートから形成してもよい。用語「シート」は、最大約５ｍｍの壁の厚さを指す。用語「プレート」は、約５ｍｍ以上の壁の厚さを指す。シートは、ロールの形でユーザに供給されてもよく、一方、プレートは、平らな材料の片の形でユーザに供給されてもよい。プロセスマイクロチャネルのそれぞれは、プロセスマイクロチャネルを通る流体の流れに垂直な、最大約５０ｍｍ、一実施態様では最大約１０ｍｍ、一実施態様では最大約２ｍｍの範囲の内部寸法（例えば、高さ、幅または直径）を有するとよい。この寸法は、約０．０５から約５０ｍｍ、一実施態様では約０．０５から約１０ｍｍ、一実施態様では約０．０５から約５ｍｍ、一実施態様では約０．０５から約２ｍｍ、一実施態様では約０．０５から約１．５ｍｍ、一実施態様では約０．０５から約１ｍｍ、一実施態様では約０．０５から約０．５ｍｍの範囲にあるとよい。プロセスマイクロチャネルを通る液体の流れに垂直な別の内部寸法（例えば、高さまたは幅）は、任意の値であってもよく、例えば、約０．０１ｃｍから約１００ｃｍ、一実施態様では約０．０１ｃｍから約７５ｃｍ、一実施態様では約０．１ｃｍから約５０ｃｍ、一実施態様では約０．２ｃｍから約２５ｃｍの範囲にあるとよい。

【００５８】

一実施態様では、プロセスマイクロチャネル（２１０、２１０ａ、３１０、３２０、３３０、３４０、４１０、５２０）は、プロセスマイクロチャネルの中の第一の液体の流れの均一な分布を提供するために、混合区域（２１３、２１３ａ、３１５、３２５、３３５、３４５、４１３）の上流の入口の中の非開口領域または非多孔質領域（２１１、２１１

ａ、３１４、３２４、３３４、３４４、４１１）を有してもよい。これは、複数のプロセスマイクロチャネルが横に並べられ、および／または上下に重ねられて配置され、複数のプロセスマイクロチャネルの中への第一の液体流が一様でないとき、有用になることがある。これらの非開口領域を設けると、混合区域に到達する前の第一の流体流の流れを安定化することがある。非開口領域または非多孔質領域を使用すると、プロセスマイクロチャネルが円形の断面（すなわち管状幾何構造）を有するとき、利点になることがある。一実施態様では、非開口領域または非多孔質領域の中のプロセスマイクロチャネルの最小内部寸法に対する、プロセスマイクロチャネルへの入口から混合区域への入口までの非開口領域の長さの比は、約０．０００１から約１００００、一実施態様では約０．００１から約１０００の範囲にあるとよい。

【００５９】

プロセスマイクロチャネル（２１０、２１０ａ、３１０、３２０、３３０、３４０、４１０、５２０）の内部壁の一つ以上は、プロセスマイクロチャネルの中の流れを変更するための表面構成要素を有してもよい。図２２～２６に、これらの表面構成要素の例が示される。表面構成要素は、三次元パターンで互いの上に重ねられるか、または絡み合った二つ以上の層を有してもよい。各別個の層の中のパターンは、同じであってもよく、あるいは異なっていてもよい。各層の中で、または一つの層の中だけで、流れが回転するか、または平行移動してもよい。バルクの流れのチャネルに隣接していなくてもよい副層を用いて、追加の表面積を作り出してもよい。例えば、これらを用いて触媒を析出させてもよい。流れは、表面構成要素の第一のレベルの中で回転し、第二の副層以降の中に分子拡散して反応を促進してもよい。金属キャスティングまたはその他のプロセスによって三次元構成要素を作ってもよい。これらの方法では、互いの上に積層されているかのように変化するパターンも個別の平面に分解しなくてよい。バルクの流れのチャネルに隣接して、三次元的に変化する表面構成要素を置くことができる。これらの構成要素は、さまざまな深さ、形状および位置を有し、さまざまな深さ、形状および位置のパターンを有する副構成要素を伴う。表面構造物は、触媒析出のために追加の表面積を必要とする化学反応、または蒸留などの化学的分離の場合に利点となることがある。

【００６０】

図２３は、三次元表面構成要素構造物の平面概略図である。図２４には、三次元表面構成要素構造物の背面図の例が示され、バルクの流れのマイクロチャネルの隣接する界面にくぼんだＶ字形があり、Ｖ字形の下には、バルクの流れの通路に隣接する構成要素に接続されるが、多彩な形状、深さおよび位置の構造物から作られた一連の三次元構造がある。開いた表面構成要素の直下にはなく、バルクの流れのマイクロチャネルに隣接するが、一つ以上の曲がりくねった二次元または三次元の通路によって接続される、副層通路を作り出すとさらに有利になることがある。この手法は、狭い滞留時間分布ではなく、広い滞留時間分布を有することが望ましい反応器の中に調整された滞留時間分布を作り出すために利点となることがある。

【００６１】

図２５は、くぼんだＶ字形がバルク流れのマイクロチャネルに接し、Ｖ字形の後ろには変化する深さおよび位置にあるさまざまな形状の追加の構成要素がある、三次元表面構成要素の前面図である。

【００６２】

表面構成要素は、約２ｍｍより小さい、一実施態様では約１ｍｍより小さい、一実施態様では約０．０１ｍｍから約０．５ｍｍの範囲にある深さを有するとよい。表面構成要素の横幅は、マイクロチャネル幅にほぼ達する（魚骨設計で示されるように）のに十分であるとよいが、一実施態様（充填構成要素など）ではマイクロチャネル幅の約６０％以下、一実施態様では約４０％以下、一実施態様では約０．１％から約６０％、一実施態様では約０．１％から約５０％の幅であるとよい。

【００６３】

表面構成要素の横幅は、約０．０５ｍｍから約１００ｃｍの範囲、一実施態様では約０

．５ｍｍから約５ｃｍの範囲、一実施態様では約１から約２ｃｍの範囲にあるとよい。

【００６４】

表面構成要素の長さおよび幅は、マイクロチャネルの長さおよび幅と同様に定めるとよい。深さは、表面構成要素がマイクロチャネル表面の中に沈む距離であってもよく、この場合は、マイクロチャネル高さまたはマイクロチャネルギャップと同じ方向である。これは、シート表面の上または中に形成された表面構成要素を有し、積層され、ボンディングされたマイクロチャネルデバイスを積層する方向に対応してもよい。表面構成要素のこれらの寸法は、表面構成要素の最大寸法を指す。例えば、角を丸めた溝の深さは、最大の深さ、すなわち、溝の底での深さを指すことがある。

【００６５】

マイクロチャネルの中に、一つ以上のマイクロチャネル壁の中にさまざまな深さでくぼむ構成要素を含む、複数の表面構成要素または表面構成要素の領域を含んでもよい。くぼみの間の間隔は、約０．０１から約１０ｍｍの範囲、一実施態様では約０．１から約１ｍｍの範囲にあるとよい。表面構成要素は、マイクロチャネルの長さ全体に存在してもよく、またはマイクロチャネルの部分または領域に存在してもよい。表面構成要素を有する部分または領域は、専用に調整された区域の中で所望の反応または単位操作を促進するように断続的であってもよい。例えば、マイクロチャネルの１インチの区間は密集した表面構成要素のアレイを有し、続く４インチは構成要素のない平坦なチャネルとし、続く２インチは疎な表面構成要素の区間としてもよい。疎に離間した表面構成要素とは、表面構成要素の長さの５倍より大きなピッチまたは構成要素間距離を有する表面構成要素を指す。

【００６６】

一実施態様では、表面構成要素は、実質的にマイクロチャネルの軸方向長さ全体にわたって延在してもよい。一実施態様では、マイクロチャネルは、その軸方向長さの約５０％以下にわたって、一実施態様ではその軸方向長さの約２０％以下にわたって表面構成要素を有するとよい。一実施態様では、表面構成要素は、マイクロチャネルの軸方向長さの約１０％から約１００％にわたって延在するとよい。

【００６７】

図２６は、表面構成要素のために用いることができる複数のさまざまなパターンを示す。これらのパターンは、本発明を限定するものではなく、複数の可能性の例を示すことだけとする。任意の表面構成要素の場合と同じく、パターンは、マイクロチャネルのさまざまな軸方向の区間または横の区間の中で用いてもよい。

【００６８】

第二の流体流チャネル（２７０、２７０ａ、３５０、３６０、４２０、４３０、５３０、５４０）および第三の流体流チャネル（４４０、４５０）は、マイクロチャネルと特徴づけるには大きすぎる寸法を有することがあるが、マイクロチャネルであるとよい。これらのチャネルのそれぞれは、任意の構成、例えば、正方形、長方形、円形、環形、楕円形、台形等の断面を有してもよい。これらのチャネルは、上記で説明したように、表面構成要素を含んでもよい。第二および第三の流体流チャネルは管状であってもよい。第二および第三の流体流チャネルは、横に並べられるか、または上下に重ねられて配置された平行な離間したシートおよび／またはプレートから形成してもよい。各第二および第三の流体流チャネルは、最大約１００ｃｍの範囲、一実施態様では約０．０５ｍｍから約１００ｃｍの範囲、一実施態様では約０．０５ｍｍから約５０ｃｍ、一実施態様では約０．０５ｍｍから約１０ｃｍ、一実施態様では約０．０５ｍｍから約５ｃｍ、一実施態様では約０．０５ｍｍから約１０ｍｍ、一実施態様では約０．０５ｍｍから約５ｍｍ、一実施態様では約０．０５ｍｍから約２ｍｍ、一実施態様では約０．０５ｍｍから約１ｍｍの、第二および第三の流体流チャネルを通る流体流に垂直な内部寸法（例えば高さ、幅または直径）を有するとよい。第二および第三の流体流チャネルを通る流体流に垂直な別の内部寸法（例えば高さまたは幅）は、約０．０１ｃｍから約１００ｃｍ、一実施態様では約０．０１ｃｍから約７５ｃｍ、一実施態様では約０．１ｃｍから約５０ｃｍ、一実施態様では約０．２ｃｍから約２５ｃｍの範囲にあるとよい。第二および第三の流体流チャネルの長さは、

任意の値、例えば、約０．１ｃｍから約５００ｃｍ、一実施態様では約０．１ｃｍから約２５０ｃｍ、一実施態様では約１ｃｍから約１００ｃｍ、一実施態様では約１ｃｍから約５０ｃｍ、一実施態様では約２ｃｍから約２５ｃｍの範囲にあるとよい。各プロセスマイクロチャネルと次の隣接する第二の流体流チャネルまたは隣接する第二および第三の流体流チャネルとの間の距離は、約０．０５ｍｍから約５０ｍｍ、一実施態様では約０．１から約１０ｍｍ、一実施態様では約０．２ｍｍから約２ｍｍの範囲にあるとよい。

【００６９】

発熱源および／または吸熱源は、冷却、加熱、あるいは冷却と加熱との両方のために用いてもよい。発熱源および／または吸熱源は、一つ以上の熱交換チャネルを含んでもよい。発熱源は、一つ以上の電熱素子または抵抗加熱器を含んでもよい。吸熱源は、一つ以上の非流体冷却素子を含んでもよい。これらは、プロセスマイクロチャネルおよび／または第二または第三の流体流チャネルに隣接してもよい。一実施態様では、発熱源および／または吸熱源は、プロセスマイクロチャネルおよび／または第二および第三の流体流チャネルに接触も隣接もせず、プロセスマイクロチャネルおよび／または第二および第三の流体流チャネルのどちらかまたは両方から離れているが、発熱源および／または吸熱源とプロセスマイクロチャネルおよび／または第二および第三の流体流チャネルとの間で熱を移動させるために、プロセスマイクロチャネルおよび／または第二および第三の流体流チャネルに十分に近くすることができる。電熱素子、抵抗加熱器および／または非流体冷却素子を用いてプロセスマイクロチャネル（２１０、３１０ａ、３１０、３２０、３３０、３４０、４１０、５２０）、第二の流体流チャネル（２７０、２７０ａ、３５０、３６０、４２０、４３０、５３０、５４０）および／または第三の流体流チャネル（４４０、４５０）の一つ以上の壁を形成してもよい。電熱素子、抵抗加熱器および／または非流体冷却素子は、プロセスマイクロチャネル、第二の流体流チャネルおよび／または第三の流体流チャネルの一つ以上の壁の中に構築してもよい。電熱素子および／または抵抗加熱器は、プロセスマイクロチャネルおよび／または液体チャネルの壁の中に埋め込まれた薄いシート、ロッド、ワイヤ、ディスクまたはその他の形状の構造物であってもよい。電熱素子および／または抵抗加熱器は、プロセスマイクロチャネル壁および／または液体チャネル壁に接着されたフォイルまたはワイヤの形状であってもよい。加熱および／または冷却は、ペルティエ型熱電冷却および／または加熱素子を用いて実現してもよい。プロセスマイクロチャネル、第二の流体流チャネルおよび／または第三の流体流チャネルの長さに沿って、複数の加熱および／または冷却区域を使用してもよい。同様に、プロセスマイクロチャネル、第二の流体流チャネルおよび／または第三の流体流チャネルの長さに沿って、一つ以上の熱交換チャネルの中のさまざまな温度の伝熱流体を使用してもよい。発熱源および／または吸熱源は、プロセスマイクロチャネル、第二の流体流チャネルおよび／または第三の流体流チャネル内の精密な温度調節を提供するために用いてもよい。

【００７０】

熱交換チャネル（２９０、３７０、３８０、５９０）は、マイクロチャネルであってもよいが、典型的マイクロチャネルとは言えないような大きな寸法を有してもよい。これらのチャネルのそれぞれは、任意の構成、例えば、正方形、長方形、円形、環形、楕円形、台形等の断面を有してもよい。熱交換チャネルは、管状であってもよい。熱交換チャネルは、横に並べられるか、または上下に重ねられて配置された平行な離間したシートおよび／またはプレートから、隣接するプロセスマイクロチャネルまたは第二および第三の流体流チャネルと一緒に形成してもよい。これらのチャネルは、上記で説明された表面構成要素を含んでもよい。熱交換チャネルのそれぞれは、最大約５０ｍｍ、一実施態様では最大約１０ｍｍ、一実施態様では最大約２ｍｍの範囲の熱交換チャネルを通る熱交換流体流に垂直な内部寸法、例えば高さ、幅または直径を有するとよい。この寸法は、約０．０５から約５０ｍｍ、一実施態様では約０．０５から約１０ｍｍ、一実施態様では約０．０５から約５ｍｍ、一実施態様では約０．０５から約２ｍｍ、一実施態様では約０．５から約１ｍｍの範囲にあるとよい。熱交換チャンルを通る熱交換流体流に垂直な別の内部寸法、例えば高さまたは幅は、任意の値、例えば約０．０１ｃｍから約１００ｃｍ、一実施態様で

は約０．０１ｃｍから約７５ｃｍ、一実施態様では約０．１ｃｍから約５０ｃｍ、一実施態様では約０．２ｃｍから約２５ｃｍの範囲にあるとよい。熱交換チャネルの長さは、例えば約０．１ｃｍから約５００ｃｍ、一実施態様では約０．１ｃｍから約２５０ｃｍ、一実施態様では約１ｃｍから約１００ｃｍ、一実施態様では約１ｃｍから約５０ｃｍ、一実施態様では約０．２ｃｍから約２５ｃｍの範囲の任意の値であるとよい。各プロセスマイクロチャネルあるいは第二または第三の流体流チャネルと次の隣接する熱交換チャネルとの間の距離は、約０．０５ｍｍから約５０ｍｍ、一実施態様では約０．１から約１０ｍｍ、一実施態様では約０．２ｍｍから約２ｍｍの範囲にあるとよい。

【００７１】

熱交換チャネル（２９０、３７０、３８０、５９０）は、チャネルを通って隣接するプロセスマイクロチャネルまたは第二および第三の流体流チャネルを通る流体の流れと平行な、並流の方向に熱交換流体が流れるようにしてもよい。あるいは、熱交換流体は、熱交換チャネルを通って、プロセスマイクロチャネルまたは第二および第三の流体流チャネルを通る流体流に対して向流となる方向に流れてもよい。あるいは、熱交換チャネルは、プロセスマイクロチャネルまたは第二および第三の流体流チャネルを通る流体流に対して交差流となる方向の熱交換流体流を提供するように、プロセスマイクロチャネルまたは第二および第三の流体流チャネルに対して配向してもよい。熱交換チャネルは、交差流と並流または向流との組み合わせを提供するために、蛇行する構成を有してもよい。

【００７２】

一実施態様では、プロセスマイクロチャネル（２１０、２１０ａ、３１０、３２０、３３０、３４０、４１０、５２０）、第二の流体流チャネル（２７０、２７０ａ、３５０、３６０、４２０、４３０、５３０、５４０）、第三の流体流チャネル（４４０、４５０）および／または熱交換チャネル（２９０、３７０、３８０、５９０）は、正方形または長方形の断面を有し、平行な離間したシートまたはプレートから形成される。これらのチャネルは、横に並べられた垂直配向の交互面、または上下に積層された水平配向の交互面に配列してもよい。平行プレート構成と呼んでもよいこれらの構成には、複数の利点がある。例えば、円形の管と比較すると、平行プレート構成は、同じ連続相物質流束での高さ、幅または直径に対して、同じせん断力を実現しながら、受ける圧力降下が小さい。例えば、長方形チャネルのアスペクト比が約１０に近づくと、すなわち平行シートまたはプレート構成に近づくと、その圧力降下は、同じ条件下の円形チャネルの中の圧力降下のわずか約５０％にすることができる。平行板構成を有するプロセスマイクロチャネル、第二の流体流チャネル、第三の流体流チャネルおよび熱伝達チャネルは、スケールアップのために、小型デバイスの中に容易に配置することができる。円形の管と比較すると、平行プレート構成を用いることによって、多相混合物形成プロセスのより高い単位体積あたり処理能力を実現することもできる。

【００７３】

平行プレート構成を用いる利点は、これらの構成が円形の管と比較してより大きな流体／壁材料比を有し、従ってより小型であり、より大きな製造能力または出力の可能性を有する点である。

【００７４】

一実施態様では、プロセスマイクロチャネル（２１０、２１０ａ、３１０、３２０、３３０、３４０、４１０、５２０）、第二の流体流チャネル（２７０、２７０ａ、３５０、３６０、４２０、４３０、５３０、５４０）、第三の流体流チャネル（４４０、４５０）および／または熱交換チャネル（２９０、３７０、３８０、５９０）は、同心状に配置された円形の管の形であるとよい。プロセスマイクロチャネルおよび第二の流体流チャネルは、互いに隣接し、一方のチャネルは環状の空間にあり、他方のチャネルは中心の空間または隣接する環状の空間にあるとよい。一実施態様では、本発明のプロセスで有用なマイクロチャネルミキサは、複数の交互に重ねられた同心円の管のプロセスマイクロチャネル、第二の流体流チャネル、および選択肢として第三の流体流チャネルを含み、マイクロチャネルミキサは円筒形の形状であるとよい。

【００７５】
開口（２４４、２４４ａ、３１３、３２３、３３３、３４３、４１６、４２６、４３６、４４６）は、開口区間を通る示された流体の流れを可能にする十分なサイズであるとよい。開口は、細孔と呼んでもよい。開口区間（２４０、２４０ａ、３１１、３２１、３３１、３４１、４１５、４２５、４３５、４４５、５５０、５６０、５７０、５８０）は、約０．０１から約５０ｍｍ、一実施態様では約０．０５から約１０ｍｍ、一実施態様では約０．１から約２ｍｍの範囲の厚さを有するとよい。開口は、最大約５０ミクロンの範囲、一実施態様では約０．００１から約５０ミクロンの範囲、一実施態様では約０．０５から約５０ミクロン、一実施態様では約０．１から約５０ミクロンの平均直径を有するとよい。一実施態様では、開口は、約０．５から約１０ナノメートル（ｎｍ）、一実施態様では約１から約１０ｎｍ、一実施態様では約５から約１０ｎｍの範囲の平均直径を有するとよい。開口区間の中の開口の数は、平方センチメートルあたり約１０から約5×10^{8}開口、一つの実施態様では平方センチメートルあたり約１から約1×10^{6}開口の範囲にあるとよい。開口は、互いに孤立していてもよく、孤立していなくてもよい。開口の一部またはすべては、開口区間内の他の開口と流体連通していてもよい。プロセスマイクロチャネル（２１０、２１０ａ、３１０、３２０、３３０、３４０、４１０、５２０）を通って流れる流体の流れの経路に沿った開口区間の長さに対する、開口区間の厚さの比は、約０．００１から約１００、一実施態様では約０．０１から約５０、一実施態様では約０．０３から約２５、一実施態様では約０．０５から約１０、一実施態様では約０．０８から約５、一実施態様では約０．１から約１の範囲にあるとよい。開口区間は、本発明のプロセスの動作を可能にするのに十分な強度および寸法安定性を提供する任意の材料で構築するとよい。これらの材料は、鋼（例えばステンレス鋼、炭素鋼および類似物）、モネル、インコネル、アルミニウム、チタン、ニッケル、白金、ロジウム、銅、クロム、真鍮、上記金属の任意のものの合金、重合体（例えば熱硬化性樹脂）、セラミック、ガラス、一つ以上の重合体（例えば熱硬化樹脂）およびガラス繊維を含むコンポジット、石英、ケイ素、カーボンナノチューブまたはカーボンモレキュラーシーブを含む微多孔質炭素、ゼオライトまたはそれらの二つ以上の組み合わせを含む。開口は、レーザ穿孔、マイクロエレクトロマシニングシステム（ＭＥＭＳ）、リソグラフィー電着および成型（ＬＩＧＡ）、電気スパークリングまたは電気化学エッチングなどの既知の技法を用いて作製してもよい。開口は、押し出しなどの構造を有するプラスチックを作るために用いられる技法、または配列カーボンナノチューブ（ＣＮＴ）膜などの膜を作るために用いられる技法を用いて、作製してもよい。開口は、金属粉末または粒子を焼結または圧縮して曲がりくねって相互連絡した毛管チャネルを形成させるなどの技法、および膜作製の技法を用いて作製してもよい。開口は、これらの方法の任意のものによって提供されるサイズから、開口を部分的に埋める開口内部側壁へのコーティングの塗布によって大きさを小さくしてもよい。選択なコーティングによって、多孔質ボディの外に薄層を形成させ、連続する流れの経路に隣接して最小の細孔サイズを提供してもよい。最小平均細孔開口は、多相混合物用の所望の液滴サイズによって、約１ナノメートルから約数百ミクロンの範囲にあるとよい。開口は、熱処理によって、ならびに、開口内部側壁上に酸化物スケールまたはコーティングを形成させる方法によって、サイズを小さくしてもよい。これらの技法は、開口を部分的に閉塞して流れに当てられる開口のサイズを減らすために用いてもよい。図１３および１４は、熱処理の前後の、同じ倍率で、同じ位置のステンレス鋼多孔基板のＳＥＭ表面構造の比較を示す。図１３は熱処理前の表面を示し、図１４は熱処理後の表面を示す。熱処理後の多孔質材料の表面は、著しく小さなギャップおよび開口部サイズを有する。対応して、開口の間の平均距離は、増加する。

【００７６】
開口区間（２４０、２４０ａ、３１１、３２１、３３１、３４１、４１５、４２５、４３５、４４５、５５０、５６０、５７０、５８０）は、約０．０１から約２００ミクロンの範囲の平均細孔サイズの相互連結チャネルまたは細孔を有する金属または非金属多孔質材料から作ってもよい。これらの細孔は、開口（２４４、２４４ａ、３１３、３２３、３

３３、３４３、４１６、４２６、４３６、４４６）として機能してもよい。多孔質材料は、平均細孔間距離が平均細孔径と同様になるように、粉末または微粒子から作ってもよい。非常に小さな細孔サイズが用いられると、細孔間距離も非常に小さくなることがあり、液滴は、プロセスマイクロチャネル（２１０、２１０ａ、３１０、３２０、３３０、４１０、５２０）または第二の流体流チャネル（４２０、４３０）の側の表面で合体して望ましくない大きな液滴を形成することがある。多孔質材料は、約３００℃から約１０００℃の範囲の高温で、約１時間から約２０日間の長さの酸化によって、またはゾルコーティングによるアルミナまたは化学蒸着法を用いるニッケルなどの別の材料の薄層を表面の上および細孔の内部にコーティングして、小さな細孔をふさぎ、大きな細孔の細孔サイズを小さくし、その結果細孔間距離を増加させることによって、調整してもよい。そのようにして、液滴の合体を減らすか、またはなくし、より小さな液滴の生成を可能にしてもよい。図１５に、調整された基板または開口区間のＳＥＭ画像が示される。

【００７７】

開口（２４４、２４４ａ、３１３、３２３、３３３、３４３、４１６、４２６、４３６、４４６）は、混合区域（２１３、２１３ａ、３１５、３２５、３３５、３４５、４１３）全体にわたって規則的に離間してもよい。開口は、小さな開口ほど、または大きな開口ほど、混合区域の前後のどちらかの近くで用いられるように、優先して離間してもよい。開口は、一緒に、混合区域の始めで互いに近く、混合区域の終わり近くで遠く離れて液滴融合を抑制する助けとしてもよい。約１ミクロンより小さな泡またはミクロスフェアサイズを有する多相混合物を提供するのに十分に小さなマイクロスケール開口または細孔（２４４、２４４ａ、３１３、３２３、３３３、３４３、４１６、４２６、４３６、４４６）を有する開口区間（２４０、２４０ａ、３１１、３２１、３３１、３４１、４１５、４２５、４３５、４４５、５５０、５６０、５７０、５８０）として用いられる基板の製作は、問題となることがある。これの理由の一つは、圧縮および／または焼結によって粉末／粒子から作られた金属多孔質基板などの未処理の通常の多孔質材料では、比較的大きな表面粗さが生じるという事実にある。一般に、これらの金属多孔質基板では、所定の名目細孔径が特定の値より低いとき、表面領域に必要な細孔サイズがない。多孔質材料のバルクは指定された名目細孔サイズを有するが、多くの場合、表面領域ははるかに大きなサイズの融合細孔および空洞を特徴とする。この問題は、これらの基板を調整して所望の細孔サイズおよび細孔間距離を表面領域の中に提供することによって、克服することができる。これは、多孔質基板から表面層を除去し、より小さな開口を有する滑らかな新しい表面を露出させるか、または加えることによって実施するとよい。これらの調整された基板を用いて形成される多相混合物の中の泡またはマイクロスフェアサイズは、基板にかかる圧力降下を増加させずに小さくすることができる。多孔質表面を直接研磨または機械加工すると、表面構造のスミアリングおよび細孔の閉塞の原因となることがあるので、多孔質構造を液体充填材で満たした後、固形化および機械研磨／磨き仕上げしてもよい。次に、充填材を除去して材料の多孔質構造を再び得る。充填材は、亜鉛またはスズなどの低い融点を有する金属またはエポキシなどの重合体の前駆体であってもよい。液体充填および除去工程は、真空の使用によって支援してもよい。研磨／磨き仕上げは、研削盤および研削粉を用いて実行してもよい。金属充填剤除去は、融解および真空吸引によって、または酸エッチングによって実現してもよい。エポキシまたはその他の重合体は、溶媒溶解によって、または空気中での燃焼除去によって除去してもよい。

【００７８】

図１６～１９を参照すると、一実施態様では、開口区間（２４０、２４０ａ、３１１、３２１、３３１、３４１、４１５、４２５、４３５、４４５、５５０、５６０、５７０、５８０）は、比較的小さな開口６０２を含む比較的薄いシート６００と、開口６００と同軸配置されるかまたは接続された比較的大きな開口６１２のアレイを含む比較的厚いシートまたはプレート６１０とで構築するとよい。比較的薄いシート６００は、比較的厚いシート６１０の上にあってボンディングされ、比較的薄いシート６００は、プロセスマイクロチャネル（２１０、２１０ａ、３１０、３２０、３３０、３４０、４１０）または第二

の流体流チャネル（４２０、４３０）の内部に対向し、比較的厚いシート６１０は、第二の流体流チャネル（２７０、２７０ａ、３５０、３６０、４２０、４３０、５３０、５４０）または第三の流体流チャネル（４４０、４５０）の内部に対向する。比較的薄いシート６００は、任意の適当な手順（例えば拡散結合）を用いて比較的厚いシート６１０にボンディングされ、機械的強度が大きくなったコンポジット構造６２０を提供することができる。比較的薄いシート６００は、約０．００１から約０．５ｍｍ、一実施態様では約０．０５から約０．２ｍｍの範囲の厚さを有するとよい。比較的小さな開口６０２は、任意の形状、例えば円形、三角形または長方形を有するとよい。比較的小さな開口６０２は、約０．０５から約５０ミクロン、一実施態様では約０．０５から約２０ミクロンの範囲の平均直径を有するとよい。比較的厚いシートまたはプレート６１０は、約０．１から約５ｍｍ、一実施態様では約０．１から約２ｍｍの範囲の厚さを有するとよい。比較的大きな開口６１２は、任意の形状、例えば円形、三角形または長方形を有するとよい。比較的大きな開口６１２は、約０．１から約４０００ミクロン、一実施態様では約１から約２０００ミクロン、一実施態様では約１０から約１０００ミクロンの範囲の平均直径を有するとよい。シート６００の中の開口６０２の数およびシートまたはプレート６１０の中の開口６１２の数は、それぞれ平方センチメートルあたり約２から約１００００開口、一実施態様では平方センチメートルあたり約２から約１０００開口の範囲にあるとよい。シート６００およびシートまたはプレート６１０は、開口区間（２４０、２４０ａ、３１１、３２１、３３１、３４１、４１５、４２５、４３５、４４５、５５０、５６０、５７０、５８０）を構築するために有用であるとして上記で説明した材料の任意のもので構築するとよい。開口６０２および６１２は、開口区間を通って流れる液体が最初に開口６１２を通り、次に開口６０２を通って流れるように同軸配置されるか、または接続されるとよい。液体が比較的小さな開口６０２を通って流れるための比較的短い通路は、開口の中の通路が開口６０２と６１２とを合わせた長さに等しい長さを有していたら起こると考えられる圧力降下と比べると比較的低い圧力降下で、液体が開口６０２を通って流れることを可能にする。

【００７９】

図１９に例が示される実施態様では、コンポジット構造物６２０ａは、開口６１２を覆う比較的薄いシート６００の凸部分６０４が提供される点を除けば、図１８に例が示されるものと同じ設計を有する。凸部分６０４は、隣接するチャネルの中の局所せん断力の増加をもたらす。図１９の方向矢印６３０は、開口６０２に隣接するチャネルの中の流体の流れを示す。せん断力がより大きいため、開口６０２を通って流れる流体の泡またはミクロスフェアサイズが小さくなる。

【００８０】

図２０に例が示される実施態様では、シートまたはプレート６４０の表面と、開口６４６の内部側壁６４４との上に表面コーティング６４２が析出される。このコーティングは、開口（２４４、２４４ａ、３１３、３２３、３３３、３４３、４１６、４２６、４３６、４４６）の直径を小さくする、より容易な方法を提供する。コーティング６４２を形成させるために用いられるコーティング材料は、アルミナ、ニッケル、金または重合材料（例えばテフロン（登録商標））を含んでもよい。コーティング６４２は、化学蒸着、金属スパッタリング、金属メッキ、焼結、ゾルコーティング、重合体コーティングおよび類似法を含む既知の技法を用いて、シートまたはプレート６４０に塗布してもよい。開口の直径は、コーティング６４２の厚さを調節することによって制御してもよい。

【００８１】

一実施態様では、開口区間（２４０、２４０ａ、３１１、３２１、３３１、３４１、４１５、４２５、４３５、４４５、５５０、５６０、５７０、５８０）は、非対称多孔質材料、例えば、複数の焼結粒子の層を有する多孔質材料で形成してもよい。層の数は、２、３または４以上であってもよい。これらの多層基板の利点は、耐久性および接着強さの増加をもたらす点である。例は、一方の側に比較的大きな細孔、他方の側に比較的小さな細孔を有する焼結セラミックスを含む。比較的小さな細孔は、約２から約１０ｎｍの範囲の

直径を有するとよい。比較的小さな細孔は、多層基板の比較的薄い層に位置するとよい。比較的薄い層は、約１から約１０ミクロンの範囲の厚さを有するとよい。比較的小さな細孔を有する側は、プロセスマイクロチャネル（２１０、２１０ａ、３１０、３２０、３３０、３４０、４１０、５２０）または第二の流体流チャネル（４２０、４３０）の内部に面して配置し、比較的高いせん断力を利用して比較的小さな多相混合物の泡またはミクロスフェアが形成されると除去するとよい。

【００８２】

プロセスマイクロチャネル（２１０、２１０ａ、３１０、３２０、３３０、３４０、４１０、５２０）、第二の流体流チャネル（２７０、２７０ａ、３５０、３６０、４２０、４３０、５３０、５４０）、第三の流体流チャネル（４４０、４５０）および熱交換チャネル（２９０、３７０、３８０、５９０）は、関連するヘッダ、フッタ、マニホルド等とともに、本発明のプロセスの動作を可能にするのに十分な強度、寸法安定性、耐食性および伝熱特性を提供する任意の材料で作ってもよい。これらの材料は、鋼（例えばステンレス鋼、炭素鋼および類似物）、モネル、インコネル、アルミニウム、チタン、ニッケル、白金、ロジウム、銅、クロム、真鍮、前述の金属の任意のものの合金、重合体（例えば熱硬化性樹脂）、セラミックス、ガラス、一つ以上の重合体（例えば熱硬化性樹脂）とガラス繊維を含むコンポジット、石英、ケイ素、またはそれらの二つ以上の組み合わせを含む。

【００８３】

第一の流体流は、気体または液体を含んでもよい。第二の流体流は、気体またはマイクロボディ形成材料を含んでもよい。第三の流体流は、気体を含んでもよい。

【００８４】

気体は、任意の気体を含んでもよい。一実施態様では、気体は、空気、酸素、窒素、二酸化炭素、水蒸気、アンモニア、オゾン、塩素ガス、水素および類似物の一種類以上を含んでもよい。気体は、一つ以上の気体炭化水素、例えば、１から約５個の炭素原子を含む炭化水素を含んでもよい。これらは、飽和および不飽和炭化水素を含む。炭化水素は、メタン、エタン、エチレン、プロパン、イソプロパン、プロピレン、ブタン類、ブチレン類、ペンタン類、シクロペンタン、ペンチレン類、シクロペンチレンおよび類似物を含む。

【００８５】

液体は、任意の液体を含んでもよい。液体は、水、有機液体またはそれらの組み合わせを含んでもよい。液体は、一つ以上の液体炭化水素を含んでもよい。これらは、１個から約２４個の炭素原子、一実施態様では約５個から約２４個の炭素原子、一実施態様では約６個から約１８個の炭素原子、一実施態様では約６個から約１２個の炭素原子を含む炭化水素化合物を含む。用語「炭化水素」は、炭化水素または主に炭化水素の性格を有する化合物を示す。これらの炭化水素化合物は、以下のものを含む。

（１）純炭化水素化合物、すなわち、脂肪族化合物（例えばアルカンまたはアルキレン）、脂環式化合物（例えばシクロアルカン、シクロアルキレン）、芳香族化合物、脂肪族および脂環式置換芳香族化合物、芳香族置換脂肪族化合物および芳香族置換脂環式化合物および類似物。例は、ヘキサン、１－ヘキセン、ドデカン、シクロヘキセン、シクロヘキサン、エチルシクロヘキサン、ベンゼン、トルエン、キシレン類、エチルベンゼン、スチレン等を含む。

（２）置換炭化水素化合物、すなわち、化合物の主に炭化水素の性格を変えない非炭化水素置換基を含む炭化水素化合物。非炭化水素置換基の例は、ヒドロキシ、アシル、ニトロ、ハロ等を含む。

（３）ヘテロ置換炭化水素化合物、すなわち性格としては主に炭化水素であるが、通常は炭素原子で構成される分子鎖または環の中に炭素以外の原子を含む炭化水素化合物。例えば、ヘテロ原子は、窒素、酸素および硫黄を含む。

【００８６】

液体は、天然オイル、合成オイルまたはそれらの混合物を含んでもよい。天然オイルは、動物オイルおよび植物オイル（例えばヒマシ油、ラード油）、ならびに液体石油系オイ

ル分およびパラフィン系、ナフテン系または混合パラフィン系－ナフテン系型の溶媒処理または酸処理鉱物オイルなどの鉱物オイルを含む。天然オイルは、石炭または頁岩から誘導されるオイルを含む。オイルは、トリグリセリドの仲間からのケン化可能なオイル、例えばダイズ油、ゴマ種子油、綿実油、サフラワー油および類似物であってよい。オイルは、シリコーンオイル（例えばシクロメチコーン、シリコンメチコーン類等）であってもよい。オイルは、ワセリン、スクアラン、スクアレンまたは一つ以上のジアルキルシクロヘキサン類、またはそれらの二つ以上の混合物などの脂肪族またはナフテン系炭化水素であってもよい。合成オイルは、重合および高分子間反応したオレフィン（例えばポリブチレン類、ポリプロピレン類、プロピレンイソブチレン共重合体等）、ポリ（１－ヘキセン類）、ポリ（１－オクテン類）、ポリ（１－デセン類）等およびそれの混合物などの炭化水素オイル、アルキルベンゼン類（例えばドデシルベンゼン類、テトラデシルベンゼン類、ジノニルベンゼン類、ジ－（２－エチルヘキシル）ベンゼン類等）、ポリフェニル類（例えばビフェニル類、テルフェニル類、アルキル化ポリフェニル類等）、アルキル化ジフェニルエーテル類およびアルキル化ジフェニルスルフィド類およびそれらの誘導体、類縁体および同族体ならびに類似物を含む。末端ヒドロキシル基がエステル化、エーテル化等によって修飾されたアルキレンオキシド重合体類およびそれらの共重合体および誘導体は、用いることができる合成オイルである。合成オイルは、ポリ－アルファ－オレフィンまたはフィッシャー－トロプシュ合成炭化水素を含んでもよい。

【００８７】

液体は、通常は液体の炭化水素燃料、例えば、ＡＳＴＭ規格Ｄ４３９で定められる自動車ガソリンなどの留出燃料、またはＡＳＴＭ規格Ｄ３９６で定められるディーゼル燃料または重油を含んでもよい。

【００８８】

液体は、脂肪族アルコール、脂肪酸エステルまたはそれらの混合物を含んでもよい。脂肪族アルコールは、ゲルベ（Ｇｕｅｒｂｅｔ）アルコールであってもよい。脂肪族アルコールは、約６個から約２２個の炭素原子、一実施態様では約６個から約１８個の炭素原子、一実施態様では約８個から約１２個の炭素原子を含むとよい。脂肪酸エステルは、約６個から約２２個の炭素原子の直鎖脂肪酸と約６個から約２２個の炭素原子の直鎖または分岐脂肪族アルコールとのエステル、約６個から約１３個の炭素原子の分岐カルボン酸と約６個から約２２個の炭素原子の直鎖または分岐脂肪族アルコールとのエステル、またはそれらの混合物であってもよい。例は、ミリスチン酸ミリスチル、パルミチン酸ミリスチル、ステアリン酸ミリスチル、イソステアリン酸ミリスチル、オレイン酸ミリスチル、ベヘン酸ミリスチル、エルシン酸ミリスチル、ミリスチン酸セチル、パルミチン酸セチル、ステアリン酸セチル、イソステアリン酸セチル、オレイン酸セチル、ベヘン酸セチル、エルシン酸セチル、ミリスチン酸ステアリル、パルミチン酸ステアリル、ステアリン酸ステアリル、イソステアリン酸ステアリル、オレイン酸ステアリル、ベヘン酸ステアリル、エルシン酸ステアリル、ミリスチン酸イソステアリル、パルミチン酸イソステアリル、ステアリン酸イソステアリル、イソステアリン酸イソステアリル、オレイン酸イソステアリル、ベヘン酸イソステアリル、オレイン酸イソステアリル、ミリスチン酸オレイル、パルミチン酸オレイル、ステアリン酸オレイル、イソステアリン酸オレイル、オレイン酸オレイル、ベヘン酸オレイル、エルシン酸オレイル、ミリスチン酸ベヘニル、パルミチン酸ベヘニル、ステアリン酸ベヘニル、イソステアリン酸ベヘニル、オレイン酸ベヘニル、ベヘン酸ベヘニル、エルシン酸ベヘニル、ミリスチン酸エルシル、パルミチン酸エルシル、ステアリン酸エルシル、イソステアリン酸エルシル、オレイン酸エルシル、ベヘン酸エルシルおよびエルシン酸エルシルを含む。脂肪酸エステルは、約１８個から約３８個の炭素原子のアルキルヒドロキシカルボン酸と、約６個から約２２個の炭素原子の直鎖または分枝脂肪族アルコールとのエステル（例えばりんご酸ジオクチル）、約６個から約２２個の炭素原子の直鎖または分枝脂肪酸と、多価アルコール（例えばプロピレングリコール、二量体ジオールまたは三量体トリオール）および／またはゲルベアルコールとのエステル、約６個から約１８個の炭素原子の一種類以上の脂肪酸から作られるトリグリセリド、約６個から

約１８個の炭素原子の一種類以上の脂肪酸から作られるモノ、ジおよび／またはトリグリセリドの混合物、約６個から約２２個の炭素原子の一種類以上の脂肪族アルコールおよび／またはゲルベアルコールと一種類以上の芳香族カルボン酸とのエステル（例えば安息香酸）、２個から約１２個の炭素原子の一種類以上のジカルボン酸と１個から約２２個の炭素原子を含む一種類以上の直鎖または分岐アルコール、２個から約１０個の炭素原子および２個から約６個のヒドロキシル基を含む一種類以上のポリオール、またはそのようなアルコールとポリオールとの混合物とのエステル、２個から約１２個の炭素原子の一種類以上のジカルボン酸（例えばフタル酸）と１個から２２個の炭素原子の一種類以上のアルコール（例えばブチルアルコール、ヘキシルアルコール）とのエステル、安息香酸と約６個から約２２個の炭素原子の直鎖および／または分岐アルコールとのエステル、またはそれらの二種類以上の混合物を含んでもよい。

【００８９】

液体は、約６個から約２２個の炭素原子の一種類以上の分岐第一アルコール、約６個から約２２個の炭素原子の一種類以上の直鎖および／または分岐脂肪族アルコール炭酸エステル、約６個から約２２個の炭素原子の一種類以上の脂肪族アルコールから作られる一種類以上のゲルベ炭酸エステル、各アルキル基が１個から約１２個の炭素原子を含む一種類以上のジアルキル（例えばジエチルヘキシル）ナフタレート、アルキル基あたり約６個から約２２個の炭素原子を含む一種類以上の直鎖または分岐、対称または非対称ジアルキルエーテル、約６個から約２２個の炭素原子のエポキシ化された脂肪酸エステルと、２個から１０個の炭素原子および２個から６個のヒドロキシル基を含むポリオールとの一種類以上の開環生成物、またはそれらの二種類以上の混合物を含んでもよい。

【００９０】

水は、任意の簡便な供給源から採取してもよい。水は、浸透法または蒸留法を用いて脱イオンまたは精製してもよい。

【００９１】

マイクロボディ形成材料は、任意のマイクロボディ形成材料を含んでもよい。マイクロボディ形成材料は、液体または固体メルトの形であってもよい。マイクロボディ形成材料は、ガラス、例えば、ガラスマイクロボディ（例えばマイクロスフェア）形成材料、重合体、例えば、重合体マイクロボディ（例えば重合体マイクロスフェア）形成材料を含んでもよい。重合体マイクロボディ形成材料は、一種類以上のアクリル樹脂、シリコン樹脂、ウレタン樹脂、酢酸ビニル樹脂、テフロン（登録商標）樹脂、ポリアミド樹脂、塩化ビニル樹脂、スチレン系樹脂、フェノール樹脂、エポキシ樹脂、スチレン－ブタジエン－スチレンブロック共重合体樹脂、スチレン－エチレン－ブチレン－スチレンブロック共重合体樹脂、スチレン－イソプレン－スチレンブロック共重合体樹脂、ｎ－ブチルゴム、クロロプレンゴム、天然ゴムまたはそれらの二種類以上の組み合わせを含んでもよい。一実施態様では、重合体マイクロボディ形成材料は、１個から約１４個の炭素原子のアルコールの（メタ）アクリル酸エステルを含んでもよい。一実施態様では、重合体マイクロボディ形成材料は、少なくとも一種類の（メタ）アクリル酸アルキルを含んでもよい。

【００９２】

本発明の一つ以上の実施態様では、乳化剤および／または界面活性剤は必要ないが、本発明のプロセスによって調製される多相混合物を形成する際に一つ以上の乳化剤および／または界面活性剤を用いてもよい。乳化剤および／または界面活性剤は、液体と予め混合してもよい。乳化剤および／または界面活性剤は、グリフィン（Ｇｒｉｆｆｉｎ）のシステムで０から約１８、一実施態様では約０．０１から約１８の範囲の親水性親油性バランス（ＨＬＢ）を有するイオン性または非イオン性化合物を含んでもよい。イオン化合物は、カチオン性または両性化合物のことがある。例は、「マッカチオンズ界面活性剤および洗剤（ＭｃＣｕｔｃｈｅｏｎｓ Ｓｕｒｆａｃｔａｎｔｓ ａｎｄ Ｄｅｔｅｒｇｅｎｔｓ）」、１９９８年版、北米版および国際版に開示されているものを含む。北米版の１～２３５頁および国際版の１～１９９頁は、そのような乳化剤の開示に関する部分が参照によって本明細書に組み込まれる。用いることができる乳化剤および／または界面活性剤は

、アルキレンオキシド繰り返し単位、カルボキシル化アルコールエトキシレート類、エトキシ化アルコール類、エトキシ化アルキルフェノール類、エトキシ化アミン類およびアミド類、エトキシ化脂肪酸、エトキシ化脂肪酸エステルおよびオイル、脂肪酸エステル、脂肪酸アミド、グリセロールエステル、グリコールエステル、ソルビタンエステル、イミダゾリン誘導体、レシチンおよび誘導体、リグニンおよび誘導体、モノグリセリドおよび誘導体、オレフィンスルホン酸エステル、リン酸エステルおよび誘導体、プロポキシル化およびエトキシル化脂肪酸またはアルコール類またはアルキルフェノール類、ソルビタン誘導体、ショ糖エステルおよび誘導体、硫酸エステルまたはアルコール類またはエトキシル化アルコール類または脂肪酸エステル類、ドデシルベンゼン類およびトリデシルベンゼン類または縮合ナフタレンまたは石油のスルホン酸エステル、スルホコハク酸エステルおよび誘導体、トリデシルベンゼンおよびドデシルベンゼンスルホン酸を含む。乳化剤および／または界面活性剤は、一種類以上のポリアルキレングリコール類、グリセロールまたはソルビタンと、約１２個から約２２個の炭素原子を含む脂肪酸との一種類以上の部分エステル、またはそれらの混合物を含んでもよい。乳化剤および／または界面活性剤は、レシチンなどの薬学上許容される材料を含んでもよい。本発明のプロセスによって作られる多相混合物の中のこれらの乳化剤および／または界面活性剤の濃度は、多相混合物の最大約２０重量％、一実施態様では約０．０１から約５重量％の範囲、一実施態様では約０．０１から約２重量％の範囲にあるとよい。一実施態様では、この濃度は、最大約２重量％、一実施態様では最大約１重量％、一実施態様では最大約０．５重量％であるとよい。

【００９３】

一実施態様では、第一の流体流は液体流を含み、第二の流体流は空気を含む。

【００９４】

一実施態様では、第一の流体流は液体廃棄流を含み、第二の流体流は空気を含む。

【００９５】

一実施態様では、第一の流体流は有害液体廃棄流を含み、第二の流体流は空気を含む。

【００９６】

一実施態様では、第一の流体流はサラダドレッシングまたはマスタードを含み、第二の流体流は窒素を含む。

【００９７】

一実施態様では、第一の流体流は液体飲料またはビールを含み、第二の流体流は二酸化炭素を含む。

【００９８】

一実施態様では、第一の流体流は紙の製造に用いられる漂白パルプを含み、第二の流体流は塩素を含む。

【００９９】

一実施態様では、第一の流体流は水の中の石炭の分散を含み、第二の流体流は空気を含む。

【０１００】

一実施態様では、第一の流体流は随伴水を含むモーター油を含み、第二の流体流は窒素を含む。

【０１０１】

一実施態様では、第一の流体流は培養反応用の細胞を含み、第二の流体流は酸素または空気を含む。

【０１０２】

一実施態様では、第一の流体流は液体反応媒質を含み、第二の流体流は空気または酸素を含む。

【０１０３】

一実施態様では、第一の流体流は水素化反応を実行するための反応媒質を含み、第二の流体流は水素を含む。

【０１０４】

一実施態様では、第一の流体流はオイルと水との混合物を含み、第二の流体流は空気または天然ガスを含む。

【０１０５】

一実施態様では、第一の流体流は紙の製造に用いられる漂白パルプを含み、第二の流体流は酸素を含む。

【０１０６】

一実施態様では、第一の流体流は食用油、ワインまたはジュースを含み、第二の流体流は窒素を含む。

【０１０７】

一実施態様では、第一の流体流は魚の養殖に用いられる水を含み、第二の流体流は酸素を含む。

【０１０８】

一実施態様では、第一の流体流は水を含み、第二の流体流はオゾンを含む。

【０１０９】

一実施態様では、第一の流体流は廃液流またはプロセス流を含み、第二の流体流は二酸化炭素またはアンモニアを含む。

【０１１０】

一実施態様では、第一の流体流は空気を含み、第二の流体流は水蒸気を含む。

【０１１１】

一実施態様では、第一の流体流は揮発性有機化合物を含む廃液流またはプロセス流を含み、第二の流体流は空気を含む。

【０１１２】

一実施態様では、第一の流体流は気体または液体を含み、第二の流体流はマイクロボディ形成材料を含む。

【０１１３】

一実施態様では、第一の流体流は水系組成物を含み、第二の流体流は水素および／または酸素を含む。これは、過酸化水素生成のための直接組み合わせのために用いてもよい。

【０１１４】

一実施態様では、第一の流体流は２‐アルキルアントラキノンを含み、第二の流は水素を含む。これは、過酸化水素の生成に用いてもよい。

【０１１５】

第一の流体流材料は、本発明のプロセスによって作られる多相混合物の中に、約０．１から約８０重量％、一実施態様では約１から約５０重量％、一実施態様では約１から約２０重量％の範囲の濃度で存在するとよい。第二の流体流材料は、本発明のプロセスによって作られる多相混合物の中に、約１から約９５重量％、一実施態様では約１０から約５０重量％、一実施態様では約１０から約２５重量％の範囲の濃度で存在するとよい。第三の流体流材料は、本発明のプロセスによって作られる多相混合物の中に、最大約０．０１％から約５０重量％、一実施態様では約１から約１５重量％、一実施態様では約０．１から約１重量％の範囲の濃度で存在するとよい。

【０１１６】

一実施態様では、第二の流体は第一の流体の中に溶解してもよい。これは、プロセスマイクロチャネルの中で起こってもよく、あるいは多相混合物がプロセスマイクロチャネルから出た後で起こってもよい。一実施態様では、第二の流体は、第一の流体と混合された後、最大約１０時間後の期間内に、一実施態様では最大約１時間の期間内に第一の流体の中に溶解するとよい。

【０１１７】

本発明の多相混合物は、一種類以上の固体粒子を含んでもよい。これらは、第一、第二および／または第三の液体と予め混合してもよい。固体粒子は、有機物、無機物またはそれらの組み合わせであってもよい。固体粒子は、触媒（例えば、CeO_2／$BaAl_{12}O_{19}$、Pt／Al_2O_3等などの燃焼触媒、重合触媒および類似物）、顔料（例えば、

TiO_2、カーボンブラック、酸化鉄等）、充填材（例えば、雲母、シリカ、滑石、硫酸バリウム、ポリエチレン類、ポリテトラフルオロエチレン、ナイロン粉、メタクリル酸メチル粉末）等を含んでもよい。固体粒子は、ナノサイズの粒子を含んでもよい。固体粒子は、約０．００１から約１０ミクロン、一実施態様では約０．０１から約１ミクロンの範囲の平均粒子直径を有するとよい。多相混合物の中の固体粒子の濃度は、多相混合物の重量を基準として最大約７０重量％、一実施態様では約０．１から約３０重量％の範囲にあるとよい。

【０１１８】

一実施態様では、本発明のプロセスによって作られる多相混合物は、連続相の中に分散した不連続相を含む。不連続相は、最大約２００ミクロン、一実施態様では約０．０１から約２００ミクロン、一実施態様では約０．０１から約１００ミクロン、一実施態様では約０．０１から約５０ミクロン、一実施態様では約０．０１から約２５ミクロン、一実施態様では約０．０１から約１０ミクロン、一実施態様では約０．０１から約５ミクロン、一実施態様では約０．０１から約２ミクロン、一実施態様では約０．０１から約１ミクロン、一実施態様では約０．０１から約０．５ミクロン、一実施態様では約０．０１から約０．２ミクロン、一実施態様では約０．０１から約０．１ミクロン、一実施態様では約０．０１から約０．０８ミクロン、一実施態様では約０．０１から約０．０５ミクロン、一実施態様では約０．０１から約０．０３ミクロンの範囲の体積基準平均寸法（例えば直径、高さ、幅、長さ）を有する泡またはマイクロボディを含むとよい。本発明のプロセスの一利点は、少なくとも一実施態様で、泡またはマイクロボディが比較的狭い平均直径（または高さ、幅または長さ）の分布を有することを特徴とする点である。

【０１１９】

「相対スパン」は、多くの場合「スパン」と呼ばれる。相対スパンは、体積分布から計算される無次元パラメータである。体積メジアン泡またはマイクロボディサイズ（ＶＭＤ）の場合と同じく、Ｄ［ｖ，０．１］およびＤ［ｖ，０．９］は、分散した泡またはマイクロボディの体積のそれぞれ１０％および９０％がそれより小さな直径の泡またはマイクロボディの中にある点を表す直径（または高さ、幅または長さ）である。スパンは、Ｄ［ｖ，０．９］からＤ［ｖ，０．１］を引いた後、ＶＭＤ（Ｄ［ｖ，０．５］）で除した商と定義してもよい。一実施態様では、本発明のプロセスによって作られる多相混合物の中の泡またはマイクロボディのスパンは、約１．３から約５、一実施態様では約１．８から約２．５の範囲にあるとよい。一実施態様では、本発明のプロセスは、単一のプロセスマイクロチャネルの中で実行され、スパンは約１．３から約２．５の範囲にあるとよい。一実施態様では、本発明のプロセスは複数のプロセスマイクロチャネルを使用するスケールアップされた多相混合プロセスの中で実行され、スパンは約１．３から約５の範囲にあるとよい。

【０１２０】

一実施態様では、本発明のプロセスによって作られる多相混合物の中の泡またはマイクロボディの体積基準の平均直径（または高さ、幅または長さ）は、約０．１から約１００ミクロンの範囲にあるとよく、スパンは、約１から約２５の範囲にあるとよい。一実施態様では、体積基準の平均直径（または高さ、幅または長さ）は、約１から約１０ミクロンの範囲にあるとよく、スパンは、約１．８から約２．５の範囲にあるとよい。

【０１２１】

一実施態様では、気泡が形成され、気泡は最大約２５ミクロンの範囲の体積基準の平均直径と、約１．９から約２．５の範囲のスパンとを有する。

【０１２２】

一実施態様では、マイクロボディが形成され、マイクロボディは最大約５ミクロンの範囲の体積基準の平均直径（または高さ、幅または長さ）と、約１．８から約２．５の範囲のスパンとを有する。

【０１２３】

本発明のプロセスによって形成されるマイクロボディは、多数の用途を有する。これら

は、密度を減らすキャストファイリング用のガラスミクロスフェア、流動床反応装置の中の選択化学種固定化用のガラスミクロスフェア、および類似物を含む。その他の例は、免疫試験および処理のために用いられるミクロスフェア重合体、ゲルまたはコロイド懸濁系発生を含む。マイクロボディ（例えばマイクロスフェア）は、第二のプロセスで処理して凝集体、触媒流動床または充填床、ドラッグデリバリシステム（例えば蛋白質酵素反応）、および最新の分離および流動床用途（例えば、磁気振動によって有利に分離または励起することができる被覆磁気担体）を含むいくつかの用途のためのカプセル化された固体を形成してもよい。

【０１２４】

少なくとも一つの実施態様では、本発明のプロセスの一利点は、プロセスが実験室用であろうと、パイロットプラント規模用であろうと、または実生産規模用であろうと、プロセスマイクロチャネル、第二の流体流チャネル、オプションとして、第三の流体流チャネル、および／または熱交換チャネルの間のギャップ距離が同じであってよいことである。その結果、マイクロチャネルミキサが実験室またはパイロットプラント規模で、または実生産規模のプラントユニットとして構築されても、本発明のプロセスで用いられるマイクロチャネルミキサによって製造される多相混合物の粒子サイズ分布は、実質的に同じにすることができる。

【０１２５】

液体制御素子（離散形）に対する速度ｕの方向のせん断力は、式　$F_X = mu * du / dy$によって計算することができる。ここで、ｍｕは粘度、ｄｕ／ｄｙは開口区間に垂直な液体の流れの速度勾配である。しかし、液体の位置（制御素子によって表される）の場合と同じく、速度は、一般に、三つの成分を有し、せん断力も三つの成分を有する。表面近くおよび表面上のチャネルの流れの場合、一次元の仮定を置くことができ、F_Xによって素子表面での液体の正味のせん断力を近似できる。ＦｌｕｅｎｔまたはＦＥＭＬＡＢなどの市販のソフトウェアパッケージを含む計算機流体力学を用いて、必要な輸送方程式を解き、その結果、表面せん断力を計算することができる。チャネル長さ方向の流れの方向に平行な表面せん断力を計算することができる。平行なチャネルの間のせん断力も、計算することができ、流れ分布効果を取り込んでそれぞれの平行なチャネル中への物質流束を詳細なチャネルおよびマニホルドの幾何形状の関数として決定する。例えば、「流体力学の基礎（Ｆｕｎｄａｍｅｎｔａｌｓ　ｏｆ　Ｆｌｕｉｄ　Ｍｅｃｈａｎｉｃｓ）」、第３版、ビー・アール・マンソン（Ｂ．Ｒ．Ｍｕｎｓｏｎ）、ディー・エフ・ヤング（Ｄ．Ｆ．Ｙｏｕｎｇ）およびティー・エイチ・オキイシ（Ｔ．Ｈ．Ｏｋｉｉｓｈｉ）、ジョン・ワイリー・アンド・サンズ社（Ｊｏｈｎ　Ｗｉｌｅｙ　＆　Ｓｏｎｓ，Ｉｎｃ）、ヴァインハイム（Ｗｅｉｎｈｅｉｍ）、１９９８年、にさらに詳しい計算方法がある。

【０１２６】

一実施態様では、単一のプロセスマイクロチャネルを使用するプロセスのせん断力偏差因子（ＳＦＤＦ）は、複数のプロセスマイクロチャネルを含むスケールアップされたプロセスのＳＦＤＦの約５０％の範囲内にすることができる。ＳＦＤＦは、式

$SFDF = (F_{max} - F_{min}) / (2F_{mean})$

を用いて計算することができる。ここで、F_{max}は、特定の液体に対するプロセスマイクロチャネルの中の最大せん断力、F_{min}は同じ液体に対するプロセスマイクロチャネルの中の最小せん断力、F_{mean}はプロセスマイクロチャネル内の開口区間（２４０、２４０ａ、３１１、３２１、３３１、３４１、４１５、４２５、４３５、４４５、５５０、５６０、５７０、５８０）の表面における同じ液体に対する算術平均せん断力である。本発明のプロセスによって動作する単一のプロセスマイクロチャネル内では、ＳＦＤＦは約２より小さく、一実施態様では約１より小さく、一実施態様では約０．５より小さく、一実施態様では約０．２より小さいとよい。

【０１２７】

一実施態様では、本発明のプロセスは、複数のプロセスマイクロチャネルを使用しながら、比較的一様なせん断力を提供することができる。複数のプロセスマイクロチャネルの

間のせん断力一様性を測定するためには、各チャネルの平均せん断力を計算し、比較する。F_{max}は平均チャネルせん断力の最大値であり、F_{min}は平均せん断力の最小値である。F_{mean}は、すべてのチャネルの平均せん断力の平均値である。ＳＦＤＦは、これらの値から計算することができる。複数のプロセスマイクロチャネルの間で、本発明のプロセスの少なくとも一つの実施態様では、ＳＦＤＦは約２より小さく、一実施態様では約１より小さく、一実施態様では約０．５より小さく、一実施態様では約０．２より小さくすることができる。

【０１２８】

熱交換流体は、任意の流体を含んでもよい。これらは、空気、蒸気、液体の水、気体窒素、液体窒素、不活性気体を含むその他の気体、一酸化炭素、二酸化炭素、融解塩、鉱油などのオイル、気体炭化水素、液化炭化水素およびダウ・ユニオンカーバイド（Ｄｏｗ－Ｕｎｉｏｎ　Ｃａｒｂｉｄｅ）から入手できるダウサームＡ（Ｄｏｗｔｈｅｒｍ　Ａ）およびサーミノール（Ｔｈｅｒｍｉｎｏｌ）などの熱交換流体を含む。

【０１２９】

熱交換流体は、多相混合物を作るのに用いられる第一、第二および／または第三の流体を含んでもよい。これによって、プロセス予備加熱または予備冷却を提供し、プロセスの総合的な熱効率を高くすることができる。

【０１３０】

一実施態様では、熱交換チャネルは、吸熱または発熱プロセスが実行されるプロセスチャネルを含む。これらの熱交換プロセスチャネルは、マイクロチャネルであってもよい。熱交換チャネル中で実行することができる吸熱プロセスの例は、水蒸気改質および脱水素反応を含む。一実施態様では、吸熱源の増強を提供する同時吸熱反応の組み込みによって、通常、対流冷却熱流束よりほぼ一桁大きな熱流束が可能になる。熱交換チャネルの中で実行することができる発熱プロセスの例は、水性ガスシフト反応、メタノール合成反応およびアンモニア合成反応を含む。

【０１３１】

一実施態様では、熱交換流体は熱交換チャネルの中で相変化を行う。この相変化によって、対流加熱または冷却によって供給される熱の他に、プロセスマイクロチャネルまたは液体チャネルからの追加の加熱または除熱が提供される。蒸発する液体熱交換流体の場合、プロセスマイクロチャネルから移動するこの追加の熱は、その熱交換流体が必要とする蒸発潜熱から生じさせることが可能である。そのような相変化の例は、核沸騰するオイルまたは水である。一実施態様では、相変化流体の沸騰の蒸気質量分率品質は、最大約１００％、一実施態様では最大約７５％、一実施態様では最大約５０％にすることができる。

【０１３２】

相変化または化学反応による伝熱促進の使用は、多相混合物発生がプロセスチャネルの中の化学反応と協同して起ると、さらに有利なものにすることができる。一実施態様では、例えば、多相混合物は、重合反応用の反応性モノマーまたはその他の追加の熱交換を必要とするものであってもよい。

【０１３３】

マイクロチャネルミキサの中の対流加熱または冷却の熱流束は、マイクロチャネルミキサの中のプロセスマイクロチャネルの表面積の平方センチメートルあたり約０．０１から約１２５ワット（Ｗ／ｃｍ^2）、一実施態様では約０．１から約５０Ｗ／ｃｍ^2、一実施態様では約１から約２５ｃｍ^2、一実施態様では約１から約１０Ｗ／ｃｍ^{2}の範囲にあるとよい。加熱または冷却用の相の熱流束は、約１から約２５０Ｗ／ｃｍ^{2}の範囲、一実施態様では約１から約１００Ｗ／ｃｍ^2、一実施態様では約１から約５０Ｗ／ｃｍ^2、一実施態様では約１から約２５Ｗ／ｃｍ^2、一実施態様では約１から約１０Ｗ／ｃｍ^{2}であるとよい。

【０１３４】

熱交換チャネルを用いて、本発明のプロセスを用いる多相混合物の作製時に無菌状態を提供することができる。バッチミキサと異なって、本発明のプロセスは環境に対して閉じ

たものにすることができ、環境から切り離すために不活性気体で覆う必要がない。熱交換チャネルは、プロセスマイクロチャネルまたは液体チャネルに隣接するので、比較的短い熱輸送および拡散距離を提供して、マイクロチャネルミキサの中の液体を迅速に加熱および冷却して温度勾配を小さくすることができる。その結果、本発明のプロセスを用いると、長時間の加熱に適さないか、または大きな温度勾配の下では劣化する可能性のある多相混合物を調製することができる。一実施態様では、プロセスマイクロチャネルの中の同じ軸位置のプロセスマイクロチャネル壁とプロセスマイクロチャネルの内のバルクの流れとの間の温度勾配を、約５℃より小さく、一実施態様では約２℃より小さく、一実施態様では約１℃より小さくすることができる。

【０１３５】

制御された加熱および／または冷却を有するプロセスマイクロチャネルおよび／または第二または第三の流体流チャネルに密着する熱交換チャネルは、複数のプロセスマイクロチャネルの間に一様な温度プロフィルを提供することができる。これによって、混合タンクなどの従来の処理設備を用いて得ることができるよりも速い速度での一様な加熱および冷却が可能になる。多重チャネルマイクロチャネルミキサの中で、プロセス流れの長さに沿って少なくともいくつかの軸位置で、プロセスマイクロチャネルの間の温度差を約５℃より小さく、一実施態様では約２℃より小さく、一実施態様では約１℃より小さくすることができる。

【０１３６】

プロセスマイクロチャネルおよび／または第二または第三の流体流液体チャネルのどちらかに隣接する熱交換チャネルは、そのようなチャネルの長さに沿った温度区域を使用することができる。一実施態様では、プロセスマイクロチャネルへの入口に近い第一の区域の中の温度は、プロセスマイクロチャネルの終わりに近い第二の区域の中の第二の温度より高い温度に維持される。プロセスマイクロチャネルの中に冷却またはクエンチ区域を組み込んで多相混合物を急速に冷却し、安定化させてもよい。原料およびまたは多相混合物生成物を加熱および／または冷却するプロセスマイクロチャネルの中の混合区域の前および／または後ろの両方の区間の可能性を含めて、プロセスマイクロチャネルの長さに沿って最適な熱プロフィルを可能にする熱プロフィルの多数の組み合わせが可能である。

【０１３７】

プロセスマイクロチャネル（２１０、２１０ａ、３１０、３２０、３３０、３４０、４１０、５２０）を通る流体の流速は、約０．０１から約５０１ｐｍ、一実施態様では約０．０１から約１０１ｐｍの範囲にあるとよい。プロセスマイクロチャネルを通って流れる流体の速度は、約０．１から約１００ｍ／ｓ、一実施態様では約０．１から約１０ｍ／ｓの範囲にあるとよい。プロセスマイクロチャネルを通って流れる流体のレイノルズ数は、約２５から約１０，０００、一実施態様では約２５０から約５０００の範囲にあるとよい。プロセスマイクロチャネルに入る流体の温度は、約１０℃から約５５０℃、一実施態様では約２５℃から約４００℃の範囲にあるとよい。プロセスマイクロチャネル内の絶対圧力は、約１から約２０気圧、一実施態様では約１から約５気圧の範囲にあるとよい。

【０１３８】

第二の流体流チャネル（２７０、２７０ａ、３５０、３６０、４２０、４３０、５３０、５４０）を通る第二の流体流および第三の流体流チャネル（４４０、４５０）を通る第三の流体流の流速は、約０．０１から約１０ｍｌ／ｓ、一実施態様では約０．１から約２ｍｌ／ｓの範囲にあるとよい。第二の流体流および第三の流体流の速度は、約０．１から約１００ｍ／ｓ、一実施態様では約０．１ｍ／ｓから約１０ｍ／ｓの範囲にあるとよい。第二の流体流および第三の流体流のレイノルズ数は、約５０から約５０００、一実施態様では約５０から約５００の範囲にあるとよい。第二の流体流チャネルに入る第二の流体流および第三の流体流チャネルに入る第三の流体流の温度は、約－１０℃から約６５０℃、一実施態様では約２５℃から約４５０℃の範囲にあるとよい。第二の流体流チャネルおよび第三の流体流チャネル内の絶対圧力は、約１から約２５気圧、一実施態様では約１から約５気圧の範囲にあるとよい。開口（２４４、２４４ａ、３１３、３２３、３３３、３４

３、４１６、４２６、４３６、４４６）を通って流れる流体の圧力降下は、約０．００５から約０．５気圧、一実施態様では約０．０５から約０．１気圧の範囲にあるとよい。

【０１３９】

本発明のプロセスによる気泡またはマイクロボディの形成の概略が図２１に示される。図２１を参照すると、気泡またはマイクロボディ６５０は、マイクロチャネル６５４の中の開口６５２から出現し、第一の流体流６５６の中に分散する。気泡またはマイクロボディは、開口６５２内の気体またはマイクロボディ形成材料基部６５８に付着している間、例えば、開口のサイズの約１０倍以上にサイズが成長してもよい。最終的には、気体またはマイクロボディ形成材料基部６５８の基部のせん断力によって泡またはマイクロボディは開口から分離され、泡またはマイクロボディは第一の流体流６５６の中に分散する。一実施態様では、比較的高い開口区間の圧力降下、または対応して、第二の流体流チャネルを通る高い第二の流体流の流速は、第一の流体流の中の第二の流体流の分散を実現するのに必要ないこともある。圧力降下が低いこと、または流速が低いことによって、開口区間を通って流れる第二の流体流のより慣性が低くなり、泡またはマイクロボディが開口から分離する前の泡またはマイクロボディ成長を減らすことがあるので、より小さな泡またはマイクロボディを生じさせることがある。

【０１４０】

プロセスマイクロチャネル（２１０、２１０ａ、３１０、３２０、３３０、３４０、４１０、５２０）から出る多相混合物は、約１０℃から約６００℃、一実施態様では約２５℃から約４５０℃の範囲の温度にあるとよい。

【０１４１】

熱交換チャネル（２９０、３７０、３８０、５９０）に入る熱交換流体は、約－４０℃から約３００℃、一実施態様では約２５℃から約１００℃の範囲の温度であるとよい。伝熱チャネルから出る熱交換流体は、約－３０℃から約５５０℃、一実施態様では約３０℃から約２００℃の範囲の温度を有するとよい。熱交換流体の圧力降下は、熱交換チャネルを通って流れるとき、約０．００５から約５気圧、一実施態様では約０．０５から約１気圧の範囲にあるとよい。熱交換チャネルを通って流れる熱交換流体流のレイノルズ数は、最大約１０，０００、一実施態様では最大約５０００、一実施態様では約１００から約５０００の範囲、一実施態様では約５００から約２０００の範囲にあるとよい。

【０１４２】

流体流は、マイクロチャネルミキサの中でまたはマイクロチャネルミキサに入る前にマイクロチャネルヒータまたはヒートパイプを含む任意の種類の伝熱デバイスを用いて予熱してもよい。一実施態様では、第一の流体流は、混合区域の上流のプロセスマイクロチャネルの非開口領域の中で予熱してもよい。マイクロチャネルミキサの中で作り出される多相混合物は、マイクロチャネルミキサの中で、またはマイクロチャネルミキサから出た後で、マイクロチャネル熱交換器を含む任意の種類の熱交換デバイスを用いて冷却してもよい。一実施態様では、多相混合物を安定化するために、または安定なままにしておくために、多相混合物をクエンチしてもよい。一実施態様では、多相混合物は、混合区域の下流のプロセスマイクロチャネルの非開口領域の中でクエンチしてもよい。一実施態様では、多相混合物は、室温に冷却してもよく、または約０．０１から約１００秒、一実施態様では約０．０１から約１０秒の範囲の時間内にクエンチしてもよい。

【０１４３】

本発明のプロセスを用いて、毎分少なくとも約０．０１リットル、一実施態様では毎分少なくとも約１リットルの速度で多相混合物を作ることができる。一実施態様では、本プロセスを用いて毎秒少なくとも約１０リットルの速度で多相混合物を作ることができる。

【０１４４】

一実施態様では、プロセスマイクロチャネルの中で、光学的または熱光学的特性を調節してもよい。これらの光学的または熱光学的特性を測定および／または調節するための技法の例は、平均液滴サイズおよびスパンを含む多相混合物品質管理および分析のためのインラインＬＳＤ（レーザ散乱回折）検出、製品粘度および固体含量を評価するための粘度

計、気泡またはマイクロスフェアサイズ測定のための写真を用いる光学測定、多相混合物の性質を調節することによる干渉計法を含むホログラフィー画像化および類似の方法を含む。

【実施例１】

【０１４５】

長方形の断面と、０．０４０×１．２５×３インチ（１．０２×３１．７５×７６．２ｍｍ）の内部寸法を有するアクリルのプロセスマイクロチャネルを含む多相混合装置が構築される。プロセスマイクロチャネルは、その側壁の一つの中に開口区間を有する。開口区間は、０．１ミクロンの名目開口または細孔サイズと、０．０１０×１×１．５インチ（０．２５４×２５．４×３８．１ｍｍ）の寸法とを有する。開口区間は、ステンレス鋼３１６Ｌで構築され、コネチカット州ファーミントン（Ｆａｒｍｉｎｇｔｏｎ，ＣＴ）のモット社（Ｍｏｔｔ　Ｃｏｒｐｏｒａｔｉｏｎ）によってカタログ番号１１１０－１２－１２－０１８－０１－Ａで供給される。開口区間は、開口区間を通ってプロセスマイクロチャネルの中に入る気体の流れを可能にするために、気体分配プレナムおよび配管に接続される。プロセスマイクロチャネルは、プロセスマイクロチャネルを通る液体の流れを可能にするために、配管に接続される。気体は、開口区間を通ってプロセスマイクロチャネルに流入し、プロセスマイクロチャネルを通って流れる液体と接触する。気体が開口区間の開口を通って流れるにつれ、プロセスマイクロチャネルの中で泡が形成される。プロセスは、空気を気体として、脱イオン水を液体として用いて実行される。空気の流速は毎分２から２０標準立方センチメートル（ＳＣＣＭ）との間で変化し、水の流速は毎分１０から８０ミリリットル（ｍｌ／分）との間で変化する。５から１５ミクロンの範囲にある直径を有する泡が形成される。

【実施例２】

【０１４６】

２ＳＣＣＭの気体流速と６０ｍｌ／分の液体流速とを用いて、実施例１に記載されたプロセスが実行される。

【実施例３】

【０１４７】

水素を気体として、１－ヘキセンを液体として用いて、実施例１に記載されたプロセスが実行される。

【実施例４】

【０１４８】

高速度の気体（１ＳＬＰＭより大きな流速）と液体（毎分０．１リットルより大きな流速）とが、プロセスマイクロチャネルの入口近くで混合されてから、表面構成要素領域を通って流れる。表面構成要素領域は、壁の片側の上に０．０１インチの深さと４５度の角度を有する構成要素を有する。表面構成要素内のバルク流路は、０．００６５インチである。平均直径が２５ミクロンより小さな一様な泡を有する発泡体が作り出される。流れの長さは１．５インチであり、チャネルの幅またはスパンは０．５インチである。プロセスマイクロチャネルは、室温および周囲圧力近くである。表面構成要素領域の上および全体に非常に小さな泡が観測される。

【実施例５】

【０１４９】

チャネルの中の層流から、チャネルの中の強い混合流れへの変化を誘起するマイクロチャネルの二つの側面への表面構成要素の追加を、Ｆｌｕｅｎｔ^{TM}を用いる計算機流体力学（ＣＦＤ）シミュレーションによって検討する。シミュレーションのために、流体の性質は一定と仮定し、密度５．０６７ｋｇ／ｍ^{3}、粘度３．６２ｅ$^{-5}$ｋｇ／ｍ・秒とした。境界条件として１２．１３ｍ／秒の一様な入口速度と、すべての壁で滑り流がないとした。３１５，１７４セルのグリッドサイズが用いられる。

【０１５０】

仮定された幾何構造は、４．０６ｍｍの幅、０．３１８ｍｍの高さおよび６３．５ｍｍ

の長さを有する連続チャネルの長方形の断面である。入口の０から３．５ｍｍ下流の区間と、出口の０から５．０ｍｍ上流の区間とは、混合用表面構成要素を含まない（簡単な長方形マイクロチャネル）。混合用表面構成要素（または溝）は、二つの対向する壁の中に切り込まれ、各構成要素は断面がほぼ長方形である。マイクロチャネルの中間区間（入口の３．５ｍｍから５８．５ｍｍ下流）は、混合用表面構成要素を含む。表面構成要素は、図２７および２８に示されるように、平均バルク層流の方向から６３°の角度でチャネル壁の一つに対角線状にまたがる。各表面構成要素は、深さ約０．２５ｍｍ、幅０．４８ｍｍ、長さ９ｍｍである。表面構成要素は、互いに平行に配置され、構成要素の間の間隔は０．４８ｍｍである。反対側の壁の上の表面構成要素は、第一の壁の上の表面構成要素と同じであり、チャネル中心線の周りに１８０°回転している（チャネル幾何構造は、入口面の中心点から出口面の中心点に延在する流れの軸の周りに対称である）。

【０１５１】

図２７は、ＣＦＤによってシミュレーションされた表面構成要素の幾何構造の平面図を示す。上部壁と下部壁との両方の混合用構成要素が重ね合わされている。図２８は、ＣＦＤによってシミュレーションされた、混合用構成要素を有するマイクロチャネルの等角投影図であり、チャネルに入る流れの方向を示す。図２９は、入口面の水平中心線（矢印の間に引かれている）に沿って開始される一般的な流れの経路線を示し、入口面から流れの軸を下に見ている。古典的な層流では、経路線は、入口面と出口面との間の直線を流れる（図２９に示される図では、古典的な層流の経路線は、矢印の間の中心線から逸脱しないと考えられる）。図３０で、入口面の水平中央線に沿って開始される流れの同じ経路線の側面図が示される（矢印は、流れの方向を示す）。図３０で、中心線からの流れ経路線の広がりと、表面構成要素の中の渦巻き運動とが、層流と比較すると改善された混合と、減少した熱および物質輸送抵抗を示す。図３１は、入口面の垂直中央線（矢印の間に引かれている）に沿って開始される流れの経路線を示し、入口面から流れの軸を下に見ている。図３１で、流れの渦巻き運動が、古典的な層流と比較すると改善された混合と、減少した熱および質量輸送抵抗を示唆する。

【０１５２】

ＣＦＤシミュレーションの結果によると、マイクロチャネルの中の層流と異なり、混合用表面構成要素は、連続チャネルの中の流れの経路線をねじれさせ、渦巻かせ、層流の場合に予想されるより速く壁に向かって押し広げる。計算された圧力降下は、５．２ｋＰａである。

【０１５３】

表面構成要素を含むマイクロチャネルに気体または第二の流体流を加えると、流れのパターンが作り出され、それによって、多相混合物は層流に近づき、泡は小さくなり、良く分散すると予測される。小さな泡とは、マイクロチャネルギャップの２５％より小さいと定義してもよい。

【０１５４】

特定の実施態様と関連させて本発明を説明してきたが、本明細書を読めば、これらの実施態様のさまざまな変更形は当業者にとって自明であると理解される。従って、本明細書に開示される本発明は、添付の請求項の範囲に属するものとしてそのような変更形を包含するものと理解される。

【図面の簡単な説明】

【０１５５】

【図１】本発明のプロセスで有用なものとすることができるマイクロチャネルの概略図である。

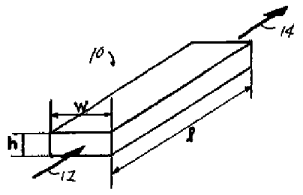
【図２】多相混合物を形成させるためにマイクロチャネルミキサが用いられる、特定の形の本発明のプロセスの例が示されるフローシートである。

【図３】本発明のプロセスで用いられる多相混合物形成ユニットの例が示されるフローシートである。第一の流体流がプロセスマイクロチャネルを通って流れ、隣接する第二の流体流チャネルからプロセスマイクロチャネルの中の開口区間を通ってプロセスマイクロチ

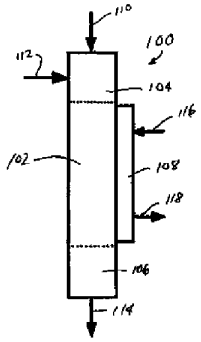
ャネルの中に流入する第二の流体流と混合される。
【図４】本発明のプロセスで用いられる多相混合物形成ユニットの例が示されるフローシートである。
【図５】本発明のプロセスで用いられる多相混合物形成ユニットの例が示されるフローシートである。
【図６】本発明のプロセスで用いられる多相混合物形成ユニットの例が示されるフローシートである。
【図７】本発明のプロセスで用いられる多相混合物形成ユニットの例が示されるフローシートである。
【図８】本発明のプロセスで用いられる多相混合物形成ユニットの例が示されるフローシートである。
【図９】本発明のプロセスで用いられる多相混合物形成ユニットの例が示されるフローシートである。
【図１０】二重多相混合物の概略図である。
【図１１】本発明のプロセスに従って用いることができるマイクロチャネル空気吹き込みユニットの概略図である。
【図１２】図１１に例を示した空気吹き込みユニットの中で用いることができるマイクロチャネル多相混合物形成ユニットの概略図である。
【図１３】多孔質ステンレス鋼基板の熱処理される前のＳＥＭ画像である。
【図１４】図８に示した基板の熱処理された後のＳＥＭ画像である。
【図１５】本発明のプロセスで有用な専用の多孔質基板のＳＥＭ画像である。
【図１６】本発明のプロセスで用いられるプロセスマイクロチャネルの開口区間を作る際に有用な開口シートの平面図である。
【図１７】本発明のプロセスで用いられるプロセスマイクロチャネルの開口区間を作る際に有用な開口シートまたはプレートの平面図である。
【図１８】本発明のプロセスで用いられるプロセスマイクロチャネルの開口区間を作る際に有用な、比較的厚い開口シートまたはプレートの上にある比較的薄い開口シートの例示である。
【図１９】本発明のプロセスで用いられるプロセスマイクロチャネルの開口区間を作る際に有用な、比較的厚い開口シートまたはプレートの上にある比較的薄い開口シートの例が示される。
【図２０】本発明のプロセスで用いられるプロセスマイクロチャネルの開口区間の中で用いることができる開口の代替実施態様の例が示される。開口は、部分的に開口を満たし、開口の側壁の上にあるコーティングを有する。
【図２１】本発明のプロセスの動作の間の気泡またはマイクロボディの形成を示す概略図である。
【図２２】本発明のプロセスで用いられるマイクロチャネルの中に設けることができる表面構成要素の概略図である。
【図２３】本発明のプロセスで用いられるマイクロチャネルの中に設けることができる表面構成要素の概略図である。
【図２４】本発明のプロセスで用いられるマイクロチャネルの中に設けることができる表面構成要素の概略図である。
【図２５】本発明のプロセスで用いられるマイクロチャネルの中に設けることができる表面構成要素の概略図である。
【図２６】本発明のプロセスで用いられるマイクロチャネルの中に設けることができる表面構成要素の概略図である。
【図２７】実施例５で説明される計算機流体力学（ＣＦＤ）によってシミュレーションされた表面構成要素の幾何構造の平面図である。上部および下部壁の上の表面構成要素が見える。
【図２８】実施例５で説明されるＣＦＤによってシミュレーションされた表面構成要素を

有するマイクロチャネルの等角投影図である。
【図２９】入口面の水平中心線（矢印の間に引かれる）に沿って開始されるマイクロチャネルの中の流れの経路線の例が示される。実施例５で説明されるように、入口面から流れの軸を下に見ている。
【図３０】入口面の水平中心線に沿って開始されるマイクロチャネルの中の流れの経路線（矢印は流れの方向を示す）を示す。実施例５で説明されるように、側面から見ている。
【図３１】入口面の垂直中心線（矢印の間に引かれる）に沿って開始されるマイクロチャネルの中の流れの経路線を示す。実施例５で説明されるように、入口面から流れの軸を下に見ている。

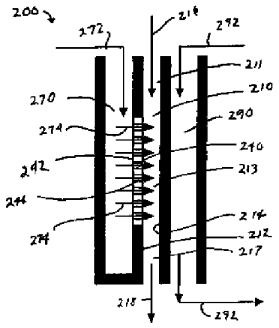
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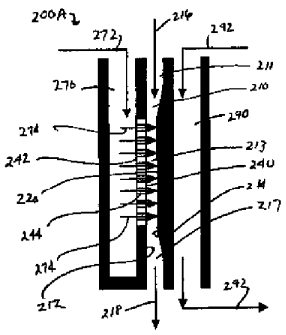
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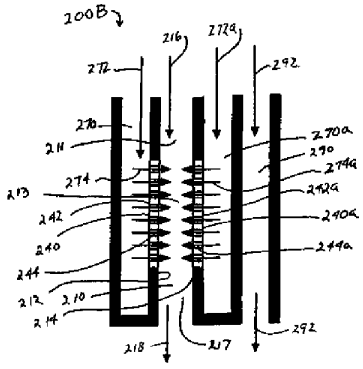
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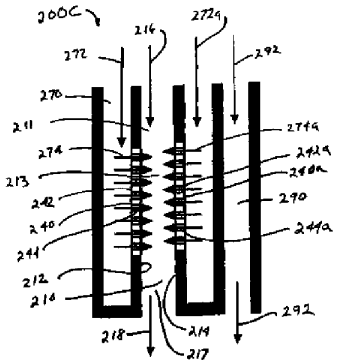
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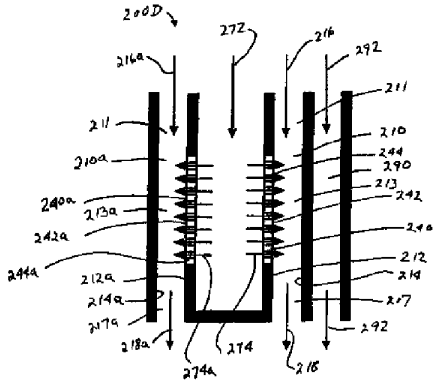
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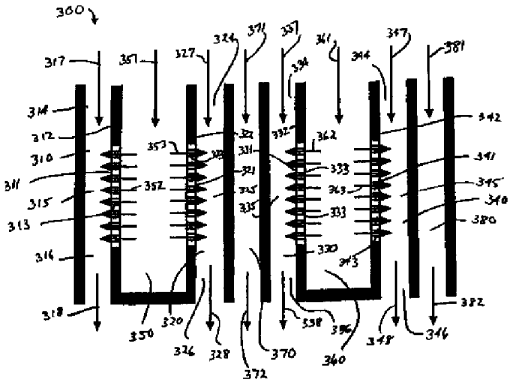
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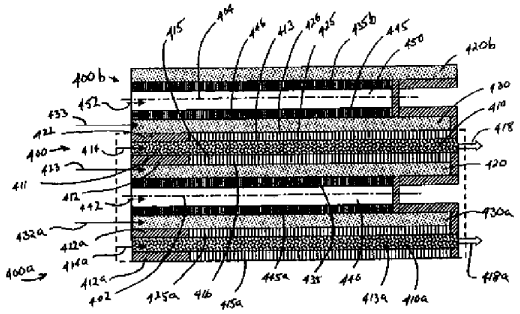
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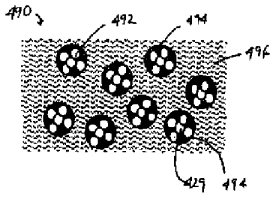
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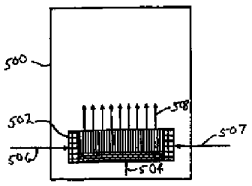
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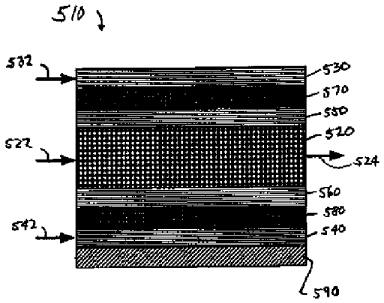
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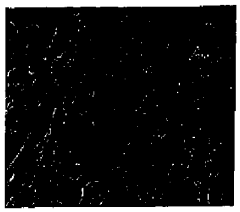
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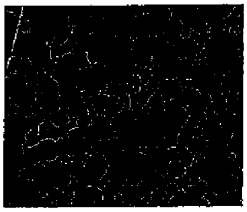
【図１２】



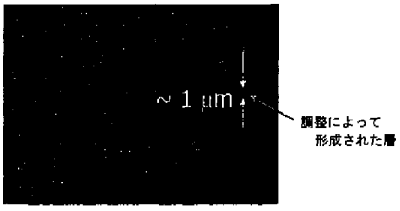
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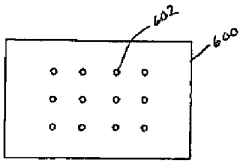
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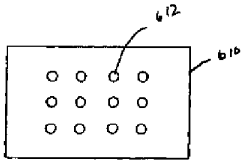
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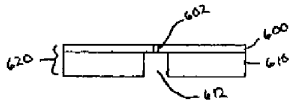
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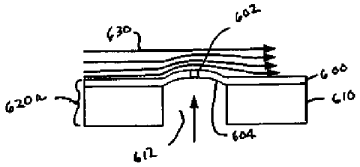
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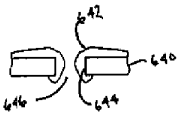
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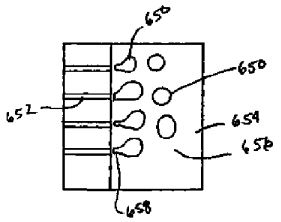
【図１９】



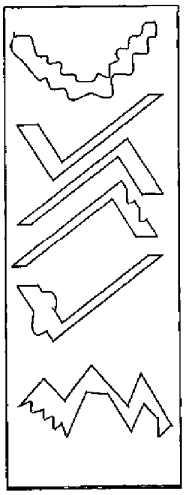
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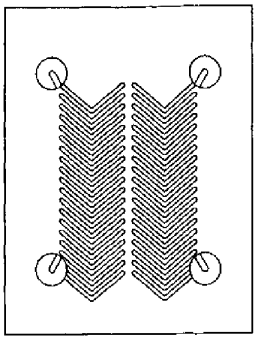
【図２１】



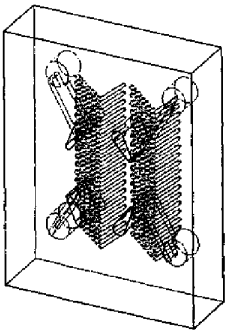
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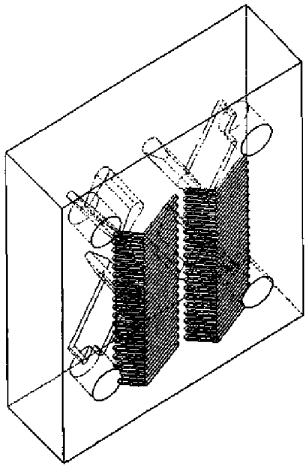
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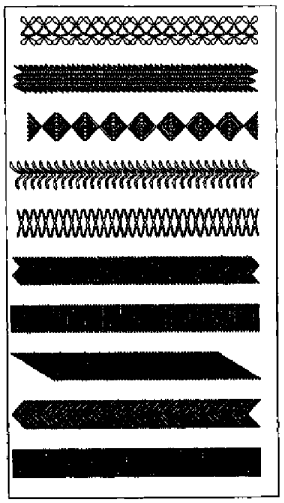
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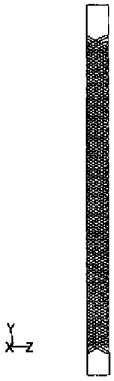
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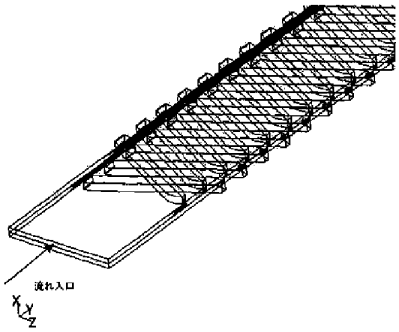
【図２６】



【図２７】



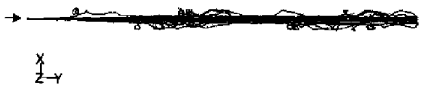
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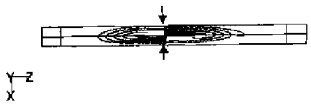
【図２９】



【図３０】



【図３１】



フロントページの続き

(51)Int.Cl. F I
B01F 15/06 Z

(72)発明者 ヘッセ, デイヴィッド ジョン
アメリカ合衆国 オハイオ州 43214 コロンバス, チャールストン アベニュー 193
(72)発明者 マルキアンド, マイケル アラン
アメリカ合衆国 オハイオ州 43140 ロンドン, ビッガート ロード 6009
(72)発明者 ラモント, マイケル ジェイ
アメリカ合衆国 オハイオ州 43026 ヒリアード, ホークストーン ロード 4877
(72)発明者 キウ, ドンミン
アメリカ合衆国 イリノイ州 62901 カーボンデール, エス. イーソン ドライブ 507
(72)発明者 ドリッツ, テレンス アンドリュー
アメリカ合衆国 オハイオ州 43085 ワージントン, グリニッジ ロード 674
(72)発明者 パグノット, クリスティーナ, エム.
アメリカ合衆国 オハイオ州 45231 シンシナティ, サウスメドウ サークル 812
(72)発明者 スティーブンソン, リック
アメリカ合衆国 オハイオ州 43064 プレイン シティ, コーポレイト ブルバード 7950
(72)発明者 ペリー, スティーブン, ティー.
アメリカ合衆国 オハイオ州 43119 ギャロウェイ, スクワッド ドライブ 8458
(72)発明者 ファネッリ, マダレナ
アメリカ合衆国 オハイオ州 43064 プレイン シティ, コーポレイト ブルバード 7950
(72)発明者 アローラ, ラヴィ
アメリカ合衆国 オハイオ州 43017 ダブリン, グリーン アーバー レーン 3069
(72)発明者 ヤン, ビン
アメリカ合衆国 オハイオ州 43064 プレイン シティ, コーポレイト ブルバード 7950
(72)発明者 フィッツジェラルド, ショーン
アメリカ合衆国 オハイオ州 43064 プレイン シティ, コーポレイト ブルバード 7950
(72)発明者 サリバン, ティム
アメリカ合衆国 オハイオ州 43064 プレイン シティ, コーポレイト ブルバード 7950
(72)発明者 ジャロッシュ, カイ トッド ポール
アメリカ合衆国 オハイオ州 43209 ベックスレー, ヴァーノン ロード 839
(72)発明者 ユシャック, トーマス
アメリカ合衆国 オハイオ州 43016 ダブリン, キャンブルック コート 5746

合議体
審判長 千葉 成就
審判官 渡邊 豊英
審判官 熊倉 強

(56)参考文献 特開2003-210957 (JP, A)
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特開平１０－１４６５２３（ＪＰ，Ａ）

(58)調査した分野(Int.Cl.，ＤＢ名)
B01F3/04

Bibliographic data: WO2008101025 (A1) — 2008-08-21

DISPOSABLE, CLOSED BLOOD SAMPLING SYSTEM FOR USE IN MEDICAL CONDUIT LINE

Inventor(s): FRAZIER JOHN A [US]; BAK-BOYCHUK GREG [US]; WRIGHT MARK [US]; MCKEOWN MORGAN T [US] ± (FRAZIER, JOHN, A, ; BAK-BOYCHUK, GREG, ; WRIGHT, MARK, ; MCKEOWN, MORGAN, T)

Applicant(s): EDWARDS LIFESCIENCES CORP [US]; FRAZIER JOHN A [US]; BAK-BOYCHUK GREG [US]; WRIGHT MARK [US]; MCKEOWN MORGAN T [US] ± (EDWARDS LIFESCIENCES CORPORATION, ; FRAZIER, JOHN, A, ; BAK-BOYCHUK, GREG, ; WRIGHT, MARK, ; MCKEOWN, MORGAN, T)

Classification: **- international:** ***A61B5/15; A61M39/02; A61M39/04;*** *A61M1/02*
- cooperative: **A61B5/15003 (EP); A61B5/150236 (EP); A61B5/150244 (EP); A61B5/150305 (EP); A61B5/150992 (EP); A61B5/153 (EP); A61B5/154 (EP); A61B5/155 (EP); A61M1/0236 (EP); A61M39/045 (EP);** A61M2039/0202 (EP); A61M39/223 (EP)

Application number: WO2008US53871 20080213 Global Dossier

Priority number(s): US20070675578 20070215

Also published as: CA2678326 (A1) CN101631498 (A) EP2117431 (A1) US2008200837 (A1)

Abstract of WO2008101025 (A1)

A disposable, closed fluid sampling system for use with a medical conduit line (70), especially for taking blood samples from a pressure monitoring line. The conduit line (70) has at least one fluid sampling site (100, 102) interposed between a distal segment of tubing and a proximal segment of tubing. The system includes a disposable subsystem (96) having a bypass cannula (110) adapted to engage the sampling site, a reservoir (112) for drawing a prime volume of fluid past the sampling site, and a fluid sampling container (114). A 3-way stopcock (116) may connect the reservoir, bypass cannula, and sampling vessel for controlling the sampling procedure. The bypass cannula (110) may simultaneously place the subsystem into fluid communication with an inner chamber (136) of the sampling site and exclude the proximal segment of the conduit line. Alternatively, a stopcock immediately adjacent the sampling site in the proximal segment may be utilized. A method of using the system includes attaching the disposable subsystem, opening the reservoir to the distal segment while excluding the proximal segment, drawing a prime volume of fluid into the reservoir, opening the sampling vessel to the distal segment and drawing a sample, re-infusing the prime volume into the distal segment, and removing and discarding the subsystem. The

reservoir remains attached between the prime volume draw and re-infusion and is thus "closed."