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

First Named Inventor:	Bobby E. Rogers	Nonprovisional Application Number (if known):	
Title of Invention:	BLOOD SAMPLE OPTIMIZATION DEVICE		

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

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

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

3. The applicable box is checked below:

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

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

---OR---

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

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

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

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

Signature /Ben Hudson/	Date July 24, 2024
Name (Print/Typed) Benjamin F. Hudson	Practitioner Registration Number 71474

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

☑ *Total of 1 forms are submitted.

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

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application is a continuation of U.S. Application No. 18/494,622 filed October 25, 2023, entitled "BLOOD SAMPLE OPTIMIZATION DEVICE," which is a continuation of U.S. Application No. 18/113,710 filed February 24, 2023, entitled "BLOOD SAMPLE OPTIMIZATION DEVICE," now U.S. Patent 11,832,994, which is a continuation of U.S. Application No. 17/538,990 filed November 11, 2021, entitled "BLOOD SAMPLE OPTIMIZATION DEVICE," now U.S. Patent 11,963,769, 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 SEQUESTRATION 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 for receiving a blood sample;

an outlet port;

a chamber connected with the inlet port and configured to collect a first portion of the blood sample when under a drawing force applied from the outlet port from a blood sample collection device; and

a sampling channel connected with the inlet port and configured to convey a subsequent portion of the blood sample to the outlet port.

2. The device in accordance with claim 1, wherein a blood impermeable membrane is configured to facilitate the chamber collecting the first portion of the blood sample.

3. The device in accordance with claim 1, wherein a blood impermeable membrane causes the first portion of the blood sample to back up into the chamber following application of the drawing force applied from the outlet port.

4. The device in accordance with claim 2, further comprising a housing, separate from the blood impermeable membrane.

5. The device in accordance with claim 1, wherein the device is configured such that, when the drawing force is applied at the outlet port, the first portion of the blood sample is drawn into the chamber to contact a material that is blood impermeable.

6. The device in accordance with claim 1, further comprising a valve configured to initially close off the sampling channel.

7. The device in accordance with claim 1, further comprising a valve configured to initially close off the sampling channel until the first portion of the blood sample is in the chamber.

8. The device in accordance with claim 1, further comprising a valve that is configured to initially close off the sampling channel until the first portion of the blood sample is in the chamber and is further configured such that, upon release, follow-on amounts of the blood sample will bypass the chamber and flow through the sampling channel toward the outlet port.

9. The device in accordance with claim 6, wherein the valve is configured to pinch, shunt, bend or otherwise close off the sampling channel before the first portion of the blood sample is collected in the chamber.

10. The device in accordance with claim 1, further comprising a housing that defines the inlet port, the sampling channel, and the outlet port.

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

12. The device in accordance with claim 1, the chamber having a volume sufficient to collect the first portion of the blood sample that is more prone to contamination and also to minimize an amount of blood to be sequestered.

13. The device in accordance with claim 1, wherein the chamber has a volume of less than 1.5 cubic centimeters.

14. A device comprising:

an inlet port for receiving blood;

an outlet port;

a chamber comprising a flexible material, the chamber connected with the inlet port and configured to collect a first portion of the blood when under a drawing force applied from the outlet port; and

a sampling channel connected with the inlet port and configured to convey a subsequent portion of the blood to the outlet port.

15. The device in accordance with claim 14, wherein the flexible material is a blood impermeable membrane configured to facilitate the chamber collecting the first portion of the blood.

16. The device in accordance with claim 14, wherein the flexible material is a blood impermeable membrane causes the first portion of the blood to back up into the chamber following application of the drawing force applied from the outlet port.

17. The device in accordance with claim 15, further comprising a housing, separate from the blood impermeable membrane.

18. The device in accordance with claim 14, wherein the device is configured such that, when the drawing force is applied at the outlet port, the first portion of the blood is drawn into the chamber to contact a material that is blood impermeable.

19. The device in accordance with claim 14, further comprising a valve configured to initially close off the sampling channel.

20. The device in accordance with claim 14, further comprising a valve configured to initially close off the sampling channel until the first portion of the blood is in the chamber.

21. The device in accordance with claim 14, further comprising a valve that is configured to initially close off the sampling channel until the first portion of the blood is in the chamber and is further configured such that, upon release, follow-on amounts of the blood will bypass the chamber and flow through the sampling channel toward the outlet port.

22. The device in accordance with claim 19, wherein the valve is configured to pinch, shunt, bend or otherwise close off the sampling channel before the first portion of the blood is collected in the chamber.

23. The device in accordance with claim 14, further comprising a housing that defines the inlet port, the sampling channel, and the outlet port.

24. The device in accordance with claim 14, further comprising a patient needle and a sample collection device.

25. The device in accordance with claim 14, the chamber having a volume sufficient to collect the first portion of the blood that is more prone to contamination and also to minimize an amount of blood to be sequestered.

26. The device in accordance with claim 14, wherein the chamber has a volume of less than 1.5 cubic centimeters.

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.

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Application Data Sheet 37 CFR 1.76	Attorney Docket Number	069366-0580418_KUR2C06US
	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:

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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	069366-0580418_KUR2C06US	**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	069366-0580418_KUR2C06US
	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)
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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.
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	18494622	2023-10-25

Prior Application Status	Patented				Remove
Application Number	Continuity Type	Prior Application Number	Filing Date (YYYY-MM-DD)	Patent Number	Issue Date (YYYY-MM-DD)
18494622	Continuation of	18113710	2023-02-24	11832944	2023-12-05

Prior Application Status	Patented				Remove
Application Number	Continuity Type	Prior Application Number	Filing Date (YYYY-MM-DD)	Patent Number	Issue Date (YYYY-MM-DD)
18113710	Continuation of	17538990	2021-11-30	11963769	2024-04-23

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

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

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

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

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

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	Application Number	
Title of Invention	BLOOD SAMPLE OPTIMIZATION DEVICE	

☐ 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	069366-0580418_KUR2C06US
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Authorization or Opt-Out of Authorization to Permit Access:

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

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

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

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

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

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

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

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

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

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Application Data Sheet 37 CFR 1.76	Attorney Docket Number	069366-0580418_KUR2C06US
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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. ☒

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Phone Number		Fax Number	
Email Address			

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Assignee Information including Non-Applicant Assignee Information:

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	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:

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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	/Ben Hudson/			Date (YYYY-MM-DD)	2024-07-24
First Name	Benjamin F.	Last Name	Hudson	Registration Number	71,474

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

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Application Data Sheet 37 CFR 1.76	Attorney Docket Number	069366-0580418_KUR2C06US
	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.**

Privacy Act Statement

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

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

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

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

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

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

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

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

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ELECTRONIC PAYMENT RECEIPT

APPLICATION #	RECEIPT DATE / TIME	ATTORNEY DOCKET #
18/783,088	07/24/2024 05:41:08 PM Z ET	069366-0580418_KUR2C06US

Title of Invention

BLOOD SAMPLE OPTIMIZATION DEVICE

Application Information

APPLICATION TYPE	Utility - Nonprovisional Application under 35 USC 111(a)	PATENT #	-
CONFIRMATION #	2051	FILED BY	Trent Tercenio
PATENT CENTER #	66504926	AUTHORIZED BY	Benjamin Hudson
CUSTOMER #	27500	FILING DATE	-
CORRESPONDENCE ADDRESS	-	FIRST NAMED INVENTOR	Bobby E. ROGERS

Payment Information

PAYMENT METHOD	PAYMENT TRANSACTION ID	PAYMENT AUTHORIZED BY
DA / 033975	E20247NH47449938	Trent Tercenio

PRE-AUTHORIZED ACCOUNT	PRE-AUTHORIZED CATEGORY
033975	37 CFR 1.16 (National application filing, search, and examination fees); 37 CFR 1.17 (Patent application and reexamination processing fees); 37 CFR 1.21 (Miscellaneous fees and charges)

FEE CODE	DESCRIPTION	ITEM PRICE($)	QUANTITY	ITEM TOTAL($)
2830	PROCESSING FEE, EXCEPT IN PROVISIONAL APPLICATIONS	56.00	1	56.00
2817	REQUEST FOR PRIORITIZED EXAMINATION	1680.00	1	1680.00
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
2202	EACH CLAIM IN EXCESS OF 20	40.00	6	240.00
			TOTAL AMOUNT:	**$2,640.00**

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.

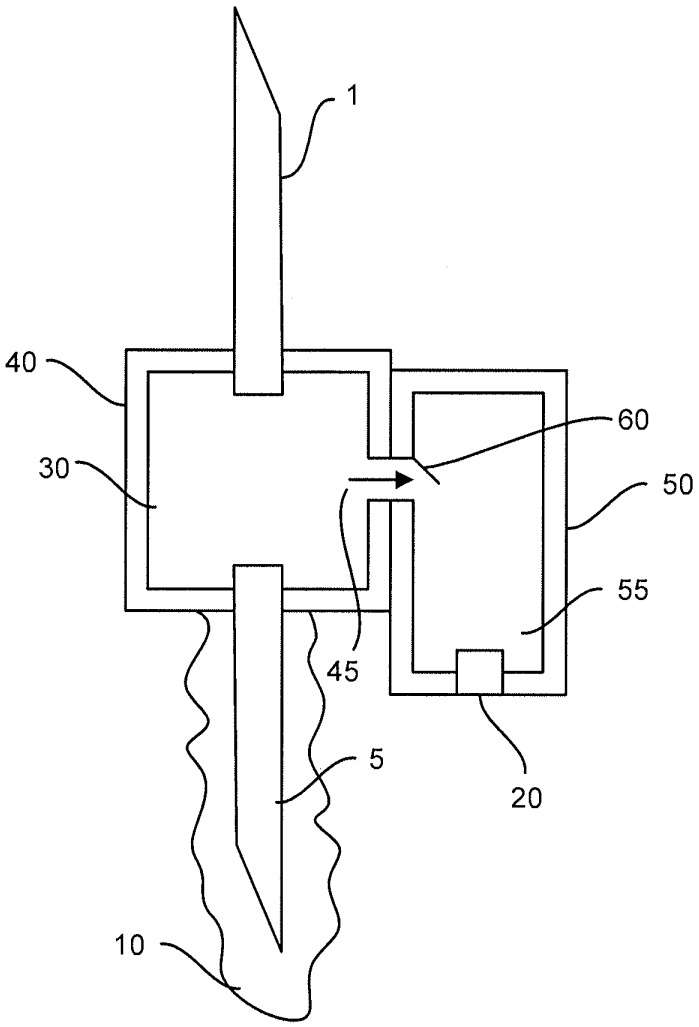


FIG. 1

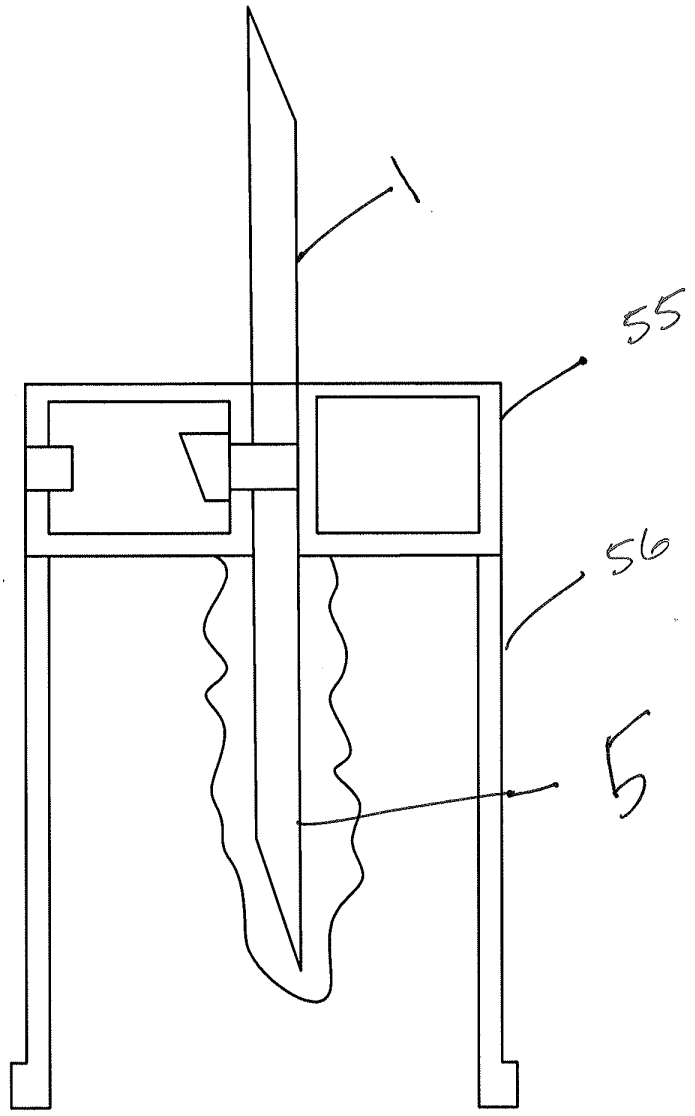


FIG. 2

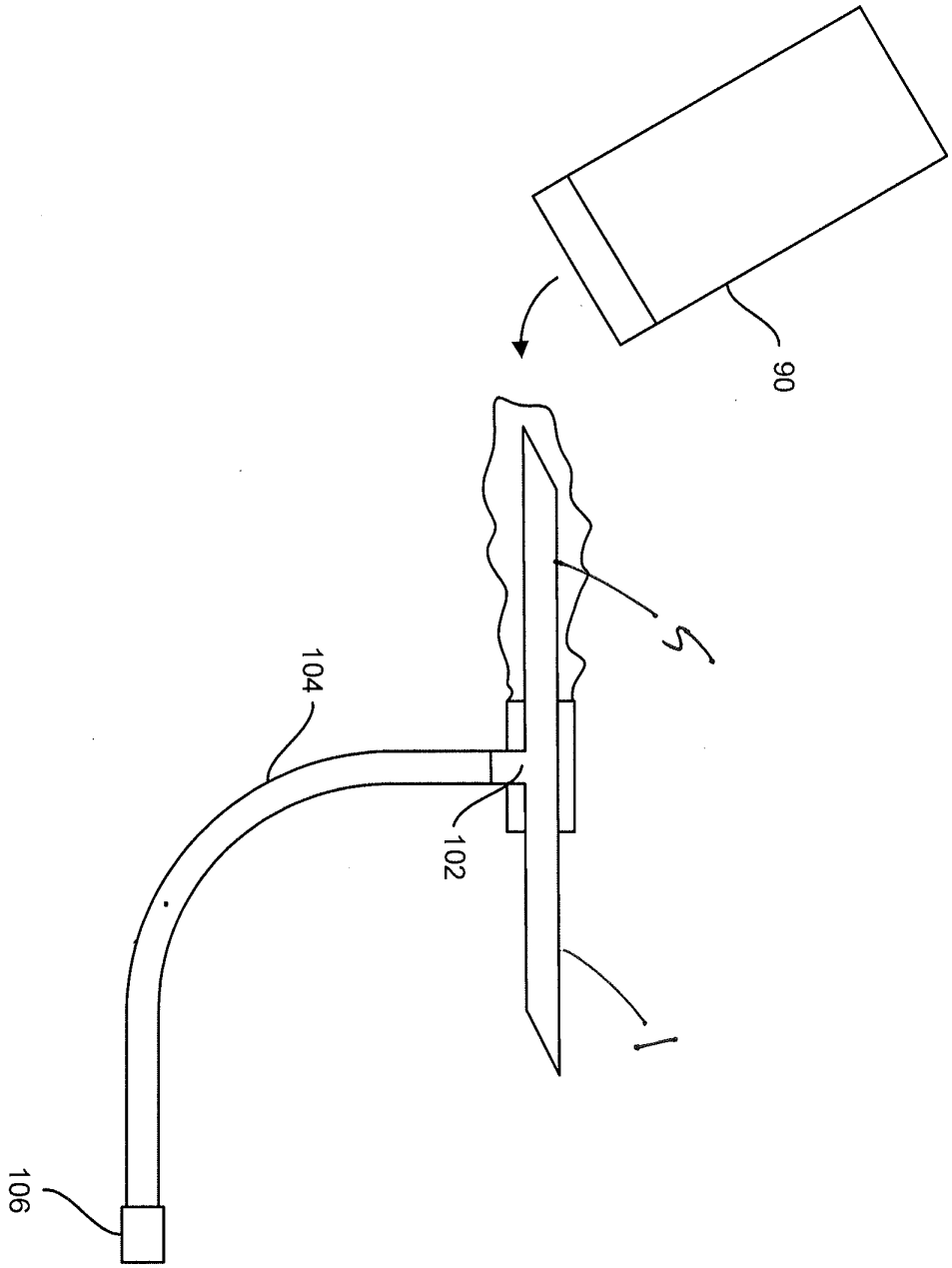


FIG. 3

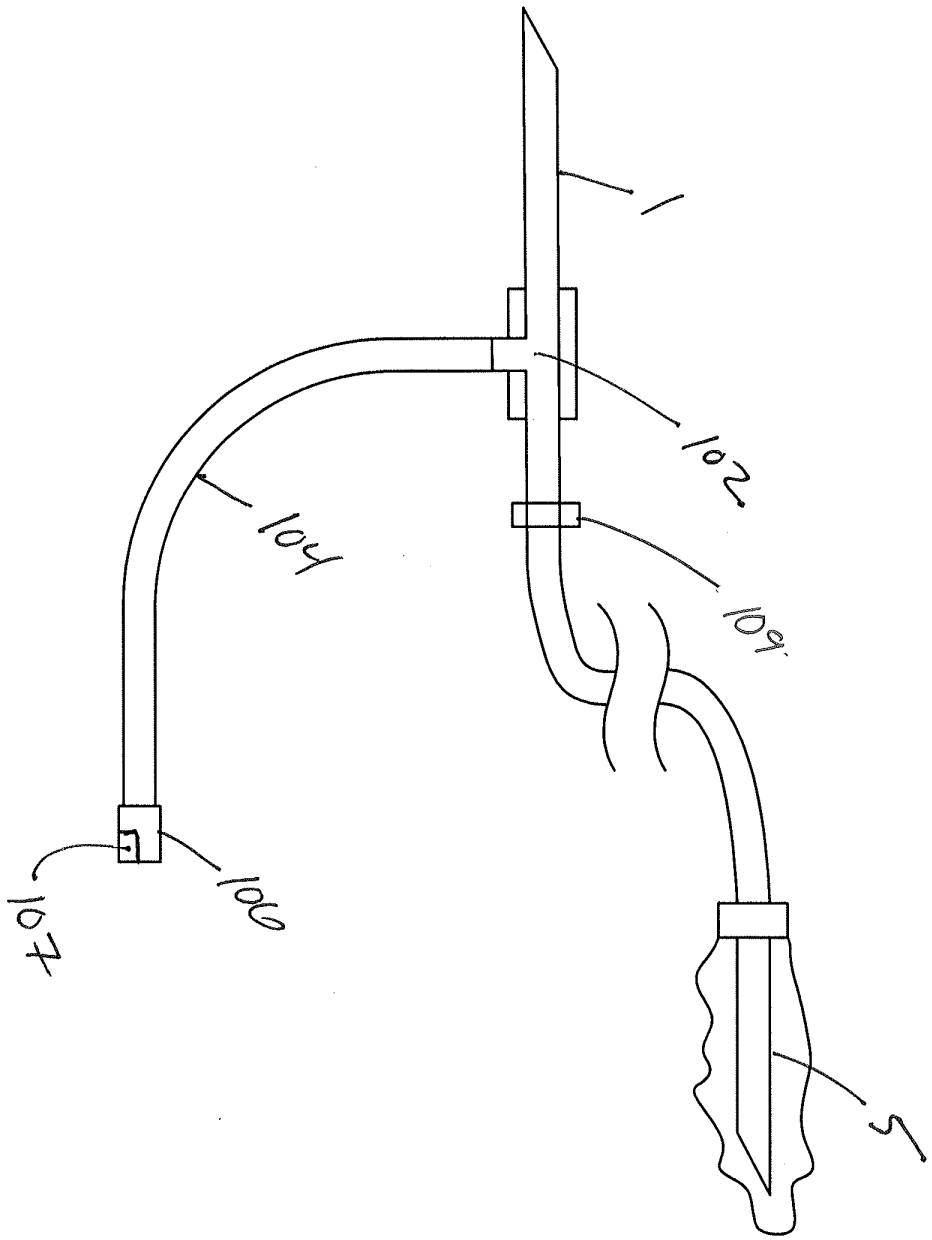


FIG. 4

FIG. 5

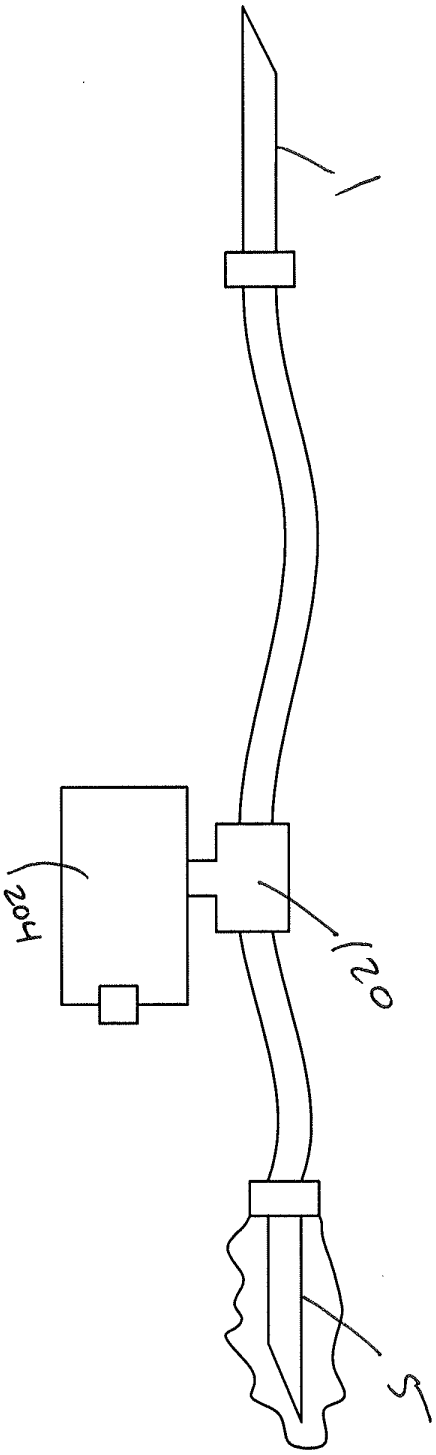
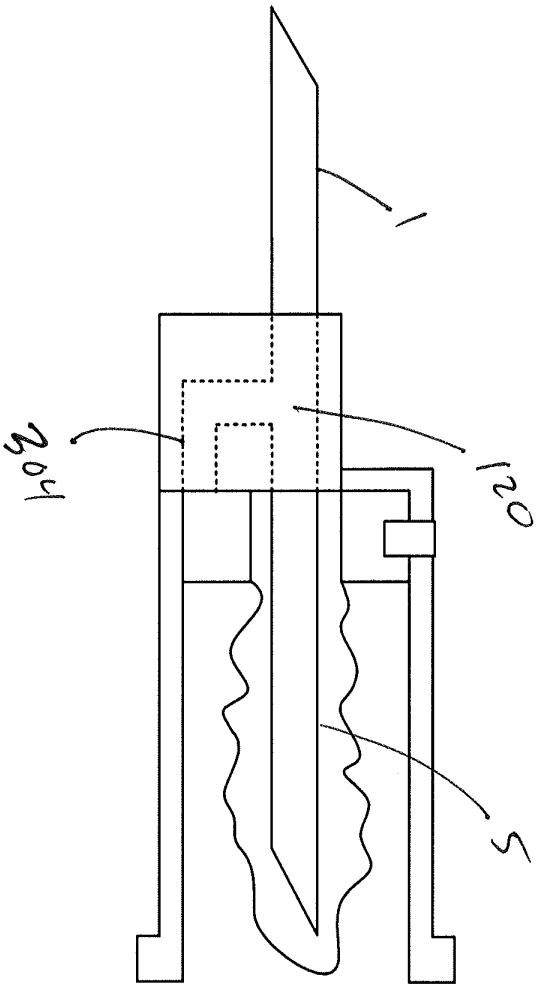


FIG. 6



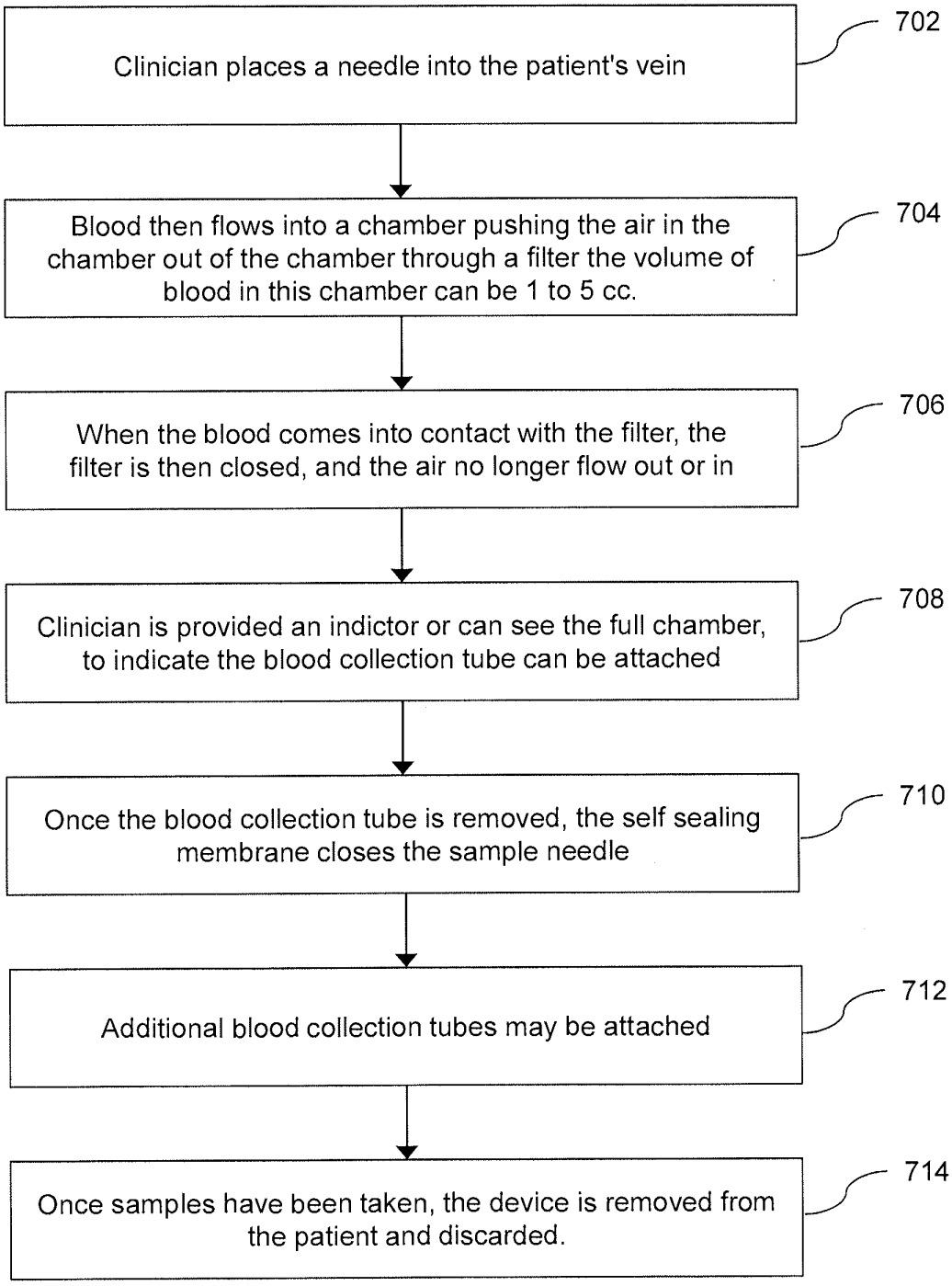
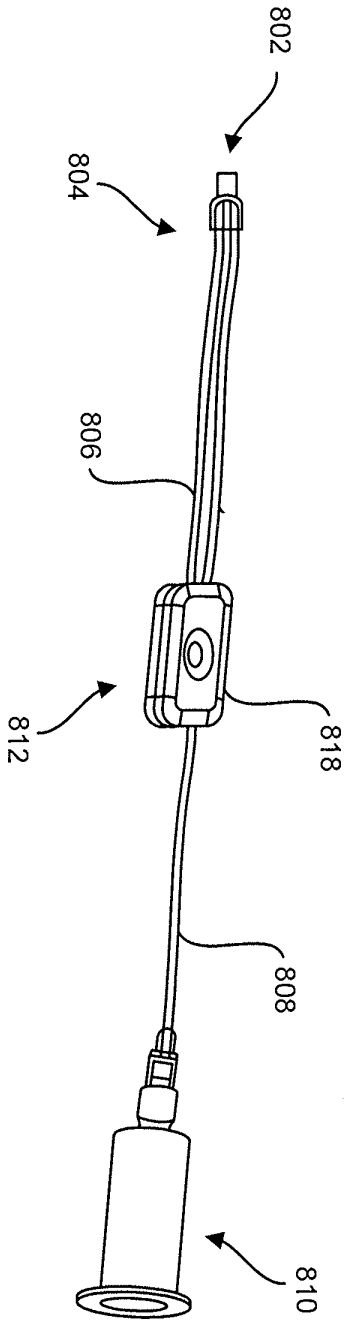

Clinician places a needle into the patient's vein
702
Blood then flows into a chamber pushing the air in the chamber out of the chamber through a filter the volume of blood in this chamber can be 1 to 5 cc.
704
When the blood comes into contact with the filter, the filter is then closed, and the air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

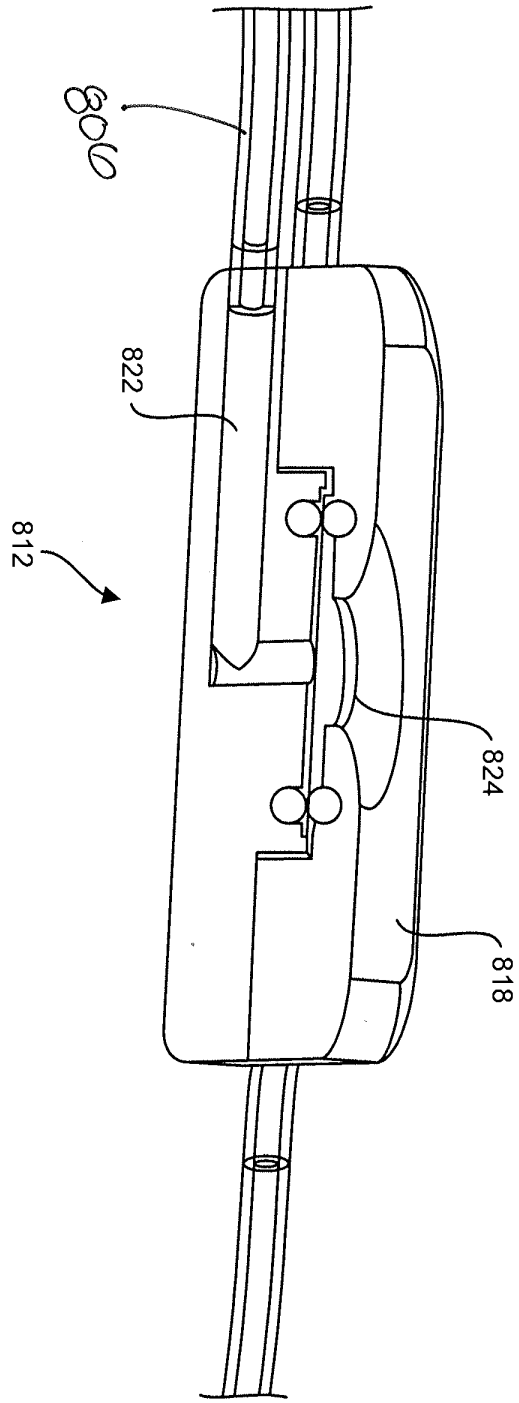


FIG. 8B

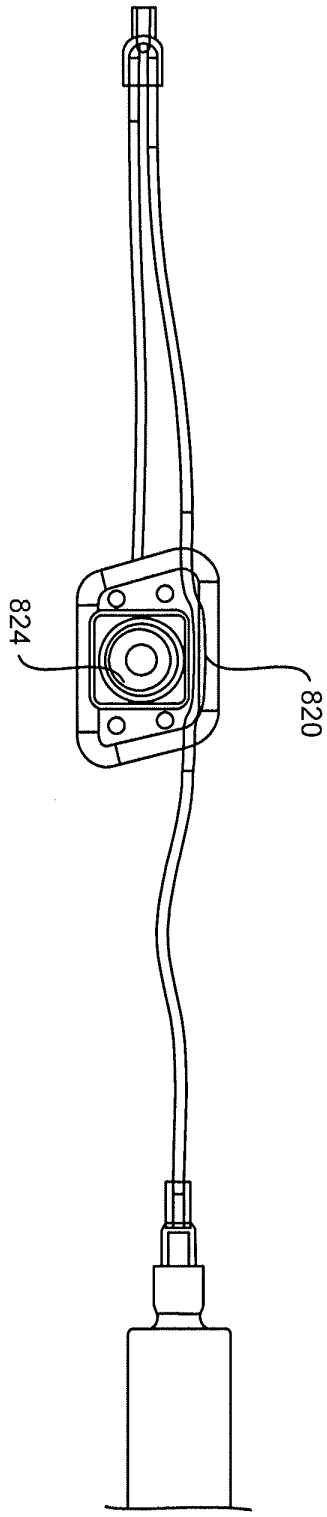
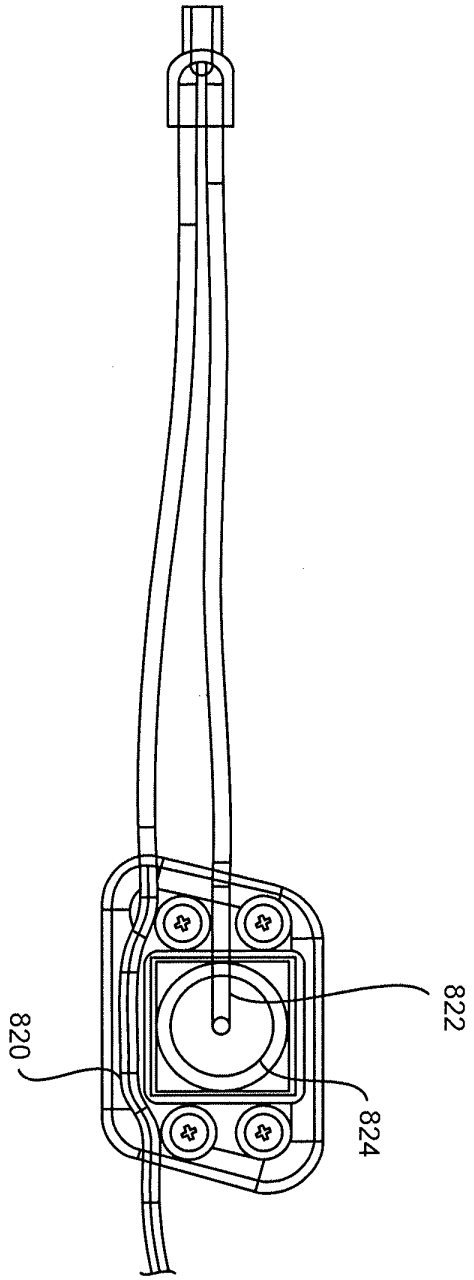


FIG. 8C

FIG. 8D



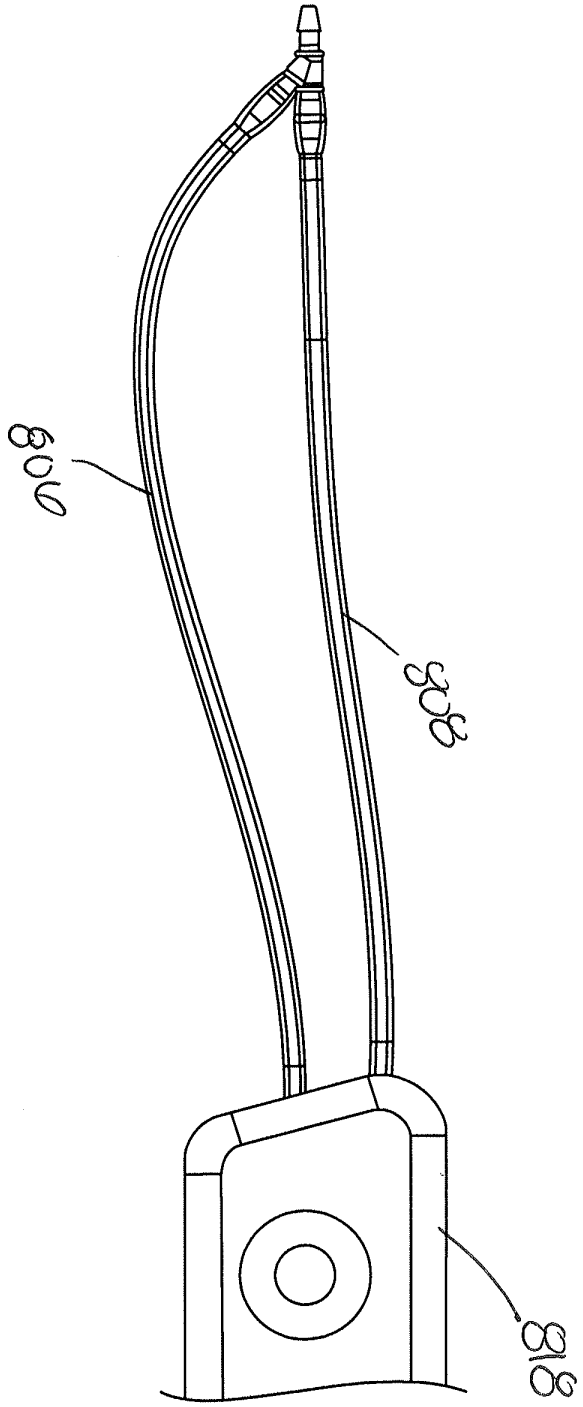
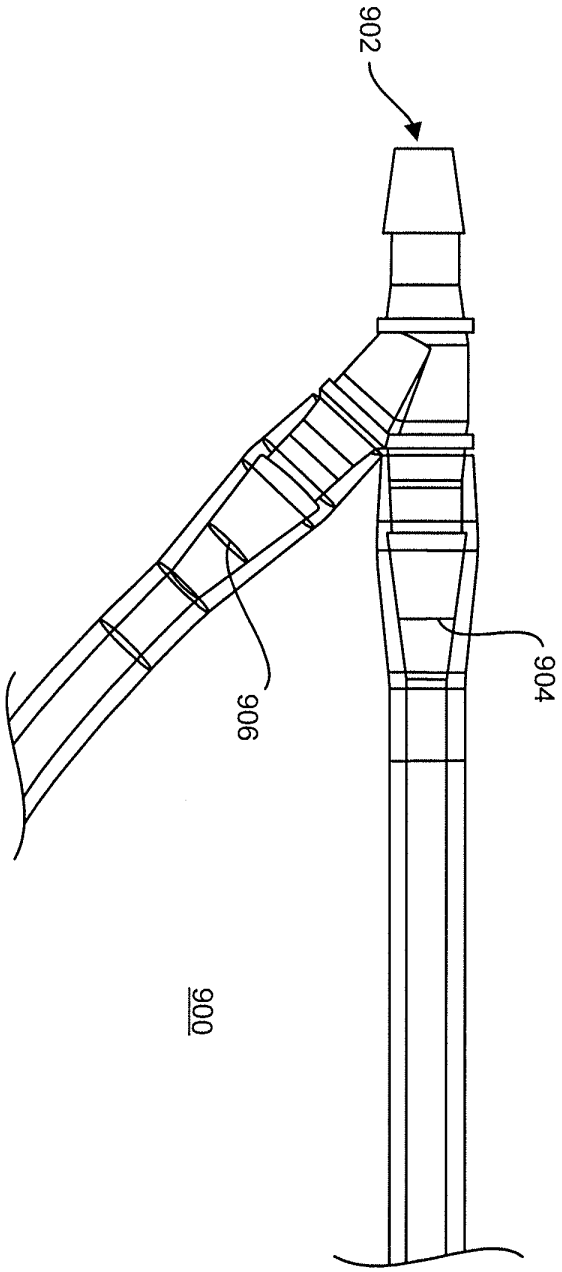


FIG. 8E

FIG. 9



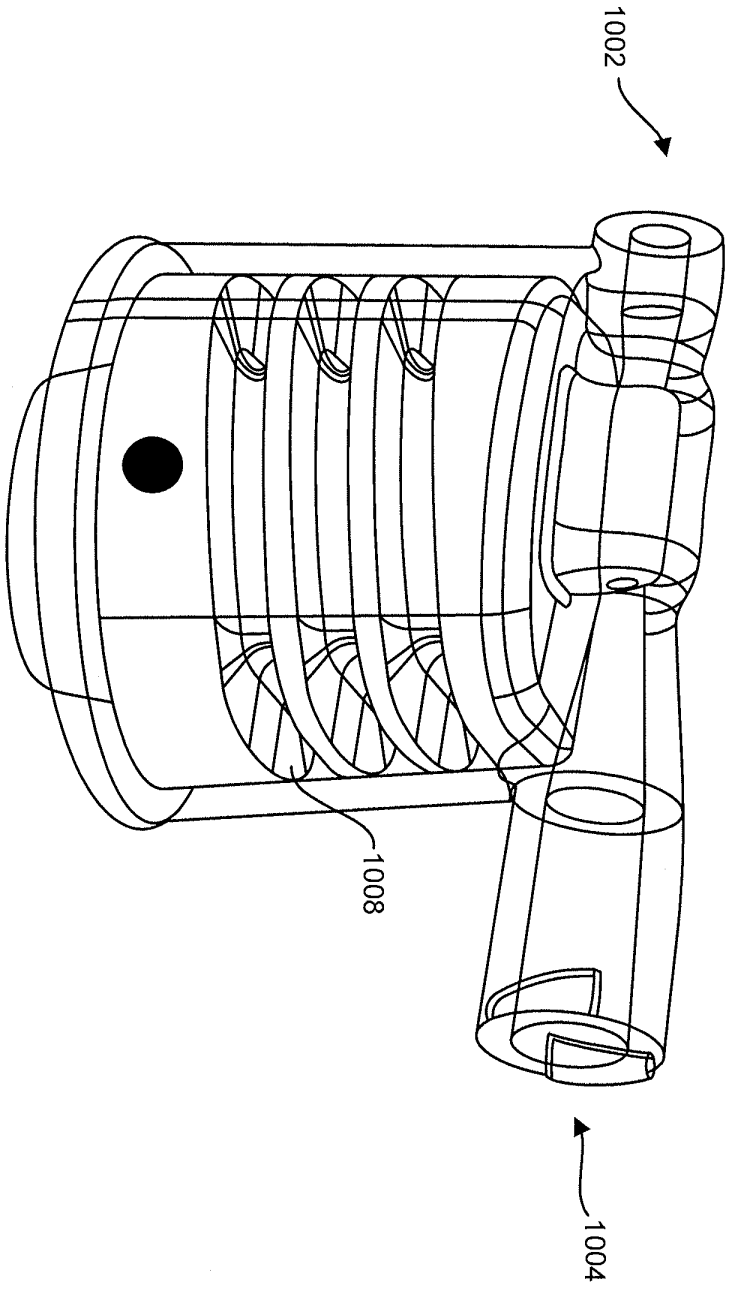


FIG. 10A

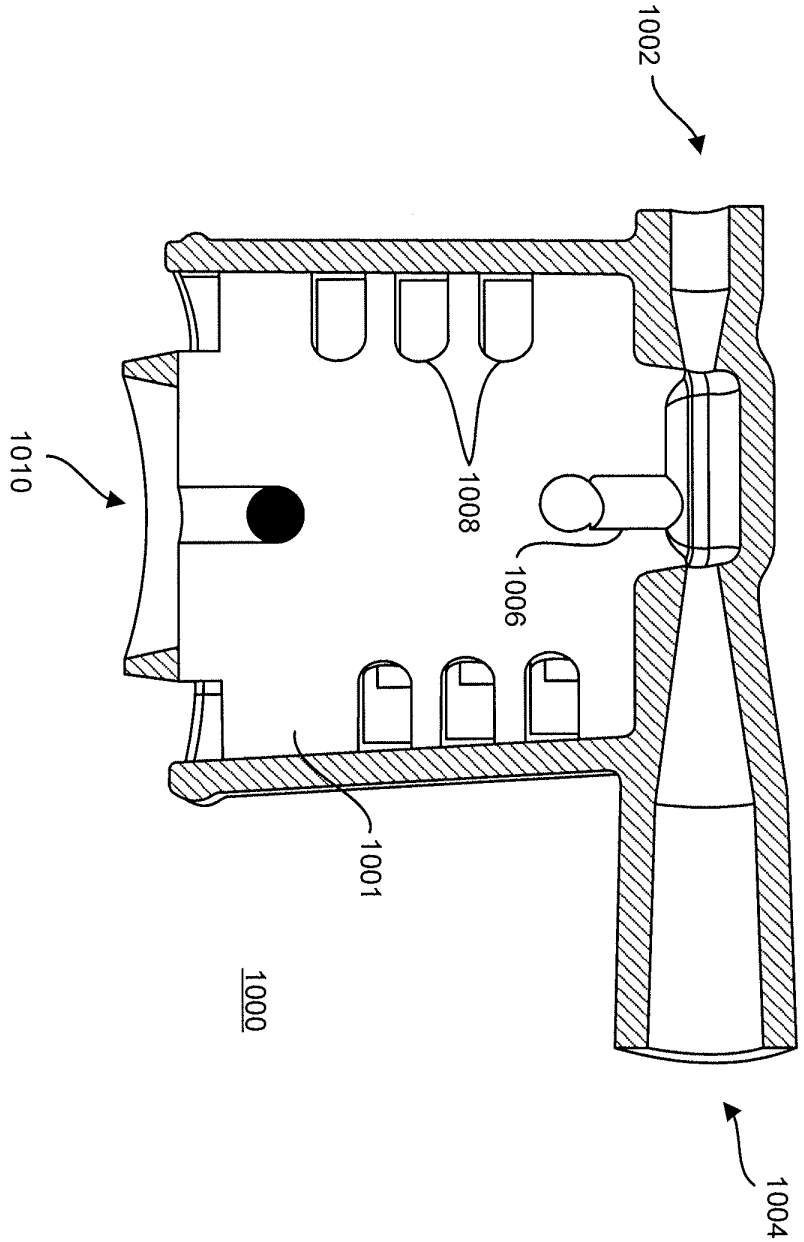


FIG. 10B

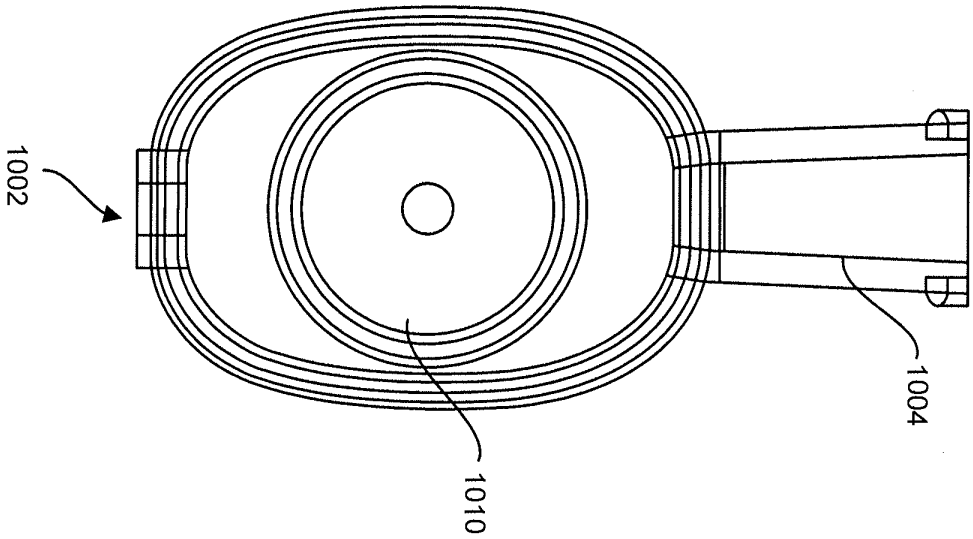
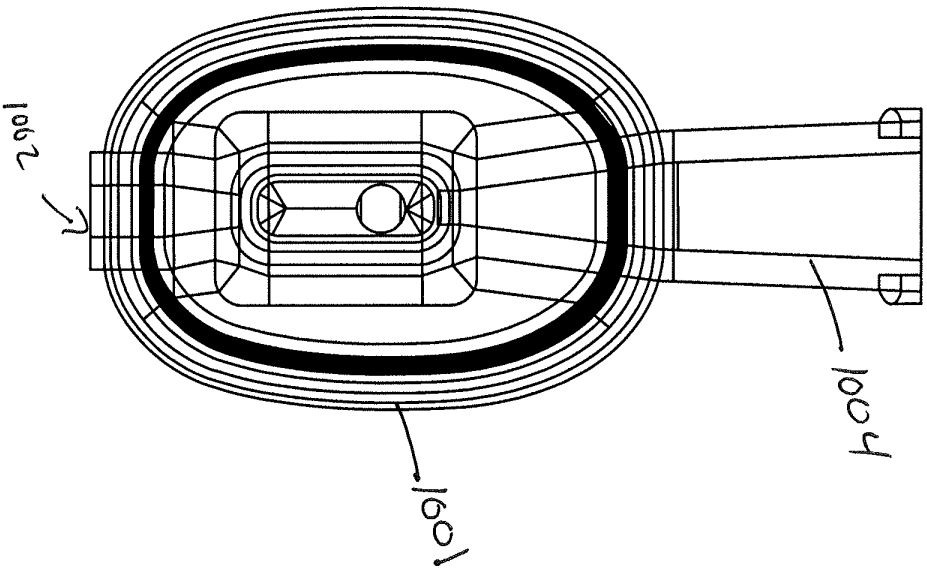


FIG. 10C

FIG. 10D



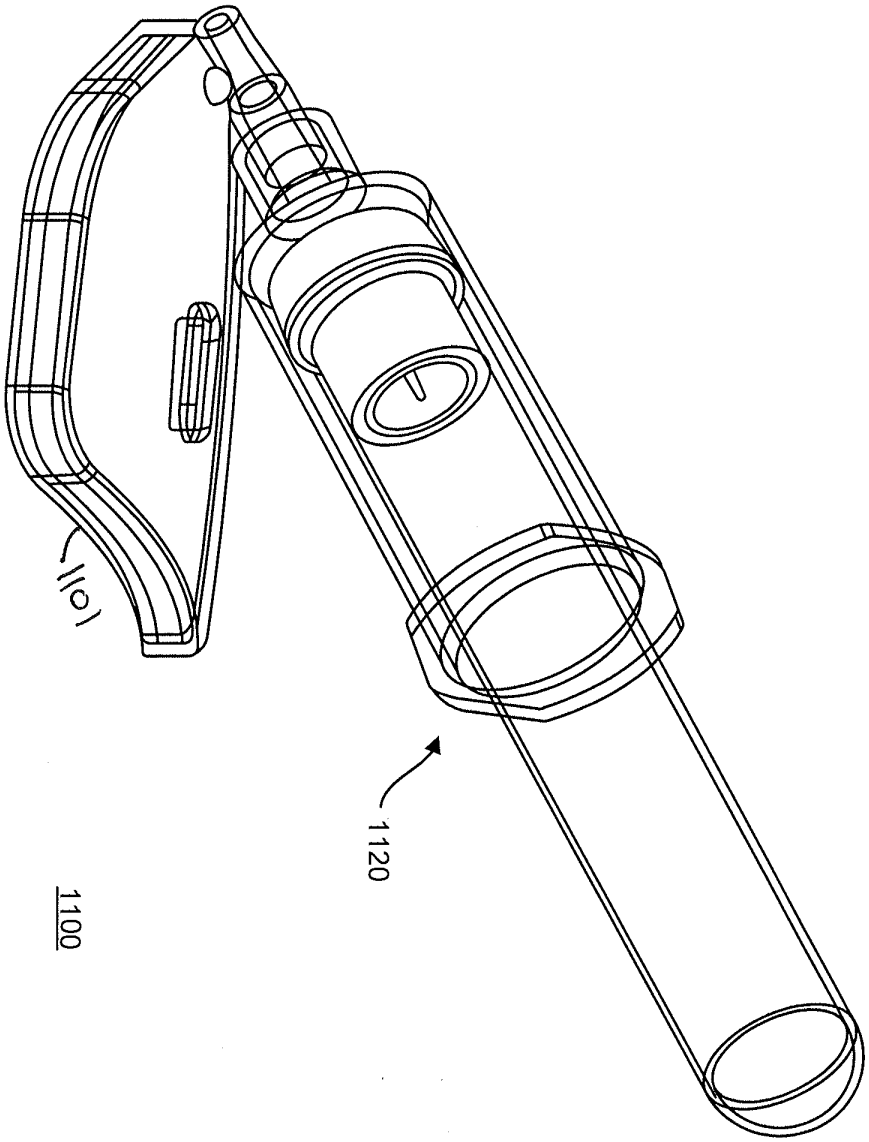


FIG. 11A

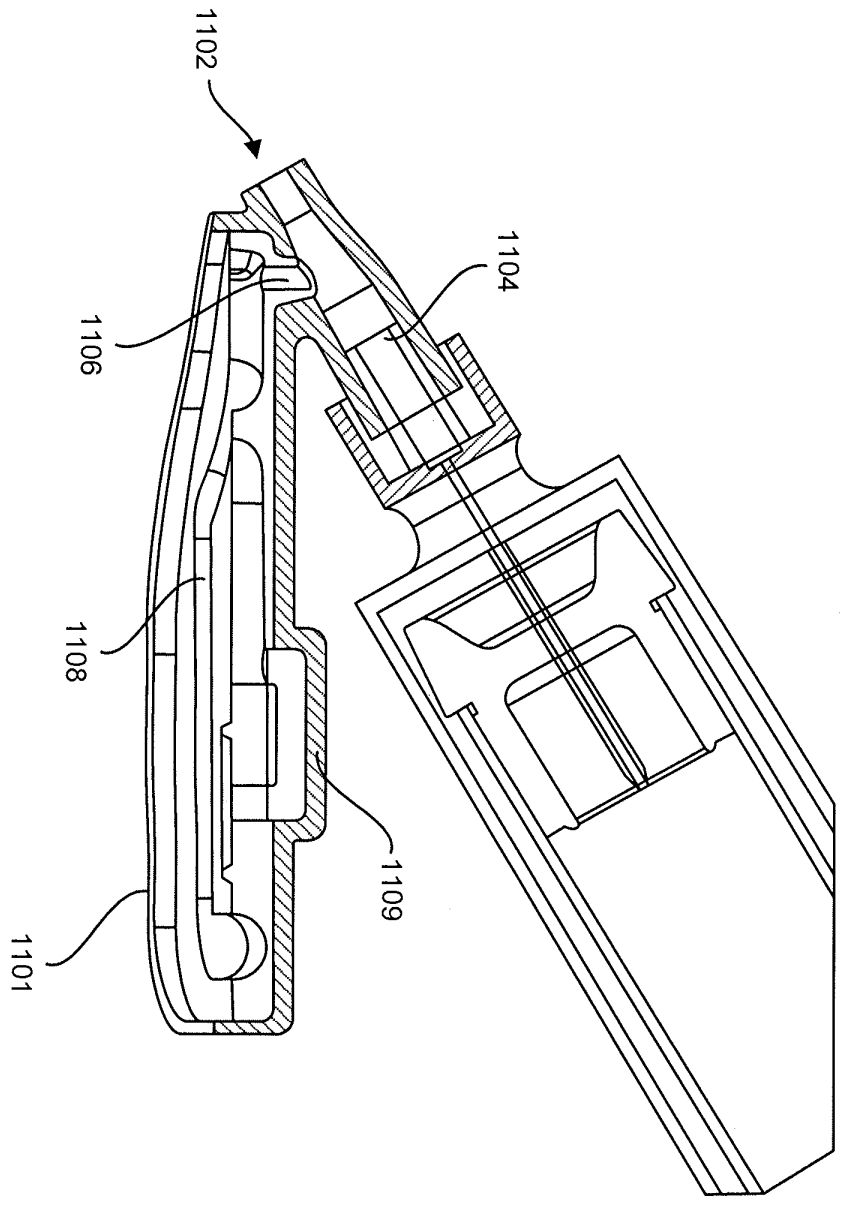


FIG. 11B

FIG. 11C

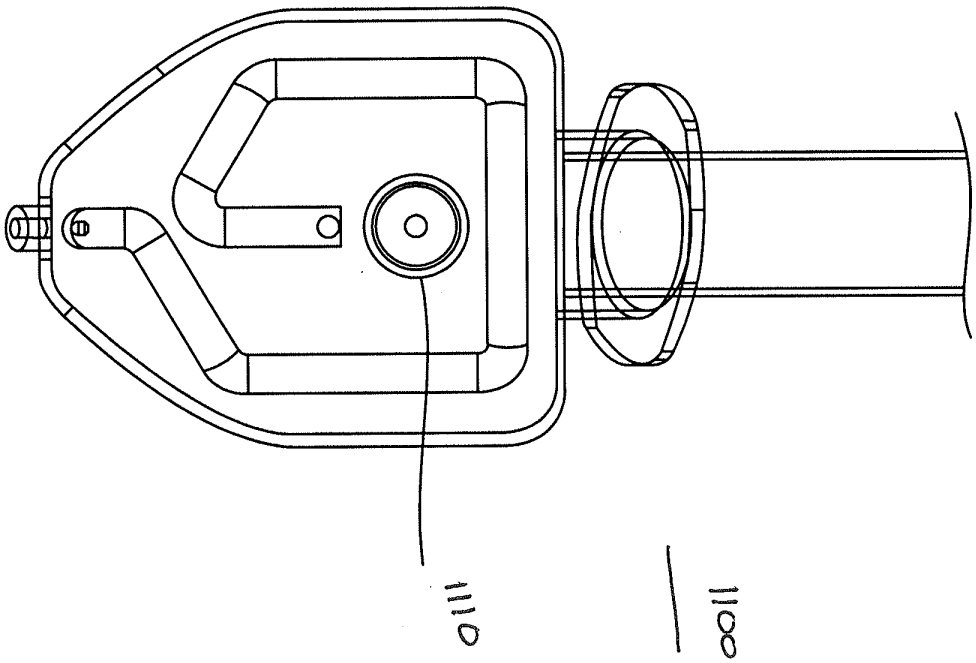
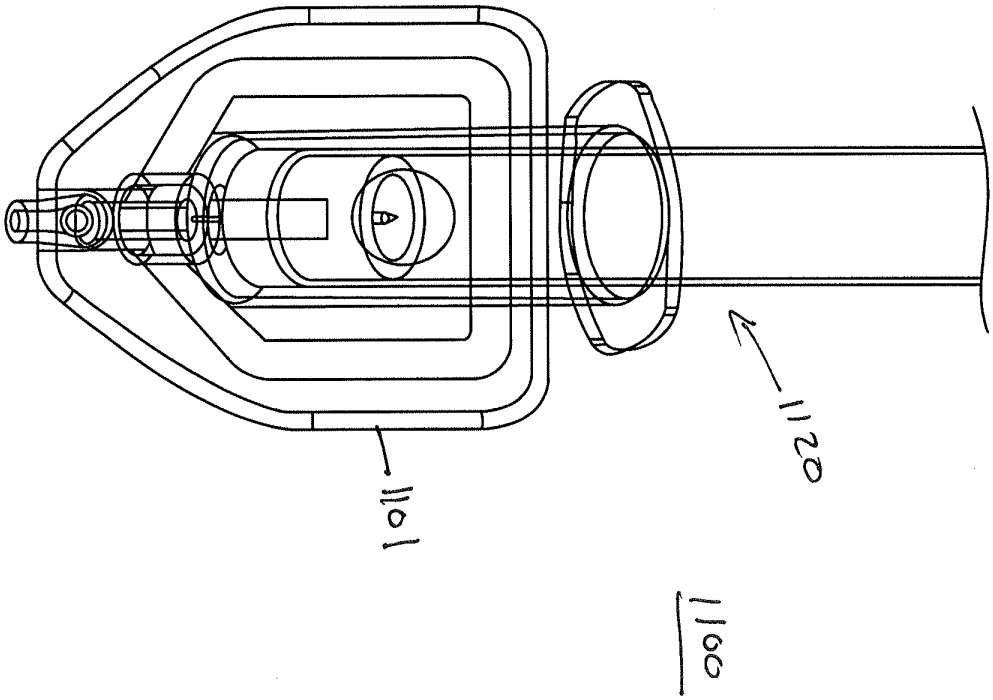


FIG. 11D



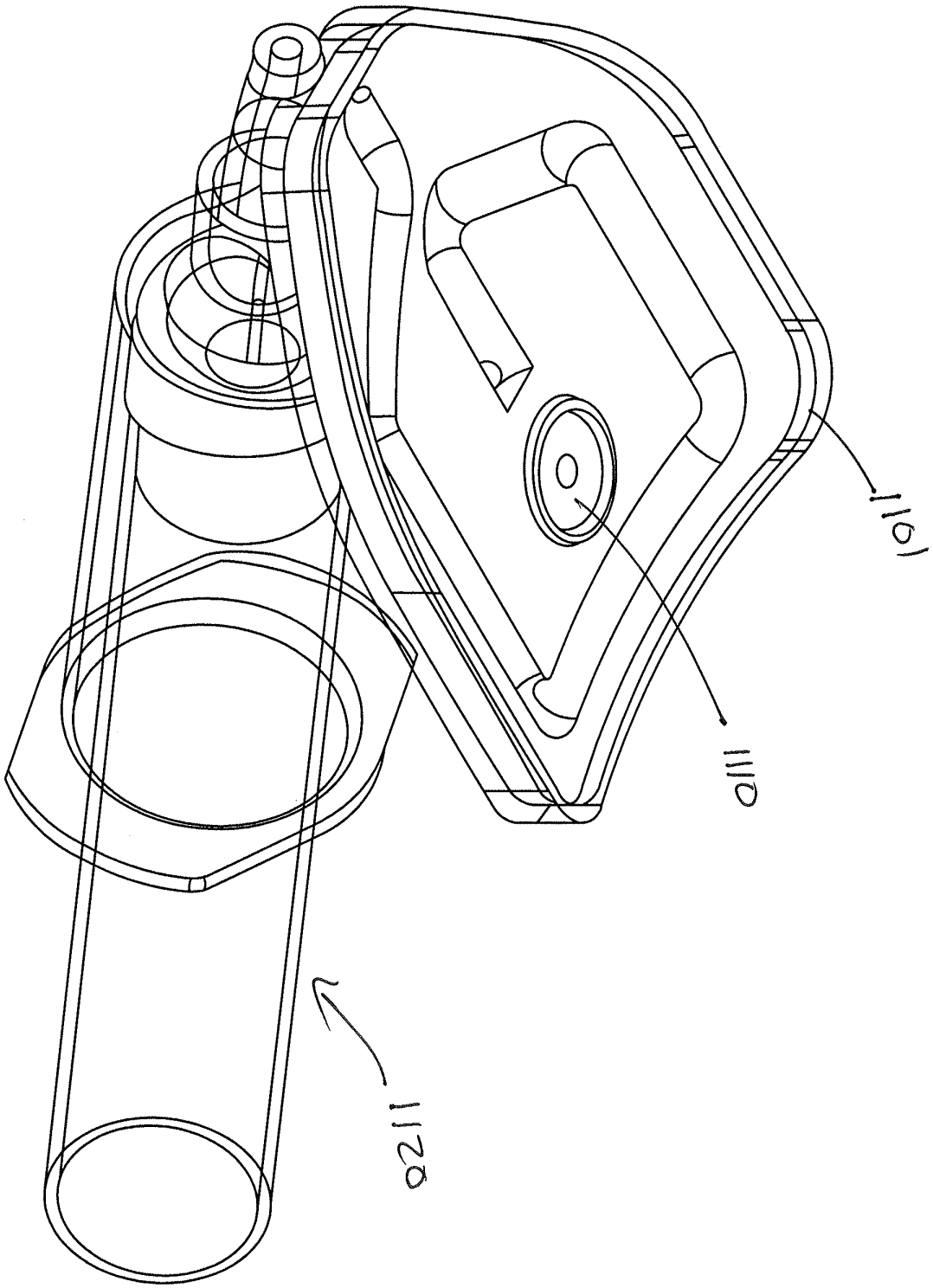


FIG. 11E

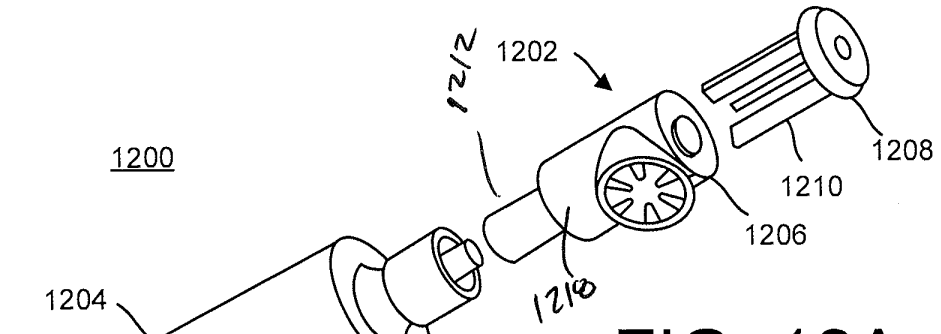


FIG. 12A

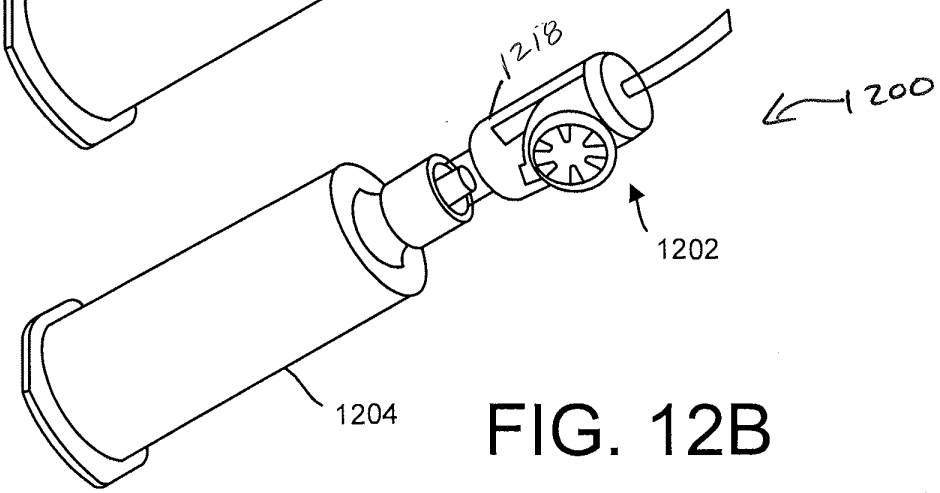


FIG. 12B

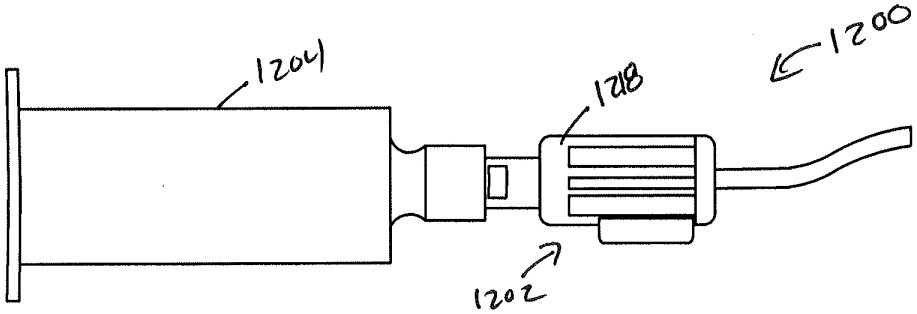


FIG. 12C

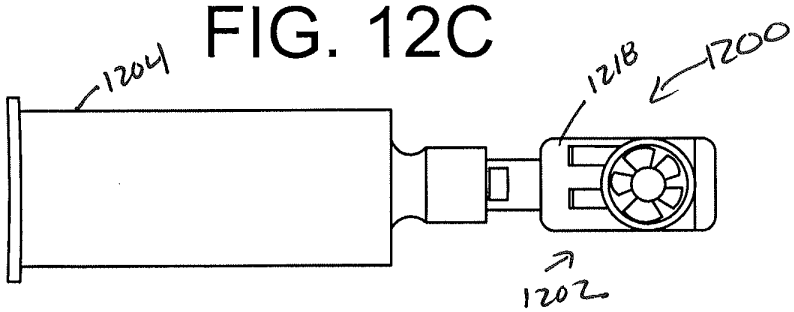


FIG. 12D

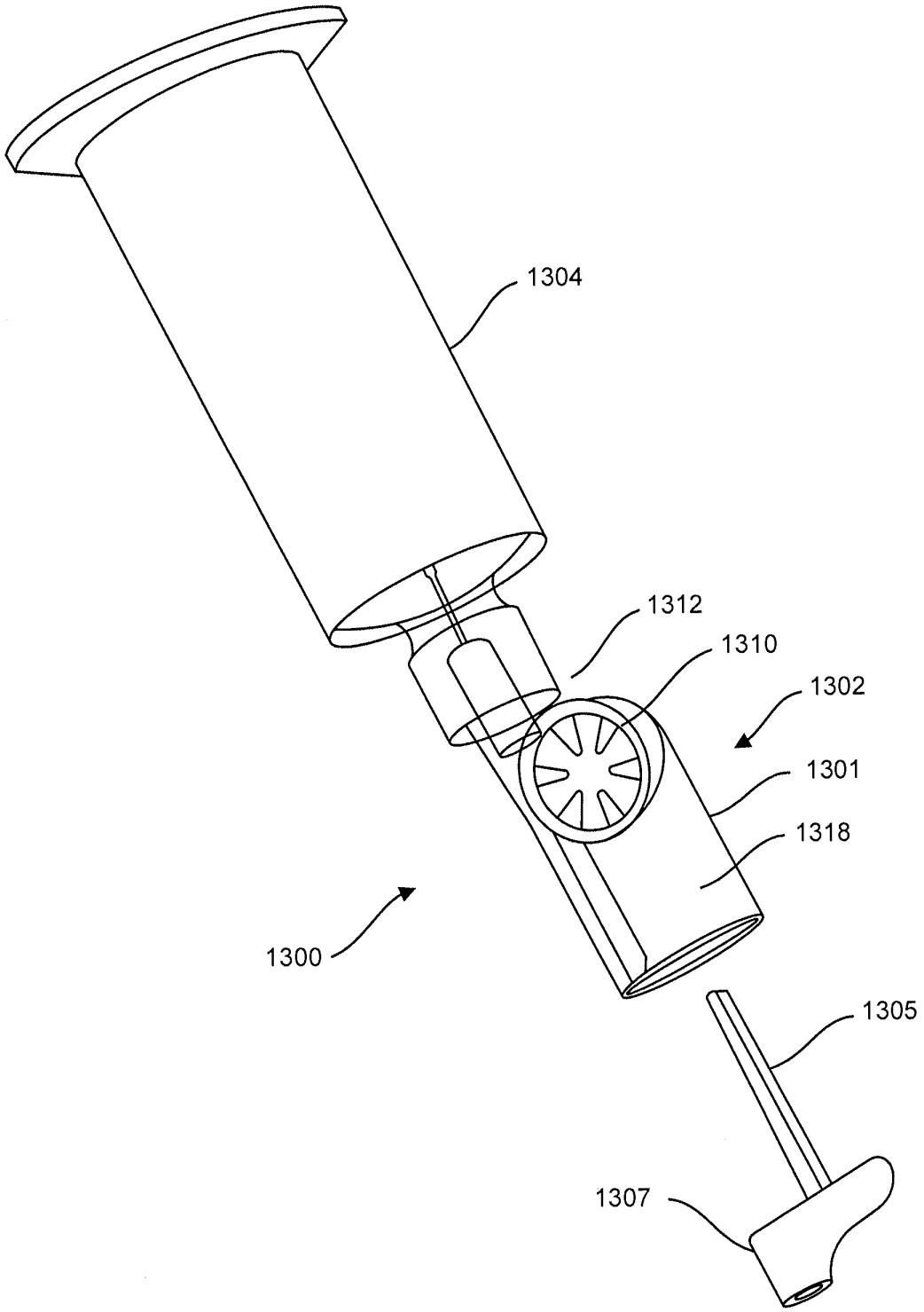


FIG. 13A

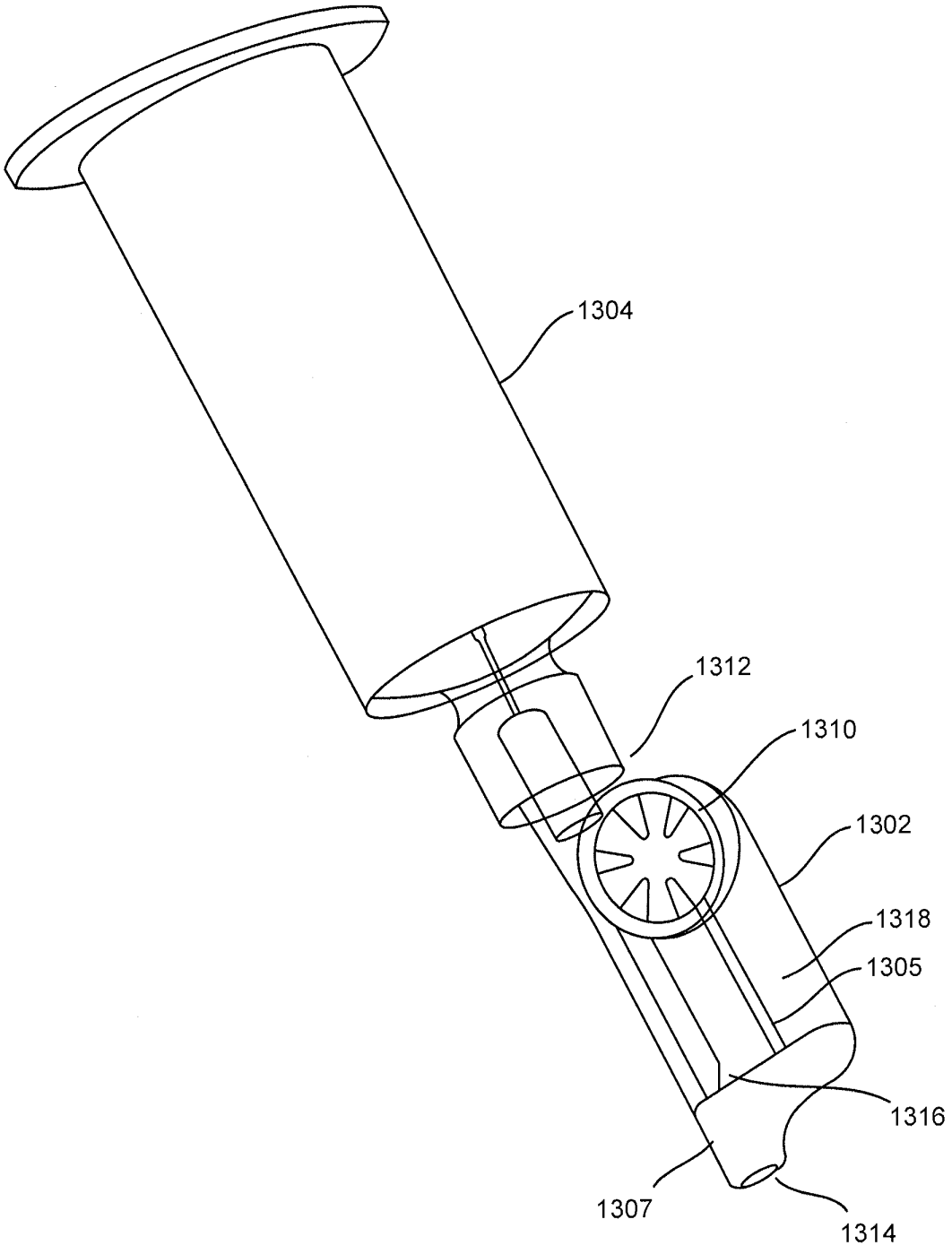


FIG. 13B

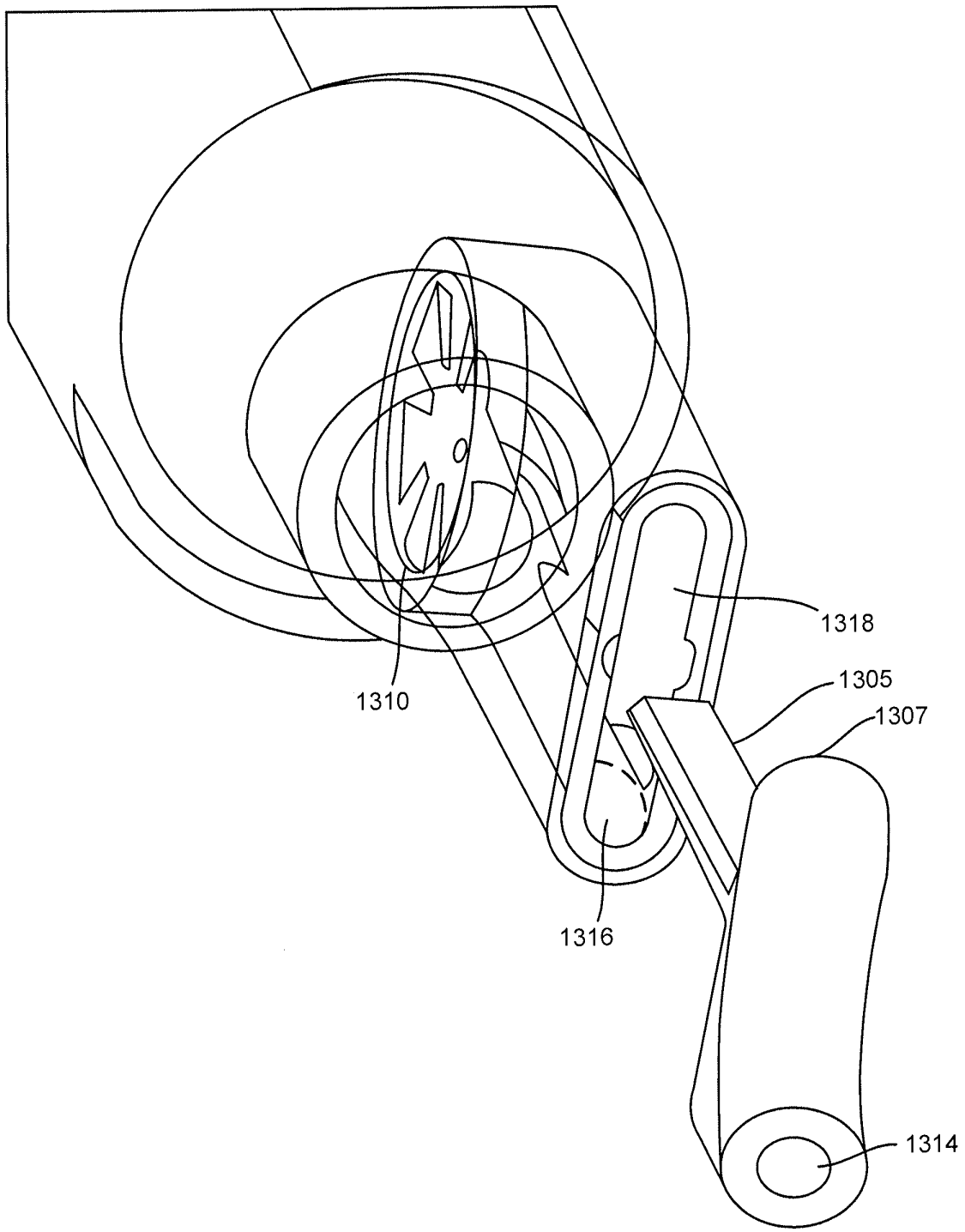


FIG. 13C

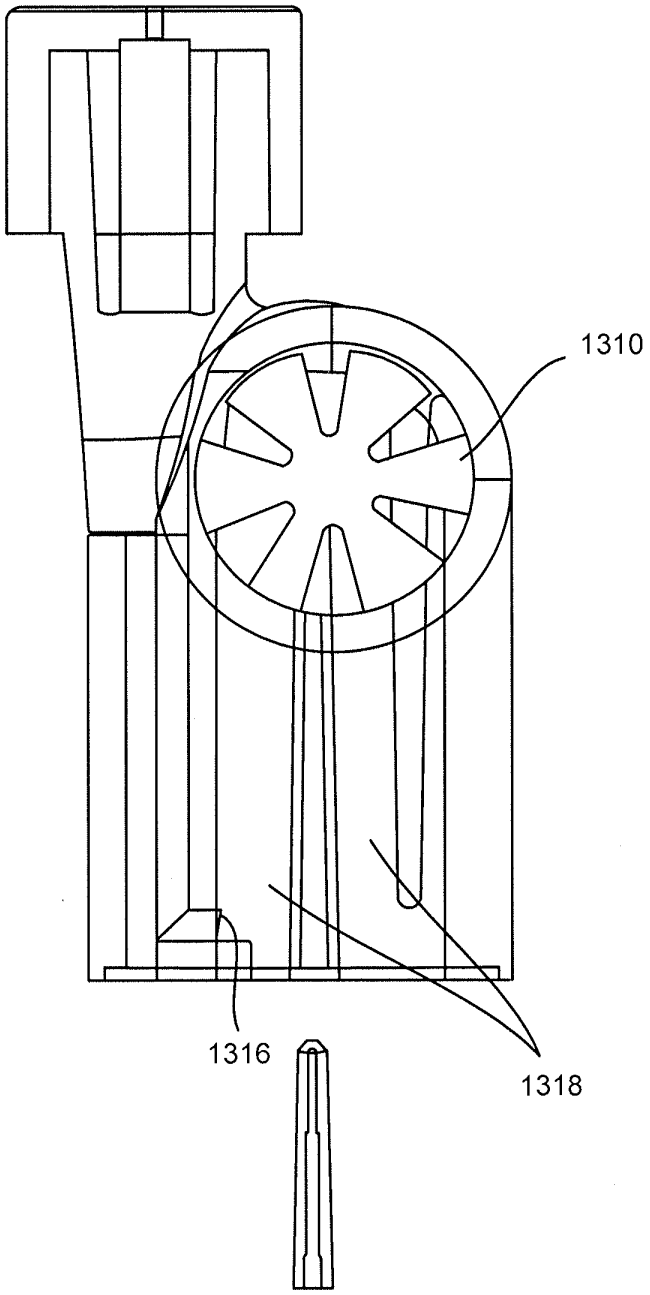


FIG. 13D

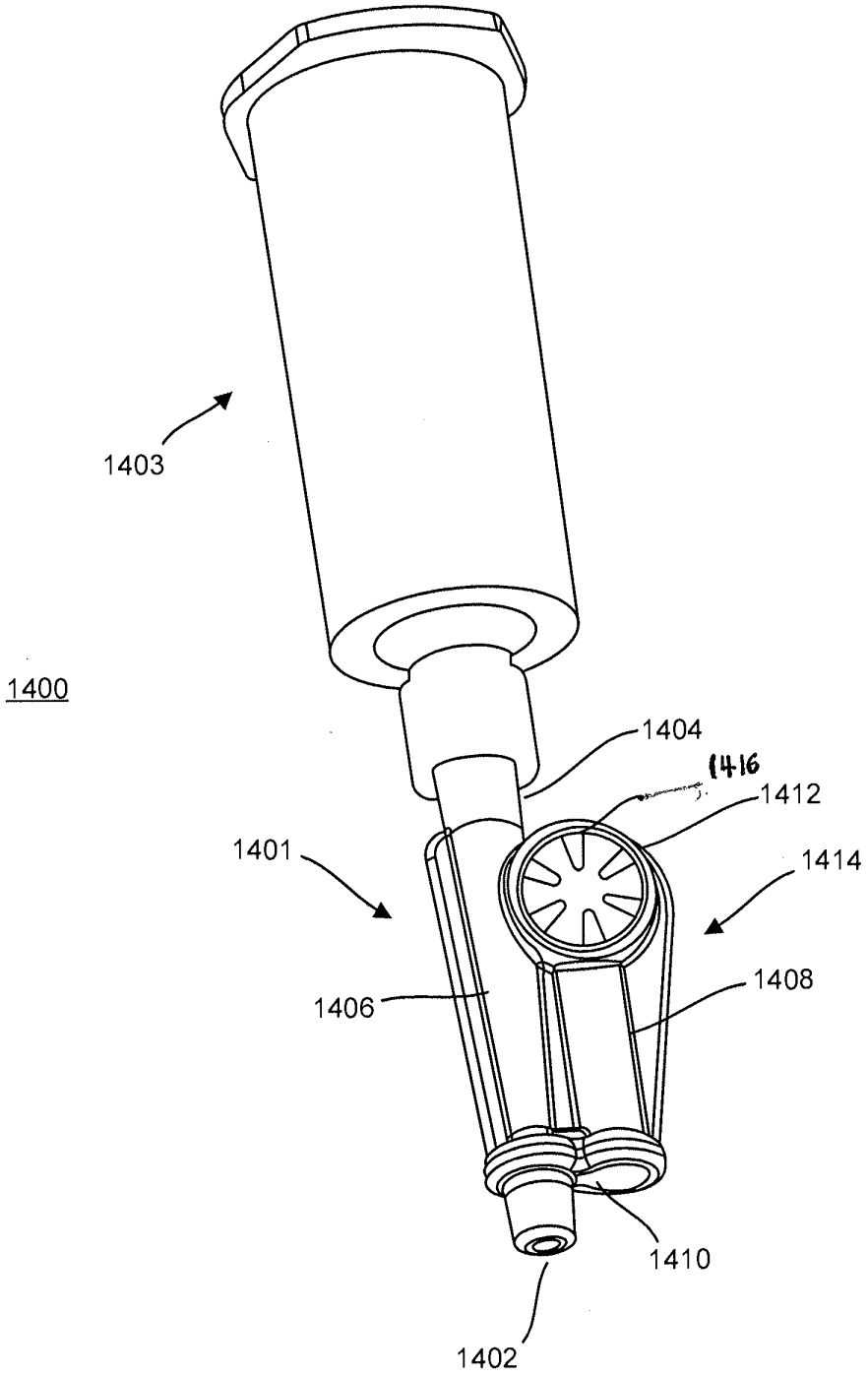


FIG. 14A

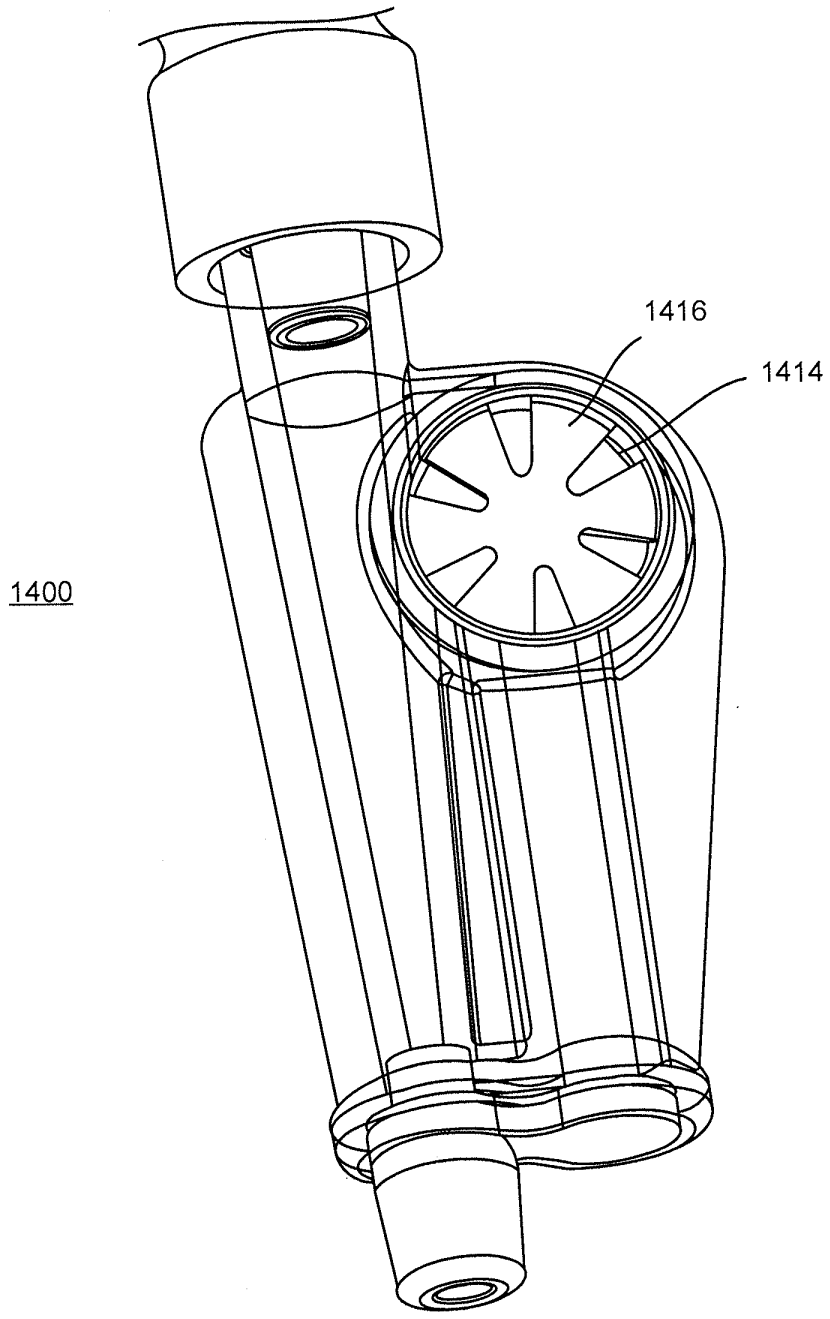


FIG. 14B

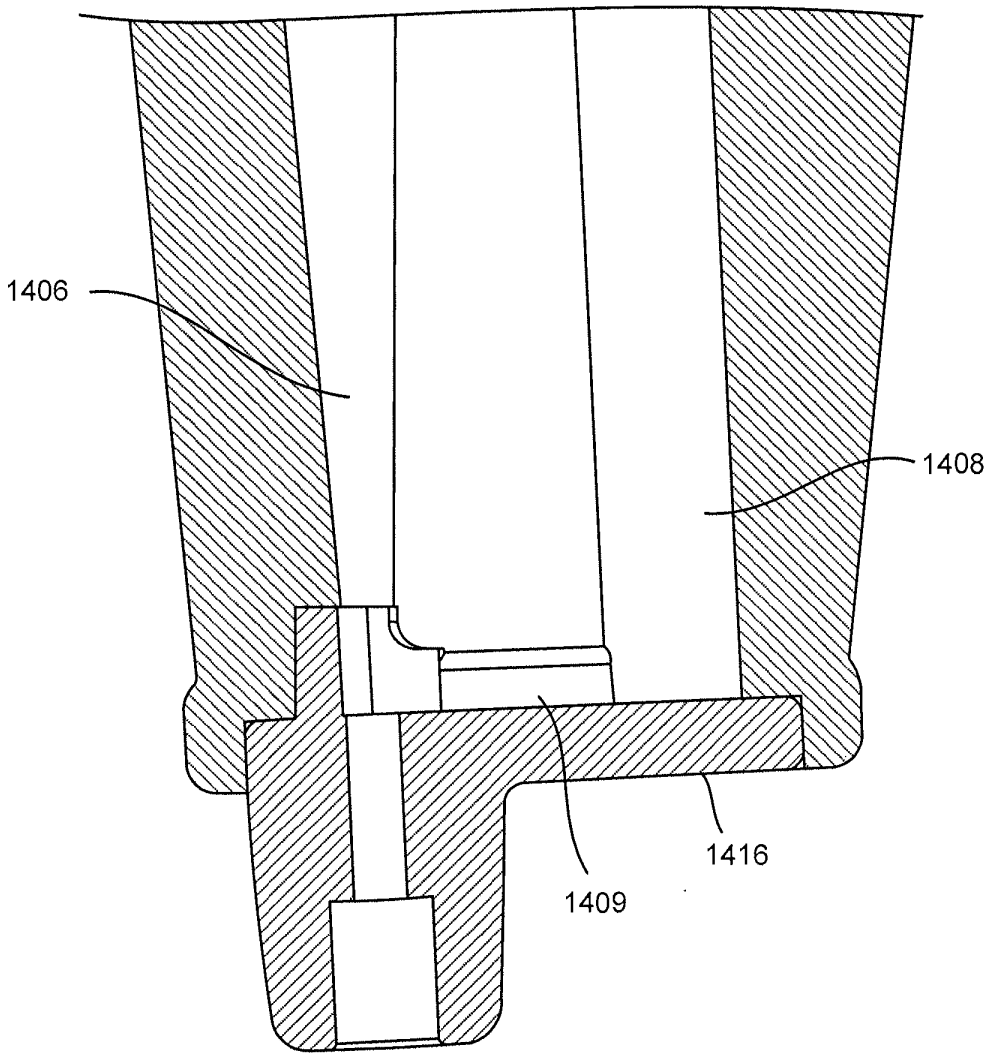


FIG. 14C

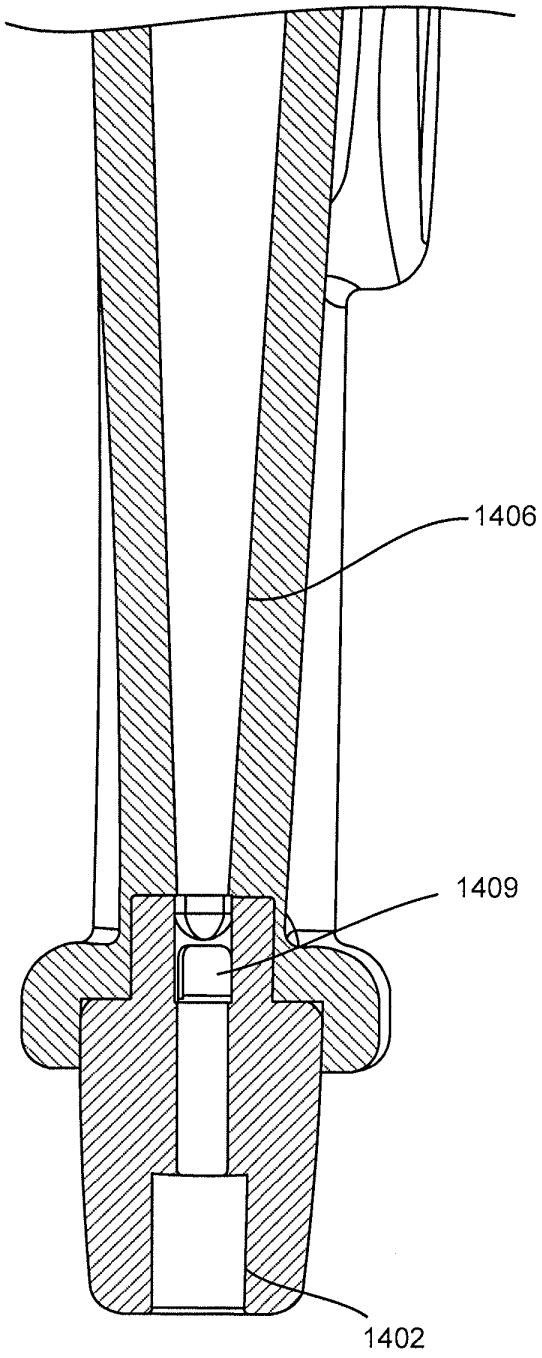


FIG. 14D

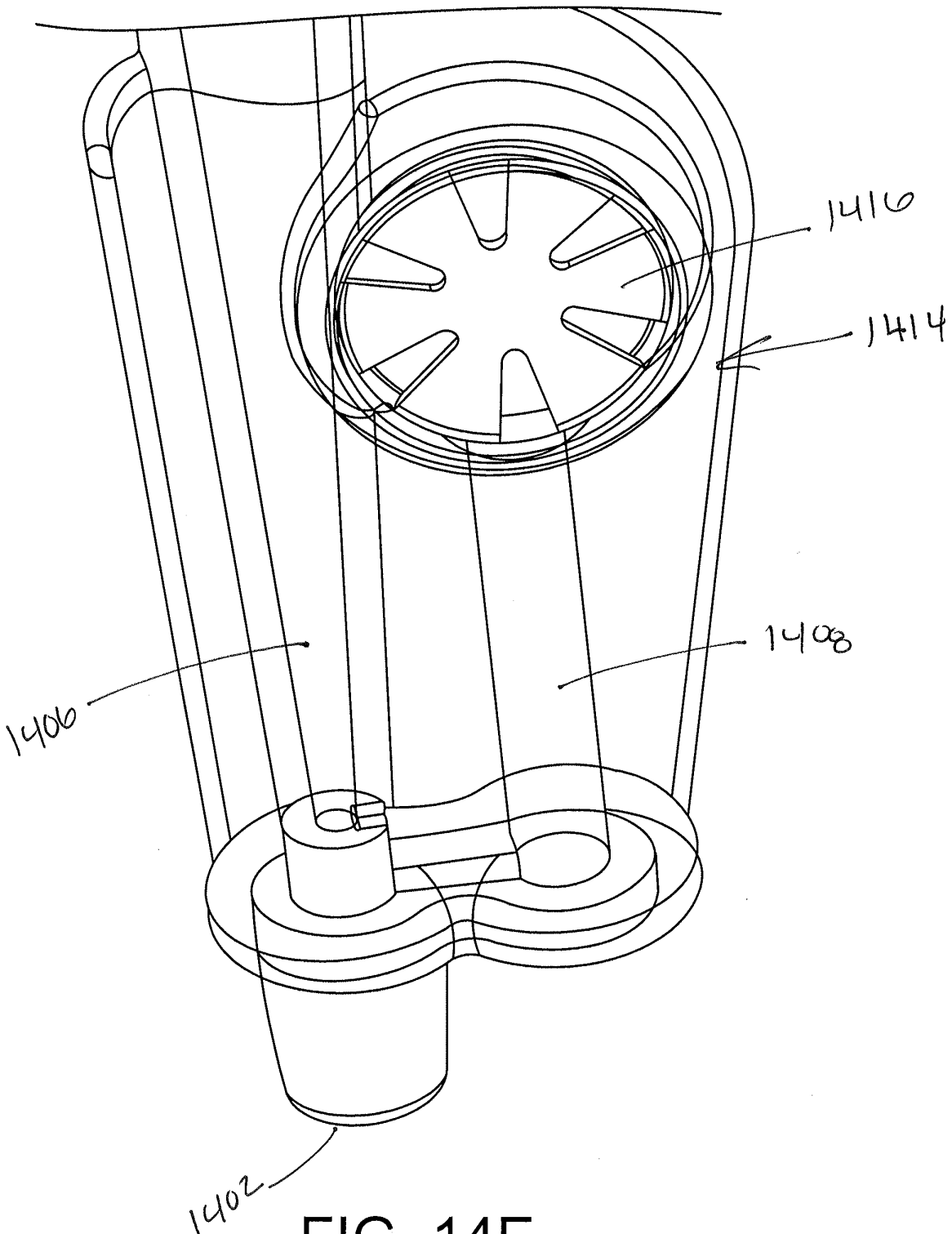


FIG. 14E

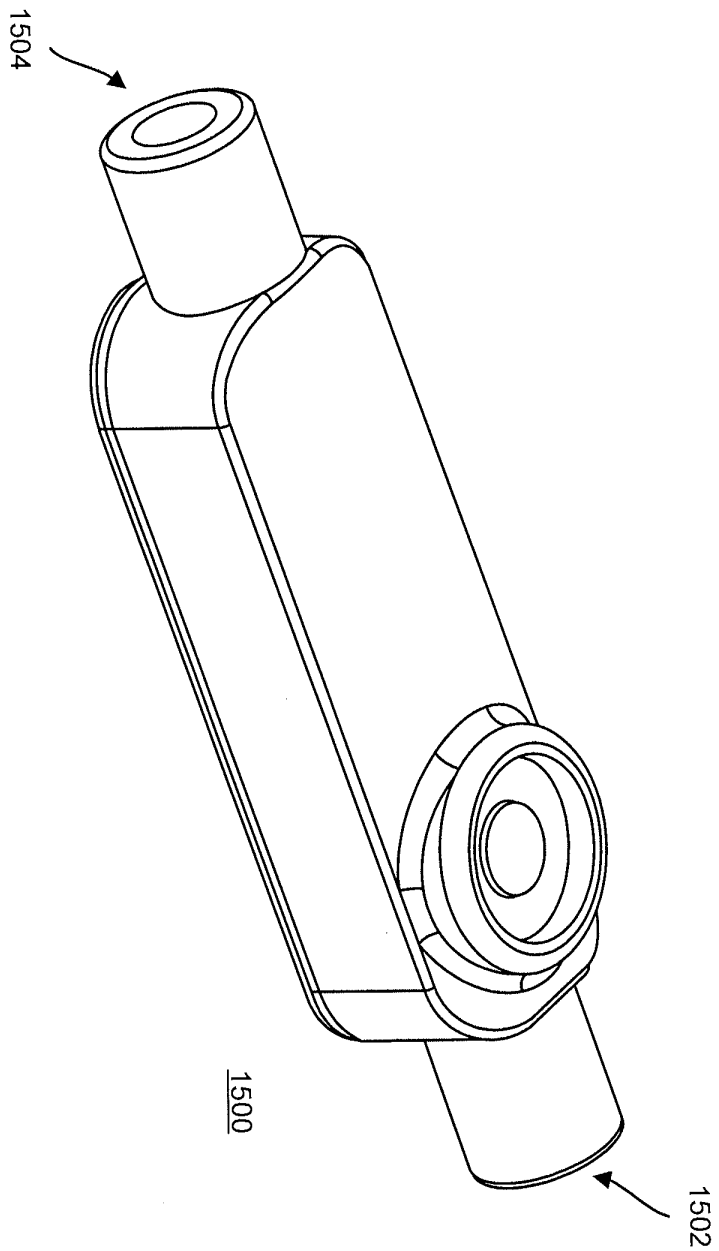


FIG. 15A

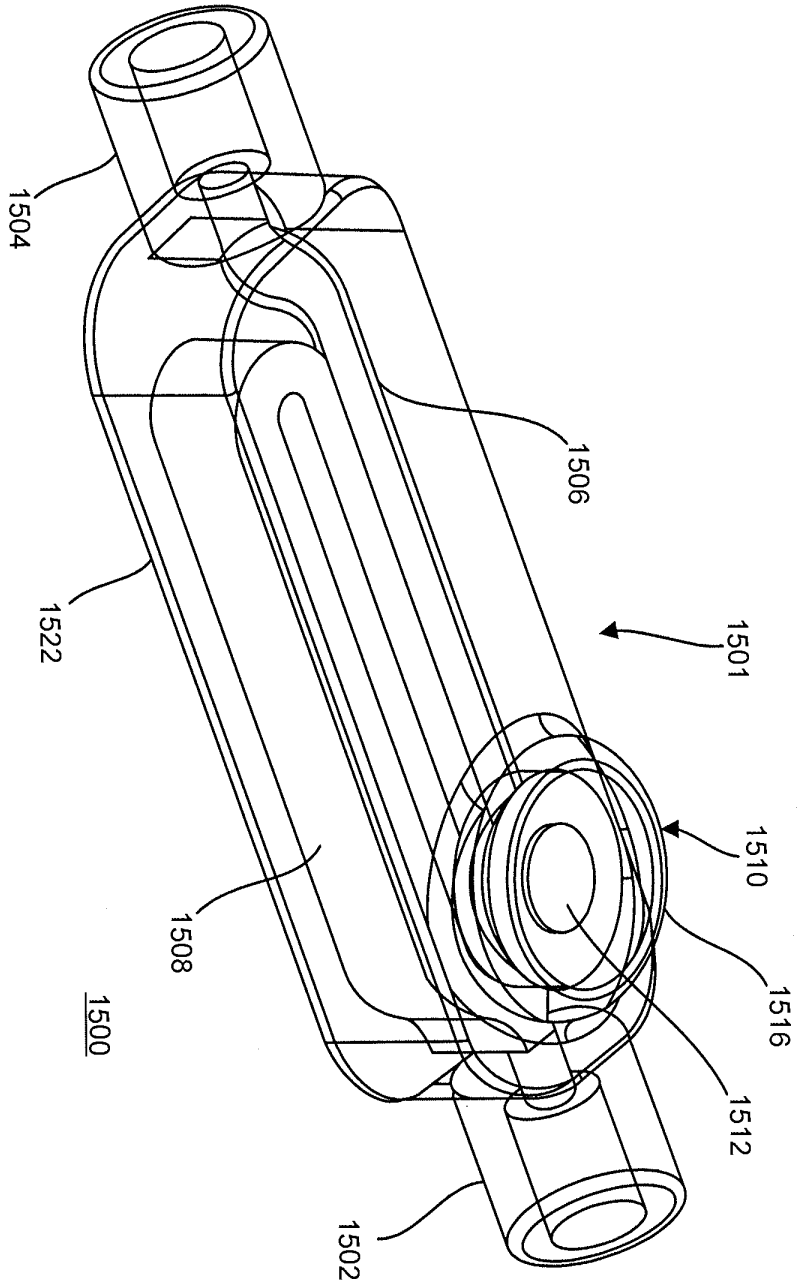


FIG. 15B

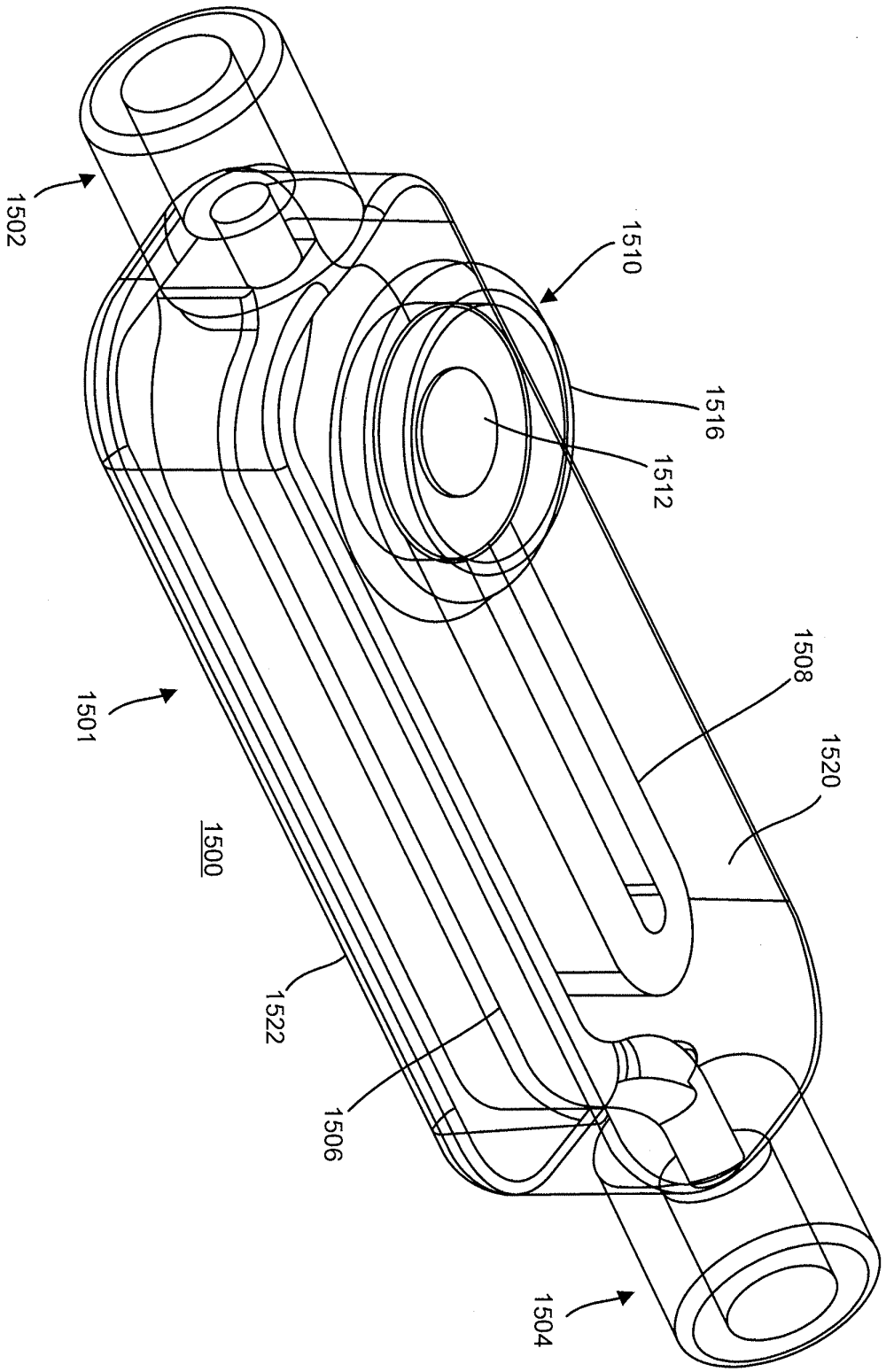


FIG. 15C

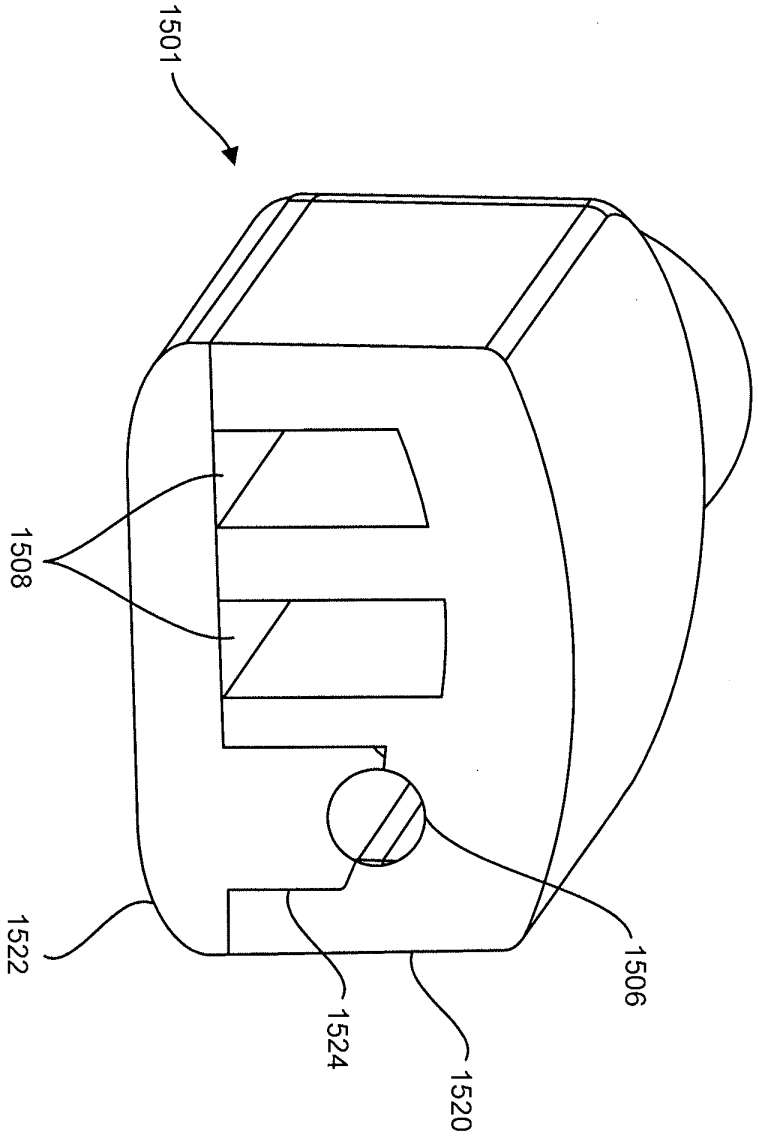


FIG. 15D

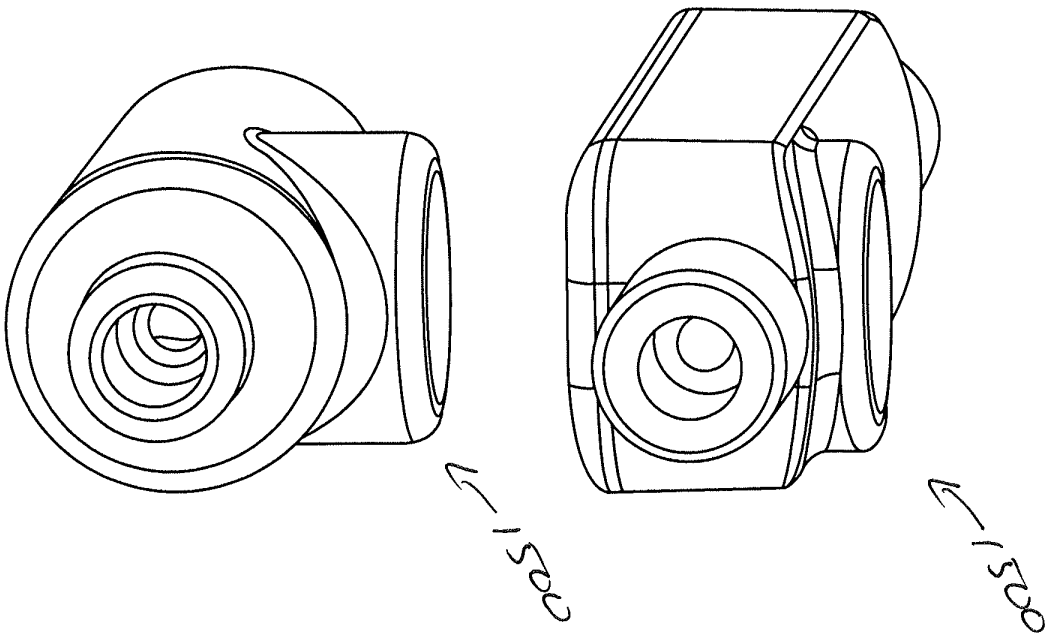


FIG. 15E

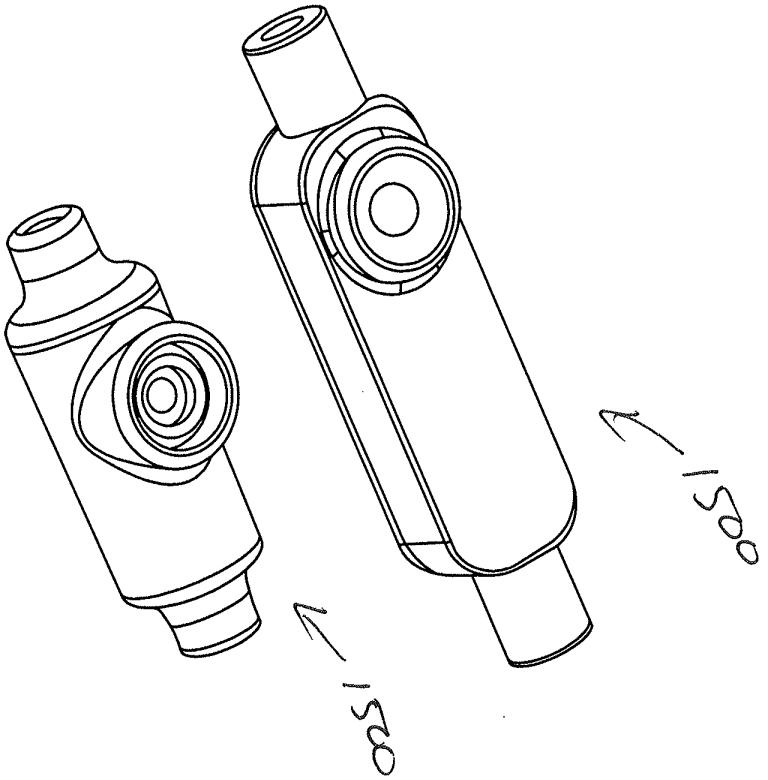


FIG. 15F

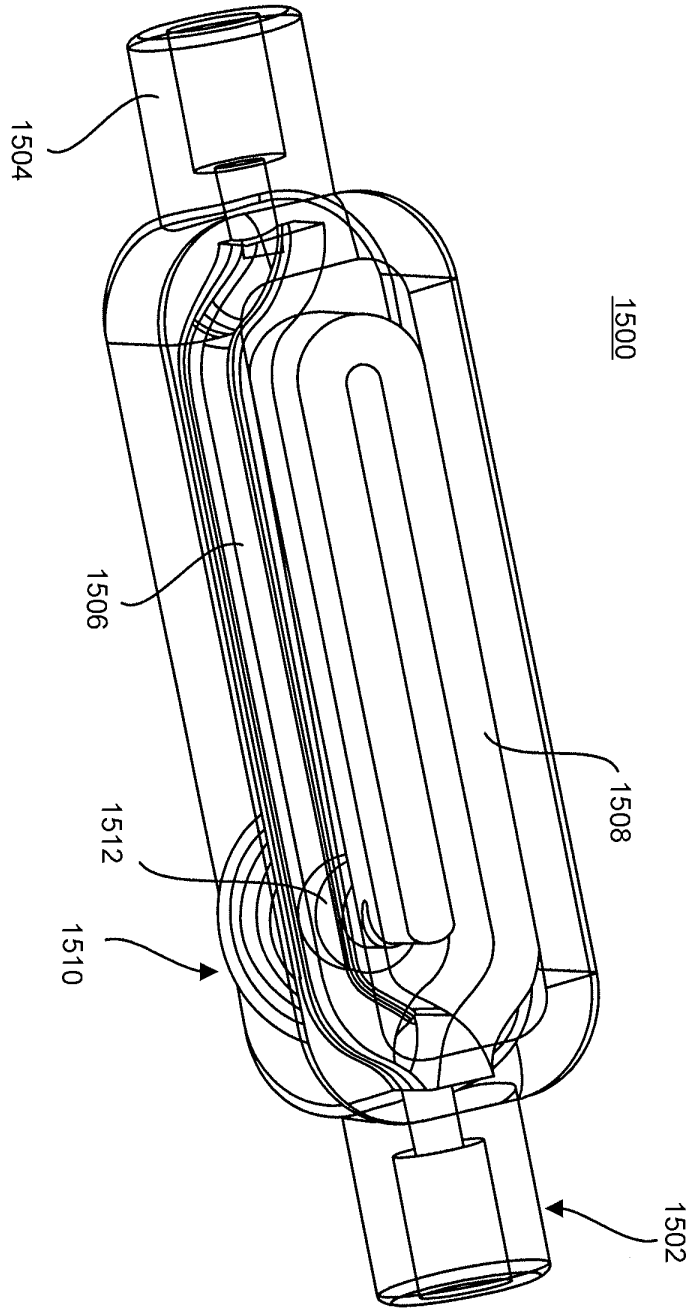


FIG. 15G

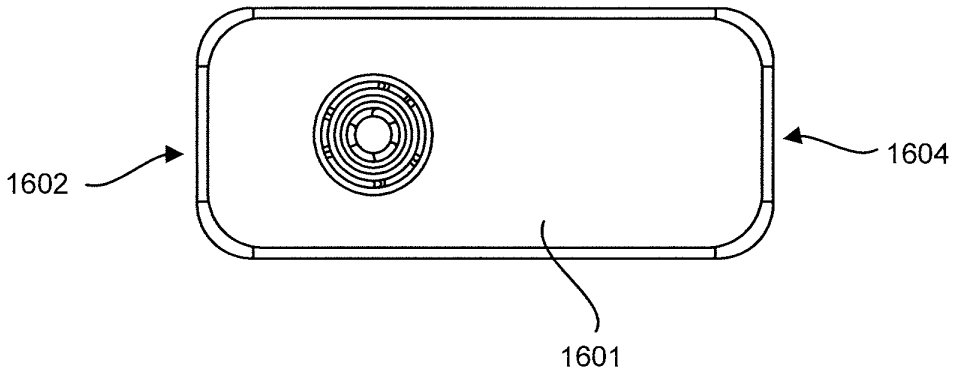


FIG. 16A

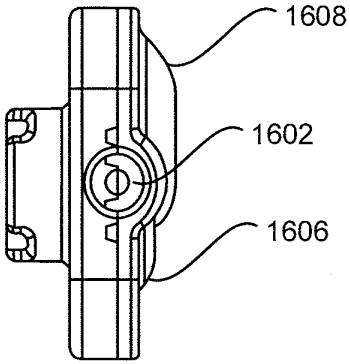


FIG. 16C

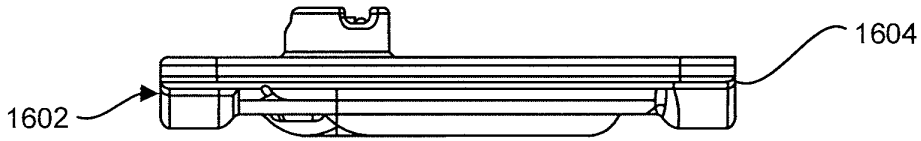


FIG. 16B

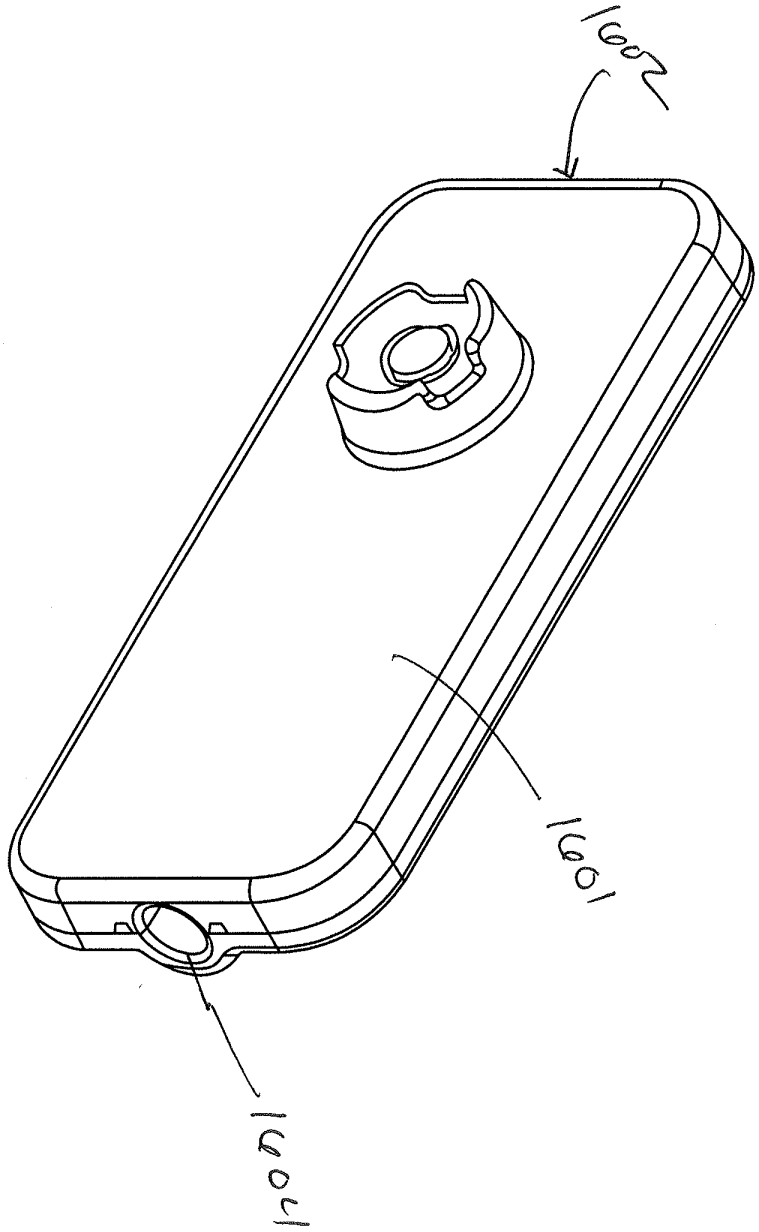


FIG. 16D

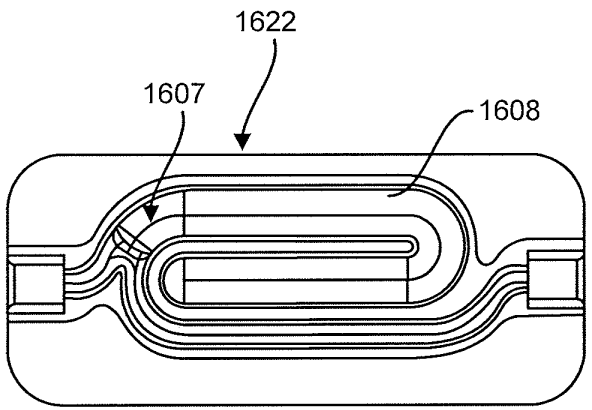


FIG. 17A

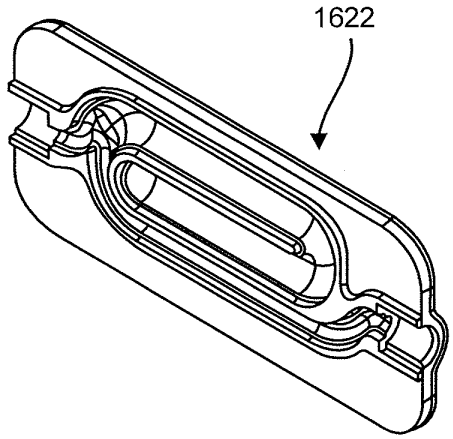


FIG. 17B

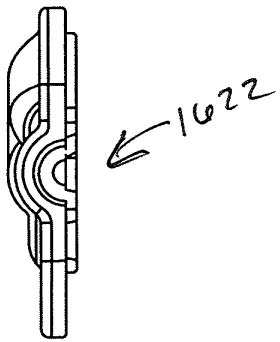


FIG. 17C

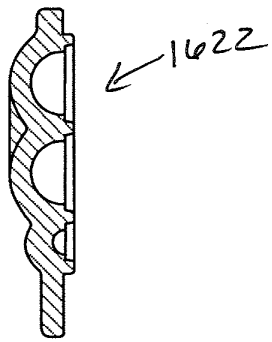


FIG. 17D

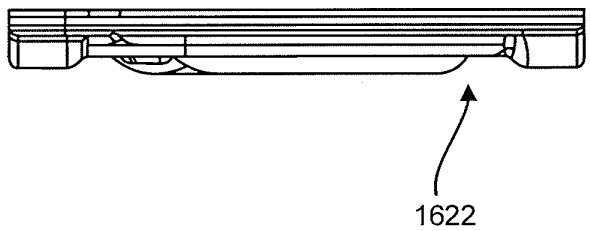


FIG. 17E

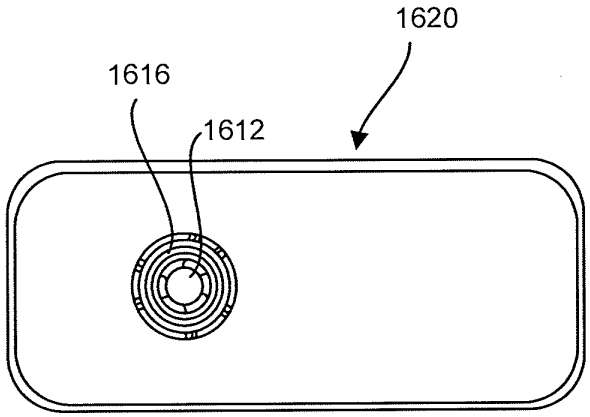


FIG. 18A

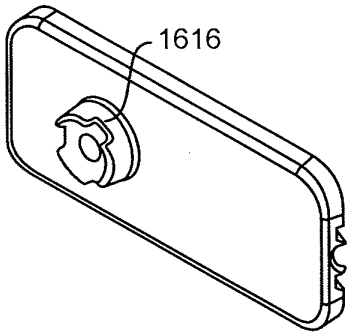


FIG. 18B

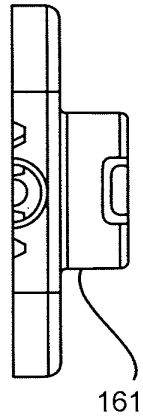


FIG. 18C

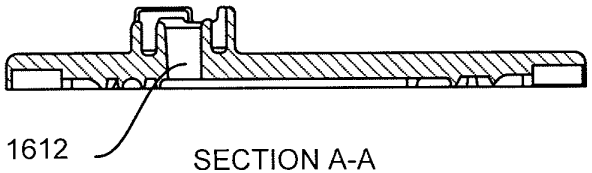


FIG. 18D

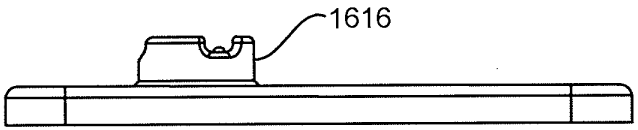


FIG. 18E

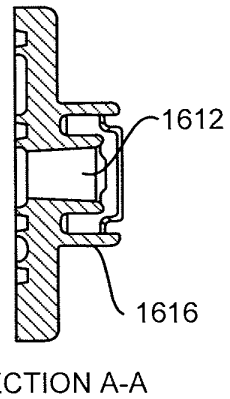


FIG. 18F

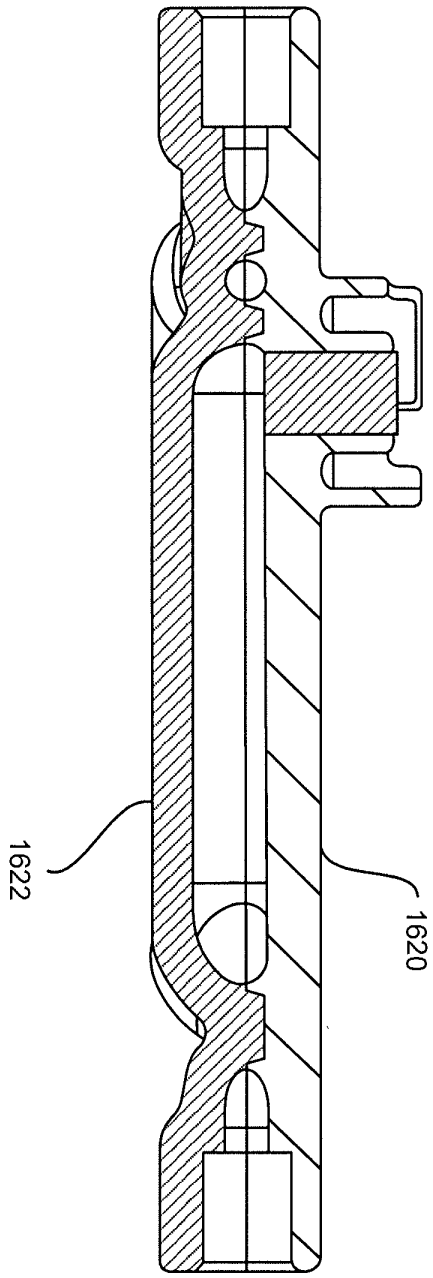


FIG. 19A

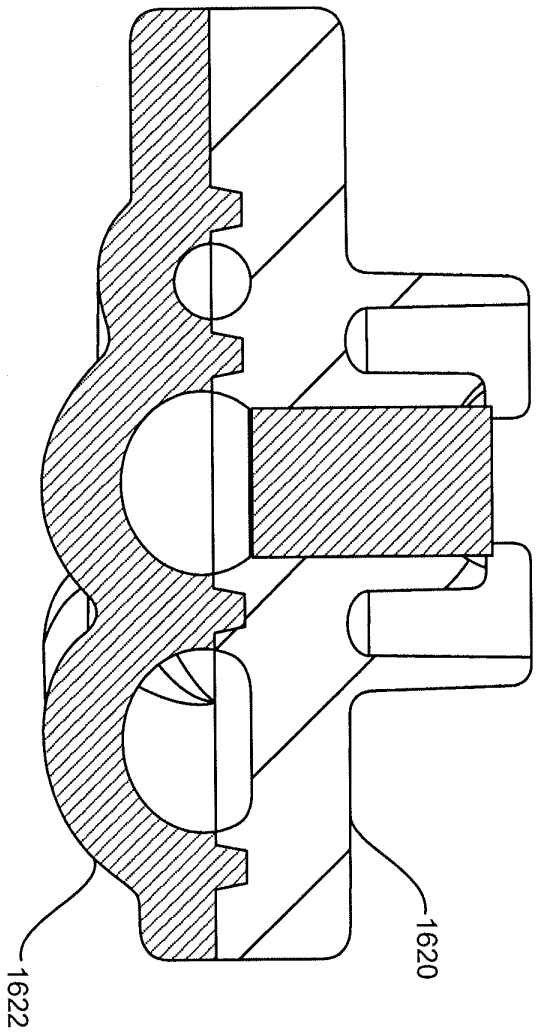


FIG. 19B

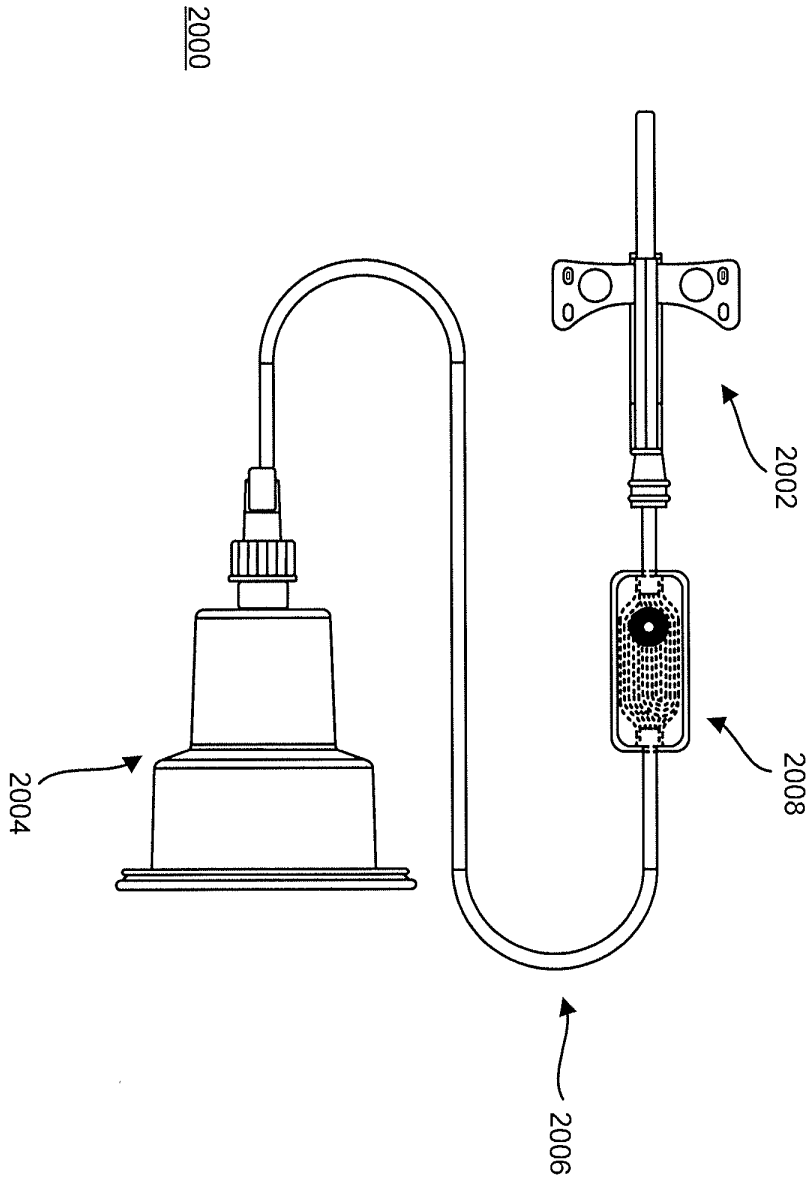


FIG. 20

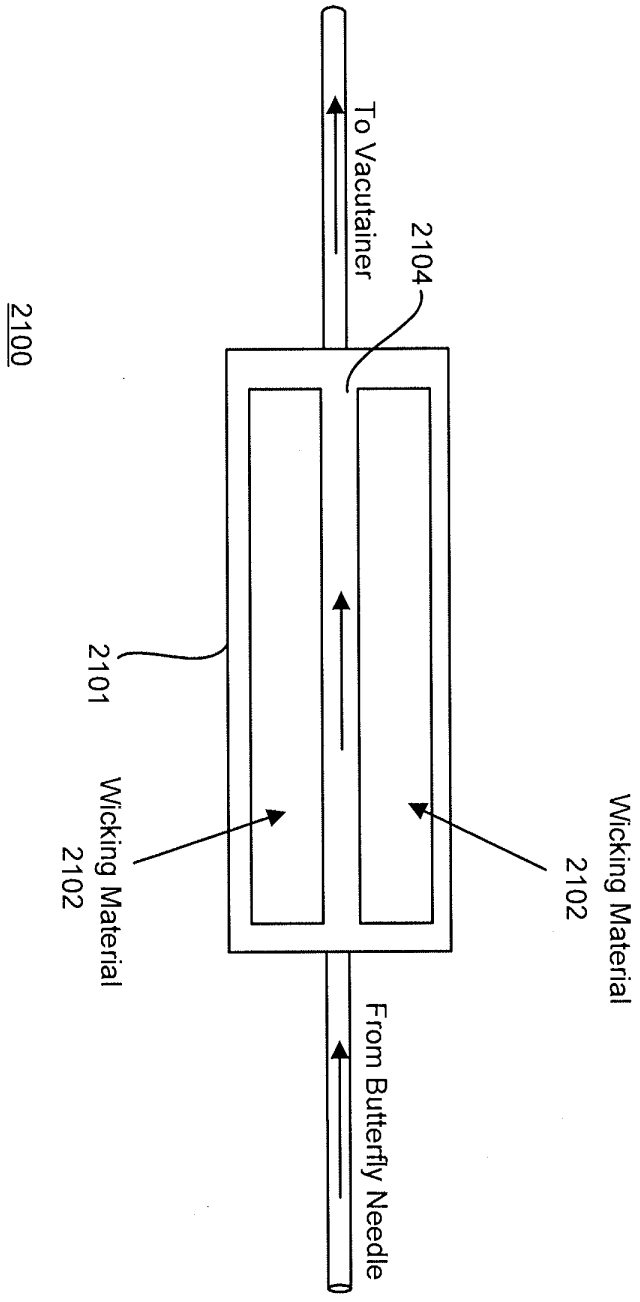

2100
To Vacutainer
2104
2101
Wicking Material
2102
Wicking Material
2102
From Butterfly Needle

FIG. 21

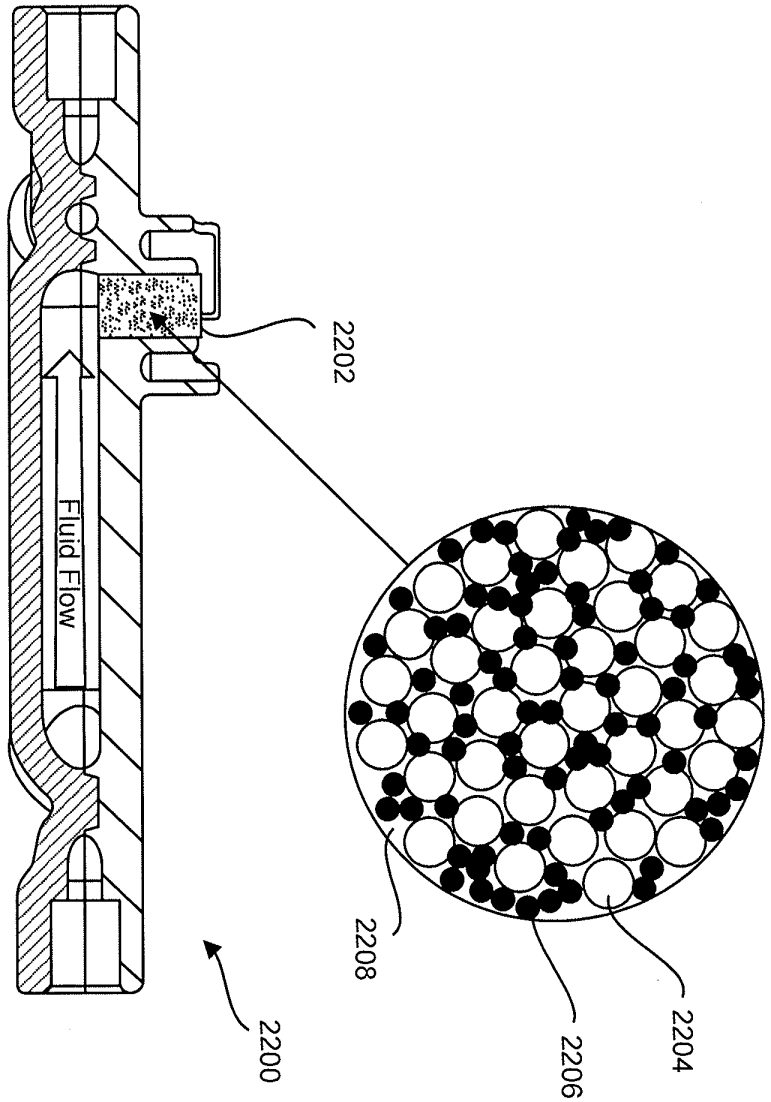


FIG. 22A

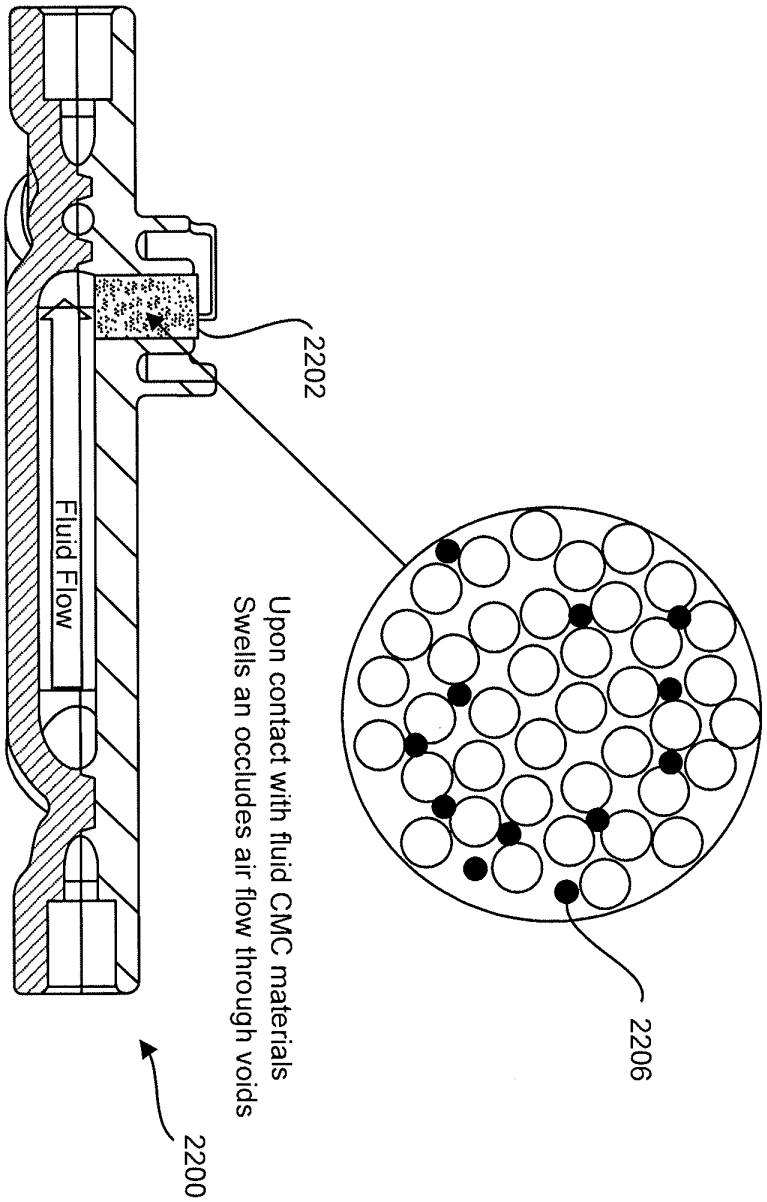

2202
Fluid Flow
Upon contact with fluid CMC materials
Swells an occludes air flow through voids
2206
2200

FIG. 22B

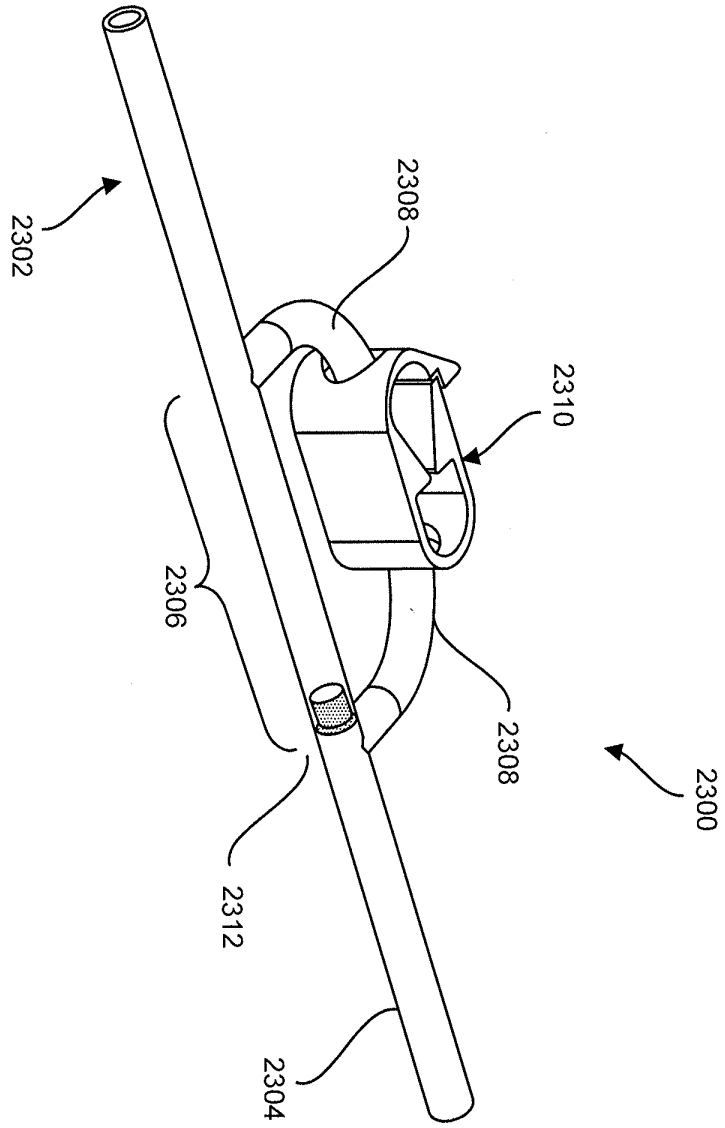


FIG. 23A

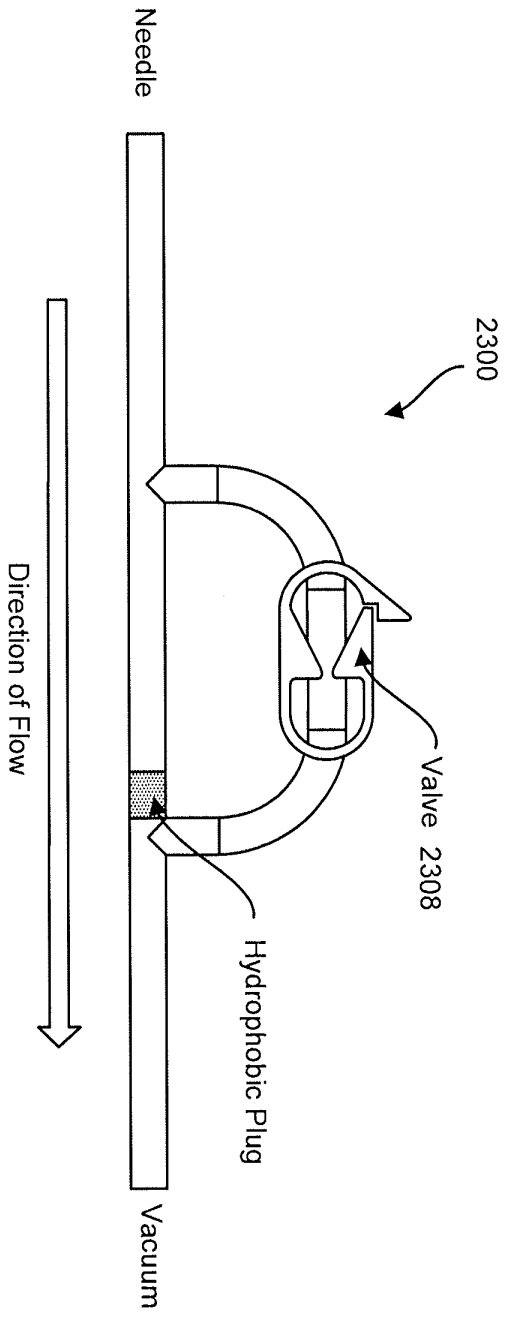

2300
Needle
Valve 2308
Hydrophobic Plug
Vacuum
Direction of Flow

FIG. 23B

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 #
18/783,088	**07/24/2024 05:41:08 PM Z ET**	**069366-0580418_KUR2C06US**

Title of Invention

BLOOD SAMPLE OPTIMIZATION DEVICE

Application Information

APPLICATION TYPE	Utility - Nonprovisional Application under 35 USC 111(a)	PATENT #	-
CONFIRMATION #	2051	FILED BY	Trent Tercenio
PATENT CENTER #	66504926	FILING DATE	-
CUSTOMER #	27500	FIRST NAMED INVENTOR	Bobby E. ROGERS
CORRESPONDENCE ADDRESS	-	AUTHORIZED BY	Benjamin Hudson

Documents

TOTAL DOCUMENTS: 5

DOCUMENT	PAGES	DESCRIPTION	SIZE (KB)
069366-0580418_KUR2C06US-ADS.pdf	9	Application Data Sheet	2175 KB
069366-0580418_KUR2C06US-Track-One-Request.pdf	2	Track One Request	122 KB
069366-0580418_KUR2C06US-Drawings.pdf	50	Drawings-only black and white line drawings	838 KB
069366-0580418_KUR2C06US-Declaration.pdf	3	Oath or Declaration filed	867 KB

069366-0580418_KUR2C06US-Specification-APP.TEXT.docx	37	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. Bookmarks were found and have been removed.

Digest

DOCUMENT	MESSAGE DIGEST(SHA-512)
069366-0580418_KUR2C06US-ADS.pdf	EB7A185D08332B83E31857CFD8DD8BDF21A5146589B470D7F9863B19E1CC56CB254AEC24C6F0C7D394A9F27319D77E3B271E81B9EC31642CCF3B6B3ED51A8937
069366-0580418_KUR2C06US-Track-One-Request.pdf	1D4DF2F208BFA9ED5976EBB17D7B287D37E7F50E52DC24B03180799A137BD1E0FA3354527D4A5D9A93B30CB8224D3085FEEE7857763141C7F5230B4E2130B9DC
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069366-0580418_KUR2C06US-Declaration.pdf	4AD43A0D0051FF165798AE089ABF7EA36C03DD6021A9A2E96BB9A2ADCB08BF21214575C900480B74B6CC265BAB55FAEC950B4240412C0489957978CC58A845DB
069366-0580418_KUR2C06US-Specification-APP.TEXT.docx	49BE87680CB906CC2BFE88D231D9D092B657340A630905E7993C956880A303F5E0B2E9DA7C18CC29C80237FD42F42CDDB5F9907B0F3BCAA7522664186C286748

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.

PTO/AIA/01 (08-12)
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DECLARATION (37 CFR 1.63) FOR UTILITY OR DESIGN APPLICATION USING AN APPLICATION DATA SHEET (37 CFR 1.76)

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

As the below named inventor, I hereby declare that:

This declaration is directed to:

☐ The attached application, or

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

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

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

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

WARNING:

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

LEGAL NAME OF INVENTOR

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

Signature: Bobby E. Rogers

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

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

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LEGAL NAME OF INVENTOR

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

Signature: _____

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

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

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

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As the below named inventor, I hereby declare that:

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

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LEGAL NAME OF INVENTOR

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

Signature: John C. Detloff

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

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

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DocCode - SCORE

Placeholder Sheet for Supplemental Content

Application Number: 18783088 Document Date: 07/24/2024

The presence of this form indicates that the following document type was received in electronic format on the date identified above. This document is stored separately from the typical case contents which are stored in image format.

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Form Revision Date: March 1, 2024

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

PTO/AIA/82A (07-13)
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TRANSMITTAL FOR POWER OF ATTORNEY TO ONE OR MORE REGISTERED PRACTITIONERS

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

Application Number	18/783,088
Filing Date	July 24, 2024
First Named Inventor	Bobby E. Rogers
Title	BLOOD SAMPLE OPTIMIZATION DEVICE
Art Unit	Not Yet Assigned
Examiner Name	Not Yet Assigned
Attorney Docket Number	069366-0580418_KUR2C06US

SIGNATURE of Applicant or Patent Practitioner

Signature	/Ben Hudson/	Date (Optional)	07-30-2024
Name	Benjamin F. Hudson	Registration Number	71,474
Title (if Applicant is a juristic entity)	Appointed Practitioner		
Applicant Name (if Applicant is a juristic entity)			

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

☑ *Total of 1 forms are submitted.

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

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

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Document Description: Power of Attorney

PTO/AIA/82B (07-13)
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POWER OF ATTORNEY BY APPLICANT

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

Application Number	Filing Date

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

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

OR

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

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

☑ The address associated with the above-mentioned Customer Number

OR

☐ The address associated with Customer Number:

OR

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

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

Kurin, Inc.

☐ Inventor or Joint Inventor (title not required below)

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

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

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

SIGNATURE of Applicant for Patent

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

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

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

☐ Total of forms are submitted.

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

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PATENT AND TRADEMARK OFFICE

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

ELECTRONIC ACKNOWLEDGEMENT RECEIPT

APPLICATION #	RECEIPT DATE / TIME	ATTORNEY DOCKET #
18/783,088	**07/30/2024 07:14:00 PM Z ET**	**069366-0580418_KUR2C06US**

Title of Invention

BLOOD SAMPLE OPTIMIZATION DEVICE

Application Information

APPLICATION TYPE	Utility - Nonprovisional Application under 35 USC 111(a)	PATENT #	-
CONFIRMATION #	2051	FILED BY	Trent Tercenio
PATENT CENTER #	66585459	FILING DATE	-
CUSTOMER #	27500	FIRST NAMED INVENTOR	Bobby E. ROGERS
CORRESPONDENCE ADDRESS	-	AUTHORIZED BY	Benjamin Hudson

Documents

TOTAL DOCUMENTS: 1

DOCUMENT	PAGES	DESCRIPTION	SIZE (KB)
069366-0580418_KUR2C06US-Power-of-Attorney.pdf	2	Power of Attorney	542 KB

Digest

DOCUMENT	MESSAGE DIGEST(SHA-512)
069366-0580418_KUR2C06US-Power-of-Attorney.pdf	A03253930E5154A4923F51BDFA54B2C4DE6932479D525DF04F051EC05126851962FC24B74F9D6E9C1AB9C1D08AA834C5E97A8FAEC128E86DCDEABE6C128BA28F

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.

PATENT ASSIGNMENT COVER SHEET

Electronic Version v1.1
Stylesheet Version v1.2

Assignment ID: PATI400239

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
Internal Address:	#257
City:	San Diego
State/Country:	CALIFORNIA
Postal Code:	92131

PROPERTY NUMBERS Total: 1

Property Type	Number
Application Number:	18783088

CORRESPONDENCE DATA

Fax Number: 7037707900

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: 7037707900
Email: Docket_ip@pillsburylaw.com
Correspondent Name: Trent Andrew Tercenio
Address Line 1: P.O. BOX 10500
Address Line 4: MCLEAN, VIRGINIA 22102

ATTORNEY DOCKET NUMBER:	069366-0580418_KUR2C06US
NAME OF SUBMITTER:	Trent Tercenio
SIGNATURE:	Trent Tercenio
DATE SIGNED:	07/31/2024
	This document serves as an Oath/Declaration (37 CFR 1.63).

Total Attachments: 3
source=069366-0580418_KUR2C06US Assignment#page1.tiff

source=069366-0580418_KUR2C06US Assignment#page2.tiff
source=069366-0580418_KUR2C06US Assignment#page3.tiff

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
18/783,088	07/24/2024		904	069366-0580418_KUR2C06US	26	2

CONFIRMATION NO. 2051

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

FILING RECEIPT

OC000000076174591

Date Mailed: 08/08/2024

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: The patent practitioners associated with Customer Number 27500

Domestic Priority data as claimed by applicant

This application is a CON of 18/494,622 10/25/2023
which 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 PAT 11,963,769
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: 08/06/2024

The country code and number of your priority application, to be used for filing abroad under the Paris Convention, is **US 18/783,088**

Projected Publication Date: 11/14/2024

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

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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).

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PATENT APPLICATION FEE DETERMINATION RECORD

Substitute for Form PTO-875

Application or Docket Number: 18/783,088

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))	26 minus 20 =	* 6	x 40 =	240	OR		
INDEPENDENT CLAIMS (37 CFR 1.16(h))	2 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	904		TOTAL	

APPLICATION AS AMENDED - PART II

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

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

* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.

** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".

*** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3".

The "Highest Number Previously Paid For" (Total or Independent) is the highest found in the appropriate box in column 1.

United States Patent and Trademark Office

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

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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).

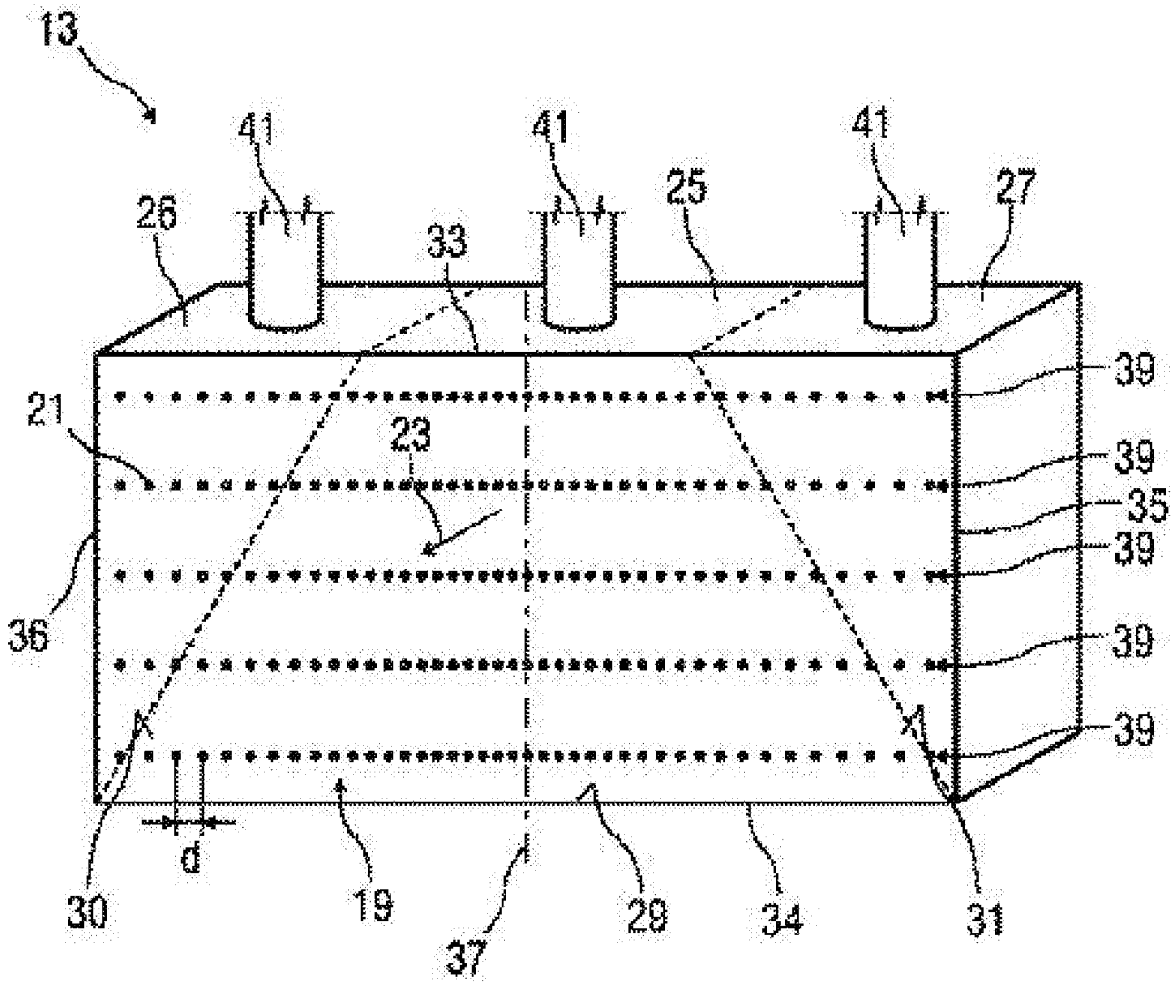


FIG 2

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 ful l jet nozzle to which the full jet nozzle is removably secured. Advantageously, this embodimen t 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 e xcess coolant to the rolled stock and/or to the roll nip where the rolled stock is guided betwee n two rolls to reduce friction between the rolled stock and the rolls. It is advantageous to be a ble 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 rod s. In this case, the advantages of using full-jet nozzles already mentioned above are also in ef fect here. That is, by using a full-jet nozzle, the distance between the spray bar and the roll b ecomes less critical over a wider range and therefore no longer needs to be adapted to the rol l diameter. Furthermore, the present invention is also particularly suitable as a retrofit to exist ing 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 accordin g to the invention, the two cooling devices being arranged on opposite sides of the rolls. The a dvantages of the rolling stand according to the invention result from the advantages of the co oling 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 ro d;

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]

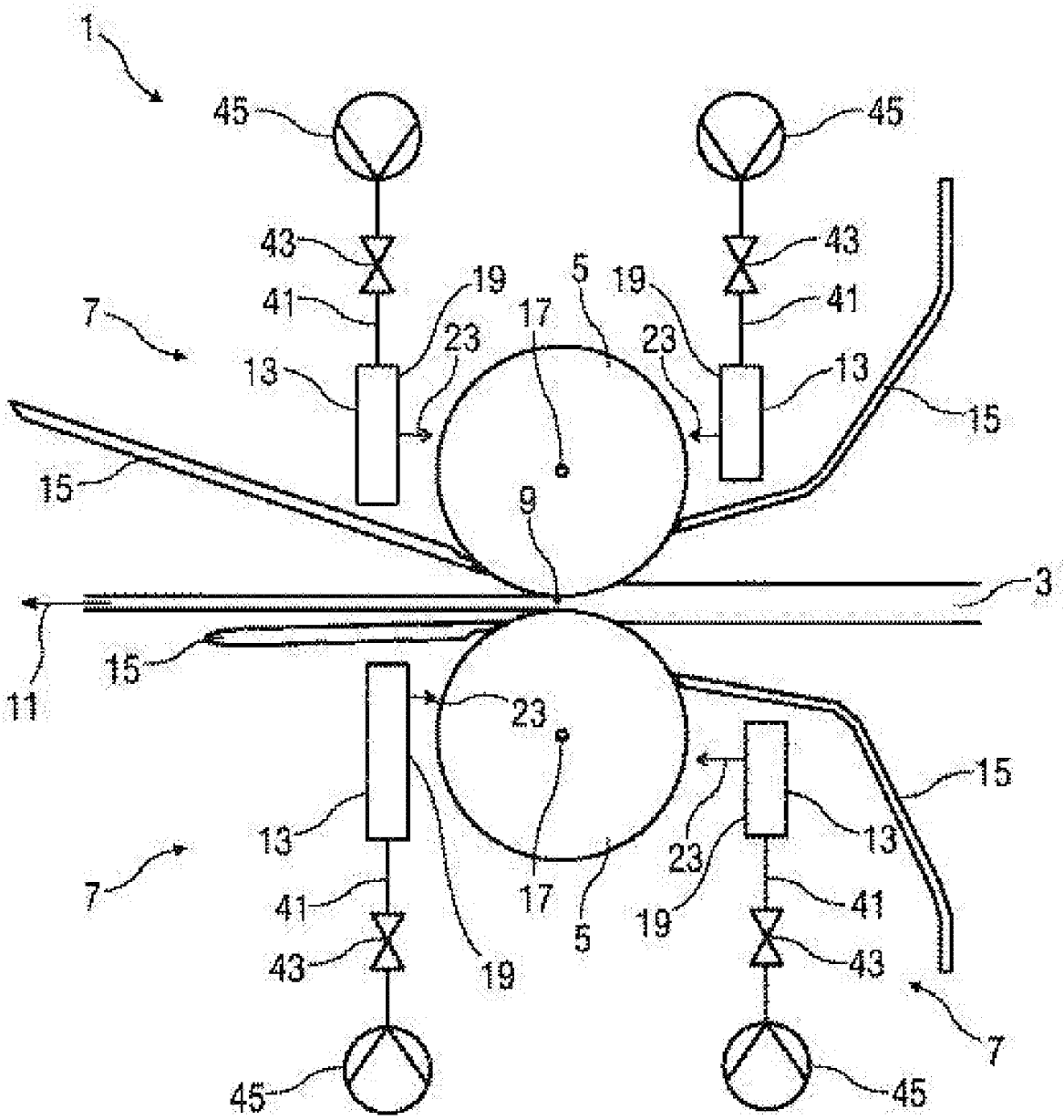


FIG 1

[Figure 2]

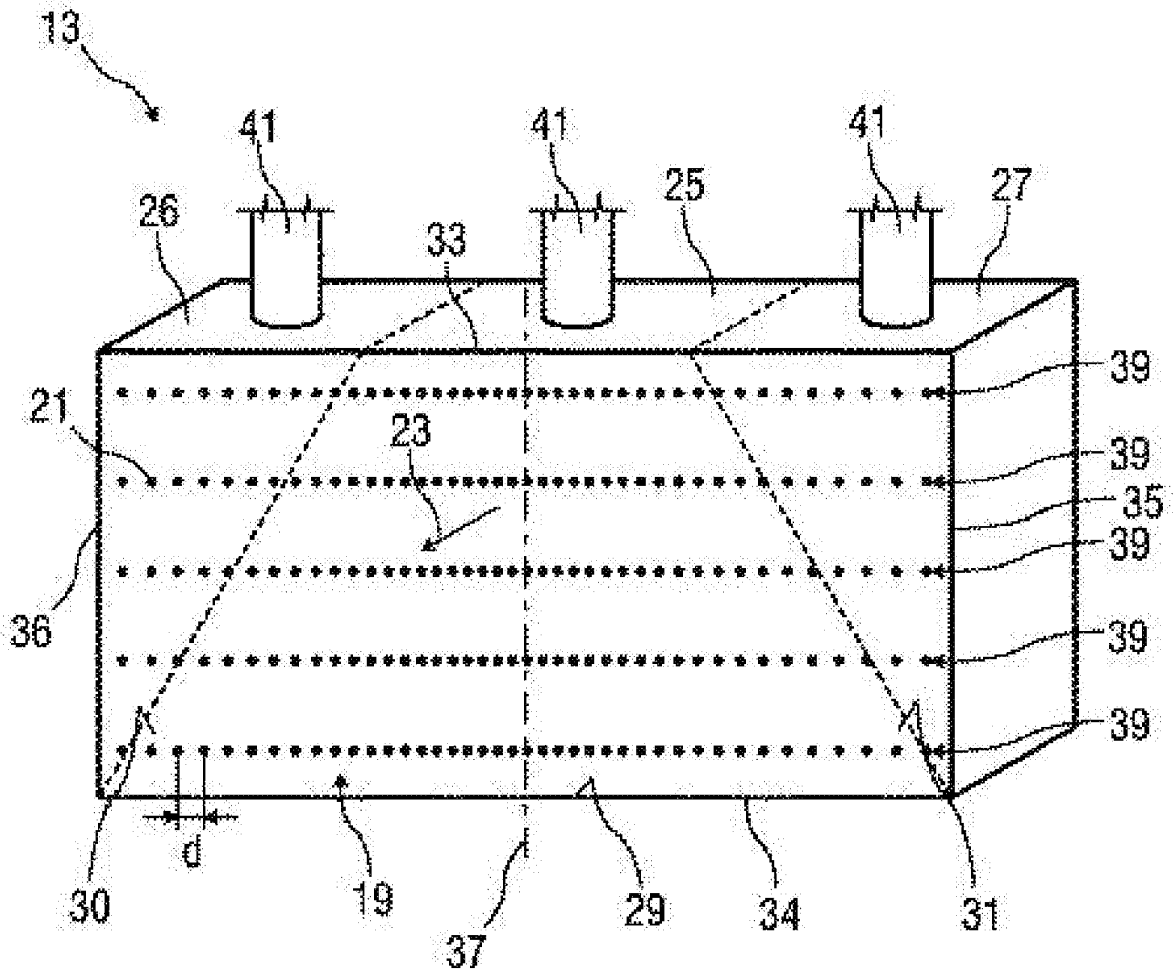


FIG 2

[Figure 3]

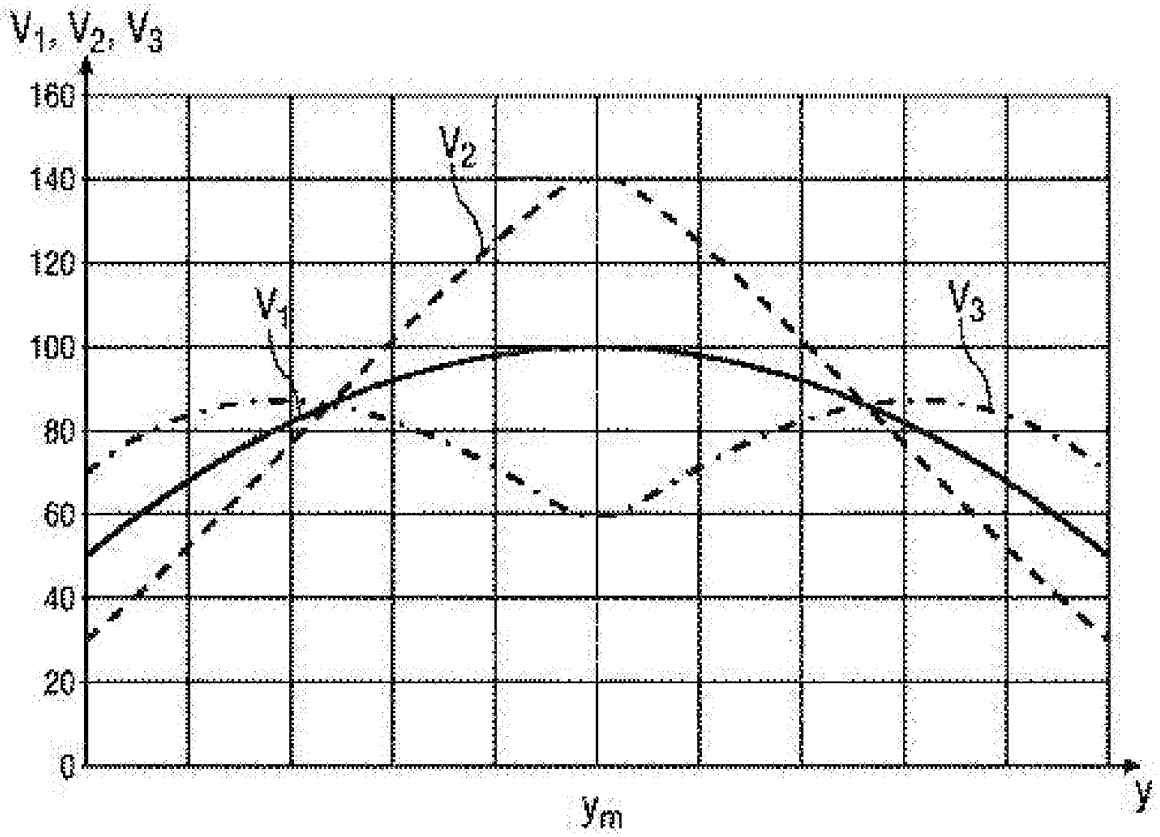


FIG 3

[Figure 4]

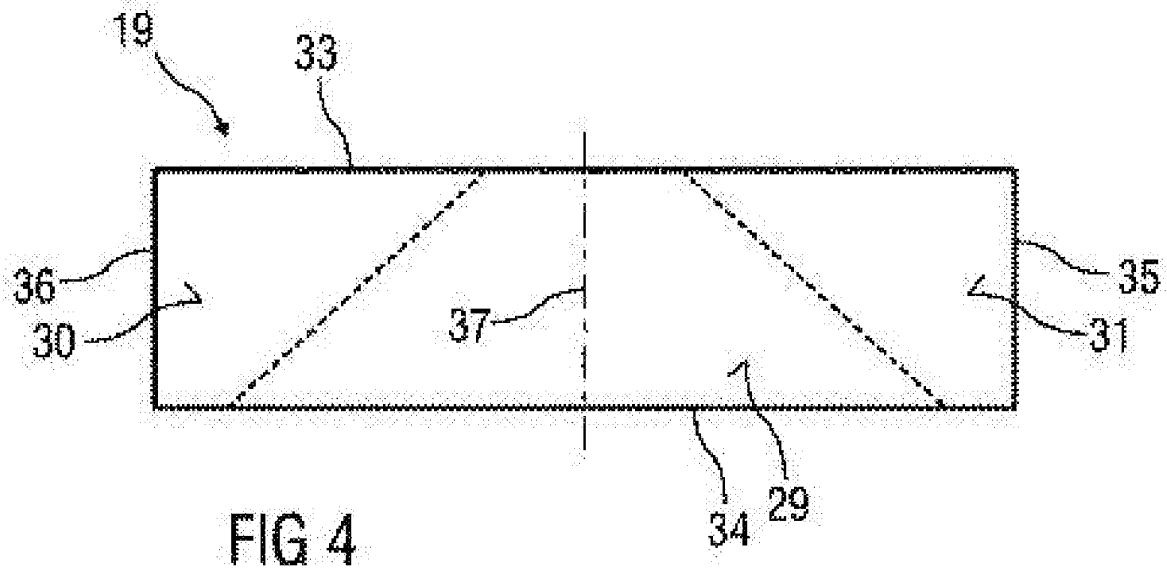


FIG 4

[Figure 5]

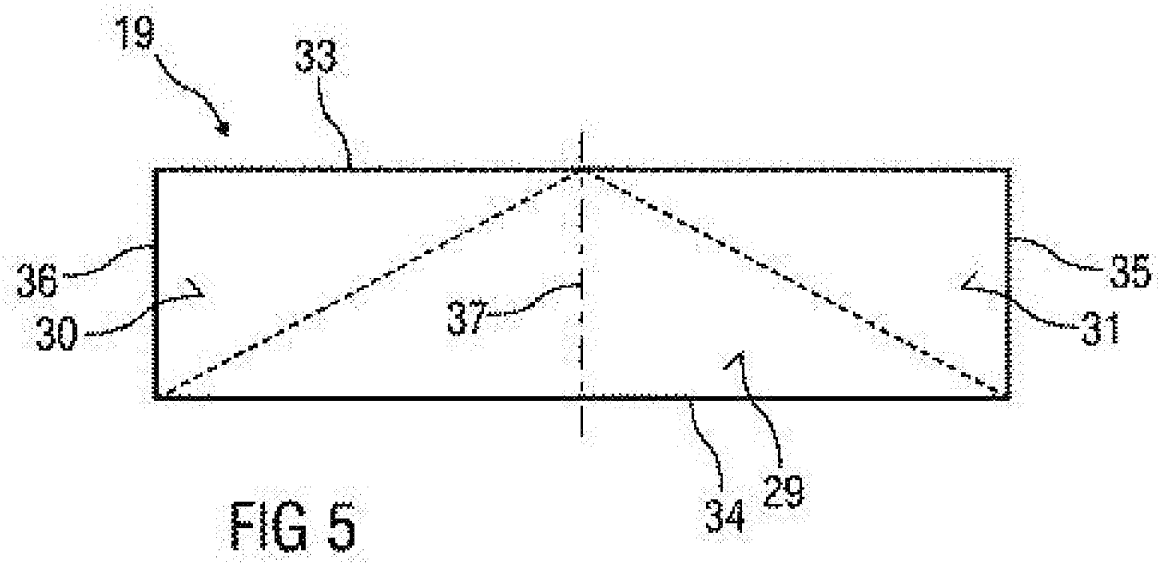


FIG 5

[Fig. 6]

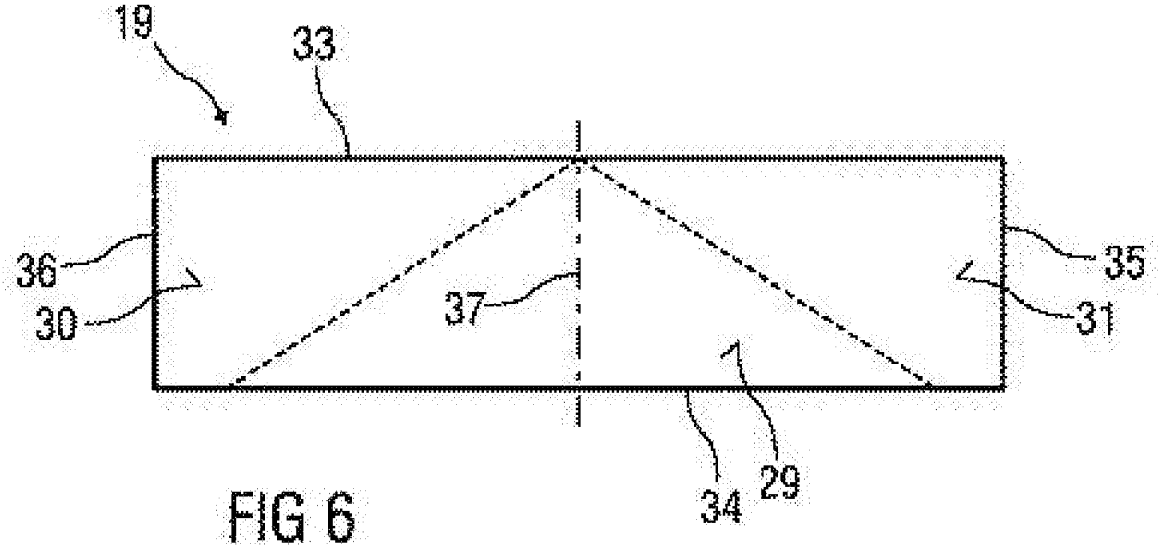


FIG 6

[Fig. 7]

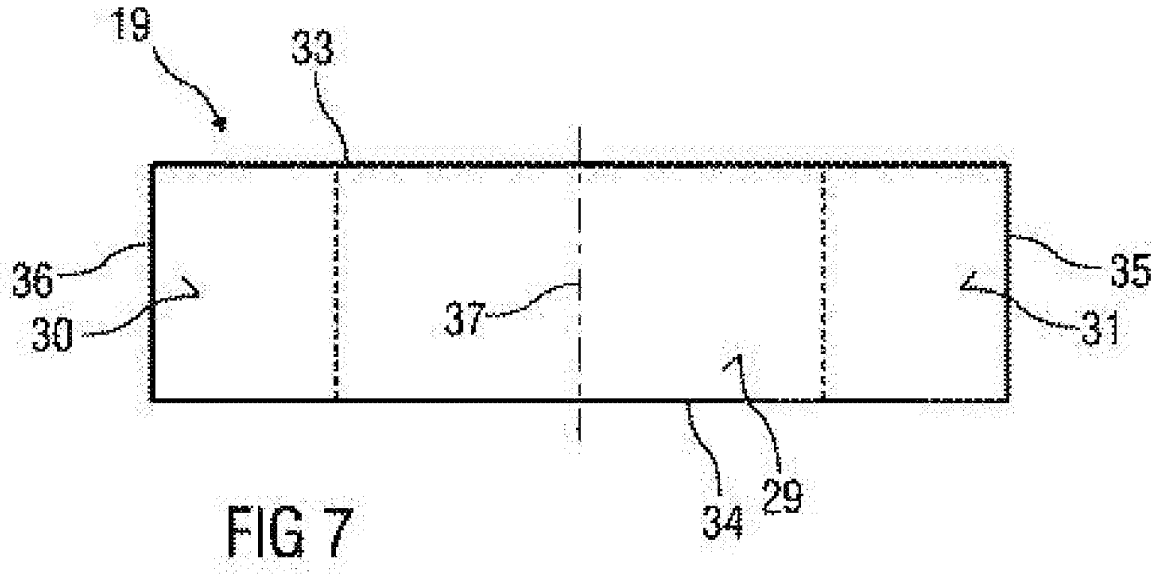


FIG 7

[Fig. 8]

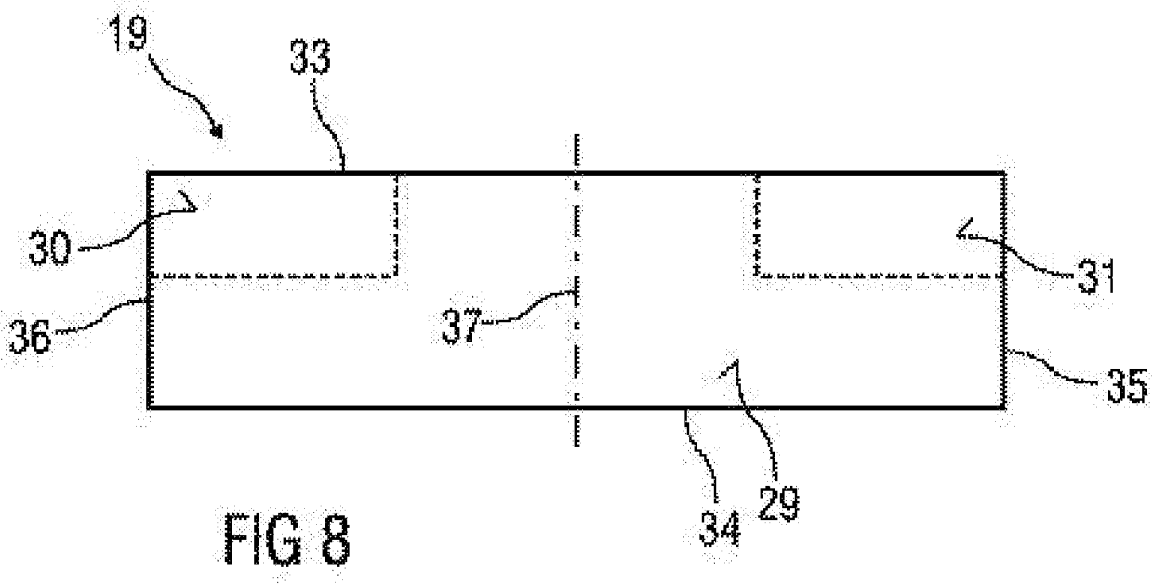


FIG 8

[Fig. 9]

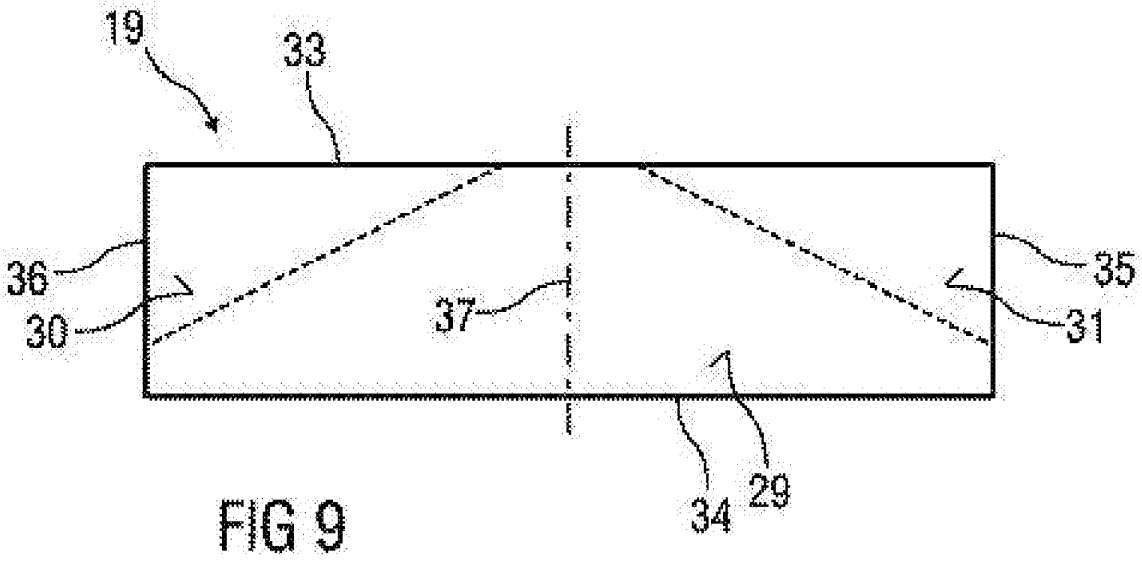


FIG 9

[Fig. 10]

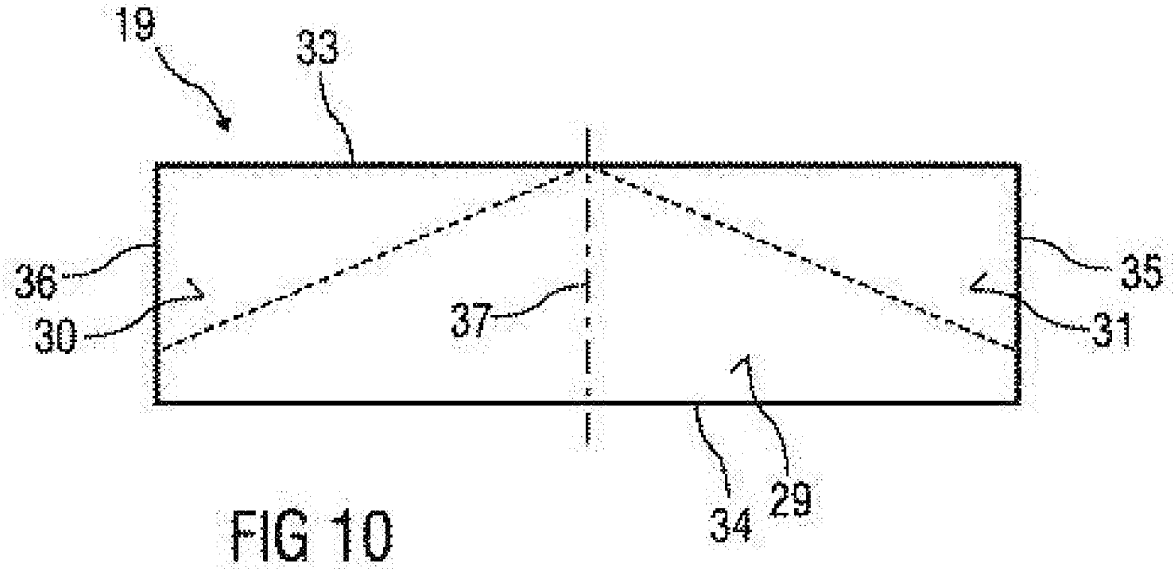


FIG 10

[Fig. 11]

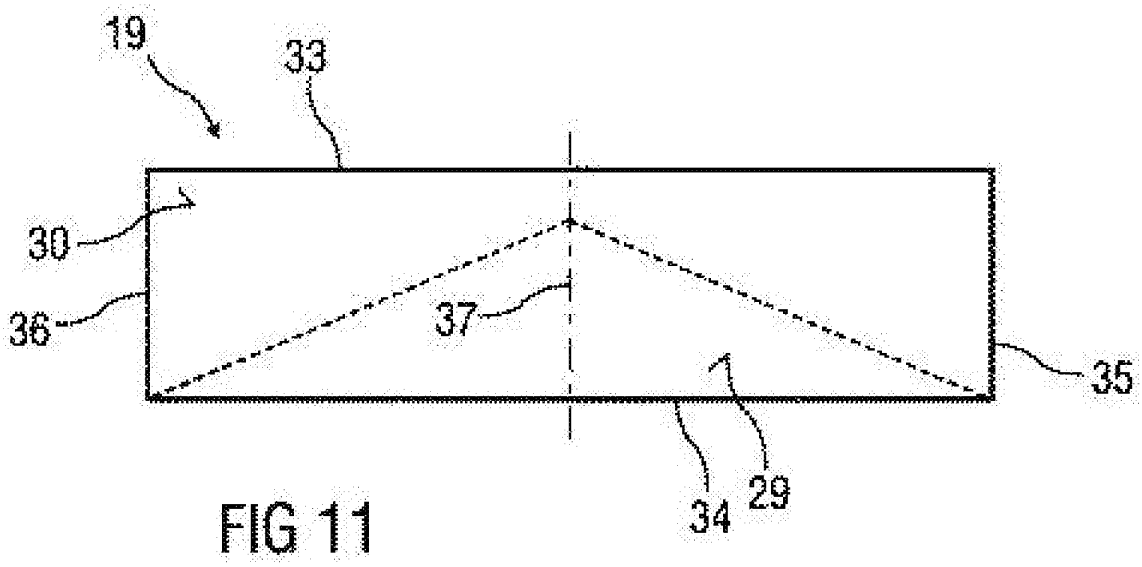


FIG 11

[Fig. 12]

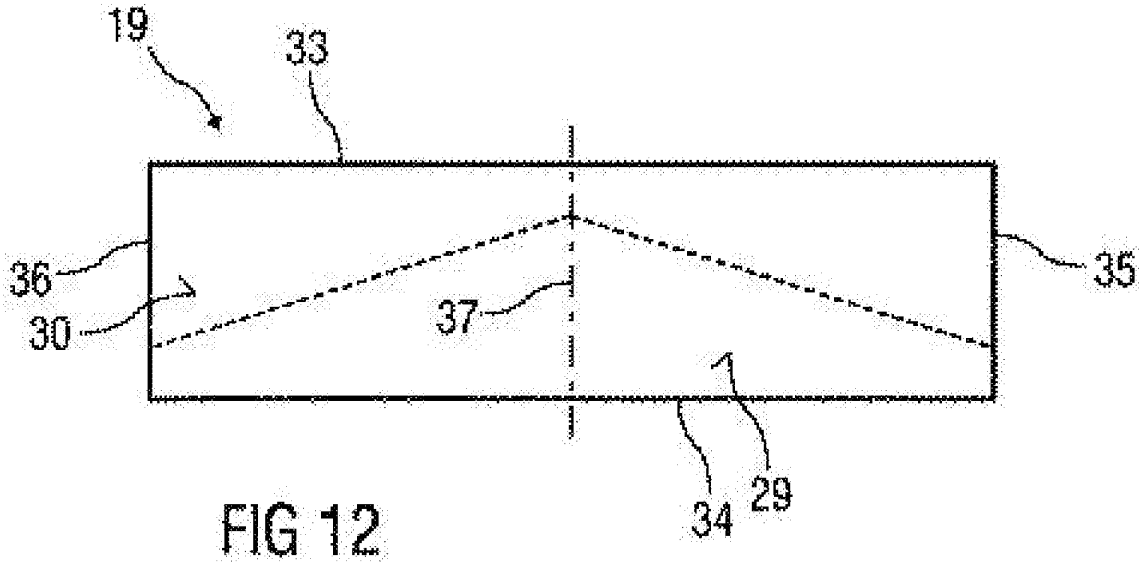


FIG 12

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

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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.

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
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		CN 101702888 A	05-05-2010
		EP 2014379 A1	14-01-2009
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		JP 5380438 B2	08-01-2014
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		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 Rechercheribericht 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.

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

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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
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drawing open

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

Magnify and Rotate

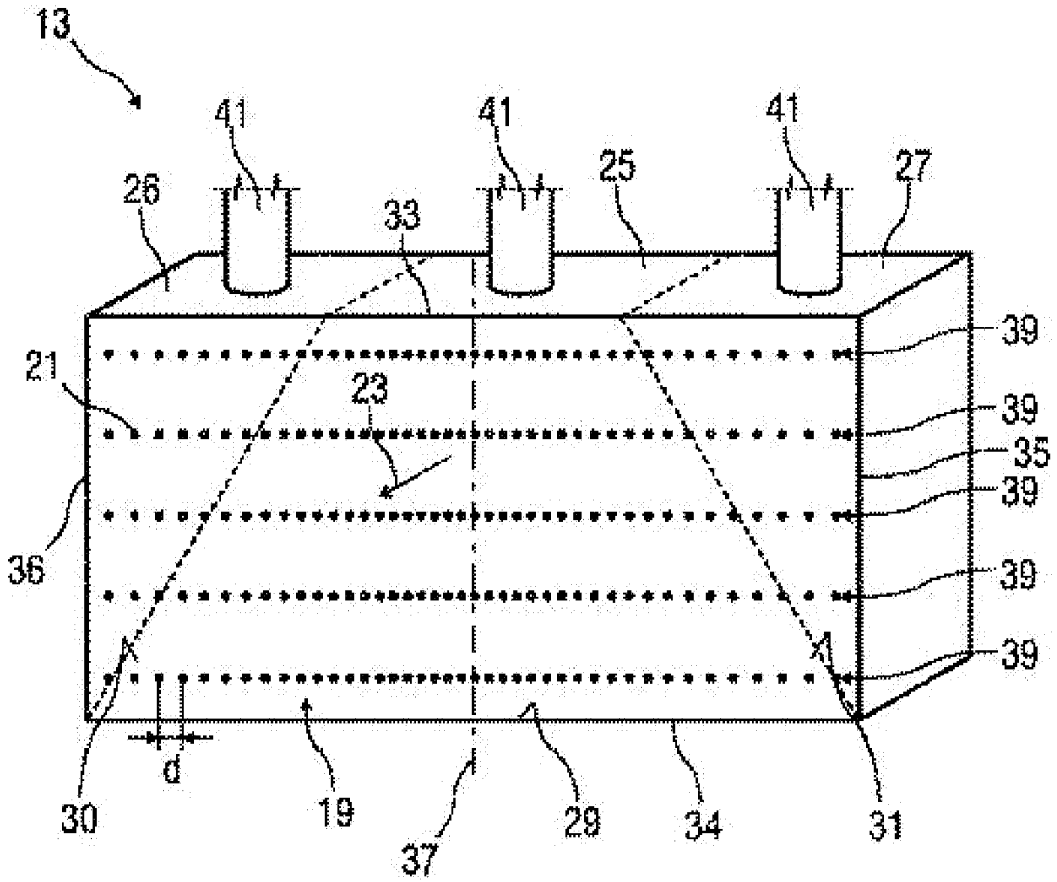


FIG 2

Representative drawing

1 / 1 display

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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).



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最終頁に続く

(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。

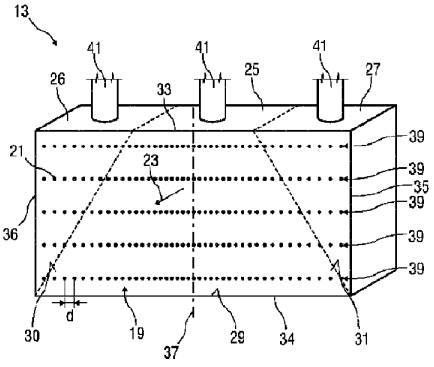


FIG 2

【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）から冷却剤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２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】

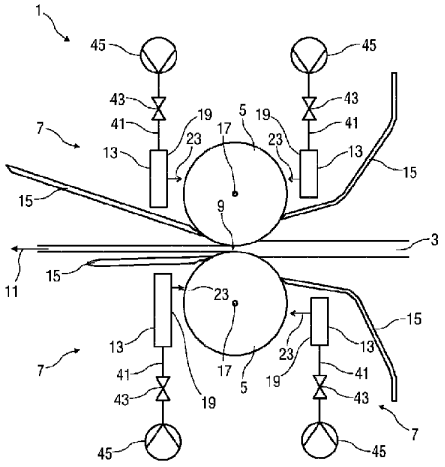


FIG 1

【図２】

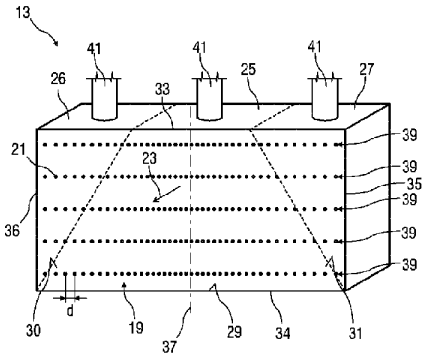


FIG 2

【図３】

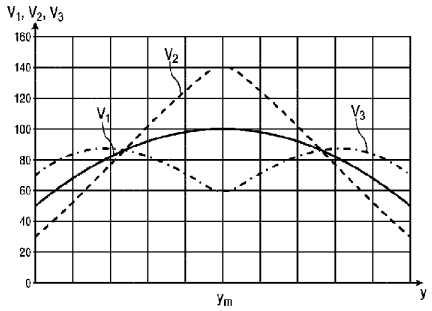


FIG 3

【図４】

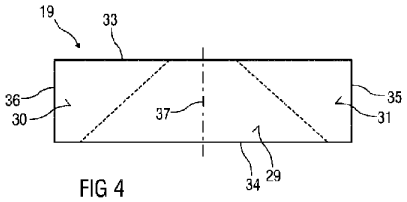


FIG 4

【図５】

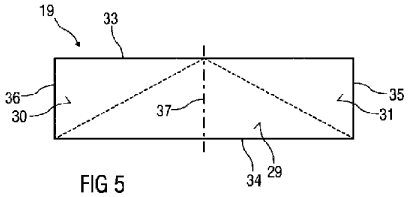


FIG 5

【図６】

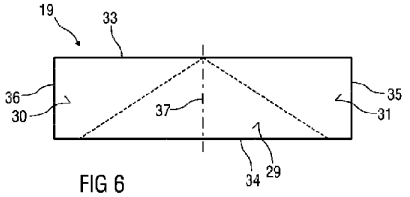


FIG 6

【図７】

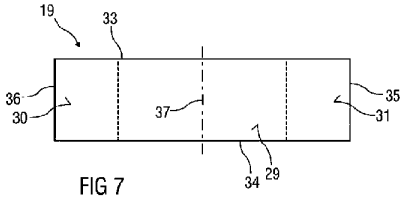


FIG 7

【図８】

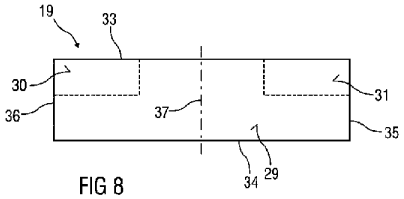


FIG 8

【図９】

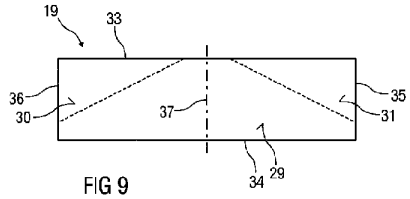


FIG 9

【図１０】

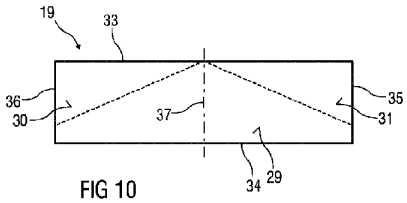


FIG 10

【図１１】

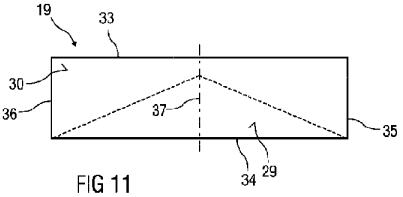


FIG 11

【図１２】

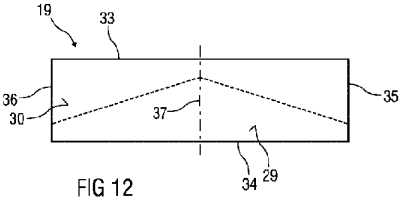


FIG 12

【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.

---

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	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 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

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

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BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE AND METHOD

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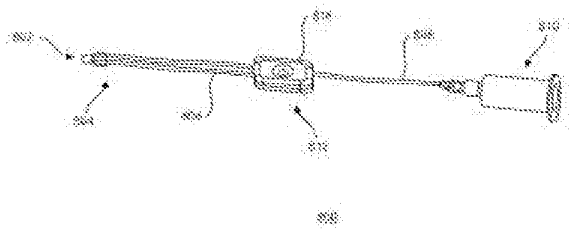
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Blood sample optimization systems and methods are described that reduce or eliminate contaminates in collected blood samples, which in turn reduces or eliminates false positive readings in blood cultures or other testing of collected blood samples.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

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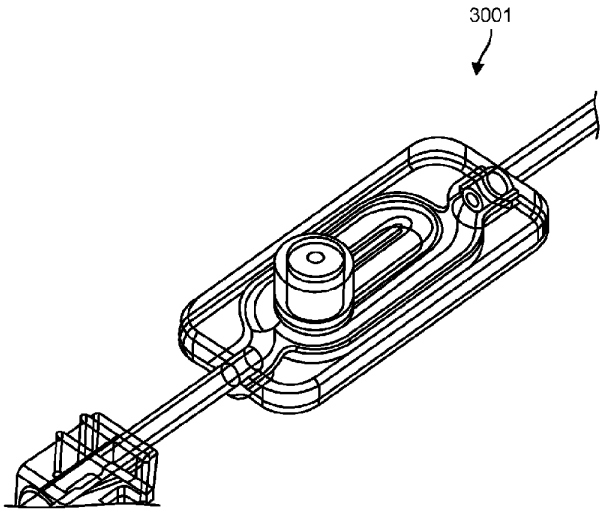


FIG. 30B

(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.

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BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE AND METHOD

BACKGROUND

[0001] Bacteraemia is the presence of microorganisms in the blood. Sepsis, on the other hand, is bacteraemia in the presence of clinical symptoms and signs such as fever, tachycardia, tachypnea and hypotension. Bacteraemia and sepsis are associated with a high mortality and an increased incidence and duration of hospital stay and associated costs. Many bacteraemias, sepsis, fungaemias and other pathogens actually occur within a hospital or other healthcare settings with catheters and venipunctures being a source of contamination as potential carriers of these pathogens.

[0002] Blood cultures are the standard test used to detect microbial pathogens related to bacteraemia and sepsis in a patient's blood. The term blood culture refers to a single venipuncture, either from a peripheral site or central or arterial line, with the blood inoculated into one or more blood culture bottles or containers. One bottle is considered a blood culture where two or more are considered a set. Multiple sets may be obtained from multiple venipunctures and are associated with different sites on the patient.

[0003] These methods allow for microbial identification and susceptibility testing to be performed, which is a critical component to managing sepsis, however the lack of rapid results and decreased sensitivity for fastidious pathogens has led to the development of improved systems and adjunctive molecular or proteomic testing.

[0004] Collection of blood samples for conducting blood cultures is a critical component of modern patient care and can either positively affect the patient outcome by providing an accurate diagnosis, or can adversely affect the outcome by prolonging unnecessary antimicrobial therapy, the length of hospital stays, and increasing costs.

[0005] One outcome of collection of blood cultures is contamination. Blood culture contamination can lead to a false positive culture result and/or significant increase in healthcare related costs. Sources of blood culture contamination include improper skin antisepsis, improper collection tube disinfection, and contamination of the initial blood draw which may then skew results.

[0006] Blood culture collection kits generally consist of a "butterfly" set, infusion set, or other type of venipuncture device as offered by companies like BD, Smiths, B. Braun and others, and aerobic and anaerobic blood culture bottles. Various different bottles are also available depending on the test requirements. These bottles are specifically designed to optimize recovery of both aerobic and anaerobic organisms. In conventional kits, a bottle used is known generally as a "Vacutainer," which is a blood collection tube formed of a sterile glass or plastic tube with a closure that is evacuated to create a vacuum inside the tube to facilitate the draw of a predetermined volume of liquid such as blood.

[0007] False positive blood cultures are typically a result of poor sampling techniques. They cause the use of antibiotics when not needed, increasing hospital costs and patient anxiety. Blood cultures are drawn from a needlestick into the skin, and then a Vacutainer is attached to capture a sample of blood. Contamination may occur from improper or incomplete disinfection of the skin area in and around the puncture site. It may also occur from the coring of the skin by the needle during insertion, with the cored skin cells and any associated contamination being pulled into the sample.

[0008] Blood flow through a hypodermic needle is laminar, and as such, a velocity gradient can be developed over the flow tube as a pressure drop is applied to the hypodermic needle. Either forceful aspiration of blood, or using a very small hypodermic needle, can cause lysis and a release of potassium from the red blood cells, thereby rendering the blood samples abnormal.

[0009] In other instances, some patients have delicate veins that can collapse under a pressure drop or vacuum, particularly as applied by a syringe's plunger that is drawn too quickly for the patient's condition. Since such condition is impossible to know beforehand, such vein collapses are a risk and very difficult to control.

[0010] Various strategies have been implemented to decrease blood culture contamination rates, e.g. training staff with regard to aseptic collection technique, feedback with regard to contamination rates and implementation of blood culture collection kits. Although skin antisepsis can reduce the burden of contamination, 20% or more of skin organisms are located deep within the dermis and are unaffected by

antisepsis. Changing needles before bottle inoculation is not advisable as it increases the risk to acquire needle stick injuries without decreasing contamination rates.

[0011] Some conventional systems and techniques for reducing blood culture contamination include discarding the initial aliquot of blood taken from central venous catheters, venipunctures, and other vascular access systems. However, these systems require the user to mechanically manipulate an intravascular device, or require a complex series of steps that are difficult to ensure being followed.

SUMMARY

[0012] This document presents systems and methods for reducing blood culture contamination, lysing of cells, and vein collapse. In some implementations, a system and method can eliminate user variability in disinfection, and also eliminate the risk of skin cells getting into the blood culture sample. The systems and methods disclosed herein do not require a change in existing clinical processes, other than to potentially indicate when a vacutainer or other blood collection device (i.e., syringe) should be attached for drawing contaminant-free blood samples.

[0013] In some implementations of the systems and methods disclosed herein the withdrawal of blood is accomplished passively by use of the patient's own blood pressure, thereby reducing the risk of vein collapse and eliminating any additional user steps over current practice. The systems and methods can be applied to accommodate short-path direct stick or butterfly venipuncture systems. They can also be used with samples drawn through a catheter.

[0014] In one aspect, a blood sequestration device is presented. The blood sequestration device includes an inlet port and an outlet port. The blood sequestration device further includes a sequestration chamber connected with the inlet port, the sequestration chamber having a vent comprising an air permeable blood barrier. The blood sequestration device further includes a sampling channel having a proximal end connected with the inlet port and a distal end connected with the outlet port.

[0015] In another aspect, a blood sequestration device connected with a blood sampling pathway is described. The blood sampling pathway has a patient needle and a sample collection device. The blood sequestration device includes an inlet port connected

with the patient needle, and a sequestration chamber connected with the inlet port, the sequestration chamber having a vent comprising an air permeable blood barrier. The blood sequestration device further includes a sampling channel having a proximal end connected with the inlet port, and an outlet port connected with a distal end of the sampling channel and with the sample collection device.

[0016] In yet another aspect, a blood sequestration device connected with a blood sampling system is described. The blood sampling system includes a patient needle for accessing a blood sample from a patient, and a sample needle that is sealed and adapted for receiving an evacuated blood collection tube. The blood sequestration device includes an inlet port connected with the patient needle to receive the blood sample from the patient. The blood sequestration device further includes a sequestration chamber connected with the inlet port and having a vent comprising an air permeable blood barrier, the sequestration chamber for receiving and sequestering a first portion of the blood sample prior to the sample needle being unsealed by the evacuated blood collection tube. The blood sequestration device further includes a sampling channel having a proximal end connected with the inlet port, the sampling channel for conveying a subsequent portion of the blood sample once the sample needle is unsealed by the evacuated blood collection tube. The blood sequestration device further includes an outlet port connected with a distal end of the sampling channel for conveying the subsequent portion of the blood sample to the sample needle.

[0017] In yet another aspect, a blood sample optimization system is disclosed and described. The blood sample optimization system includes a blood sampling system for accessing and acquiring one or more samples of a patient's blood, and a blood sequestration device for receiving and sequestering a first portion of the one or more samples of the patient's blood which might be contaminated by a venipuncture process and which could result in a false positive identification of a pathogen in the patient's blood.

[0018] The blood sampling system includes a patient needle configured for a venipuncture of a patient to access a sample of blood of a patient, a blood sampling pathway connected with the patient needle for conveying the sample of blood, and a sample needle configured for receiving an evacuated blood collection container to collect and contain a subsequent portion of the sample of blood.

[0019] In yet another aspect, a blood sequestration device is disclosed and described. In some implementations, the blood sequestration device can include an inlet port, an outlet port connected with the inlet port, and a sequestration chamber connected with the inlet port. The sequestration chamber can have a vent comprising an air permeable blood barrier.

[0020] The blood sequestration device, in one aspect can include an inlet port, an outlet port, a sequestration chamber connected with the inlet port via a junction, the sequestration chamber having a vent that includes an air permeable blood barrier, the vent being defined by an outer wall that at least partially circumscribes the air permeable blood barrier and includes one or more air vents, the vent further includes a cap that at least partially covers the wall and a one-way seal abutting the air permeable blood barrier that inhibits air from entering the sequestration chamber, and a sampling channel having a proximal end connected with the inlet port via the junction, and a distal end connected with the outlet port. In certain related aspects, the sequestration chamber, the sampling channel and the junction are sized and configured such that a first portion of blood flows into the sequestration chamber toward the air permeable blood barrier for sequestration therein, and a second portion of blood bypasses the sequestration chamber and the first portion of blood sequestered therein and is directed into the sampling channel toward the outlet port.

[0021] In another aspect, the sampling channel and the junction is sized and configured such that a first portion of blood flows into and fills the sequestration chamber to displace air therein through the vent, and such that a second portion of blood bypasses the sequestration chamber and the first portion of blood sequestered therein and is directed into the sampling channel toward the outlet port.

[0022] The blood sequestration and sampling system sequestration device, in certain aspects can include a blood sampling pathway having a patient needle on a proximal end and a sample collection device on a distal end; and a blood sequestration device attached on the blood sampling pathway between the proximal end and distal end of the blood sampling pathway. The blood sequestration device in one aspect can include an inlet port coupled with the blood sampling pathway toward the patient needle, an outlet port coupled with the blood sampling pathway toward the sample collection device, a sequestration chamber connected with the inlet port via a junction, which chamber has a

vent that includes an air permeable blood barrier, the vent being defined by an outer wall that at least partially circumscribes the air permeable blood barrier and includes one or more air vents, the vent further including a cap that at least partially covers the wall and a one-way seal abutting the air permeable blood barrier that inhibits air from entering the sequestration chamber; and a sampling channel having a proximal end connected with the inlet port via the junction, and a distal end connected with the outlet port. In a certain related aspect, the sequestration chamber, the sampling channel and the junction can be sized and configured such that a first portion of blood flows into the sequestration chamber toward the air permeable blood barrier for sequestration therein, and a second portion of blood bypasses the sequestration chamber and the first portion of blood sequestered therein and is directed into the sampling channel toward the outlet port.

[0023] The blood sequestration device is connected along the blood sampling pathway between the patient needle and the sample needle, and includes an inlet port for receiving the sample of blood. The blood sequestration device further includes a sequestration chamber connected with the inlet port for receiving a first amount of the sample of blood, the sequestration chamber having a vent comprising an air permeable blood barrier for sequestering at least a first portion of the first amount of the sample of blood. The blood sequestration device may further include a sampling channel having a proximal end connected with the inlet port, the sampling channel conveying a subsequent amount of the sample of blood to the evacuated blood collection container upon the sequestration chamber sequestering at least the first portion of the first amount of the sample of blood. The blood sequestration device further includes an outlet port connected with a distal end of the sampling channel, the outlet port for outputting the subsequent amount of the sample of blood.

[0024] The details of one or more embodiments are set forth in the accompanying drawings and the description below. Other features and advantages will be apparent from the description and drawings, and from the claims.

BRIEF DESCRIPTION OF THE DRAWINGS

[0025] These and other aspects will now be described in detail with reference to the following drawings.

[0026] FIG. 1 illustrates a blood sample optimization system.

[0027] FIG. 2 illustrates a blood sample optimization system in accordance with an alternative implementation.

[0028] FIG. 3 illustrates a blood sample optimization system in accordance with another alternative implementation.

[0029] FIG. 4 illustrates a blood sample optimization system in accordance with another alternative implementation.

[0030] FIG. 5 illustrates a blood sample optimization system in accordance with another alternative implementation.

[0031] FIG. 6 illustrates a blood sample optimization system in accordance with an alternative implementation.

[0032] FIG. 7 is a flowchart of a method for optimizing a quality of a blood culture.

[0033] FIGS. 8A – 8E illustrate a blood sequestration system for non-contaminated blood sampling, in accordance with some implementations.

[0034] FIG. 9 illustrates a pathway splitter for use in a blood sequestrations system.

[0035] FIGS. 10A – 10D illustrate a blood sequestration system for non-contaminated blood sampling, in accordance with alternative implementations.

[0036] FIGS. 11A – 11E illustrate a blood sequestration system for non-contaminated blood sampling, in accordance with other alternative implementations.

[0037] FIGS. 12A-12D illustrate a blood sample optimization system including a blood sequestration device in accordance with yet other alternative implementations.

[0038] FIGS. 13A-13D illustrate a blood sample optimization system 1300 in accordance with yet another alternative implementations.

[0039] FIGS. 14A-14E illustrate yet another implementation of a blood sampling system to sequester contaminates of an initial aliquot or sample to reduce false positives in blood cultures or tests performed on a patient's blood sample.

[0040] FIGS. 15A-15G illustrate a blood sequestration device and method of using the same, in accordance with yet another implementation.

[0041] FIGS. 16A-16D illustrate a blood sequestration device in accordance with yet another implementation.

[0042] FIGS. 17A – 17E illustrate a bottom member of a housing for a blood sequestration device.

[0043] FIGS. 18A – 18F illustrate a top member of a housing for a blood sequestration device.

[0044] FIGS. 19A and 19B illustrate a blood sequestration device having a top member mated with a bottom member.

[0045] FIG. 20 shows a blood sample optimization system including a blood sequestration device.

[0046] FIG. 21 illustrates a non-vented blood sequestration device using a wicking material chamber.

[0047] FIGS. 22A and 22B illustrate a material makeup of a filter for sequestering blood in a sequestration chamber of a blood sequestration device.

[0048] FIGS. 23A – 23E illustrate another implementation of a blood sequestration device that uses a vacuum force from a blood collection device.

[0049] FIGS. 24A – 24D illustrate another implementation of a blood optimization system and blood sequestration device.

[0050] FIGS. 25A – 25D illustrate another implementation of a blood optimization system and blood sequestration device.

[0051] FIGS. 26A – 26E illustrate another implementation of a blood optimization system and blood sequestration device.

[0052] FIGS. 27A – 27D illustrate another implementation of a blood optimization system and blood sequestration device.

[0053] FIGS. 28A – 28F illustrate another implementation of a blood optimization system and blood sequestration device.

[0054] FIGS. 29A – 29C illustrate another implementation of a blood optimization system and blood sequestration device.

[0055] FIGS. 30A – 30G illustrate another implementation of a blood optimization system and blood sequestration device.

[0056] Like reference symbols in the various drawings indicate like elements.

DETAILED DESCRIPTION

[0057] This document describes blood sample optimization systems and methods for reducing or eliminating contaminates in collected blood samples, which in turn reduces or eliminates false positive readings in blood cultures or other testing of collected blood samples. In some implementations, a blood sample optimization system includes a patient needle for vascular access to a patient's bloodstream, a sample needle for providing a blood sample to a blood collection container, such as an evacuated blood collection container or tube like a Vacutainer™ or the like, or other sampling device, and a blood sequestration device located between the patient needle and the sample needle. The blood sequestration device includes a sequestration chamber for sequestering an initial, potentially contaminated aliquot of blood, and may further include a sampling channel that bypasses the sequestration chamber to convey likely uncontaminated blood between the patient needle and the sample needle after the initial aliquot of blood is sequestered in the sequestration chamber.

[0058] FIG. 1 illustrates a blood sample optimization system in accordance with some implementations. The system includes a patient needle 1 to puncture the skin of a patient to access the patient's vein and blood therein. The system further includes a sample needle (i.e., a resealably closed needle for use with Vacutainers™ or the like) 5, which may be contained within and initially sealed by a resealable boot 10, a Luer activated valve, or another collection interface or device. The resealable boot 10 can be

pushed aside or around the sample needle 5 by application of a Vacutainer™ bottle (not shown) for drawing the patient's blood. The system can further include a low volume chamber 30 that leads to the sample needle 5, but also includes an orifice or one or more channels 45 that lead to a sequestration chamber 55 formed by a housing 50.

[0059] The sequestration chamber 55 is a chamber, channel, pathway, lock, or other structure for receiving and holding a first aliquot of the patient's blood, which may be in a predetermined or measured amount, depending on a volume of the sequestration chamber 55. The first draw of blood typically contains or is more susceptible to containing organisms that cause bacteraemia and sepsis or other pathogens than subsequent blood draws. The sequestration chamber 55 can be a vessel encased in a solid housing, formed in or defined by the housing itself, or can be implemented as tubing or a lumen. The sequestration chamber 55, regardless how formed and implemented, may have a predetermined volume. In some implementations, the predetermined volume may be based on a volume of the patient needle, i.e. ranging from less than the volume of the patient needle to any volume up to or greater than 20 times or more of the volume of the patient needle. The predetermined volume of the sequestration chamber 55 may also be established to economize or minimize an amount of blood to be sequestered and disposed of.

[0060] The sequestration chamber 55 can be formed, contained or housed in a chamber housing 50, and can be made of plastic, rubber, steel, aluminum or other suitable material. For example, the sequestration chamber 55 could be formed of flexible tubing or other elastomeric materials. The sequestration chamber 55 further includes an air permeable blood barrier 20 that allows air to exit the sequestration chamber 55. As used herein the term "air permeable blood barrier" means an air permeable but substantially blood impermeable substance, material, or structure. Examples may include hydrophobic membranes and coatings, a hydrophilic membrane or coating combined with a hydrophobic membrane or coating, mesh, a filter, a mechanical valve, antimicrobial material, or any other means of allowing air to be displaced from the sequestration chamber 55 as it is filled with blood. In various exemplary embodiments, an air permeable blood barrier may be formed by one or more materials that allow air to pass through until contacted by a liquid, such material then becomes completely or partially sealed to prevent or inhibit the passage of air and/or liquid. In other words, prior to contact with liquid, the material forms a barrier that is air permeable. After contact with a

liquid, the material substantially or completely prevents the further passage of air and/or liquid.

[0061] The orifice or channel 45 can be any desired length, cross-sectional shape or size, and/or can be formed to depart from the low volume chamber 30 at any desired angle or orientation. The orifice or channel 45 may also include a one-way flap or valve 60 that maintains an initial aliquot of blood sample within the sequestration chamber 55. In some specific implementations, the orifice or channel 45 can include a "duck bill" or flapper valve 60, or the like, for one-way flow of blood from low volume chamber 30 to the sequestration chamber 55. The air permeable blood barrier 20 can also be constructed of a material that allows air to exit but then seals upon contact with blood, thereby not allowing external air to enter sequestration chamber 55. This sealing would eliminate the need for a valve.

[0062] Valve 60 can be any type of valve or closing mechanism. Chamber 30 is designed to hold virtually no residual blood, and can be designed to be adapted to hold or allow pass-through of a particular volume or rate of blood into sequestration chamber 55. Likewise, sequestration chamber 55 may also include any type of coating, such as an anti-microbial coating, or a coating that aids identification and/or diagnosis of components of the first, sequestered blood draw.

[0063] Housing 50 and 40 can be formed of any suitable material, including plastic, such as acrylonitrile butadiene styrene (ABS) or other thermoplastic or polymeric material, rubber, steel, or aluminum. The air permeable blood barrier 20 can include a color-providing substance, or other signaling mechanism, that is activated upon contact with blood from the initial blood draw, or when air displacement is stopped, or any combination of events with blood in the sequestration chamber 55. The air permeable barrier may also include an outer layer such as a hydrophobic membrane or cover that inhibits or prevents the inadvertent or premature sealing of the filter by an external fluid source, splash etc. Sequestration chamber 55 can also be translucent or clear to enable a user to visually confirm the chamber is filled.

[0064] FIG. 2 illustrates a blood sample optimization system in accordance with some alternative implementations. In the implementation shown in FIG. 2, a sequestration chamber 55, or waste chamber, surrounds the patient needle 1, with an

open-ended cuff or housing connected with the waste chamber and encircling the sample needle housing base and housing. The patient needle 1 and sample needle 5 are connected together by a boot 56, which forms a continuous blood draw channel therethrough. The boot 56 includes a single orifice or channel leading from the blood draw channel into sequestration chamber 55. The device can include more than one single orifice or channel, in other implementations. Each orifice or channel can include a one-way valve, and can be sized and adapted for predetermined amount of blood flow.

[0065] The sequestration chamber 55 includes an air permeable blood barrier. The filter can further include a sensor or indicator to sense and/or indicate, respectively, when a predetermined volume of blood has been collected in the sequestration chamber 55. That indication will alert a user to attach an evacuated blood collection tube or bottle, such as a Vacutainer™ to the sample needle 5. The housing for the sequestration chamber 55 can be any size or shape, and can include any type of material to define an interior space or volume therein. The interior space is initially filled only with air, but can also be coated with an agent or substance, such as a decontaminate, solidifying agent, or the like. Once evacuated blood collection tube is attached to the sample needle 5, blood will flow automatically into the patient needle 1, through the blood draw channel and sample needle 5, and into the bottle. The sample needle 5 is covered by a resealable boot, coating or membrane that seals the sample needle when a blood collection bottle is not attached thereon or thereto.

[0066] FIG. 3 illustrates a blood sample optimization system in accordance with some alternative implementations. In the implementation shown, a sample needle 5 is surrounded by a resealable boot or membrane, and is further connected with a patient needle 1. A blood flow channel is formed through the sample needle and the patient needle. The connection between the sample needle and patient needle includes a "T" or "Y" connector 102, which includes a channel, port or aperture leading out from the main blood flow channel to a sequestration chamber 104.

[0067] The T or Y connector 102 may include a flap or one-way valve, and have an opening that is sized and adapted for a predetermined rate of flow of blood. The sequestration chamber 104 can be formed from tubing, or be formed by a solid housing, and is initially filled with air. The sequestration chamber 104 will receive blood that flows out of a patient automatically, i.e. under pressure from the patient's own blood

pressure. The sequestration chamber 104 includes an air permeable blood barrier 106, preferably at the distal end of tubing that forms the sequestration chamber 104, and which is connected at the proximal end to the T or Y connector 102. The T or Y connector 102 can branch off at any desired angle for most efficient blood flow, and can be formed so as to minimize an interface between the aperture and channel and the main blood flow channel, so as to minimize or eliminate mixing of the initial aliquot of blood with main blood draw samples.

[0068] In some alternative implementations, the sample needle may be affixed to a tubing of any length, as shown in FIG. 4, connecting at its opposite end to the T or Y connector 102. The sequestration chamber 104 can be any shape or volume so long as it will contain a predetermined amount of blood sample in the initial aliquot. The T or Y connector 102 may also include an opening or channel that is parallel to the main blood flow channel. The air permeable blood barrier may further include an indicator 107 or other mechanism to indicate when a predetermined amount of blood has been collected in the sequestration chamber, or when air being expelled reaches a certain threshold, i.e. to zero. The tubing can also include a clip 109 that can be used to pinch off and prevent fluid flow therethrough.

[0069] Once the air permeable blood barrier and primary chamber are sealed the initial aliquot of blood is trapped in the sequestration chamber 104, an evacuated blood collection tube, such as a Vacutainer™ bottle may be attached to the sample needle 5 to obtain the sample. The blood collection tube can be removed, and the sample needle 5 will be resealed. Any number of follow-on blood collection tubes can then be attached for further blood draws or samples. Upon completion of all blood draws, the system can be discarded, with the initial aliquot of blood remaining trapped in the sequestration chamber 104.

[0070] FIG. 5 illustrates a blood sample optimization system in accordance with some alternative implementations. In the implementation shown, a sample needle 5 is connected with a patient needle by tubing. A "T" or "Y" connector 120 is added along the tubing at any desired location, and includes an aperture, port or channel leading to a sequestration chamber 204, substantially as described above.

[0071] FIG. 6 illustrates a blood sample optimization system in accordance with some alternative implementations, in which a sequestration chamber 304, formed as a primary collection channel, receives an initial aliquot of blood, and is provided adjacent to the blood sampling channel. The sequestration chamber 304 can encircle the blood sampling channel, the patient needle 1, and/or the sample needle 5. The primary collection channel can include a T or Y connector 120, or other type of aperture or channel. The sequestration chamber 304 includes an air permeable blood barrier, which can also include an indicator of being contacted by a fluid such as blood, as described above.

[0072] In some implementations, either the patient needle 1 or the sample needle 5, or both, can be replaced by a Luer lock male or female connector. However, in various implementations, the connector at a sample needle end of the blood sample optimization system is initially sealed to permit the diversion of the initial aliquot of blood to the sequestration chamber, which is pressured at ambient air pressure and includes the air outlet of the air permeable blood barrier. In this way, the system passively and automatically uses a patient's own blood pressure to overcome the ambient air pressure of the sequestration chamber to push out air through the air permeable blood barrier and displace air in the sequestration chamber with blood.

[0073] FIG. 7 is a flowchart of an exemplary method for optimizing the quality of a blood culture. At 702, a clinician places a needle into a patient's vein. At 704, blood then flows into a sequestration chamber, pushing the air in the sequestration chamber out of the sequestration chamber through an air permeable blood barrier. In some implementations, the volume of the sequestration chamber is less than 0.1 to more than 5 cubic centimeters (cc's), or more. The sequestration chamber is sized and adapted to collect a first portion of a blood sample, which is more prone to contamination than secondary and other subsequent portion of the blood sample or subsequent draws. Since the sequestration chamber has an air-permeable blood barrier through which air can be displaced by blood pushed from the patient's vein, such blood will naturally and automatically flow into the sequestration chamber before it is drawn into or otherwise enters into a Vacutainer or other bottle for receiving and storing a blood sample.

[0074] When the sequestration chamber fills, the blood will gather at or otherwise make contact with the air permeable blood barrier, which will inhibit or prevent blood

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

[0075] Prior to an evacuated blood collection tube being attached, communication between the needle, sampling channel, and the sequestration chamber is restricted by the sealing of the sequestration chamber blood barrier thereby not permitting air to reenter the system through the sequestration. Sealing the communication path could also be accomplished with a mechanical twist or other movement, a small orifice or tortuous pathway, eliminating the need for a separate valve or mechanical movement or operation by the clinician. At 710, once the evacuated blood collection tube is removed, the self-sealing membrane closes the sample needle, and at 712, additional subsequent evacuated blood collection tubes may be attached. Once samples have been taken, at 714 the device is removed from the patient and discarded.

[0076] FIGS. 8A – 8E illustrate an exemplary blood sample optimization system 800 for non-contaminated blood sampling, in accordance with some implementations. The blood sample optimization system 800 includes an inlet port 802 that can be connected to tubing, a patient needle (or both), or other vascular or venous access device, and a pathway splitter 804 having a first outlet to a sequestration chamber tubing 806 and a second outlet to sample collection tubing 808. One or both of the sequestration chamber tubing 806 and the sample collection tubing 808 can be formed of tubing. In some implementations, the sequestration chamber tubing 806 is sized so as to contain a particular volume of initial blood sample. The sample collection tubing 808 will receive a blood sample once the sequestration chamber tubing 806 is filled. The sample collection tubing 808 can be connected to a Vacutainer™ base or housing 810, or other blood sample collection device.

[0077] The blood sequestration system 800 further includes a blood sequestration device 812 which, as shown in more detail in FIGS. 8B – 8D, includes a housing 818 that

includes a sampling channel 820 defining a pathway for the non-contaminated sample collection tubing 808 or connected at either end to the non-contaminated sample collection tubing 808. The sampling channel 820 can be curved through the housing 818 so as to better affix and stabilize the housing 818 at a location along the non-contaminated sample collection tubing 808.

[0078] The blood sequestration device 812 further includes a sequestration chamber 822 connected with the sequestration chamber tubing 806 or other chamber. The sequestration chamber 822 terminates at an air permeable blood barrier 824. The air permeable blood barrier 824 can also include a coloring agent that turns a different color upon full contact with blood, as an indicator that the regular collection of blood samples (i.e. the non-contaminated blood samples) can be initiated. Other indicators may be used, such as a small light, a sound generation mechanism, or the like. In some implementations, the air permeable blood barrier is positioned at a right angle from the direction of sequestration chamber 822, but can be positioned at any distance or orientation in order to conserve space and materials used for the housing 818. The housing 818 and its contents can be formed of any rigid or semi-rigid material or set of materials.

[0079] FIG. 9 illustrates a pathway splitter 900 for use in a blood sequestrations system, such as those shown in FIGS. 8A – 8E, for example. The pathway splitter 900 includes an inlet port 902, a main line outlet port 904, and a sequestration channel outlet port 906. The inlet port 902 can be connected to main tubing that is in turn connected to a patient needle system, or directly to a patient needle. The main line outlet port 904 can be connected to main line tubing to a blood sampling system, such as a vacutainer base or housing, or directly to such blood sampling system. The sequestration channel outlet port 906 can be connected to sequestration tubing for receiving and sequestering a first sample of blood, up to a measured amount or predetermined threshold. Alternatively, the sequestration channel outlet port 906 can be connected to a sequestration chamber. The sequestration channel outlet port 906 is preferably 20-70 degrees angled from the main line outlet port 904, which in turn is preferably in-line with the inlet port 902. Once the predetermined amount of initial blood sample is sequestered in the sequestration tubing or chamber, in accordance with mechanisms and techniques described herein, follow-on blood samples will flow into the inlet port 902 and directly out the main line outlet port 904, without impedance.

[0080] FIGS. 10A – 10D illustrate a blood sequestration device 1000 in accordance with alternative implementations. The blood sequestration device 1000 includes an inlet port 1002, a main outlet port 1004, and a sequestration channel port 1006. The inlet port 1002 can be connected to a patient needle or related tubing. The main outlet port 1004 can be connected to a blood sample collection device such as a Vacutainer, associated tubing, or a Luer activated valve, or the like. The sequestration channel port 1006 splits off from the main outlet port 1004 to a sequestration chamber 1008. In some implementations, the sequestration chamber 1008 is formed as a helical channel within a housing or other container 1001.

[0081] The sequestration chamber 1008 is connected at the distal end to an air permeable blood barrier 1010, substantially as described above. Air in the sequestration chamber 1008 is displaced through the air permeable blood barrier 1010 by an initial aliquot of blood that is guided into the sequestration channel port 1006. Once the sequestration chamber 1008 is filled, further blood draws through the main outlet port 1004 can be accomplished, where these samples will be non-contaminated.

[0082] FIGS. 11A – 11E illustrate a blood sequestration device 1100 in accordance with other alternative implementations. The blood sequestration device 1100 includes an inlet port 1102, similar to the inlet ports described above, a main outlet port 1104, and a sequestration channel port 1106 that splits off from the main outlet port 1104 and inlet port 1102. The sequestration channel port is connected to a sequestration chamber 1108. In the implementation shown in FIGS. 11A – 11E, the blood sequestration device includes a base member 1101 having a channel therein, which functions as the sequestration chamber 1108. The channel can be formed as a tortuous path through the base member 1101, which is in turn shaped and formed to rest on a limb of a patient.

[0083] A portion of the sequestration chamber 1108 can protrude from the base member or near a top surface of the base member, just before exiting to an air permeable blood barrier 1110, to serve as a blood sequestration indicator 1109. The indicator 1109 can be formed of a clear material, or a material that changes color when in contact with blood.

[0084] In some implementations, the blood sequestration device 1100 can include a blood sampling device 1120 such as a normally closed needle, Vacutainer™ shield or other collection device. The blood sampling device 1120 can be manufactured and sold with the blood sequestration device 1100 for efficiency and convenience, so that a first aliquot of blood that may be contaminated by a patient needle insertion process can be sequestered. Thereafter, the blood sampling device 1120 can draw non-contaminated blood samples to reduce the risk of false positive testing and ensure a non-contaminated sample.

[0085] FIGS. 12A-12D illustrate a blood sample optimization system 1200 in accordance with yet other alternative implementations. The system 1200 includes a blood sequestration device 1202 for attaching to a blood sampling device 1204, such as a Vacutainer™ or other collection and sampling device. The blood sequestration device 1202 is configured and arranged to receive, prior to a Vacutainer™ container or vial being attached to a collection needle of the blood sampling device 1204, a first aliquot or amount of blood, and sequester that first aliquot or amount in a sequestration channel of the blood sequestration device 1202.

[0086] In some implementations, the blood sequestration device 1202 can include an inlet port 1212, a main outlet port, and a sequestration channel port. The inlet port 1212 can be connected to a patient needle or related tubing. The main outlet port 1214 can be connected to a normally closed needle or device to enable connection with an evacuated blood collection container or other collection device such as a Vacutainer™, associated tubing, luer connectors, syringe, a Luer activated valve, or the like. The sequestration channel port splits off from the main outlet port to a sequestration chamber 1218.

[0087] In some implementations, the sequestration chamber 1218 is formed as a channel within the body of a sequestration device 1202. The sequestration chamber 1218 can be a winding channel, such as a U-shaped channel, an S-shaped channel, a helical channel, or any other winding channel. The sequestration device 1202 can include a housing or other containing body, and one or more channels formed therein. As shown in FIGS. 12A and 12B, the sequestration device 1202 includes a main body 1206 and a cap 1208. The main body 1206 is formed with one or more cavities or channels, which are further formed with one or more arms 1210 that extend from the cap 1208, and which

abut the cavities or channels in the main body 1206 to form the primary collection port and main outlet port.

[0088] FIGS. 13A-13D illustrate a blood sample optimization system 1300 in accordance with yet other alternative implementations. The system 1300 includes a blood sequestration device 1302 for attaching to a blood sampling device 1304, such as a Vacutainer or other bodily fluid collection and sampling device. The blood sequestration device 1302 is configured and arranged to receive, prior to a Vacutainer container or vial being attached to a collection needle of the blood sampling device 1304, a first aliquot or amount of blood, and to sequester that first aliquot or amount of blood or other bodily fluid in a sequestration channel of the blood sequestration device 1302.

[0089] The blood sequestration device 1302 includes a housing 1301 having an inlet port 1314, a main outlet port 1312, and a sequestration channel port 1316. The inlet port 1314 can be connected to a patient needle or associated tubing. The main outlet port 1312 can be connected to a normally closed needle or device to enable connection with an evacuated blood collection container or other collection device such as a Vacutainer™, associated tubing, luer connectors, syringe, a Luer activated valve, or the like. The sequestration channel port 1316 splits off from the main inlet port 1314 to a sequestration chamber 1318.

[0090] In the implementation shown in FIGS. 13A-D, the sequestration chamber 1318 is formed as a cavity or chamber within housing 1301 or formed by walls that define housing 1301. The sequestration chamber 1318 can be a winding channel, such as a U-shaped channel, an S-shaped channel, a helical channel, or any other winding channel, that is defined by the cooperation and connection of housing 1301 with cap 1307 which cap 1307 can include a protrusion 1305 that provides one or more walls or directors for the winding channel in the sequestration chamber 1318. The protrusion 1305 from the cap 1307 can be straight or curved, and may have various channels, apertures or grooves embedded therein, and can extend from the cap 1307 any angle or orientation. When the cap 1307 is connected with the housing 1301 to complete the formation of the sequestration chamber 1318, the protrusion 1305 forms at least part of the winding channel to sequester a first aliquot or amount of blood or other bodily fluid in a sequestration channel formed in the sequestration chamber 1318 and by the winding channel.

[0091] The sequestration chamber 1318 includes an air permeable blood barrier 1310, substantially as described above. Air in the sequestration chamber 1318 is displaced through the air permeable blood barrier 1310 by an initial aliquot of blood that is provided into the sequestration chamber 1318 by the blood pressure of the patient. Once the sequestration chamber 1318 is filled and the air in the sequestration chamber 1318 displaced, the blood pressure of the patient will be insufficient to drive or provide further blood into the blood sequestration device 1302, and in particular the outlet port 1312, until a force such as a vacuum or other pressure, such as provided by the blood sample collection device like Vacutainer is provided to draw out a next aliquot or amount of blood or bodily fluid. Further blood draws through the main outlet port 1312 can be accomplished, where these samples will be non-contaminated since any contaminants would be sequestered in the sequestration chamber 1318 with the first aliquot of blood.

[0092] FIGS. 14A-14E illustrate yet another implementation of a blood sampling system 1400 to sequester contaminates of an initial aliquot or sample to reduce false positives in blood cultures or tests performed on a patient's blood sample. The blood sampling system 1400 includes a blood sequestration device 1401 that can be connected between a blood sample collection device 1403 and a patient needle (not shown). The blood sample collection device 1403 can be a Vacutainer or the like. The blood sequestration device 1401 includes an inlet port 1402 that can be connected with a patient needle that is inserted into a patient's vascular system for access to and withdrawing of a blood sample. The inlet port 1402 may also be connected with tubing or other conduit that is in turn connected with the patient needle.

[0093] The inlet port 1402 defines an opening into the blood sequestration device 1401, which opening can be the same cross sectional dimensions as tubing or other conduit connected with the patient needle or the patient needle itself. For instance, the opening can be circular with a diameter of approximately 0.045 inches, but can have a diameter of between 0.01 inches or less to 0.2 inches or more. The blood sequestration device 1401 further includes an outlet port 1404, which defines an opening out of the blood sequestration device 1401 and to the blood sample collection device 1403. The outlet port 1404 may also be connected with tubing or other conduit that is in turn connected with the blood sequestration device 1403. The outlet port 1404 can further include a connector device such as a threaded cap, a Luer connector (male or female), a

non threaded interference or glue joint fitting for attachment of various devices including but not limited to tubing, or the like.

[0094] The blood sequestration device 1401 further includes a sampling channel 1406 between the inlet port 1402 and the outlet port 1404, and which functions as a blood sample pathway once a first aliquot of blood has been sequestered. The sampling channel 1406 can be any sized, shaped or configured channel, or conduit. In some implementations, the sampling channel 1406 has a substantially similar cross sectional area as the opening of the inlet port 1402. In other implementations, the sampling channel 1406 can gradually widen from the inlet port 1402 to the outlet port 1404.

[0095] The blood sequestration device 1401 further includes a sequestration chamber 1408 that is connected to and split off or diverted from the sampling channel 1406 at any point between the inlet port 1402 and the outlet port 1404, but preferably from a proximal end of the sampling channel 1406 near the inlet port 1402. The sequestration chamber 1408 is at first maintained at atmospheric pressure, and includes an air outlet 1412 at or near a distal end of the sequestration chamber 1408 opposite the diversion point from the sampling channel 1406. The air outlet 1412 includes an air permeable blood barrier 1412. As shown in FIG. 14B, the air permeable blood barrier 1412 can be overlaid with a protective cover 1416. The protective cover 1416 can be sized and configured to inhibit a user from touching the air permeable blood barrier 1412 with their finger or other external implement, while still allowing air to exit the air permeable blood barrier 1412 as the air is displaced from the sequestration chamber 1408 by blood being forced into the sequestration chamber 1408 by a patient's own blood pressure. In addition the protective cover 1416 can be constructed to inhibit or prevent accidental exposure of the air permeable blood barrier to environmental fluids or splashes. This can be accomplished in a variety of mechanical ways including but not limited to the addition of a hydrophobic membrane to the protective cover.

[0096] As shown in FIGS. 14C and 14D, the sampling channel 1406 can be cylindrical or frusto-conical in shape, going from a smaller diameter to a larger diameter, to minimize a potential to lyse red blood cells. Likewise, the sampling channel 1406 is formed with a minimal amount of or no sharp turns or edges, which can also lyse red blood cells. The sampling channel 1406 splits off to the sequestration chamber 1408 near the inlet port 1402 via a diversion pathway 1409. The diversion pathway 1409 can have

any cross-sectional shape or size, but is preferably similar to the cross-sectional shape of at least part of the inlet port 1402.

[0097] In some implementations, the sampling channel 1406 and the sequestration chamber 1408 are formed by grooves, channels, locks or other pathways formed in housing 1414. The housing 1414 can be made of plastic, metal or other rigid or semi-rigid material. The housing 1414 can have a bottom member that sealably mates with a top member. One or both of the bottom member and the top member can include the sampling channel 1406 and the sequestration chamber 1408, as well as the diversion pathway 1409, the inlet port 1402, and the outlet port 1404. In some other implementations, one or more of the diversion pathway 1409, the inlet port 1402, and/or the outlet port 1404 can be at least partially formed by a cap member that is connected to either end of the housing 1414. In some implementations, the top member and the bottom member, as well as the cap member(s), can be coupled together by laser welding, heat sealing, gluing, snapping, screwing, bolting, or the like. In other implementations, some or all of the interior surface of the diversion pathway 1409 and/or sequestration chamber 1408 can be coated or loaded with an agent or substance, such as a decontaminate, solidifying agent, or the like. For instance, a solidifying agent can be provided at the diversion pathway 1409 such that when the sequestration chamber 1408 is filled and the initial aliquot of blood backs up to the diversion pathway 1409, that last amount of sequestered blood could solidify, creating a barrier between the sequestration chamber 1408 and the sampling channel 1406.

[0098] FIGS. 15A-15G illustrate a blood sequestration device 1500. The blood sequestration device 1500 can be connected to a normally closed needle or device to enable connection with an evacuated blood collection container or other collection device such as a Vacutainer™, associated tubing, luer connectors, syringe, a Luer activated valve, or the like.

[0099] The blood sequestration device 1500 includes an inlet port 1502 that can be connected with a patient needle that is inserted into a patient's vascular system for access to and withdrawing of a blood sample. The inlet port 1502 may also be connected with tubing or other conduit that is in turn connected with the patient needle. The inlet port 1502 defines an opening into the blood sequestration device 1500, which opening may be the same cross sectional dimensions as tubing or other conduit connected with the

patient needle or the patient needle itself. For instance, the opening can be circular with a diameter of approximately 0.045 inches, but can have a diameter of between 0.01 inches or less to 0.2 inches or more.

[00100] The inlet port 1502 can also include a sealing or fluid-tight connector or connection, such as threading or Luer fitting, or the like. In some implementations, tubing or other conduit associated with the patient needle can be integral with the inlet port 1502, such as by co-molding, gluing, laser weld, or thermally bonding the parts together. In this manner, the blood sequestration device 1500 can be fabricated and sold with the patient needle as a single unit, eliminating the need for connecting the patient needle to the blood sequestration device 1500 at the time of blood draw or sampling.

[00101] The blood sequestration device 1500 further includes an outlet port 1504, which defines an opening out of the blood sequestration device 1500 and to the blood sample collection device. The outlet port 1504 may also be connected with tubing or other conduit that is in turn connected with the blood sequestration device, and may also include a sealing or fluid-tight connector or connection, such as threading or Luer fitting, or the like. Accordingly, as discussed above, the blood sequestration device 1500 can be fabricated and sold with the patient needle and/or tubing and the blood sample collection device as a single unit, eliminating the need for connecting the patient needle and the blood sample collection device to the blood sequestration device 1500 at the time of blood draw or sampling.

[00102] The blood sequestration device 1500 further includes a sampling channel 1506 between the inlet port 1502 and the outlet port 1504, and which functions as a blood sample pathway once a first aliquot of blood has been sequestered. The sampling channel 1506 can be any sized, shaped or configured channel or conduit. In some implementations, the sampling channel 1506 has a substantially similar cross sectional area as the opening of the inlet port 1502. In other implementations, the sampling channel 1506 can gradually widen from the inlet port 1502 to the outlet port 1504.

[00103] The blood sequestration device 1500 further includes a sequestration chamber 1508 that is connected to and split off or diverted from the sampling channel 1506 at any point between the inlet port 1502 and the outlet port 1504, but preferably from a proximal end of the sampling channel 1506 near the inlet port 1502. In some

implementations, the diversion includes a Y-shaped junction. The sequestration chamber 1508 is preferably maintained at atmospheric pressure, and includes a vent 1510 at or near a distal end of the sequestration chamber 1508. The vent 1510 includes an air permeable blood barrier 1512. FIG. 15C illustrates the blood sequestration device 1500 with the sequestration chamber 1508 filled with a first aliquot or sample of blood from the patient.

[00104] The air permeable blood barrier 1512 can be covered with a protective cover 1516. The protective cover 1516 can be sized and configured to inhibit a user from touching the air permeable blood barrier 1512 with their finger or other external implement, while still allowing air to exit the air permeable blood barrier 1512 as the air is displaced from the sequestration chamber 1508 by blood being forced into the sequestration chamber 1508 by a patient's own blood pressure. The protective cover 1516 can be constructed to inhibit or prevent accidental exposure of the filter to environmental fluids or splashes. This can be accomplished in a variety of mechanical ways including but not limited to the addition of a hydrophobic membrane to the protective cover.

[00105] FIG. 15B is a perspective view of the blood sequestration device 1500 from the outlet port 1504 and top side of a housing 1501 of the blood sequestration device 1500 that includes the vent 1510, and illustrating an initial aliquot of blood filling sequestration chamber 1508 while the sampling channel 1506 is empty, before a sample collection device is activated. FIG. 15G is a perspective view of the blood sequestration device 1500 from the outlet port 1504 and bottom side of the housing 1501 of the blood sequestration device 1500, and illustrating the initial aliquot of blood filling sequestration chamber 1508 while the sampling channel 1506 is empty, before the sample collection device is activated. FIG. 15C is another perspective view of the blood sequestration device 1500 from the inlet port 1502 and top side of a housing 1501 of the blood sequestration device 1500 that includes the vent 1510, and illustrating blood now being drawn through sampling channel 1506 while the sequestered blood remains substantially in the sequestration chamber 1508.

[00106] FIG. 15D is a cross section of the blood sequestration device 1500 in accordance with some implementations, showing the housing 1501 that defines the sampling channel 1506 and the sequestration chamber 1508. FIGS. 15E and 15F

illustrate various form factors of a housing for a blood sequestration device, in accordance with one or more implementations described herein.

[00107] The sequestration chamber 1508 can have a larger cross-sectional area than the sampling channel 1506, and the cross-sectional area and length can be configured for a predetermined or specific volume of blood to be sequestered or locked. The sampling channel 1506 can be sized to be compatible with tubing for either or both of the patient needle tubing or the blood collection device tubing.

[00108] The housing 1501 can be formed of multiple parts or a single, unitary part. In some implementations, and as illustrated in FIG. 15D, the housing 1501 includes a top member 1520 and a bottom member 1522 that are mated together, one or both of which having grooves, channels, locks, conduits or other pathways pre-formed therein, such as by an injection molding process or by etching, cutting, drilling, etc. The top member 1520 can be connected with the bottom member 1522 by any mating or connection mechanism, such as by laser welding, thermal bonding, ultrasonic welding, gluing, using screws, rivets, bolts, or the like, or by other mating mechanisms such as latches, grooves, tongues, pins, flanges, or the like.

[00109] In some implementations, such as shown in FIG. 15D, the top member 1520 can include the grooves, channels, locks, conduits or other pathways, while the bottom member 1522 can include a protrusion 1524 that is sized and adapted to fit into at least one of the grooves, channels, locks or other pathways of the top member 1520. The protrusion 1524 can provide a surface feature, such as a partial groove or channel, for instance, to complete the formation of either the sampling channel 1506 and/or the sequestration chamber 1508. In some implementations, the protrusion 1524 can be formed with one or more angled sides or surfaces for a tighter fit within the corresponding groove, channel, lock or other pathway. In yet other implementations, both the top member 1520 and the bottom member can include grooves, channels, locks or other pathways, as well as one or more protrusions 1524.

[00110] In some implementations, the sampling channel 1506 and the sequestration chamber 1508 are formed by grooves, channels, locks or other pathways formed in housing 1501. The housing 1501 can be made of any suitable material, including rubber, plastic, metal or other material. The housing 1501 can be formed of a clear or translucent

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

[00111] After a venipuncture by a patient needle of a patient (not shown), which could gather a number of pathogens from the patient's skin, a first amount of the patient's blood with those pathogens will make its way into the inlet port 1502 blood sequestration device 1500 and flow into the sequestration chamber 1508 by following the path of least resistance, as the patient's own blood pressure overcomes the atmospheric pressure in the sequestration chamber 1508 to displace air therein through the air permeable blood barrier 1512. The patient's blood pressure will not be sufficient to overcome the air pressure that builds up in the sealed sampling channel 1506. Eventually, the sequestration chamber 1508, which has a predetermined volume, is filled with blood that displaces air through the air permeable blood barrier 1512. Once the blood hits the air permeable blood barrier, the blood interacts with the air permeable blood barrier 1512 material to completely or partially seal the vent 1510. A signal or indication may be provided that the practitioner can now utilize the Vacutainer capsule or other blood sample collection device to acquire a next amount of the patient's blood for sampling. The blood in the sequestration chamber 1508 is now effectively sequestered in the sequestration chamber.

[00112] Upon filling the blood sequestration pathway 1508 but prior to use of the Vacutainer or other blood sample collection device, the patient's blood pressure may drive compression of the air in the sampling channel 1506, possibly resulting in a small amount of blood moving past the diversion point to the sequestration chamber 1508 and into the sampling channel 1506, queuing up the uncontaminated blood to be drawn through the sampling channel 1506.

[00113] In some instances, as shown in FIG. 15H, an inlet port 1532 can include a male luer connector for connecting to a removable patient needle, and an outlet port 11534 can include a female luer connector for connecting with a syringe. This implementation of the inlet port and outlet port can be used with any device described herein, for avoiding a propensity of a Vacutainer-type device collapsing a patient's vein. In this implementation, a clinician can use the syringe in a modulated fashion to obtain a blood sample. In operation, the syringe is attached to the outlet port 1004, and the needle is attached to the inlet port 1002. A venipuncture is performed with the needle, and without the clinician pulling on the syringe. An initial aliquot of blood fills a sequestration chamber, and then the syringe can be used to draw a sample of blood through the collection channel, bypassing the sequestered blood in the sequestration chamber.

[00114] FIGS. 16-19 illustrate yet another implementation of a blood sequestration device. FIGS. 16A-16D illustrate a blood sequestration device 1600 that can be connected between a blood sample collection device, such as an evacuated blood collection container like a Vacutainer™ (not shown), and a patient needle (not shown) and/or associated tubing. FIG. 17 illustrates a bottom member of the blood sequestration device, and FIG. 18 illustrates a top member of the blood sequestration device, which top member and bottom member can be mated together to form an inlet port, and outlet port, a sequestration chamber and a sampling channel, as explained more fully below. FIGS. 19A and B show the top member and bottom member mated together. It should be understood that FIGS. 16-19 illustrate one exemplary manner of constructing a blood sequestration device as described herein, and other forms of construction are possible.

[00115] Referring to FIGS. 16A – D, the blood sequestration device 1600 includes an inlet port 1602 that can be connected with a patient needle that is inserted into a patient's vascular system for access to and withdrawing of a blood sample. The inlet port 1602 may also be connected with tubing or other conduit that is in turn connected with the patient needle. The inlet port 1602 defines an opening into the blood sequestration device 1600, which opening can be the same cross sectional dimensions as tubing or other conduit connected with the patient needle or the patient needle itself. For instance, the opening can be circular with a diameter of approximately 0.045 inches, but can have a diameter of between 0.01 inches or less to 0.2 inches or more.

[00116] The inlet port 1602 can also include a sealing or fluid-tight connector or connection, such as threading or Luer fitting, or the like. In some implementations, tubing or other conduit associated with the patient needle can be integral with the inlet port 1602, such as by co-molding, gluing, laser weld, or thermally bonding the parts together. In this manner, the blood sequestration device 1600 can be fabricated and sold with the patient needle and/or tubing as a single unit, eliminating the need for connecting the patient needle to the blood sequestration device 1600 at the time of blood draw or sampling.

[00117] The blood sequestration device 1600 further includes an outlet port 1604, which defines an opening out of the blood sequestration device 1600 and to the blood sample collection device. The outlet port 1604 may also be connected with tubing or other conduit that is in turn connected with the blood sequestration device, and may also include a sealing or fluid-tight connector or connection, such as threading or Luer fitting, or the like. Accordingly, as discussed above, the blood sequestration device 1600 can be fabricated and sold with the patient needle and/or tubing and the blood sample collection device as a single unit, eliminating the need for connecting the patient needle and the blood sample collection device to the blood sequestration device 1600 at the time of blood draw or sampling.

[00118] The blood sequestration device 1600 further includes a sampling channel 1606 between the inlet port 1602 and the outlet port 1604, and a sequestration chamber 1608 that is connected to and split off or diverted from the sampling channel 1606 at any point between the inlet port 1602 and the outlet port 1604. The sampling channel 1606 functions as a blood sampling pathway once a first aliquot of blood has been sequestered in the sequestration chamber 1608. The sampling channel 1606 can be any sized, shaped or configured channel, or conduit. In some implementations, the sampling channel 1606 has a substantially similar cross sectional area as the opening of the inlet port 1602. In other implementations, the sampling channel 1606 can gradually widen from the inlet port 1602 to the outlet port 1604. The sequestration chamber 1608 may have a larger cross section to form a big reservoir toward the sequestration channel path so that the blood will want to enter the reservoir first versus entering a smaller diameter on the sampling channel 1606, as is shown more fully in FIGS. 17 and 19.

[00119] In some exemplary implementations, the diversion between the sampling channel 1606 and the sequestration chamber 1608 is by diverter junction 1607. Diverter junction 1607 may be a substantially Y-shaped, T-shaped, or U-shaped. In some preferred exemplary implementations, and as shown in FIG. 17A – 17B, the diverter junction 1607 is configured such that the flow out of the inlet port 1602 is preferentially directed toward the sequestration chamber 1608. The sequestration chamber 1608 may also include or form a curve or ramp to direct the initial blood flow toward and into the sequestration chamber 1608.

[00120] The sequestration chamber 1608 is preferably maintained at atmospheric pressure, and includes a vent 1610 at or near a distal end of the sequestration chamber 1608. The vent 1610 may include an air permeable blood barrier 1612 as described above.

[00121] The blood sequestration device 1600 can include a housing 1601 that can be formed of multiple parts or a single, unitary part. In some implementations, and as illustrated in FIGS. 17A – 17E and FIGS. 18A – 18F, the housing 1601 includes a top member 1620 and a bottom member 1622 that are mated together. The blood sequestration device 1600 can also include a gasket or other sealing member (not shown) so that when the top member 1620 is mechanically attached with the bottom member 1622, the interface between the two is sealed by the gasket or sealing member. The FIGS. 17A – 17E illustrate a bottom member 1622 of a housing for a blood sequestration device 1600. The bottom member 1622 can include grooves, channels, locks, conduits or other pathways pre-formed therein, such as by an injection molding process or by etching, cutting, drilling, etc., to form the sampling channel 1606, the sequestration chamber 1608, and diverter junction 1607.

[00122] The sequestration chamber 1608 may have a larger cross section than the sampling channel 1606 so that the blood will preferentially move into the sequestration chamber first versus entering a smaller diameter on the sampling channel 1606.

[00123] FIGS. 18A – 18F illustrate the top member 1620, which can be connected with the bottom member 1622 by any mating or connection mechanism, such as by laser welding, thermal bonding, gluing, using screws, rivets, bolts, or the like, or by other mating mechanisms such as latches, grooves, tongues, pins, flanges, or the like. The top

member 1620 can include some or all of the grooves, channels, locks, conduits or other pathways to form the sampling channel 1606, the sequestration chamber 1608, and the diverter junction 1607. In yet other implementations, both the top member 1620 and the bottom member 1622 can include the grooves, channels, locks or other pathways.

[00124] In some implementations, the sampling channel 1606 and the sequestration chamber 1608 are formed by grooves, channels, locks or other pathways formed in housing 1601. The housing 1601 can be made of rubber, plastic, metal or any other suitable material. The housing 1601 can be formed of a clear or translucent material, or of an opaque or non-translucent material. In other implementations, the housing 1601 can be mostly opaque or non-translucent, while the housing surface directly adjacent to the sampling channel 1606 and/or the sequestration chamber 1608 may be clear or translucent, giving a practitioner a visual cue or sign that the sequestration chamber 1608 is first filled to the extent necessary or desired, and/or then a visual cue or sign that the sequestered blood remains sequestered while a clean sample of blood is drawn through the sampling channel 1606. Other visual cues or signs of the sequestration can include, without limitation: the air permeable blood barrier 1612 turning a different color upon contact, saturation, or partial saturation with blood; a color-coded tab or indicator at any point along or adjacent to the sequestration chamber; an audible signal; a vibratory signal; or other signal.

[00125] As shown in FIGS. 18A – 18F, the air permeable blood barrier 1612 can be covered with, or surrounded by, a protective member 1616. The protective member 1616 can be sized and configured to inhibit a user from touching the air permeable blood barrier 1612 with their finger or other external implement, while still allowing air to exit the air permeable blood barrier 1612 as the air is displaced from the sequestration chamber 1608. In some implementations, the protective member 1616 includes a protrusion that extends up from a top surface of the top member 1620 and around the air permeable blood barrier 1612. The protective member 1616 can be constructed to inhibit or prevent accidental exposure of the filter to environmental fluids or splashes. This can be accomplished in a variety of mechanical ways including but not limited to the addition of a hydrophobic membrane to the protective cover.

[00126] In use, the blood sequestration device 1600 includes a sampling channel 1606 and a sequestration chamber 1608. Both pathways are initially air-filled at

atmospheric pressure, but the sampling channel 1606 is directed to an outlet port 1604 that will be initially sealed by a Vacutainer or other such sealed blood sampling device, and the sequestration chamber 1608 terminates at a vent 1610 to atmosphere that includes an air permeable blood barrier 1612.

[00127] After a venipuncture by a patient needle of a patient (not shown), which could gather a number of pathogens from the patient's skin, a first amount of the patient's blood with those pathogens will pass through inlet port 1602 of blood sequestration device 1600. This initial volume of potentially contaminated blood will preferentially flow into the sequestration chamber 1608 by finding the path of least resistance. The patient's own blood pressure overcomes the atmospheric pressure in the vented sequestration chamber 1608 to displace air therein through the air permeable blood barrier 1612, but is not sufficient to overcome the air pressure that builds up in the sealed sampling channel 1606. In various exemplary embodiments, the sequestration chamber 1608 and sampling channel 1606 can be configured such that the force generated by the patient's blood pressure is sufficient to overcome any effect of gravity, regardless of the blood sequestration device's orientation.

[00128] Eventually, the sequestration chamber 1608 fills with blood that displaces air through the air permeable blood barrier 1612. Once the blood contacts the air permeable blood barrier, the blood interacts with the air permeable blood barrier 1612 material to completely or partially seal the vent 1610. A signal or indication may be provided that the practitioner can now utilize the Vacutainer or other blood sampling device.

[00129] Upon filling the blood sequestration pathway 1608 but prior to use of the Vacutainer or other blood sample collection device, the patient's blood pressure may drive compression of the air in the sampling channel 1606, possibly resulting in a small amount of blood moving past the diversion point into the sampling channel 1606, queuing up the uncontaminated blood to be drawn through the sampling channel 1606.

[00130] FIG. 19A is a side view, and FIG. 19B is a cross-sectional view, of the blood sequestration device 1600, illustrating the top member 1620 mated with the bottom member 1622.

[00131] FIG. 20 shows a blood sample optimization system 2000 that includes a patient needle 2002 for vascular access to a patient's bloodstream, a blood sample collection device 2004 to facilitate the collecting of one or more blood samples, and a conduit 2006 providing a fluid connection between the patient needle 2002 and the blood sample collection device 2004. In some implementations, the blood sample collection device 2004 includes a protective shield that includes a sealed collection needle on which a sealed vacuum-loaded container is placed, which, once pierced by the collection needle, draws in a blood sample under vacuum pressure or force through the conduit 2006 from the patient needle 2002.

[00132] The blood sample optimization system 2000 further includes a blood sequestration device 2008, located at any point on the conduit 2006 between the patient needle 2002 and the blood sample collection device 2004 as described herein.

[00133] FIG. 21 illustrates a non-vented blood sequestration device 2100 using a wicking material chamber. The blood sequestration device 2100 includes a housing 2101 that has a sampling channel 2104 that is at least partially surrounded or abutted by a sequestration chamber 2102 that is filled with a wicking material. An initial aliquot of blood is drawn in from the patient needle into the sampling channel 2104 where it is immediately wicked into the wicking material of the sequestration chamber 2102. The wicking material and/or sequestration chamber 2102 is sized and adapted to receive and hold a predetermined amount of blood, such that follow-on or later blood draws pass by the wicking material and flow straight through the sampling channel 2104 to a sampling device such as a Vacutainer. The wicking material can include a substance such as a solidifier, a decontaminate, or other additive.

[00134] As described herein, an air permeable blood barrier may be created using a wide variety of different structures and materials. As shown in FIGS. 22A and B, an air permeable blood barrier 2202 of a blood sequestration device 2200 can include a polymer bead matrix 2204, in which at least some beads are treated to make them hydrophilic. The air permeable blood barrier 2202 further includes a self-sealing material 2206, such as carboxymethyl cellulose (CMC) or cellulose gum, or other sealing material. The air permeable blood barrier 2202 can further include voids 2208 that permit air flow before contact or during partial contact with a fluid such as blood. As shown in FIG. 22B,

contact with a fluid causes the self-sealing material 2206 to swell and close off the voids 2208, occluding air flow through the voids 2208 and creating a complete or partial seal.

[00135] FIGS. 23A and B illustrate yet another implementation of a blood sequestration device 2300, having an inlet port 2302 to connect with a patient needle, an outlet port 2304 to connect with a blood sample collection device, a sequestration chamber 2306, and a sampling channel 2308 that bypasses the sequestration chamber 2306 once the sequestration chamber is filled to an initial aliquot of potentially contaminated blood to be sequestered. The sequestration chamber 2306 includes a hydrophobic plug 2312 at a distal end of the sequestration chamber 2306 that is farthest from the inlet port 2302. A vacuum or other drawing force applied from the outlet port 2304, such as from a Vacutainer or the like, draws in blood into the inlet port 2302 and directly into the sequestration chamber 2306, where the initial aliquot of blood will contact the hydrophobic plug 2312 and cause the initial aliquot of blood to back up into the sequestration chamber 2306 and be sequestered there. A small amount of blood may make its way into the sampling channel 2308, which is initially closed off by valve 2308. Upon release of the valve 2308, and under further force of the vacuum or other force, follow-on amounts of blood will flow into inlet port 2302, bypass the sequestration chamber 2306, and flow into and through sampling channel 2308 toward the outlet port 2304 and to the collection device.

[00136] The sampling channel 2308 can have any suitable geometry and can be formed of plastic tubing or any other suitable material. Valve 2308 can be a clip or other enclosing device to pinch, shunt, bend or otherwise close off the sampling channel 2308 before the initial aliquot of blood is sequestered in the sequestration chamber 2306. For instance, valve 2308 can also be formed as a flap, door or closable window or barrier within the sampling channel 2308.

[00137] FIGS. 23C – 23E illustrate an alternative implementation of the blood sequestration device 2300', in which a sequestration chamber 2320 branches off from a main collection channel 2322 between an inlet port 2316 to connect with a patient needle and an outlet port 2318 to connect with a blood sample collection device, such as a Vacutainer, a syringe, or the like. The sequestration chamber 2320 includes an air-permeable, blood impermeable blood barrier 2324, such as a hydrophobic plug of material, or a filter formed of one or more layers, for example. A valve 2324 closes off

and opens the collection channel 2322, and the device 2300' can be used similarly as described above.

[00138] FIG. 24A – 24D illustrate a blood sample optimization system 2400 that includes a patient needle 2402 for vascular access to a patient's bloodstream, a blood sample collection device 2404 to facilitate the collecting of one or more blood samples for blood testing or blood cultures, and a conduit 2406 providing a fluid connection between the patient needle 2402 and the blood sample collection device 2404. In some implementations, the blood sample collection device 2404 includes a protective shield that includes a sealed collection needle on which a sealed vacuum-loaded container is placed, which, once pierced by the collection needle, draws in a blood sample under vacuum pressure or force through the conduit 2006 from the patient needle 2402.

[00139] The blood sample optimization system 2400 further includes a blood sequestration device 2408, located at any point on the conduit 2406 between the patient needle 2402 and the blood sample collection device 2404. The location of the blood sequestration device 2408 can be based on a length of the conduit between the blood sequestration device 2408 and the patient needle 2402, and the associated volume that length provides.

[00140] The blood sequestration device 2408 includes an inlet port 2412 for being connected to the conduit 2406 toward the patient needle 2402, and an outlet port 2414 for being connected to the conduit 2406 toward the blood sample collection device 2404, and a housing 2416. The housing 2416 can be any shape, although it is shown in FIGS. 24A – D as being substantially cylindrical, and includes the inlet port 2412 and outlet port 2414, which can be located anywhere on the housing although shown as being located on opposite ends of the housing 2416.

[00141] The blood sequestration device 2408 further includes a blood sequestration chamber 2418 connected with the inlet port 2412. The blood sequestration chamber 2418 is defined by an inner chamber housing 2419 that is movable from a first position to receive and sequester a first aliquot of blood, to a second position to expose one or more apertures 2424 at a proximal end of the inner chamber housing 2419 to allow blood to bypass and/or flow around the inner chamber housing 2419 and through a blood sample channel 2422 defined by the outer surface of the inner chamber housing 2419 and the

inner surface of the housing 2416. The blood sequestration chamber 2418 includes an air permeable blood barrier 2420 at a distal end of the blood sequestration chamber 2418.

[00142] In operation, the inner chamber housing 2419 is in the first position toward the inlet port 2412, such that the one or more apertures 2424 are closed, and the blood sequestration chamber 2418 is in a direct path from the patient needle. Upon venipuncture of a patient, and drawing of blood by way of a syringe or Vacutainer, or other blood collection device 2404, the initial aliquot of blood flows into the blood sequestration chamber 2418. As the initial aliquot of blood flows into the blood sequestration chamber, it displaces air therein and eventually the blood contacts the blood barrier 2420, forcing the inner chamber housing to the second position. The inner chamber housing 2419 and/or housing 2416 can include a locking mechanism of one or more small tabs, grooves, detents, bumps, ridges, or the like, to maintain the inner chamber housing 2419 in the first position until the blood sequestration chamber 2418 is filled, providing force to overcome the locking mechanism to enable movement of the inner chamber housing 2419 to the second position. Once in the second position, the initial aliquot of blood is sequestered in the blood sequestration chamber 2418 and the one or more apertures 2424 are opened to create a pathway from the inlet port 2412 to the blood sampling channel 2422, bypassing and/or flowing around the blood sequestration chamber 2418.

[00143] As described above, the housing 2416 and/or inner chamber housing 2419 can be formed as cylindrical and concentric, but can be any shape, such as squared, rectangular, elliptical, oval, or other cross-sectional shape. The outer surface of the distal end of the inner chamber housing 2419 can have one or more outwardly projecting tangs 2421with gaps therebetween. The tangs 2421 contact the inner surface of the housing 2416 to help define the blood sampling channel 2422 therebetween, and to help stop the inner chamber housing 2419 in the second position. The gaps between the tangs 2421 enable blood to flow through the blood sampling channel 2422 and to the outlet port 2414. When the inner chamber housing 2419 is in the second position and the blood sequestration chamber 2418 is filled with the first aliquot of blood, further blood samples will automatically flow through the inlet port 2412, through the one or more apertures 2424, through the blood sampling channel 2422, through the gaps between the tangs 2421, and ultimately through the outlet port 2414 to be collected by a blood sampling device 2404.

[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.

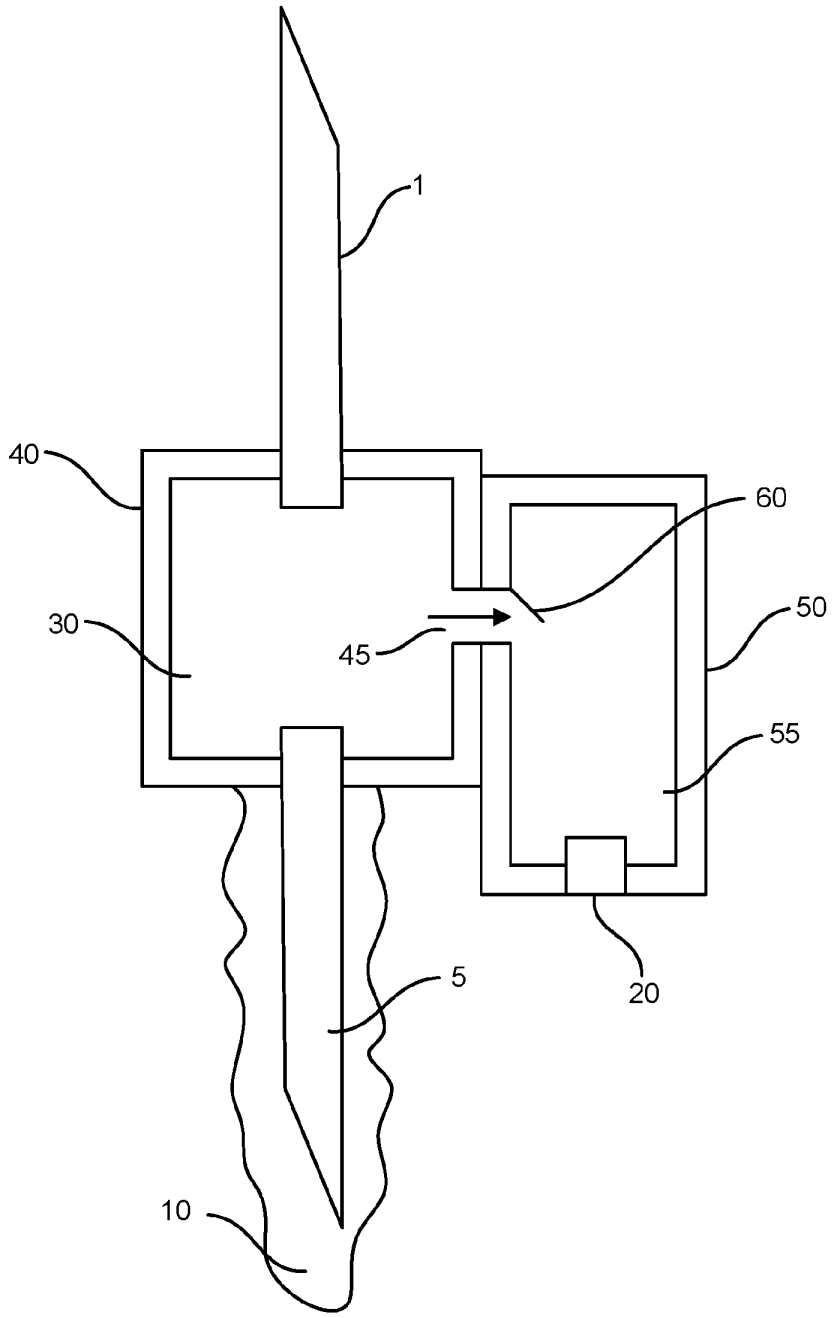


FIG. 1

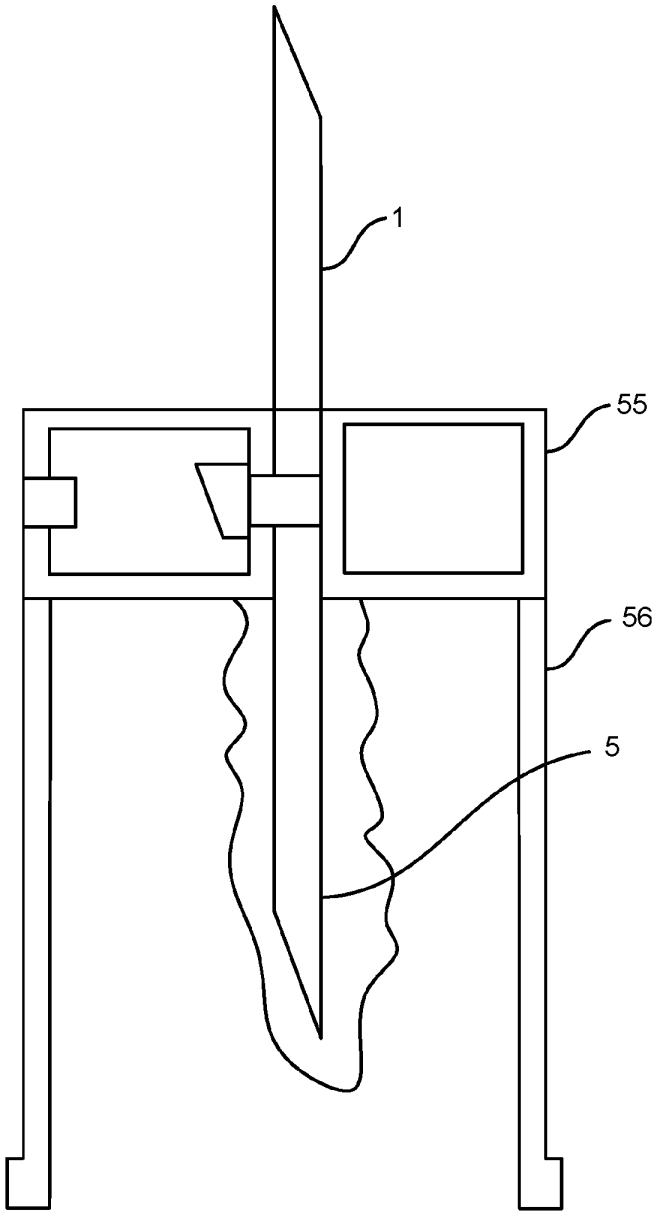


FIG. 2

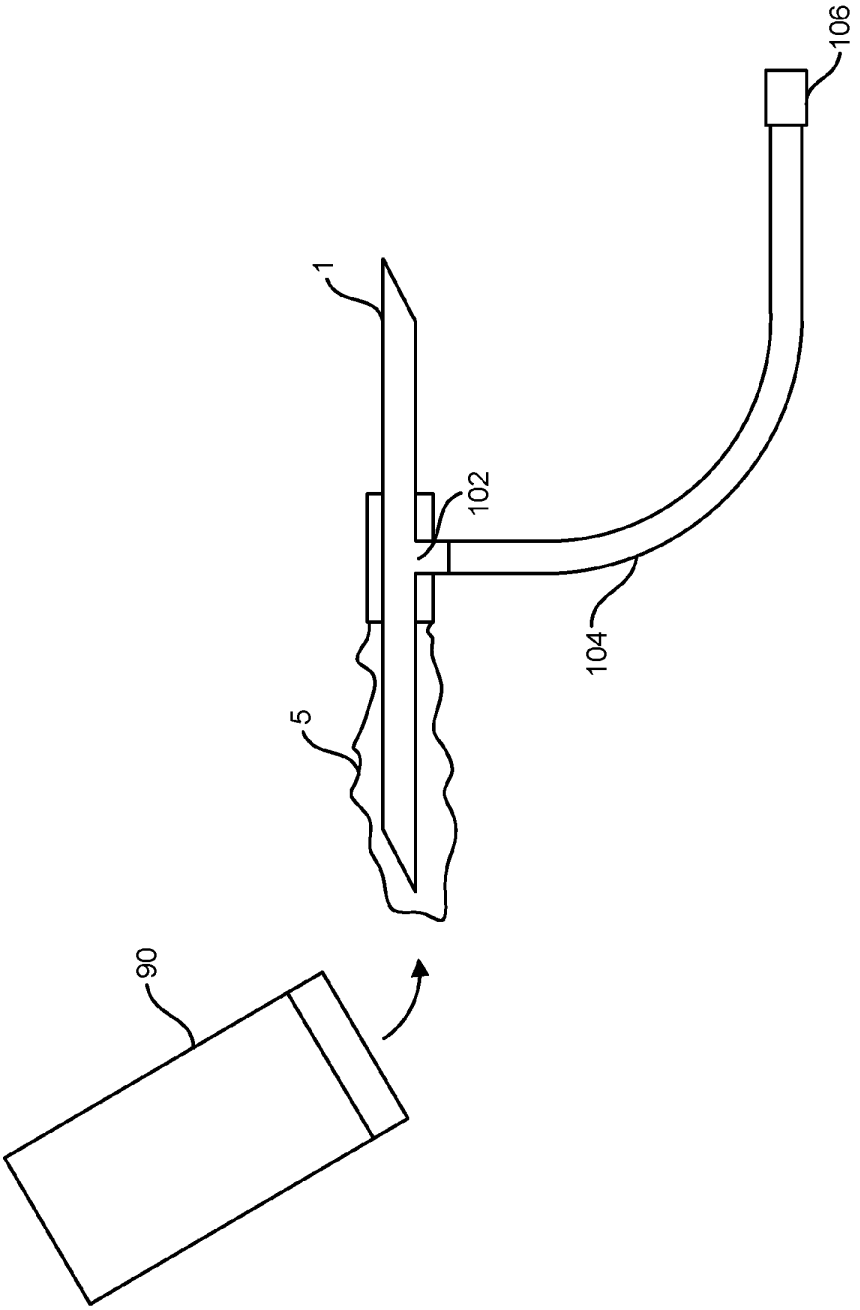


FIG. 3

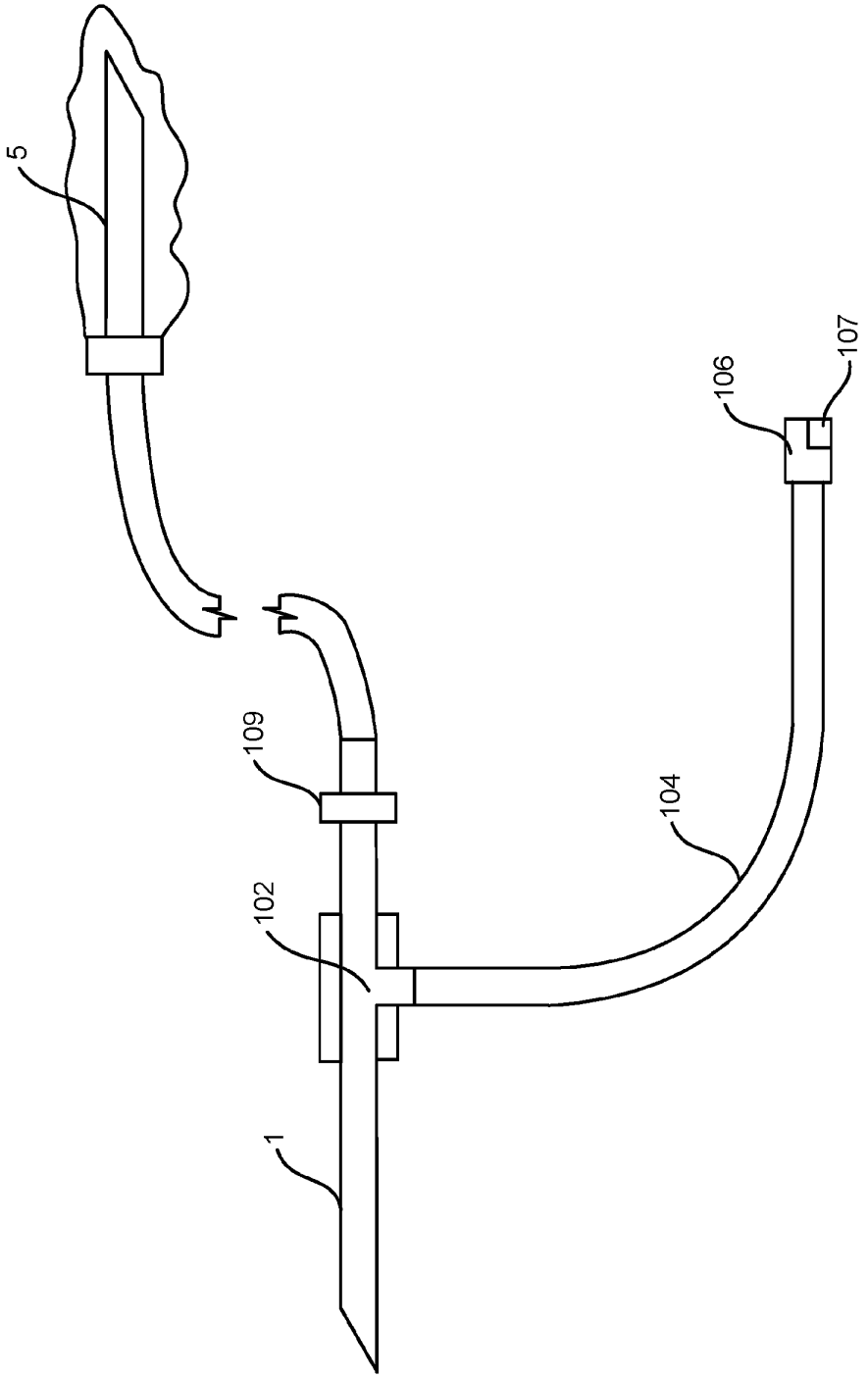


FIG. 4

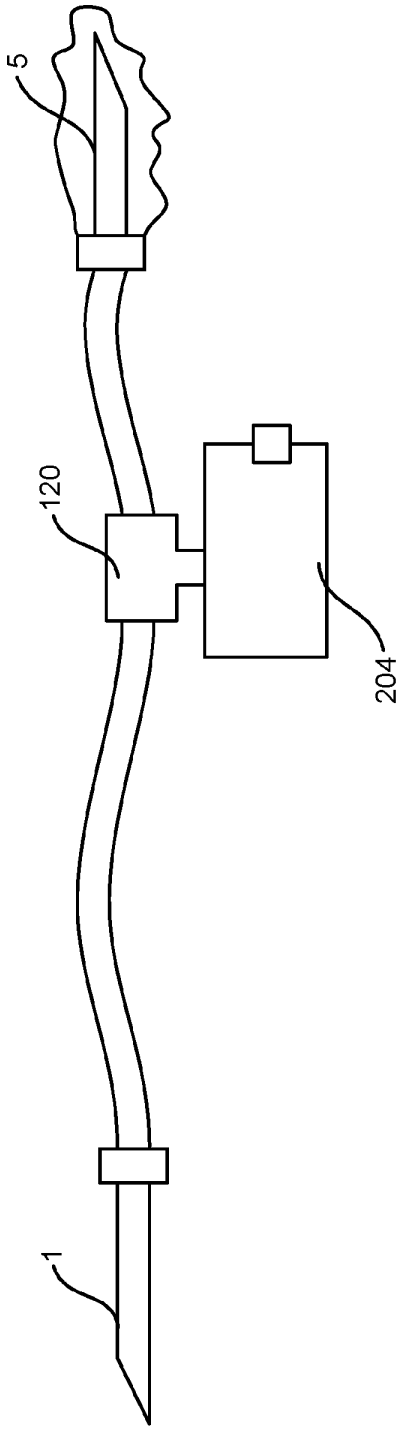


FIG. 5

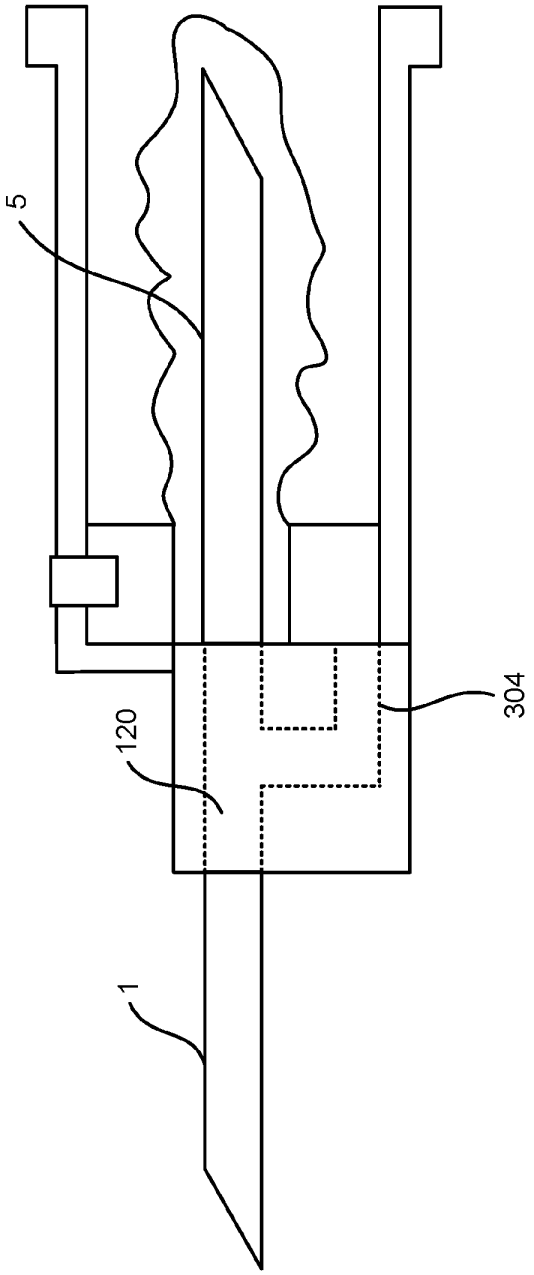


FIG. 6

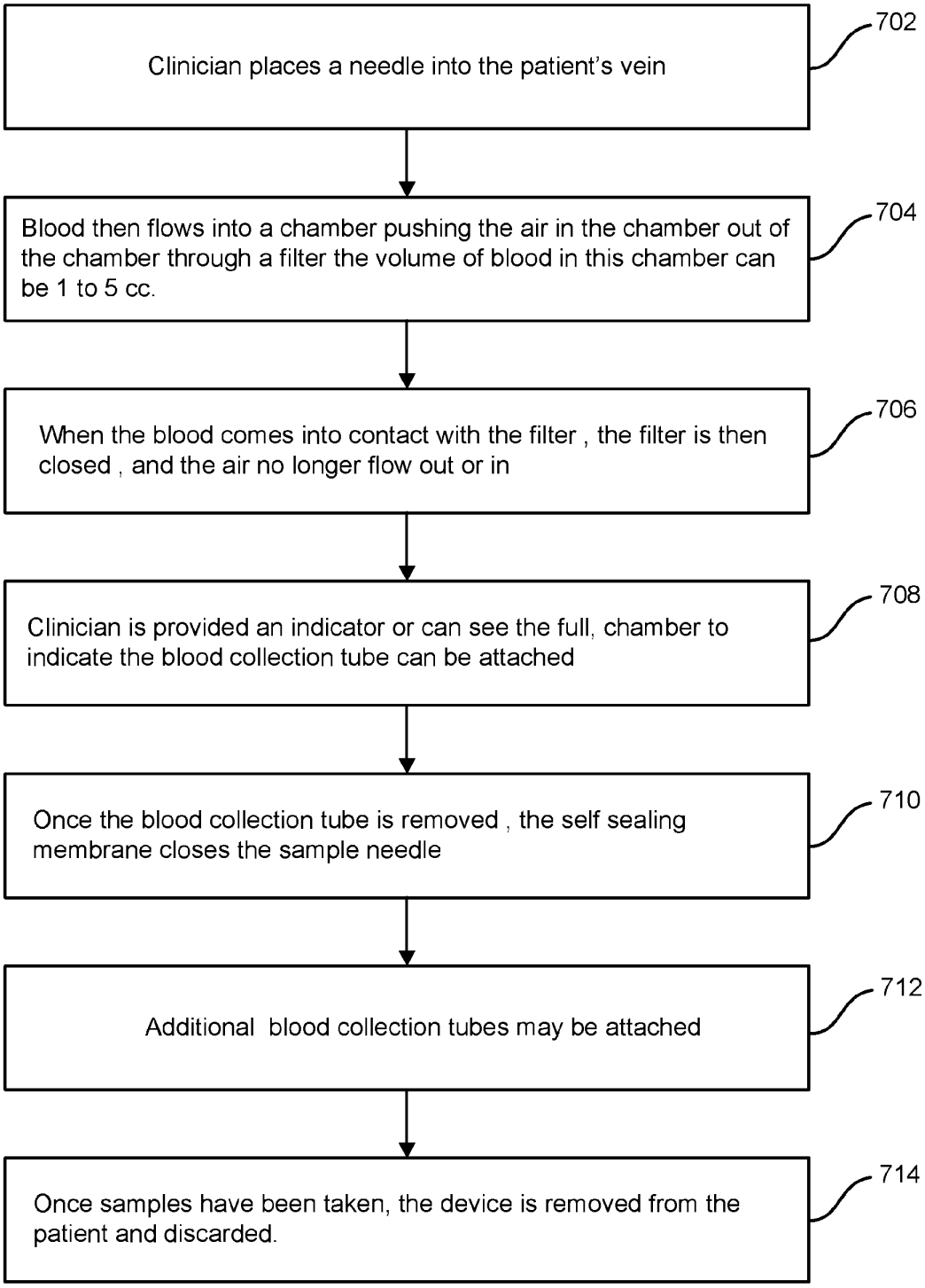

Clinician places a needle into the patient's vein
702
Blood then flows into a chamber pushing the air in the chamber out of the chamber through a filter the volume of blood in this chamber can be 1 to 5 cc.
704
When the blood comes into contact with the filter , the filter is then closed , and the air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

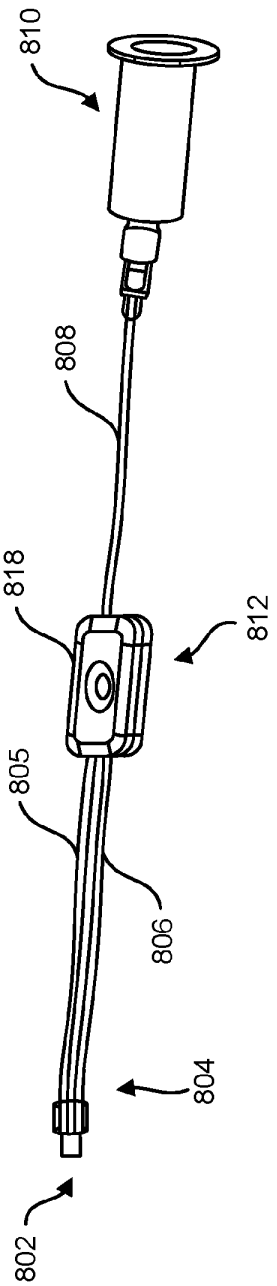


FIG. 8A

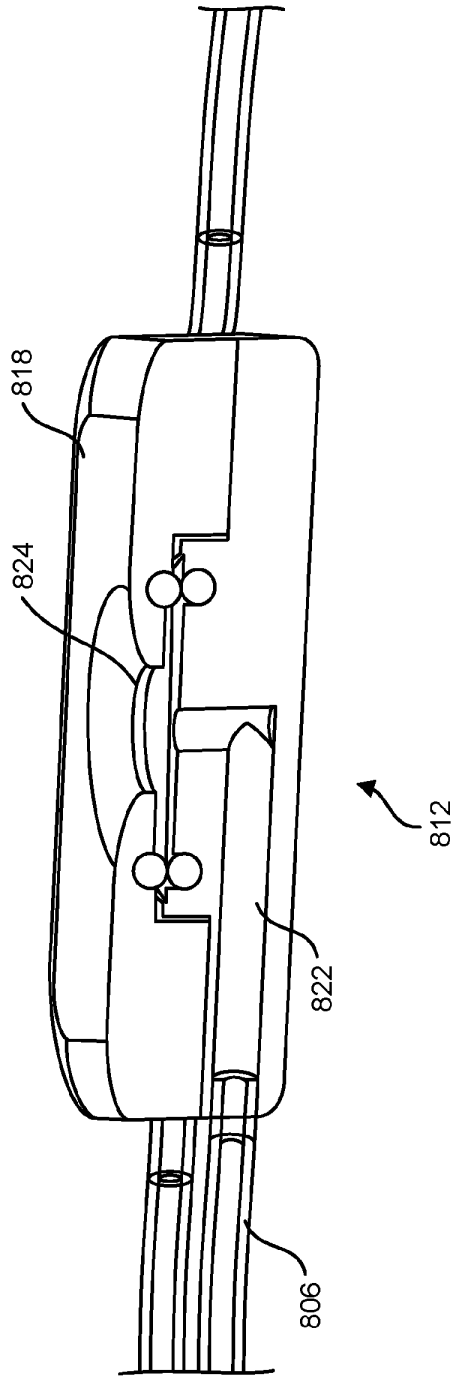


FIG. 8B

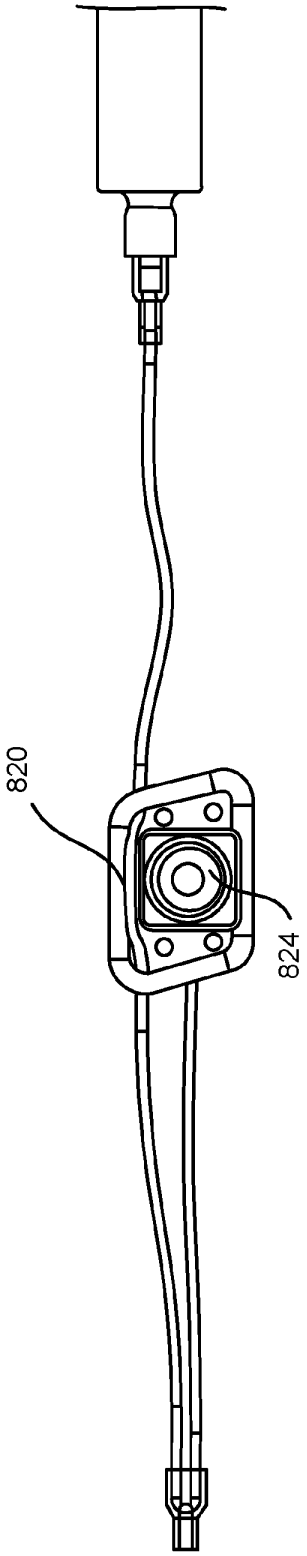


FIG. 8C

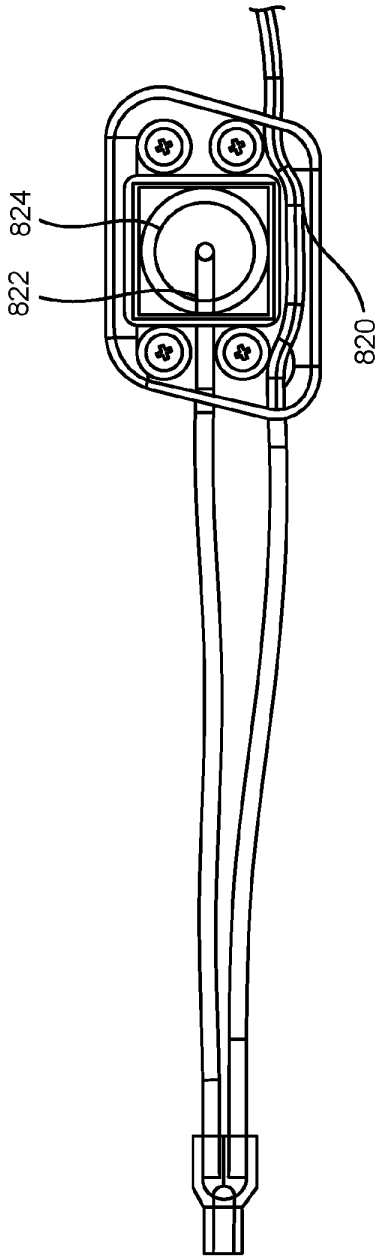


FIG. 8D

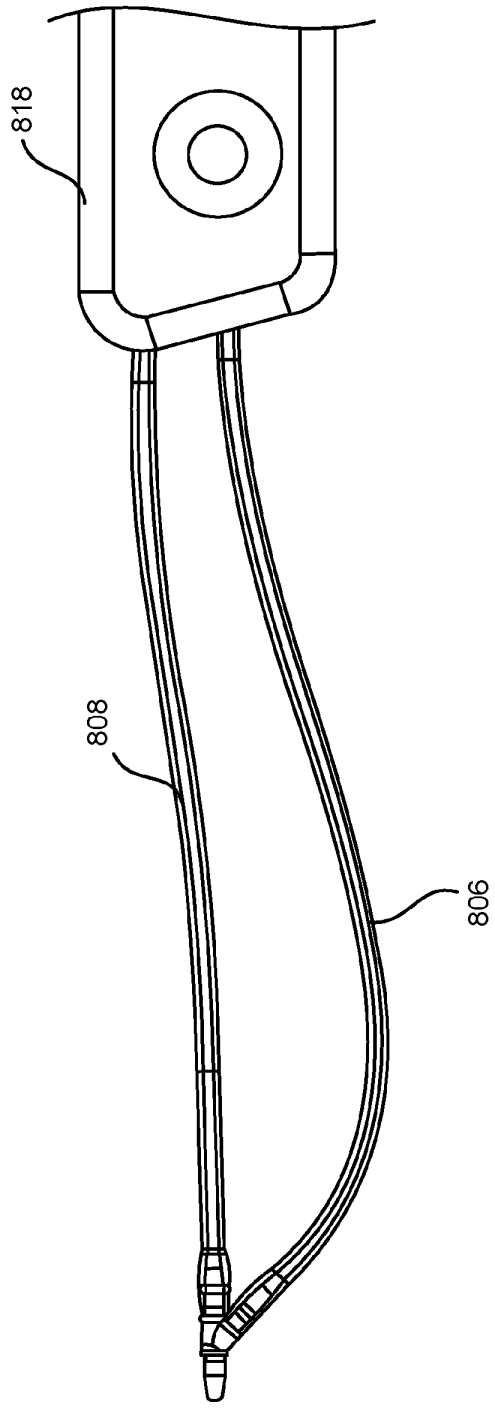


FIG. 8E

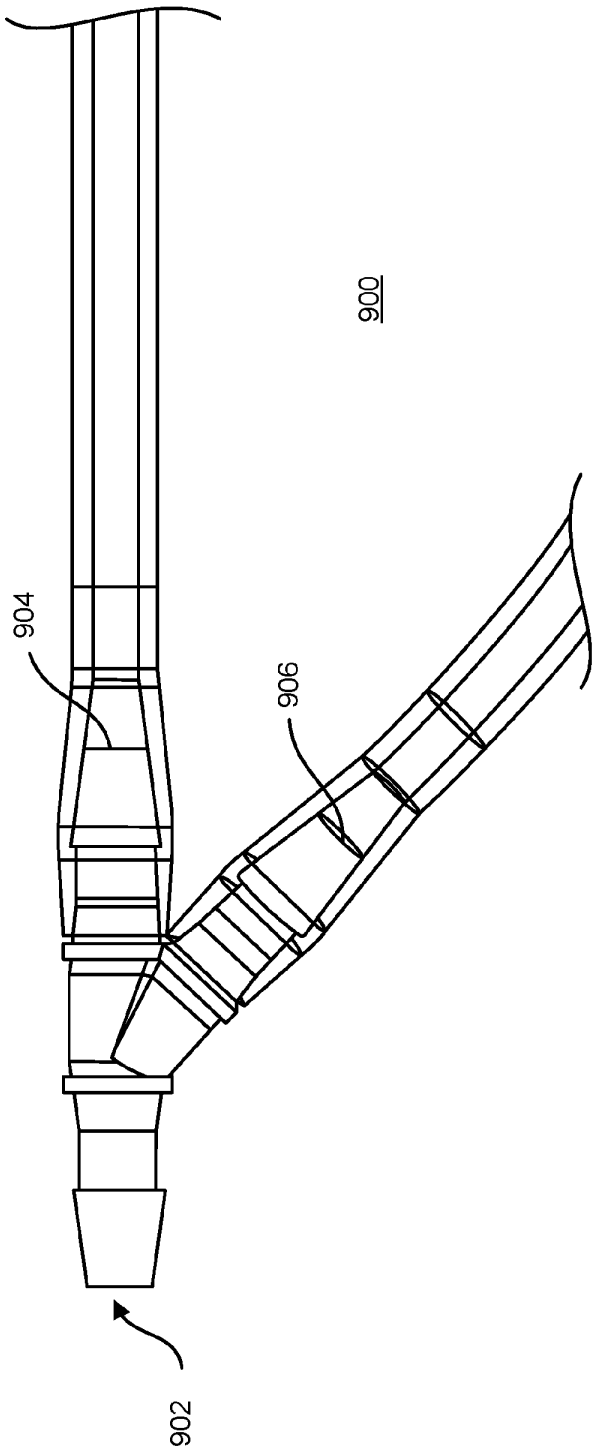


FIG. 9

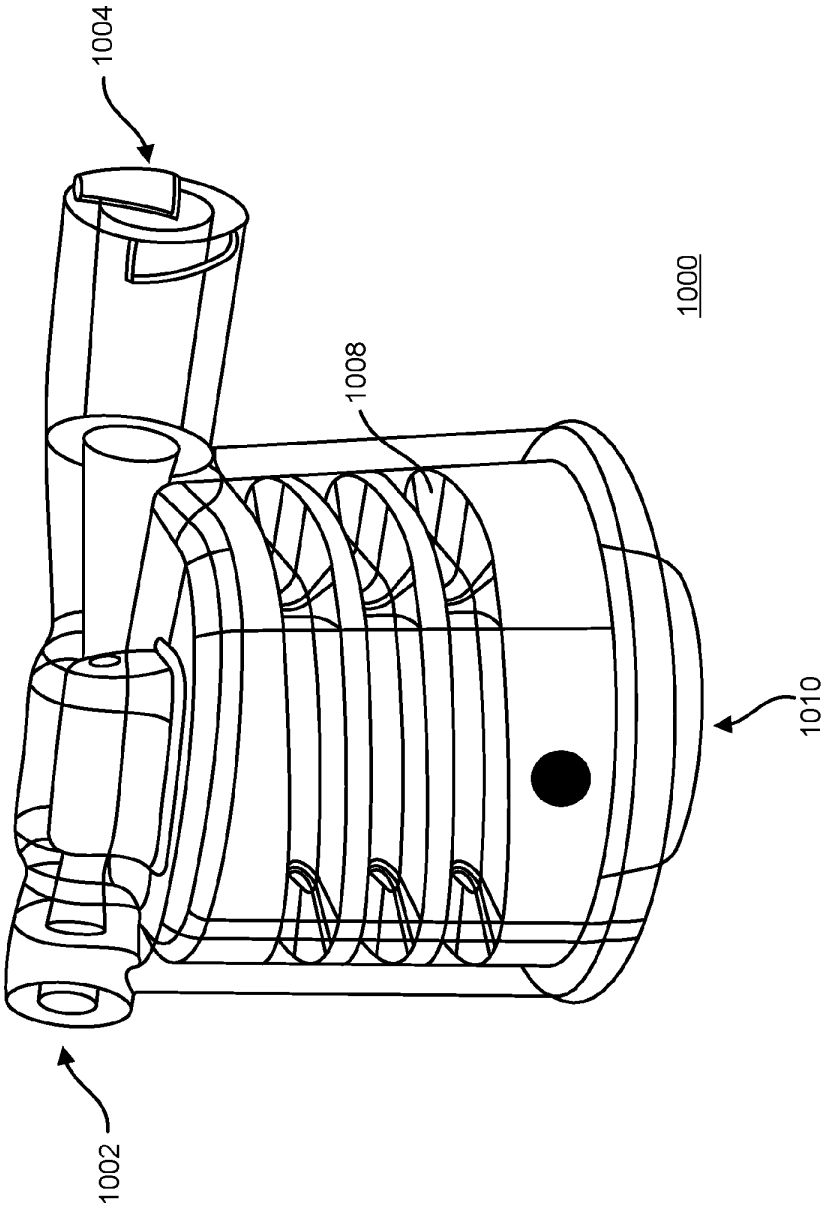


FIG. 10A

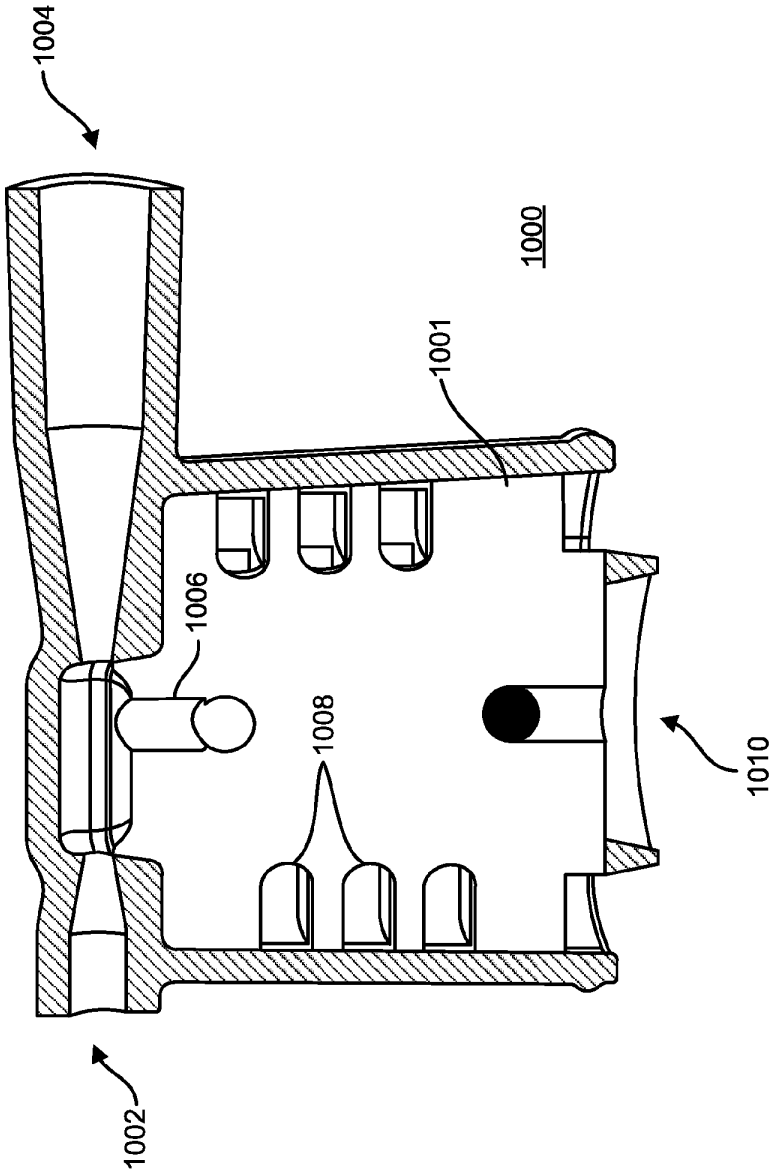


FIG. 10B

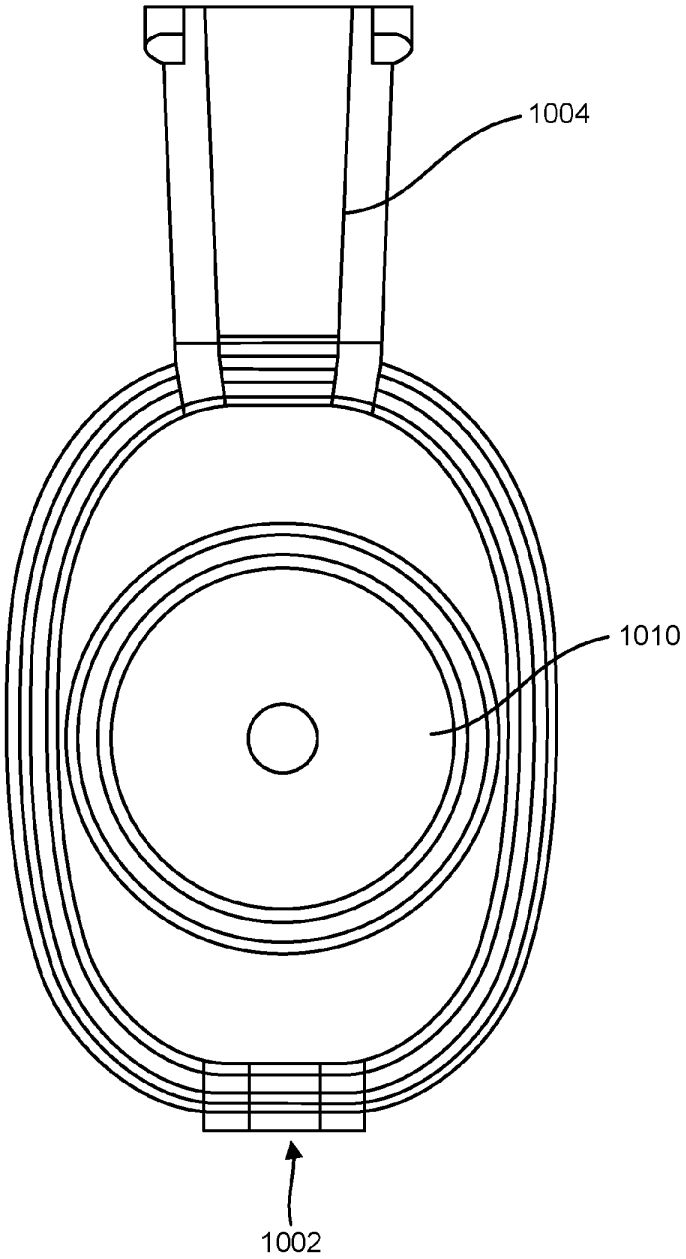


FIG. 10C

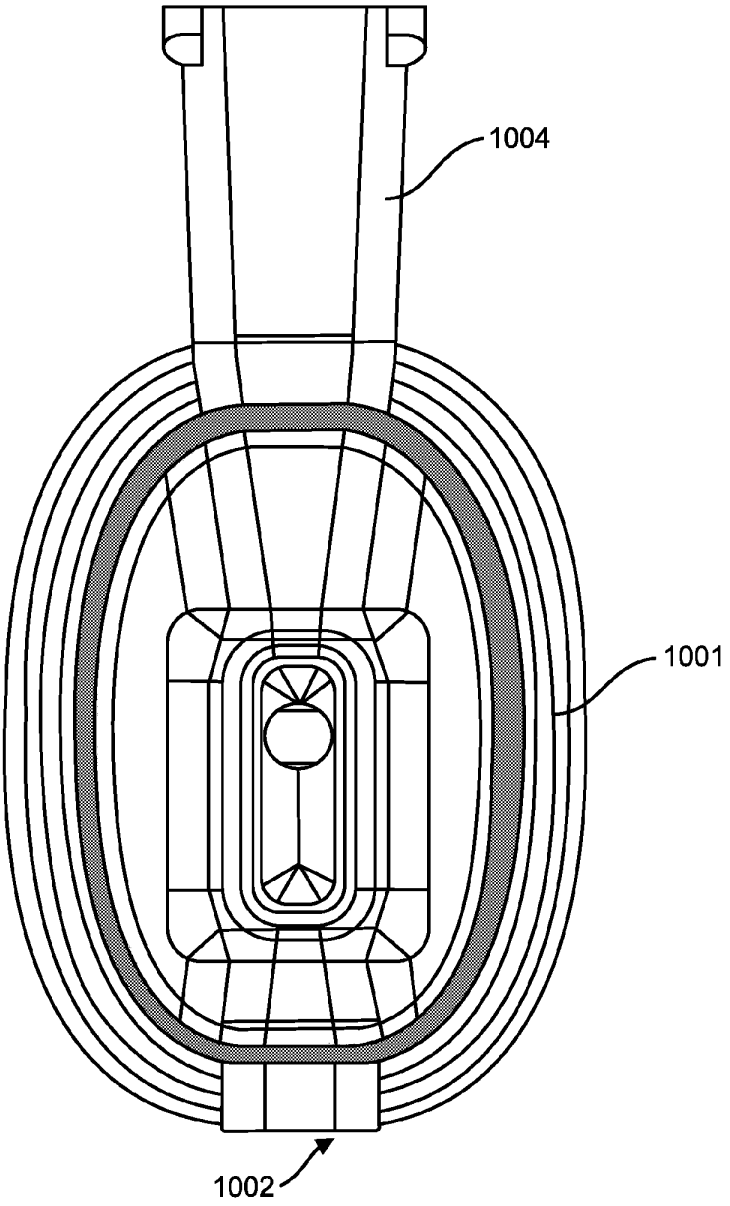


FIG. 10D

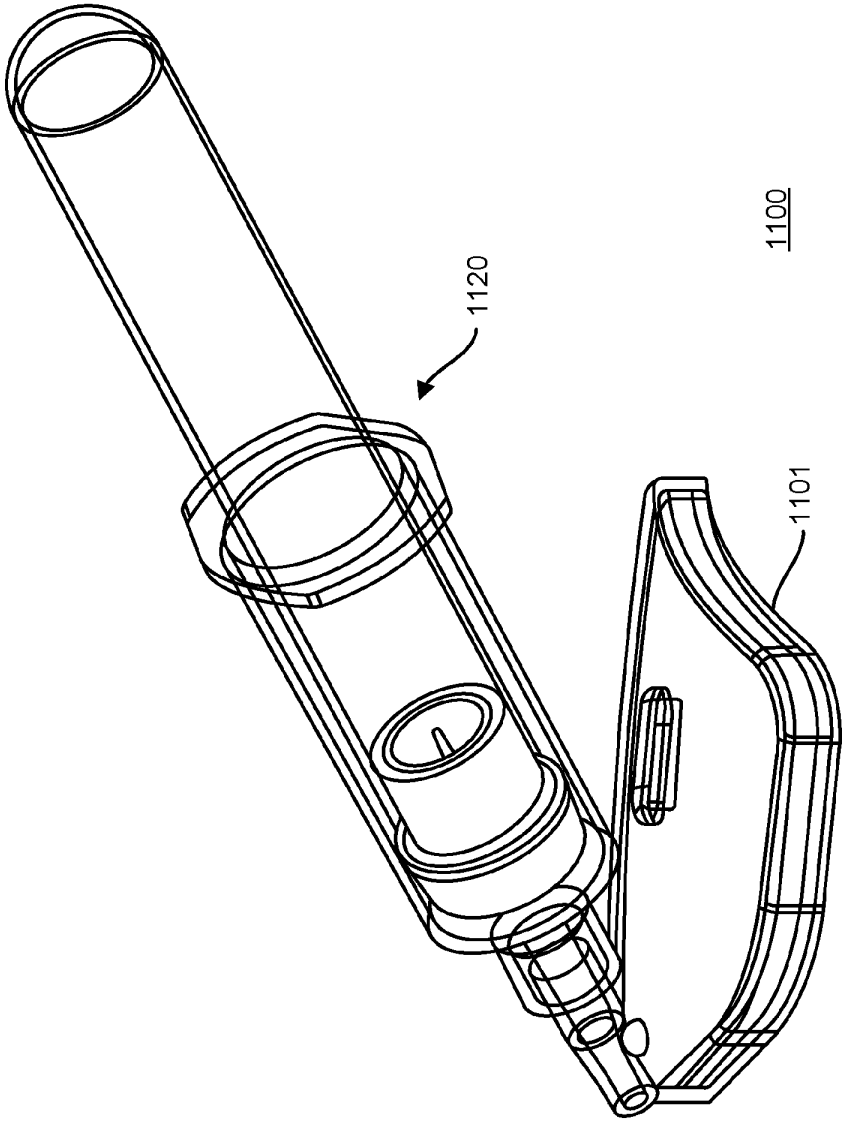


FIG. 11A

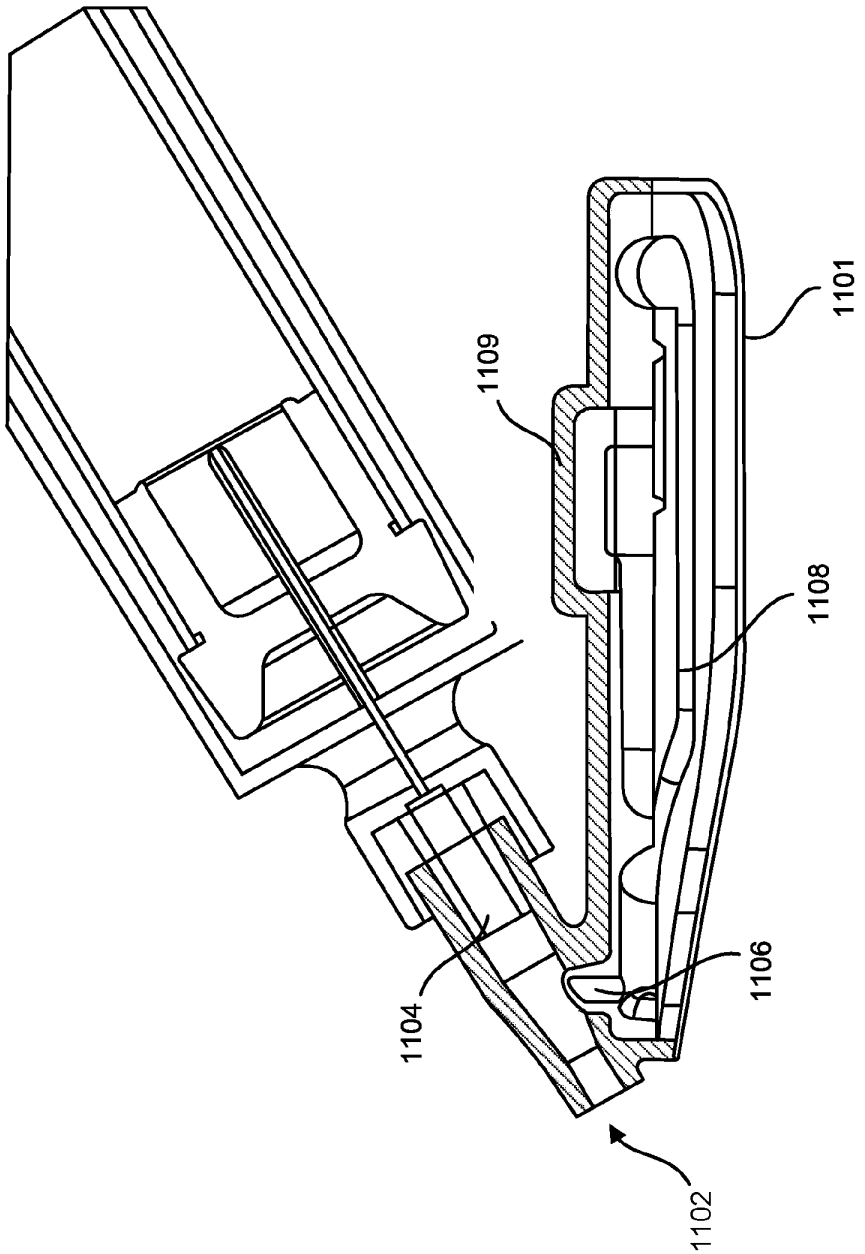


FIG. 11B

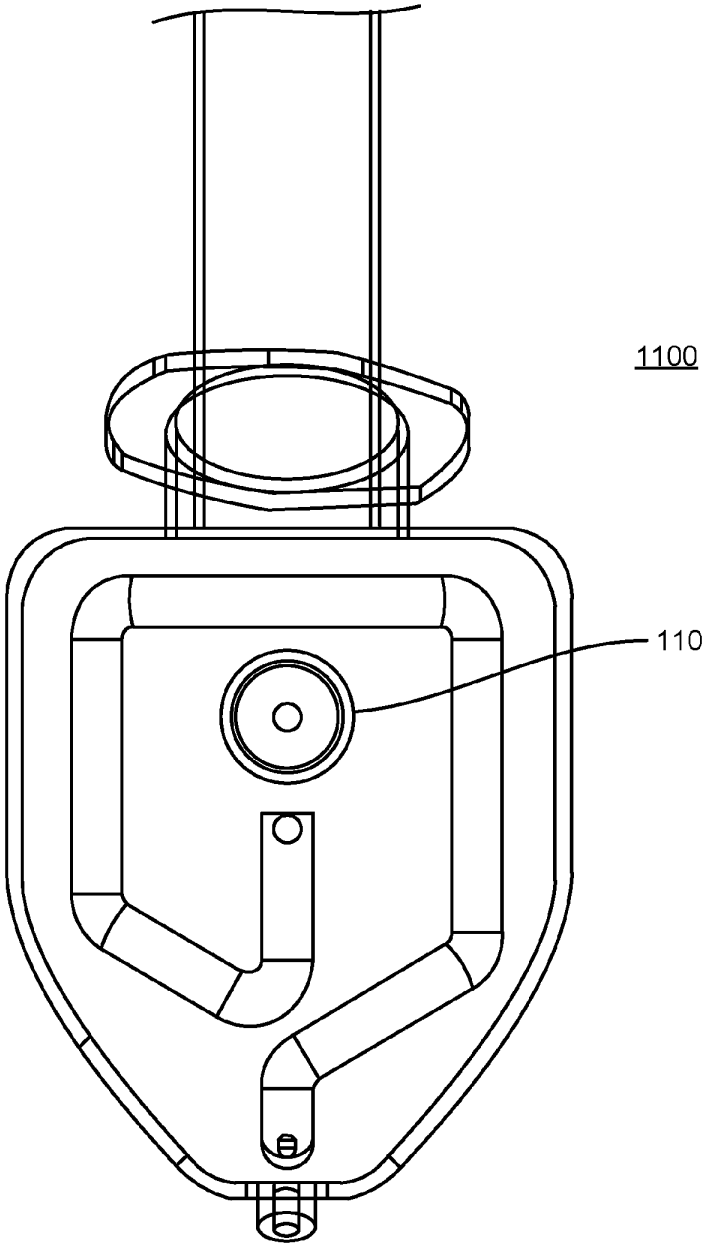


FIG. 11C

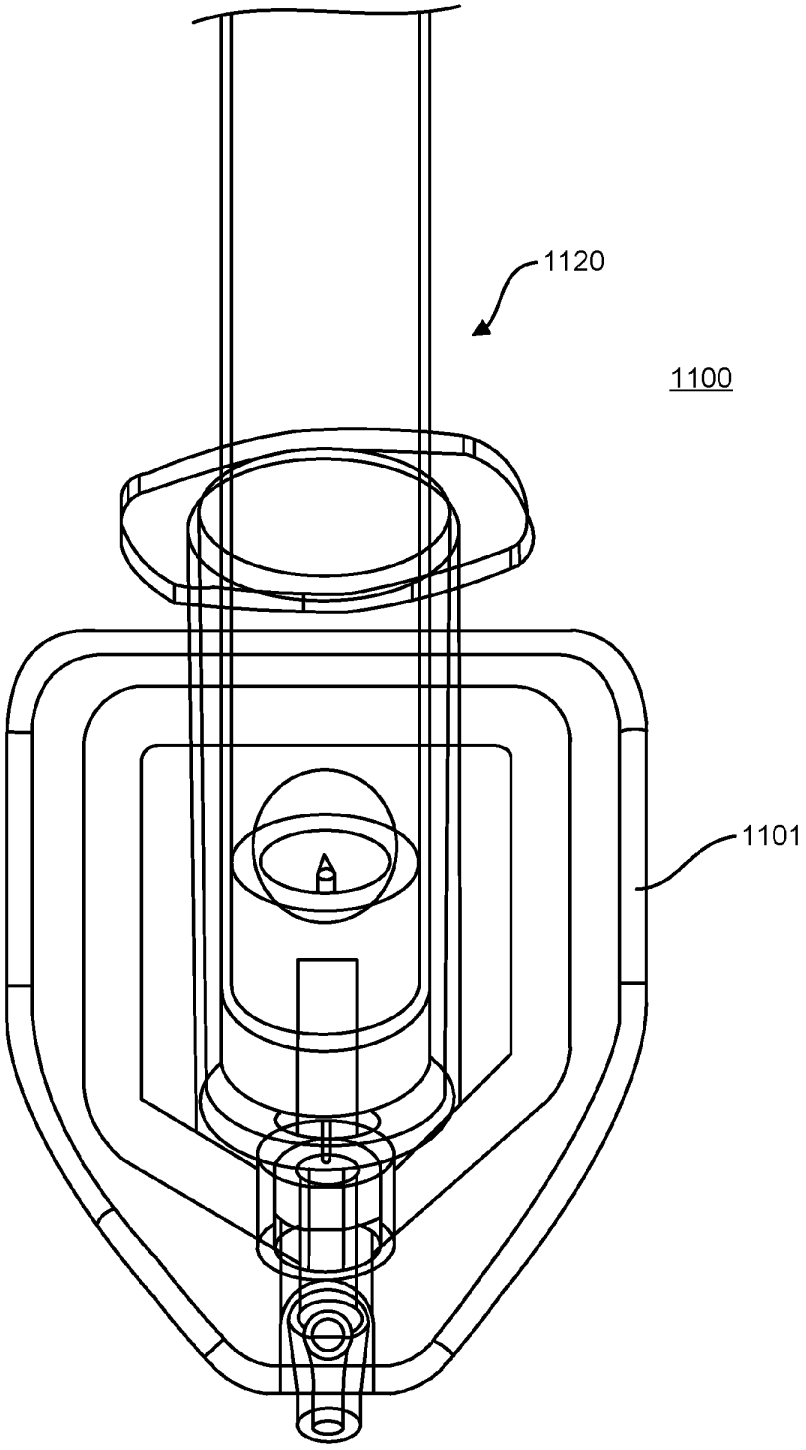


FIG. 11D

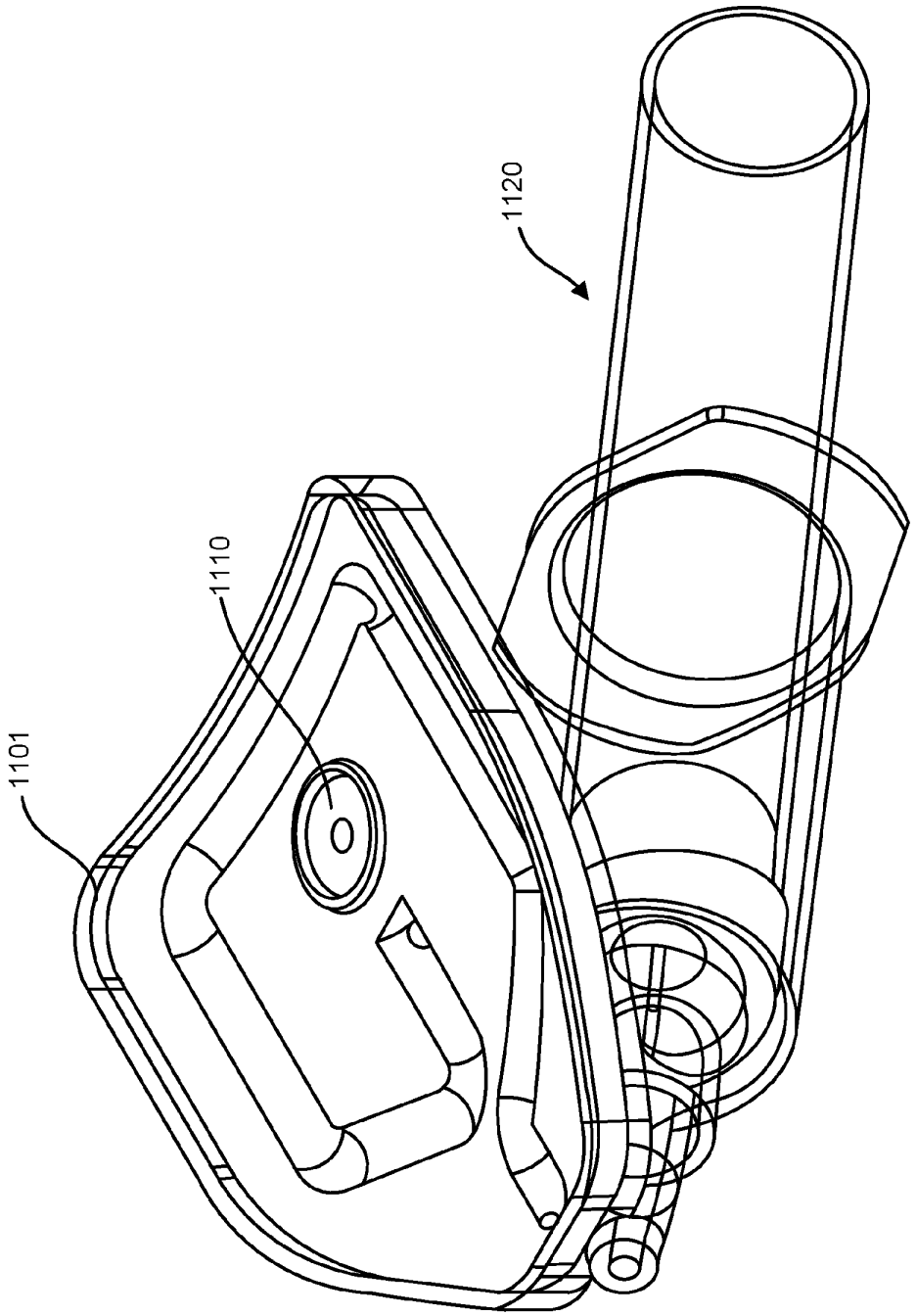


FIG. 11E

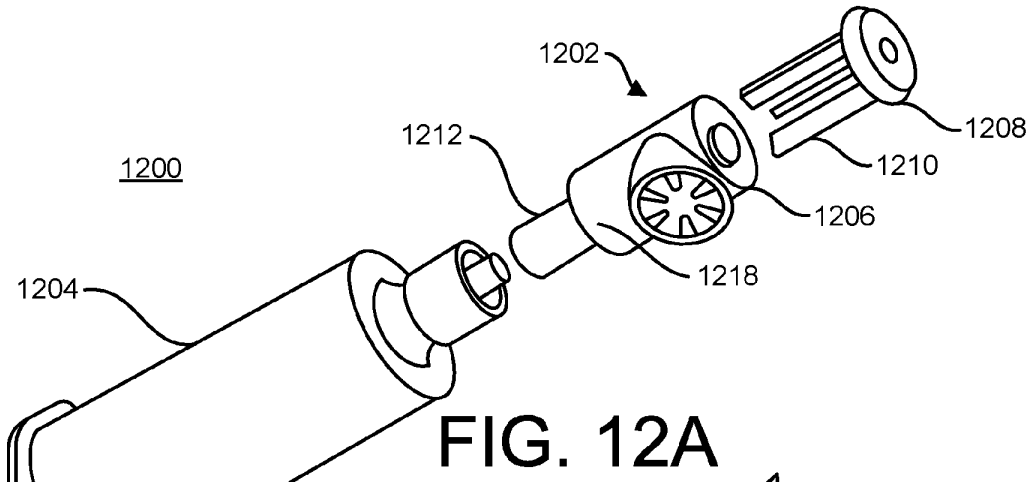


FIG. 12A

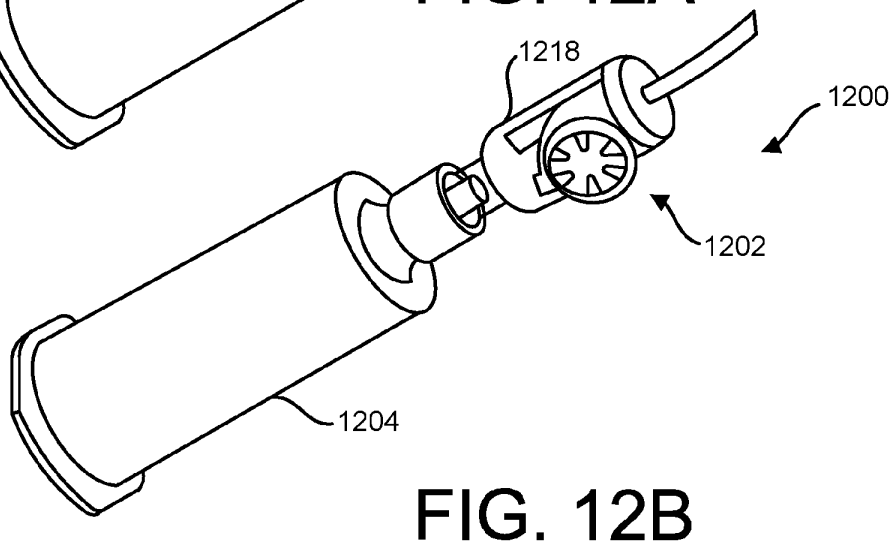


FIG. 12B

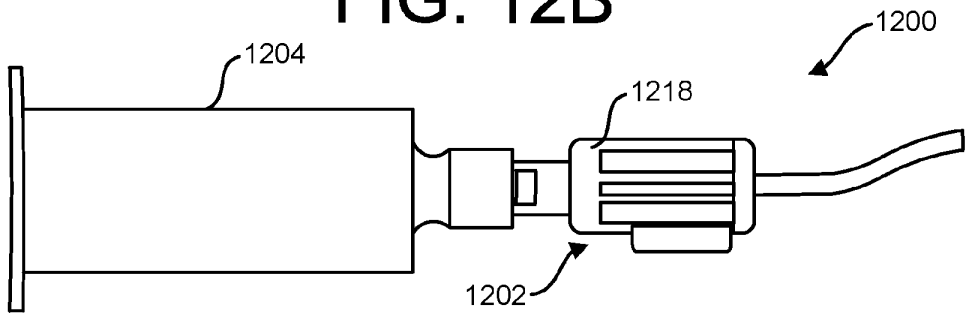


FIG. 12C

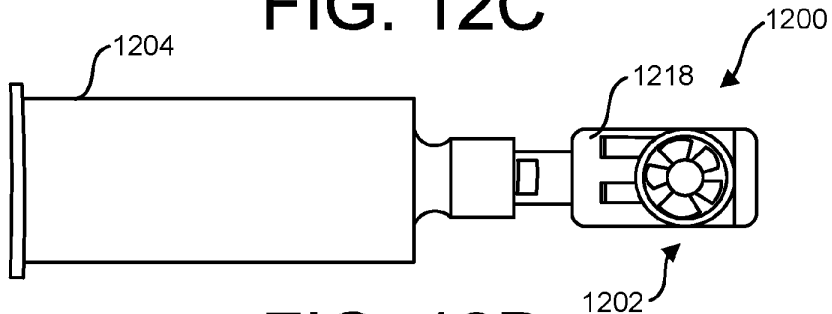


FIG. 12D

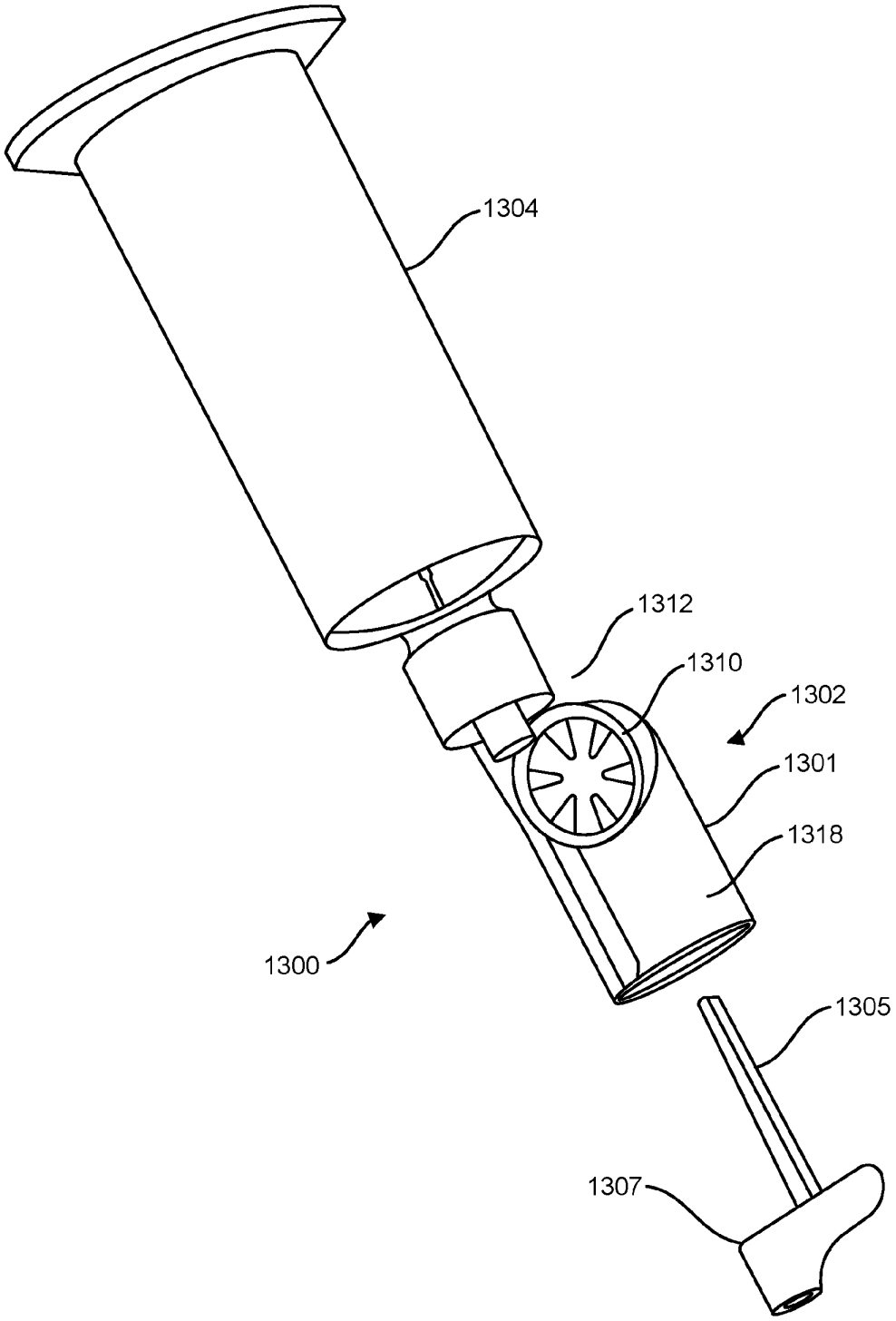


FIG. 13A

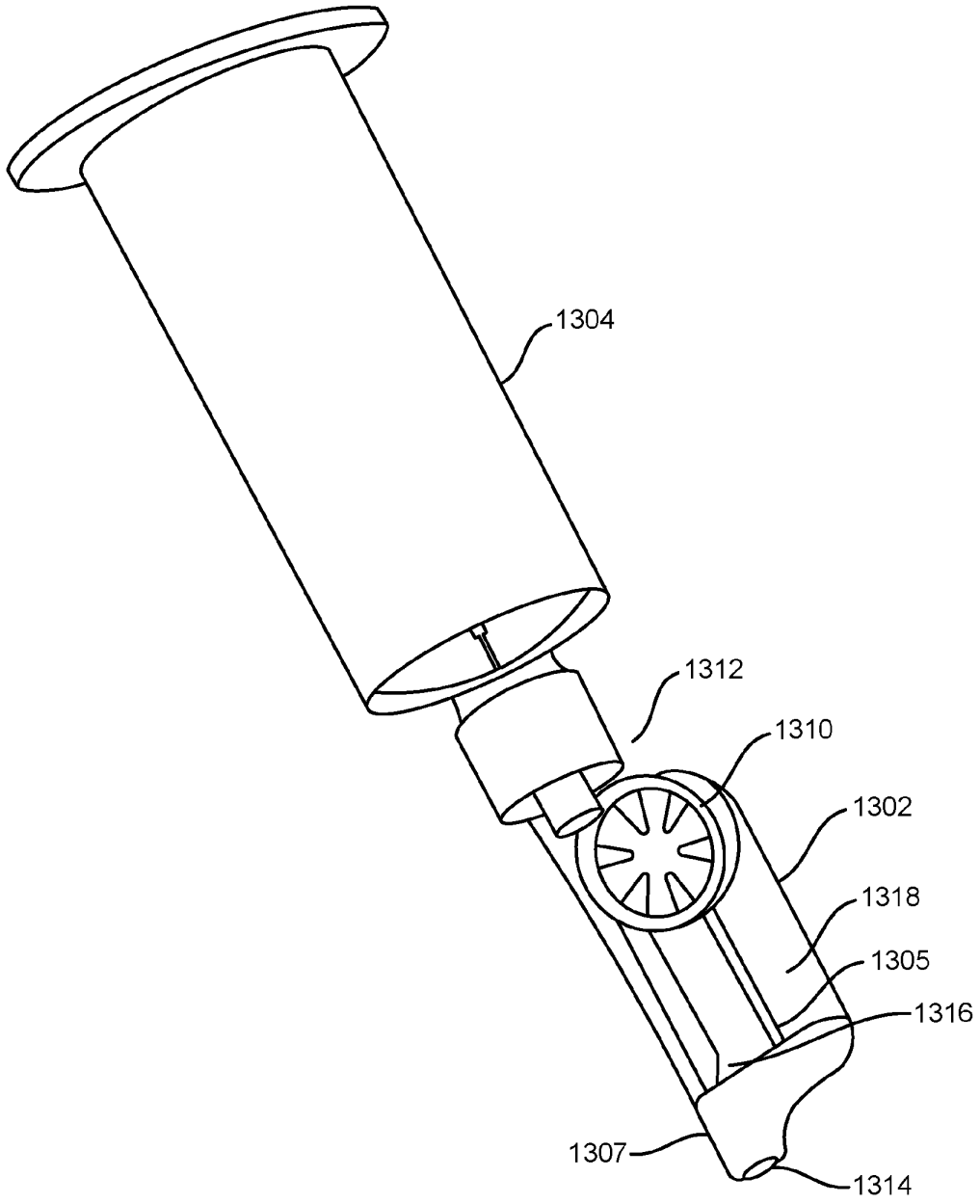


FIG. 13B

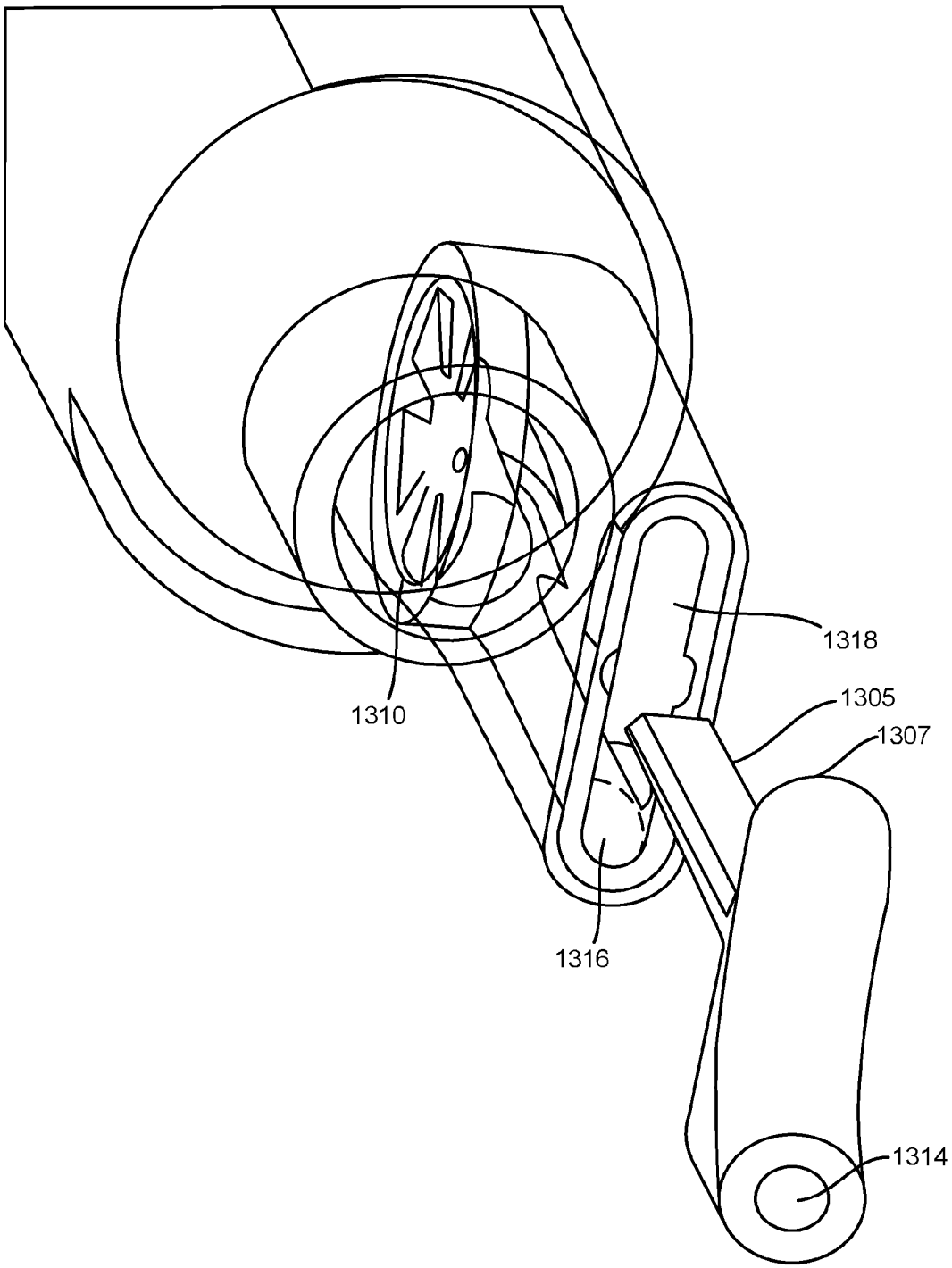


FIG. 13C

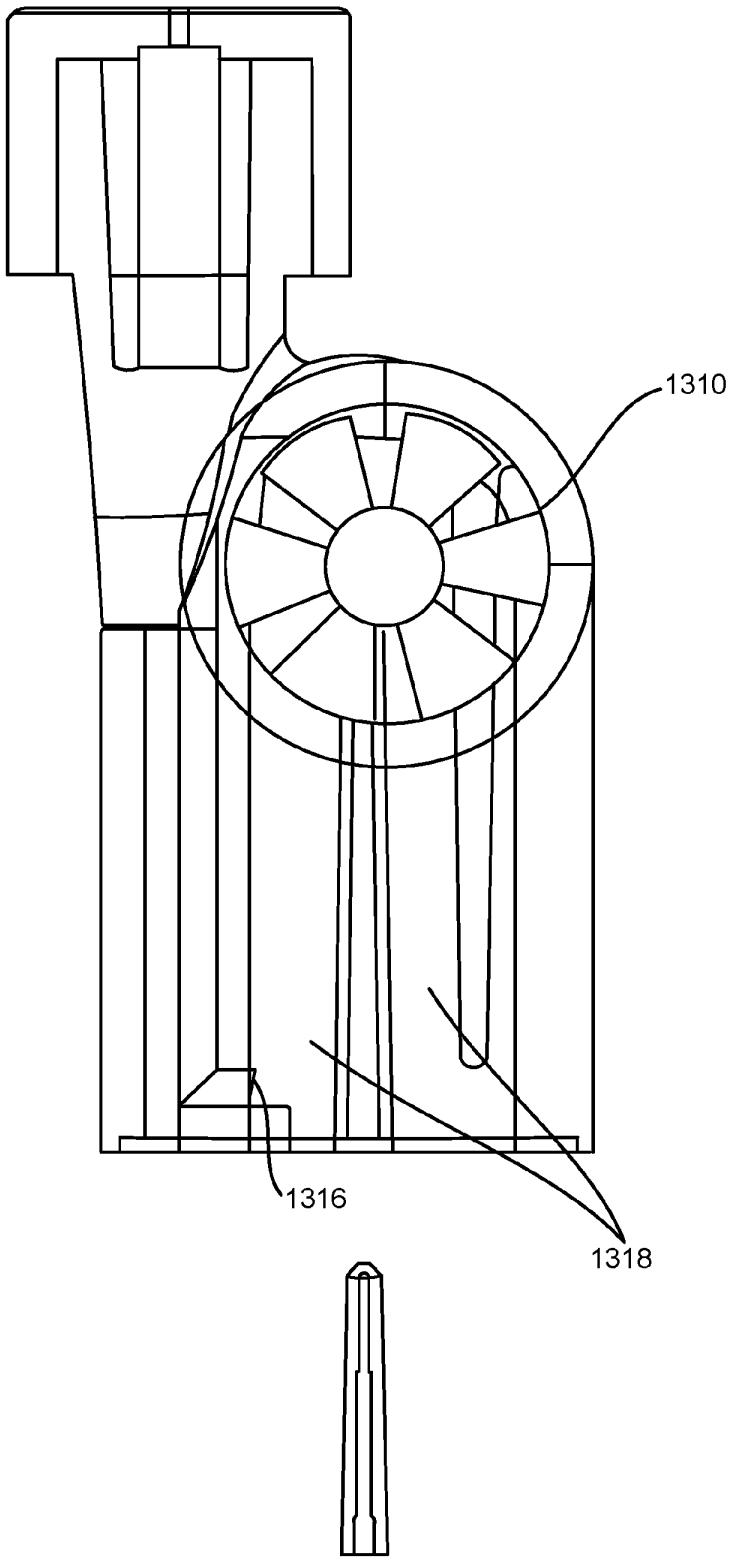


FIG. 13D

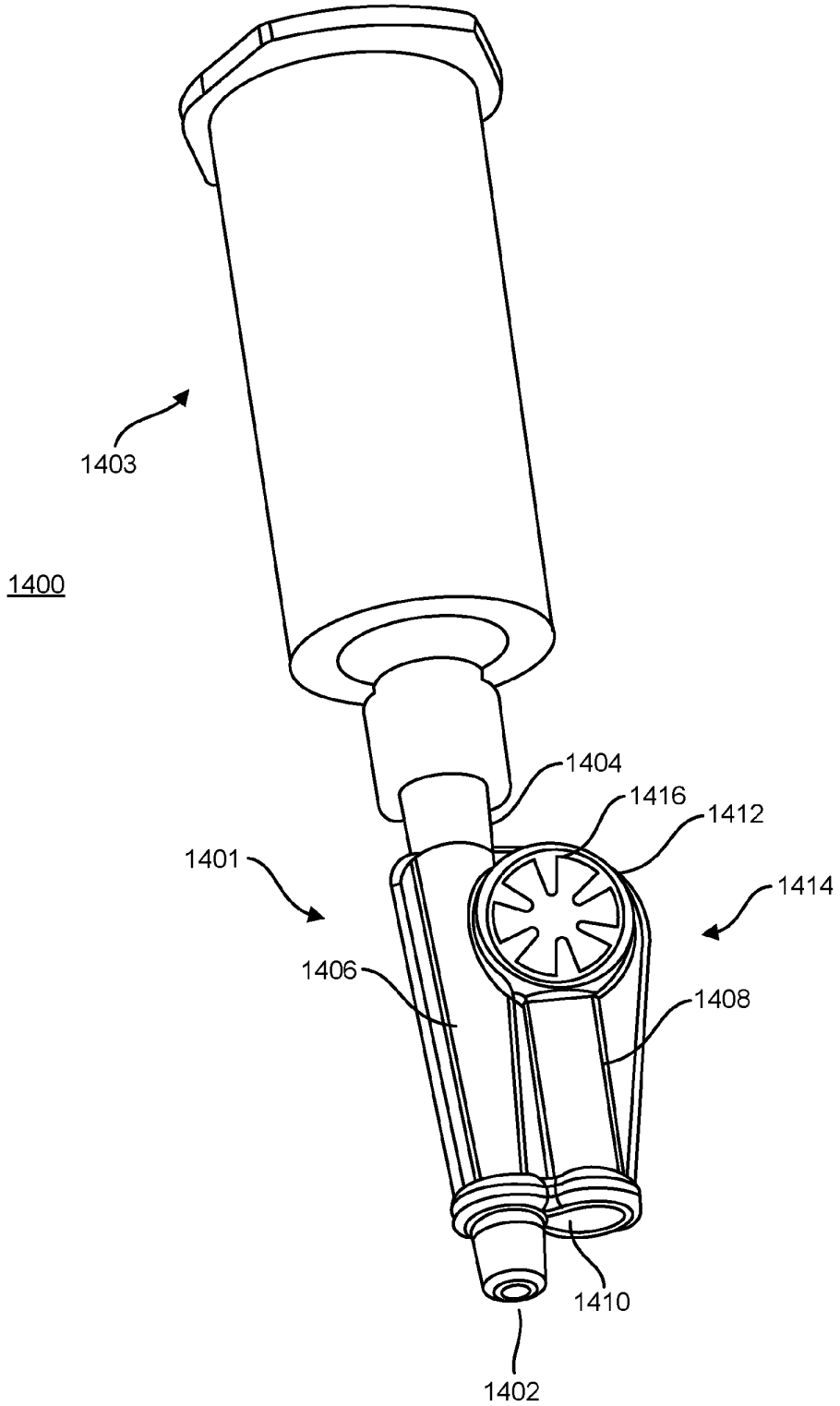


FIG. 14A

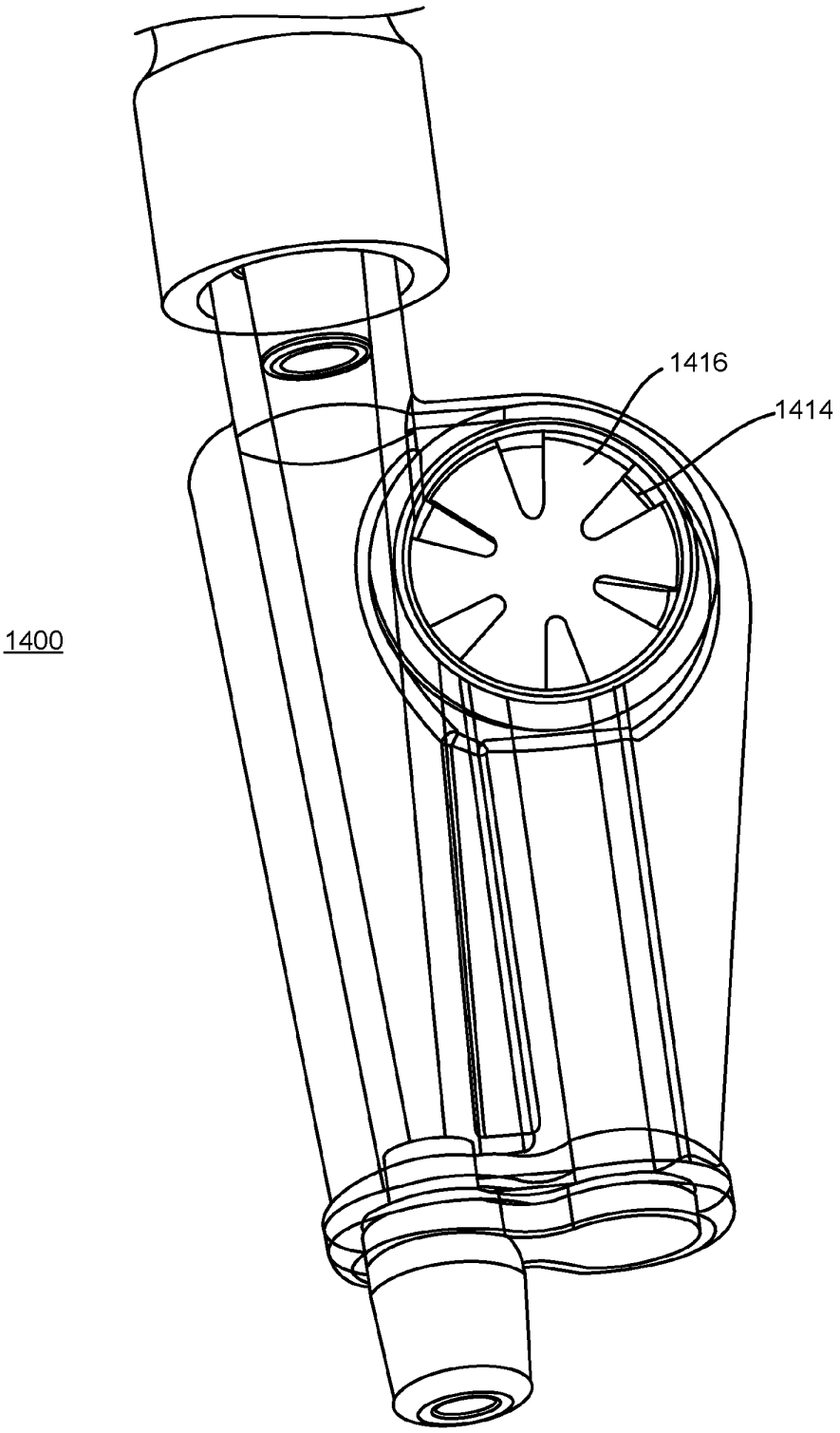


FIG. 14B

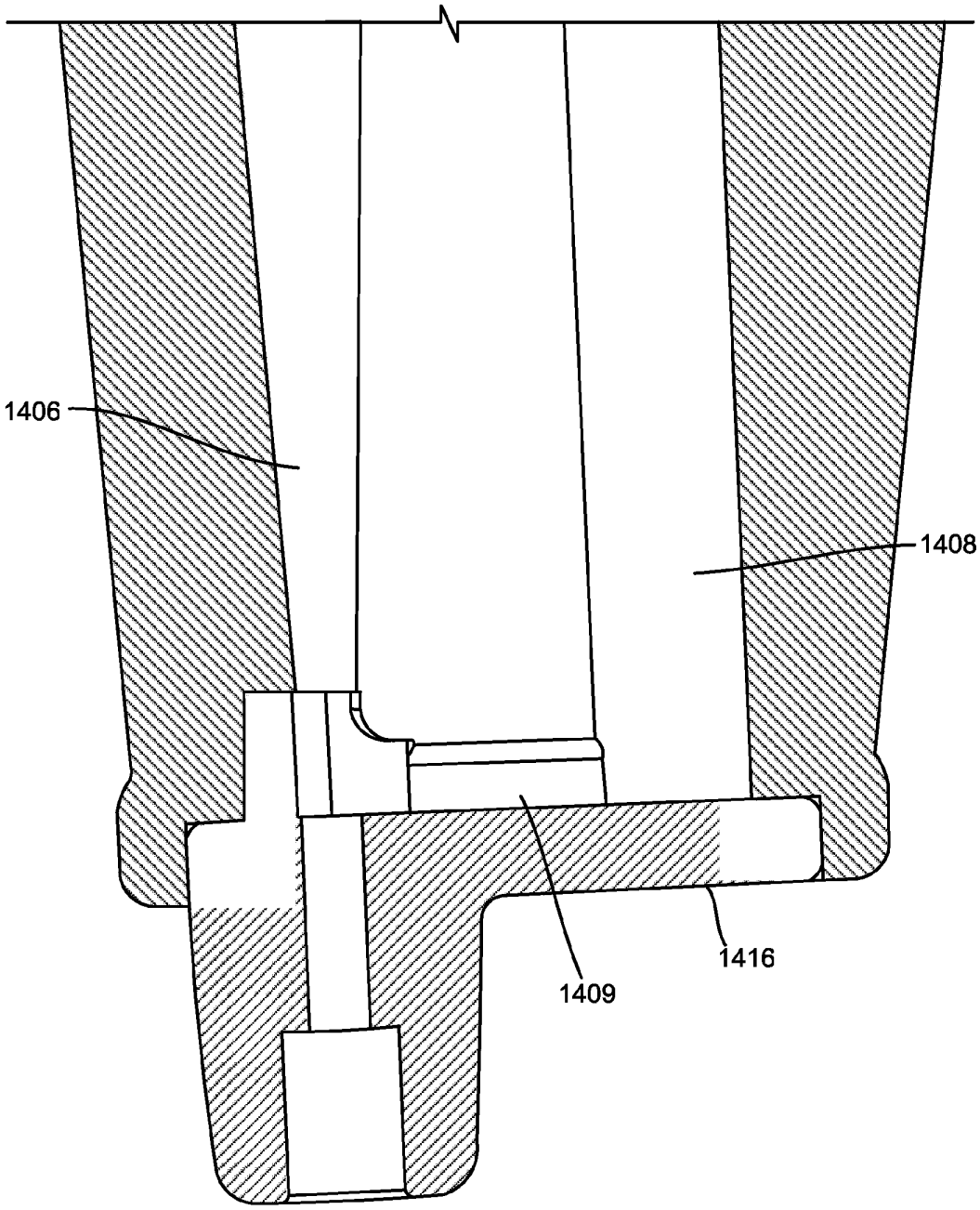


FIG. 14C

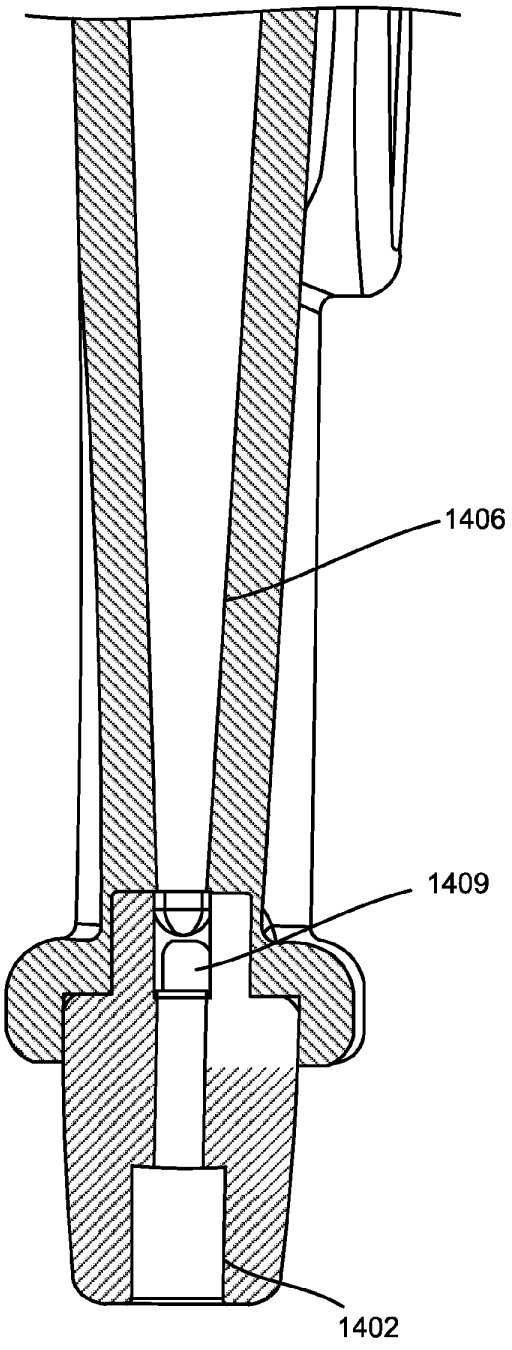


FIG. 14D

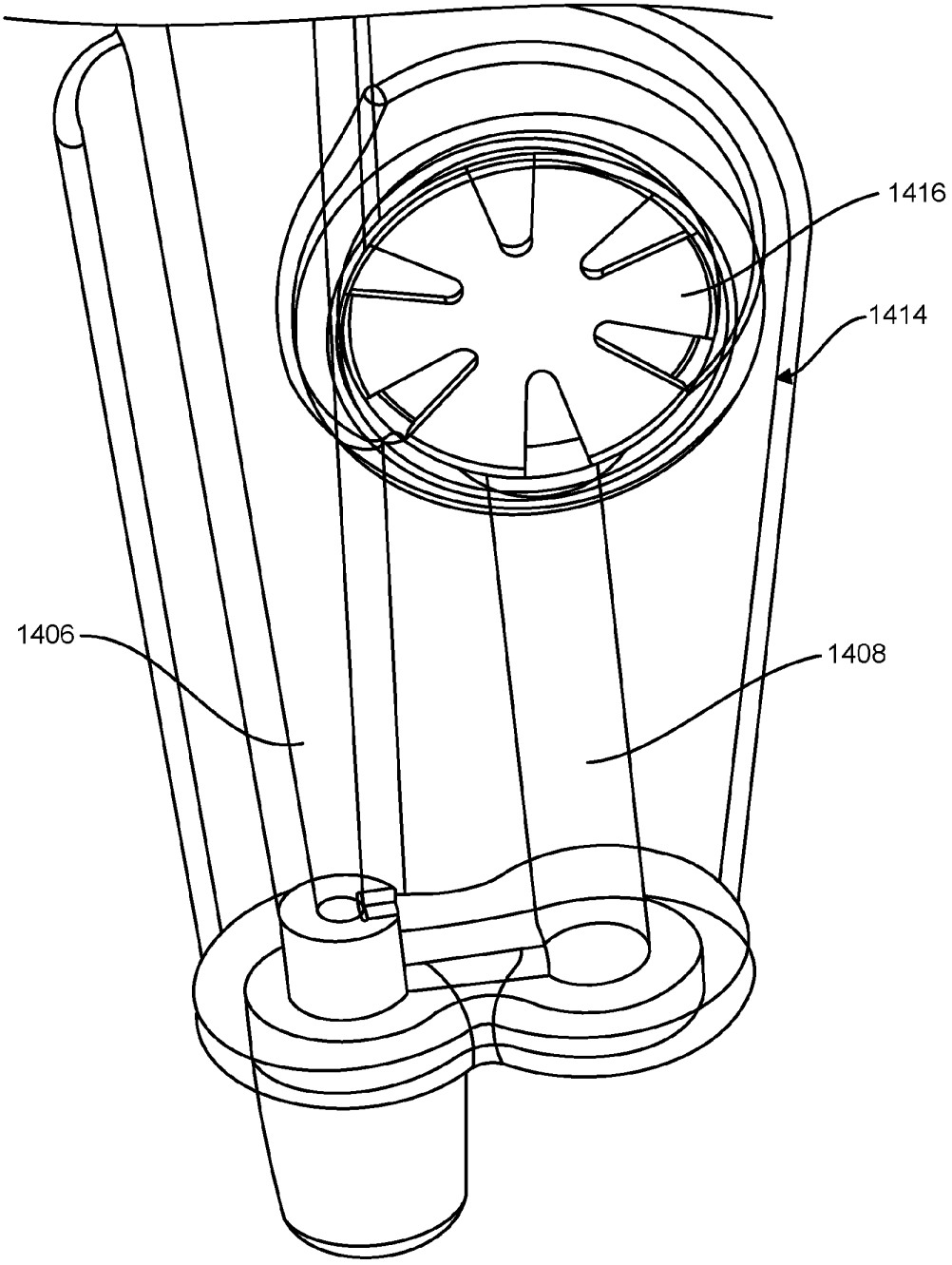


FIG. 14E

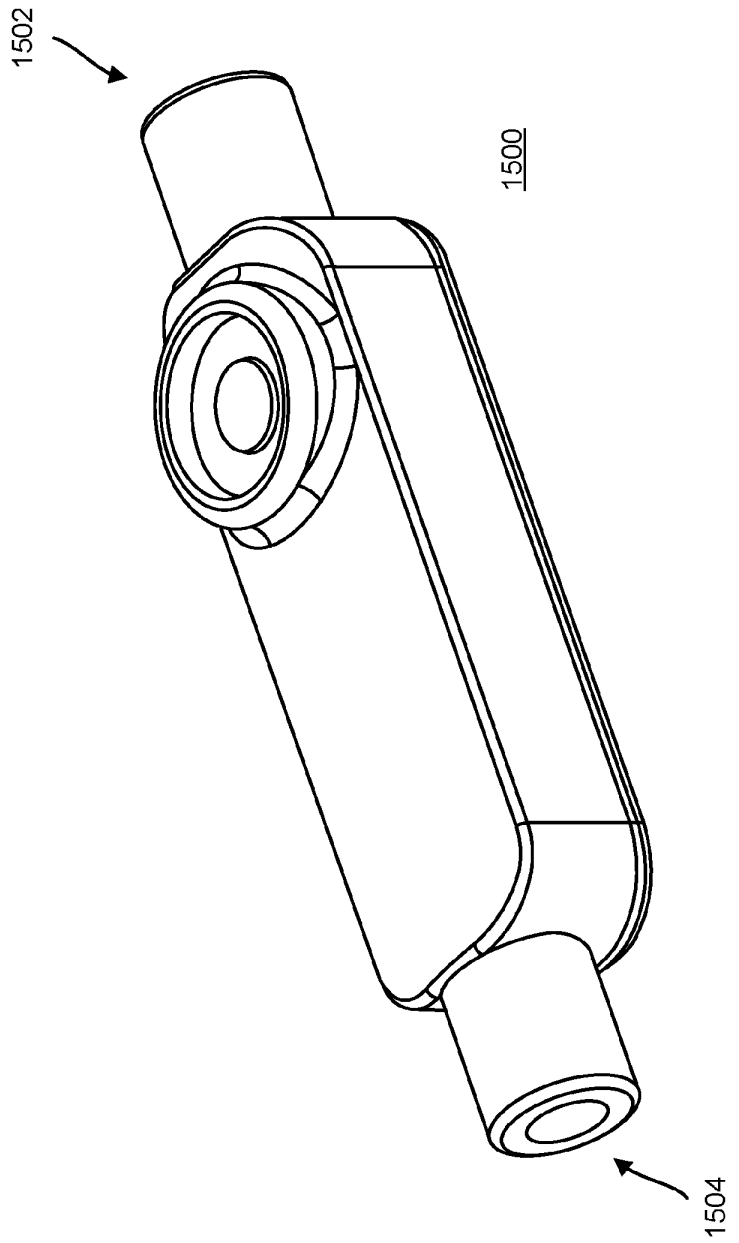


FIG. 15A

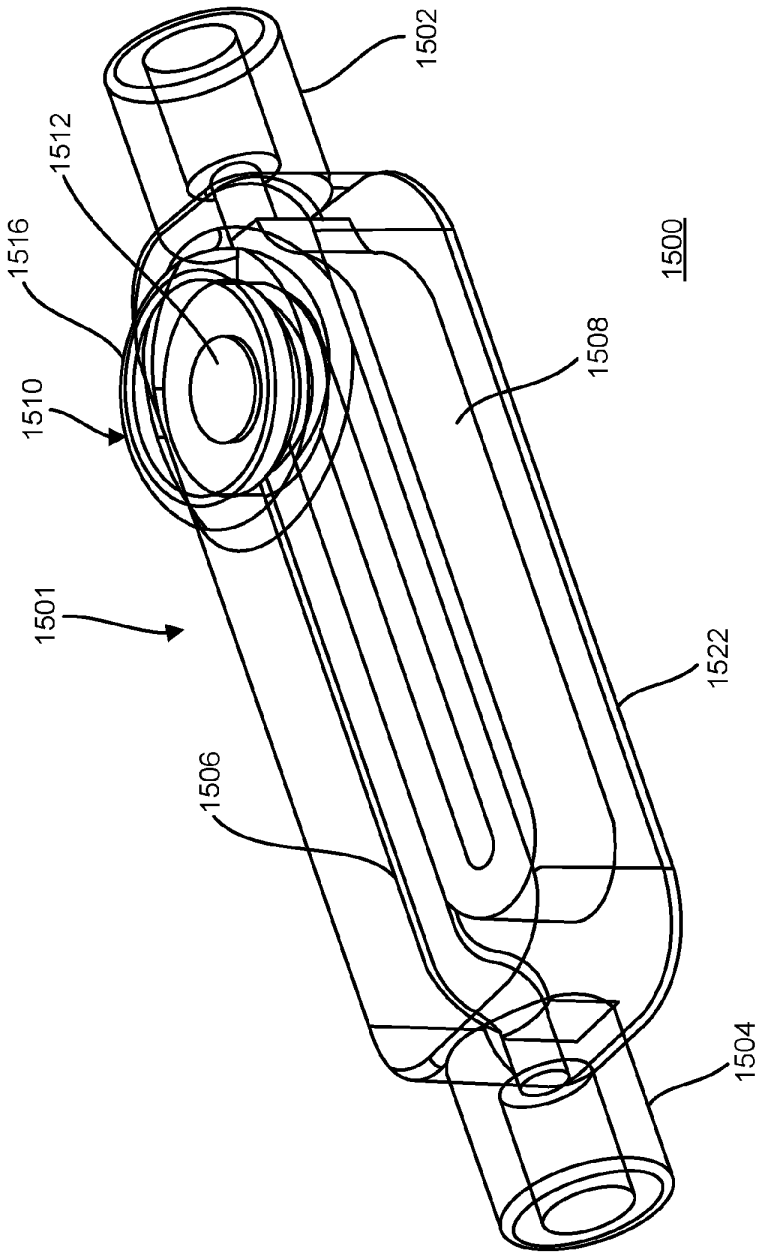


FIG. 15B

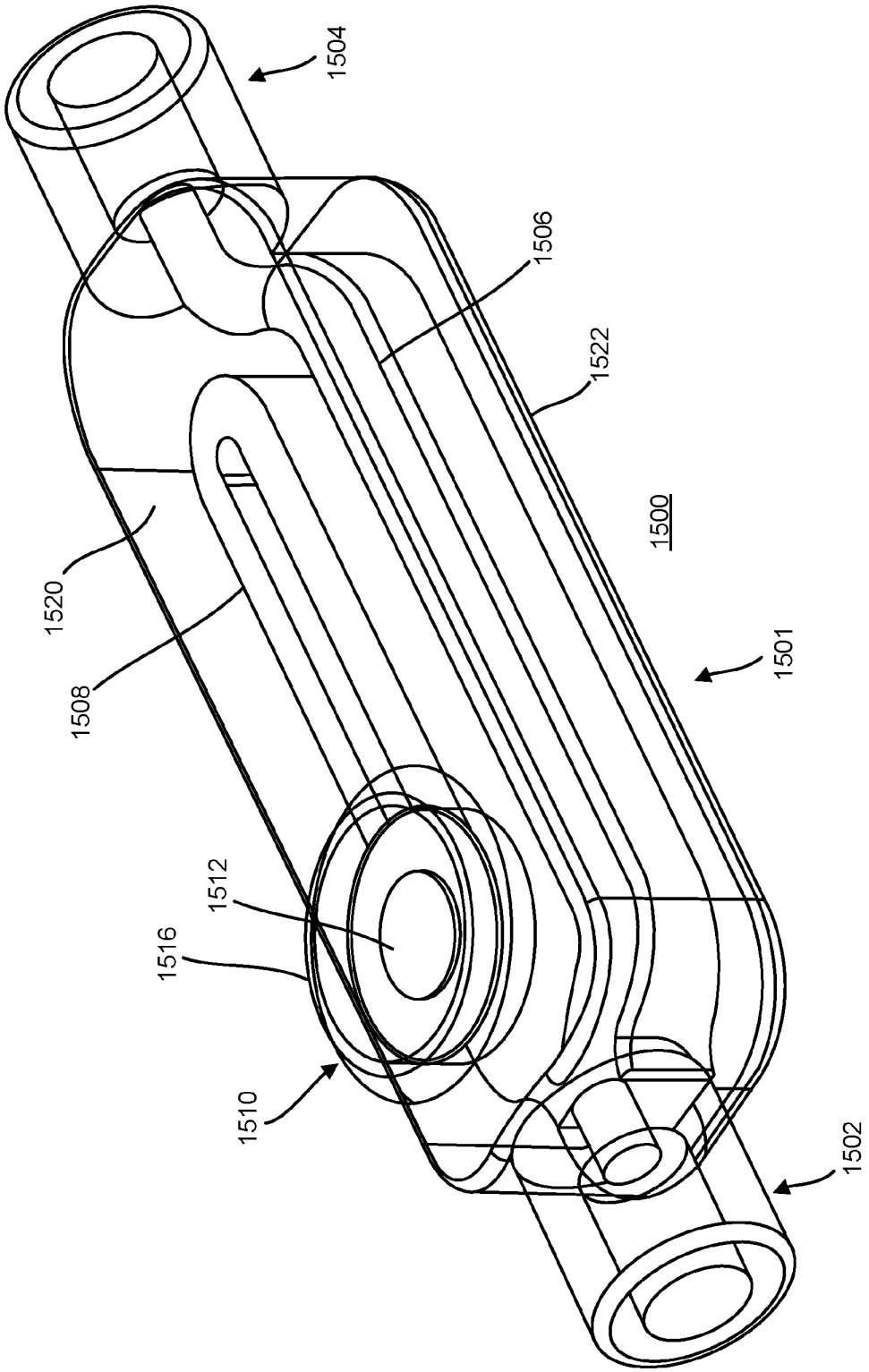


FIG. 15C

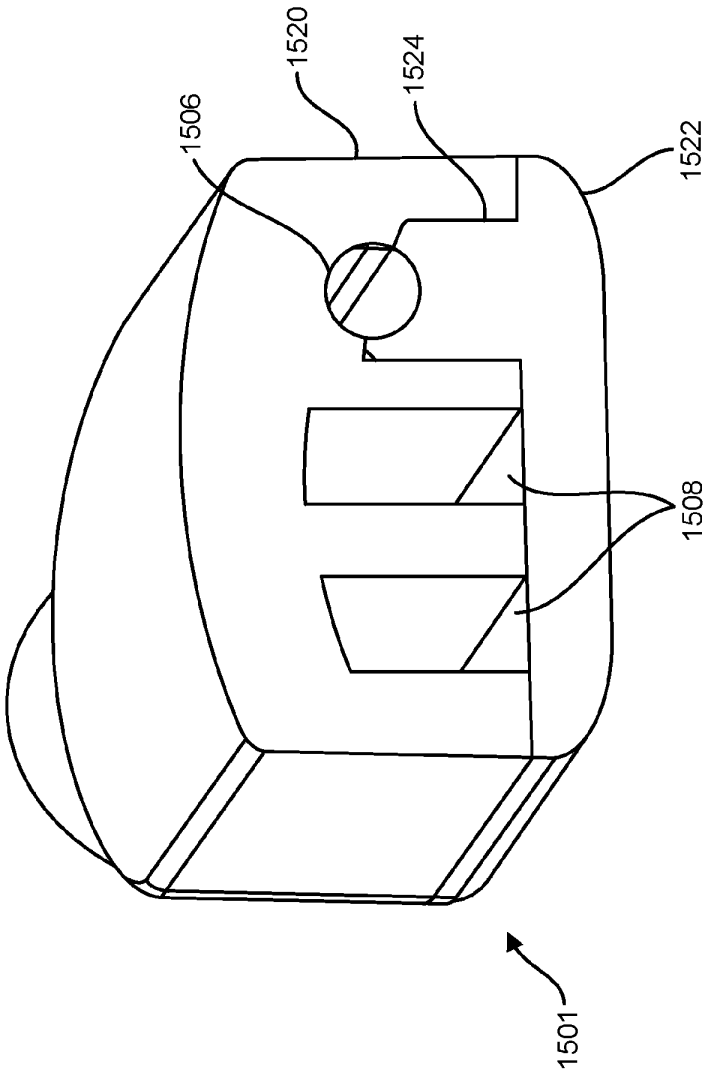


FIG. 15D

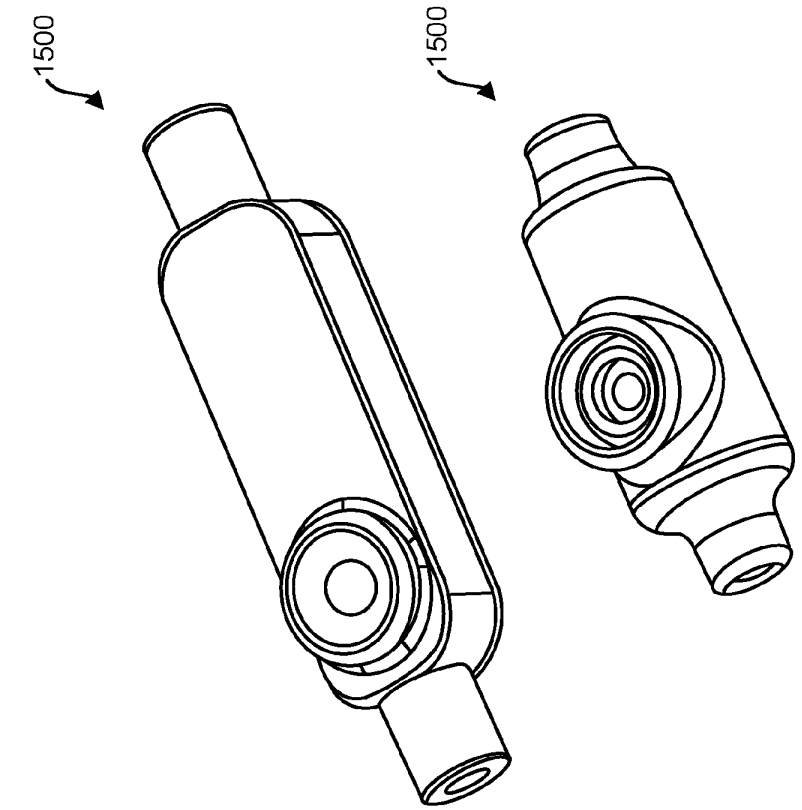


FIG. 15F

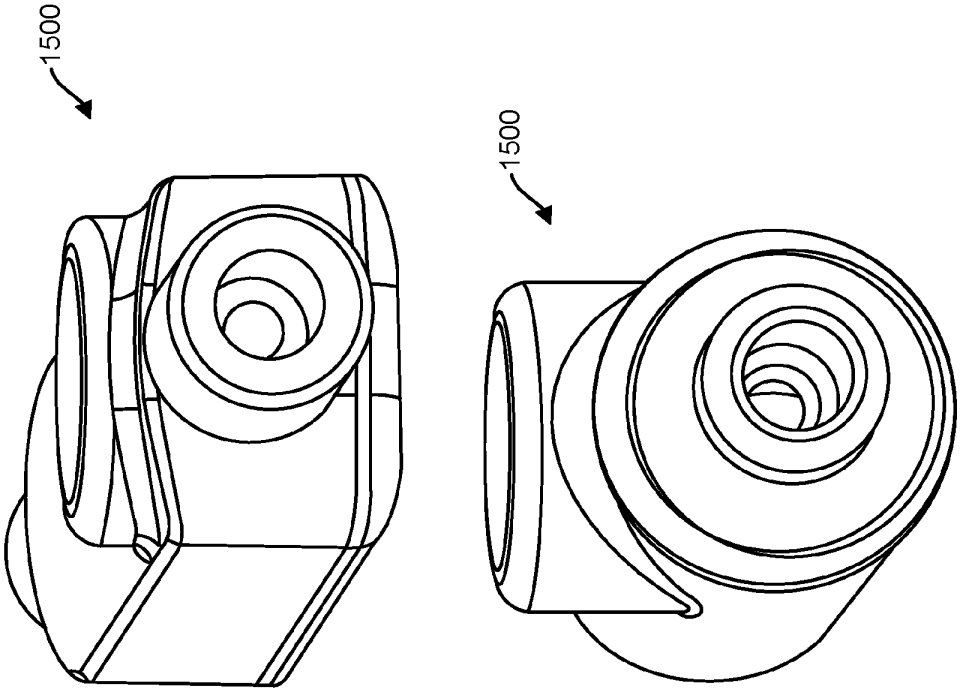


FIG. 15E

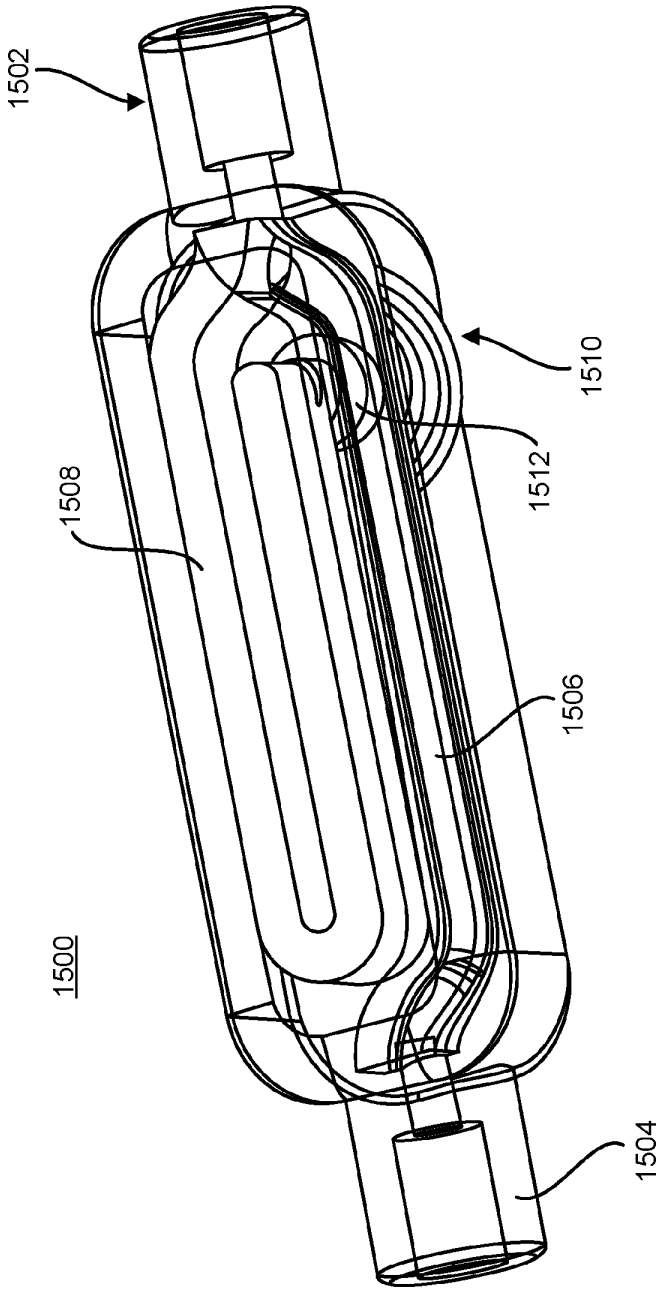


FIG. 15G

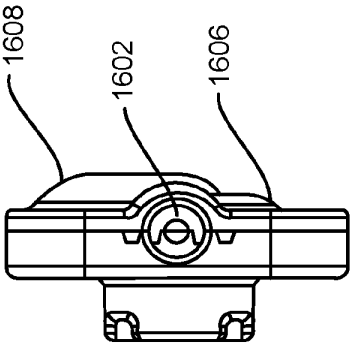


FIG. 16C

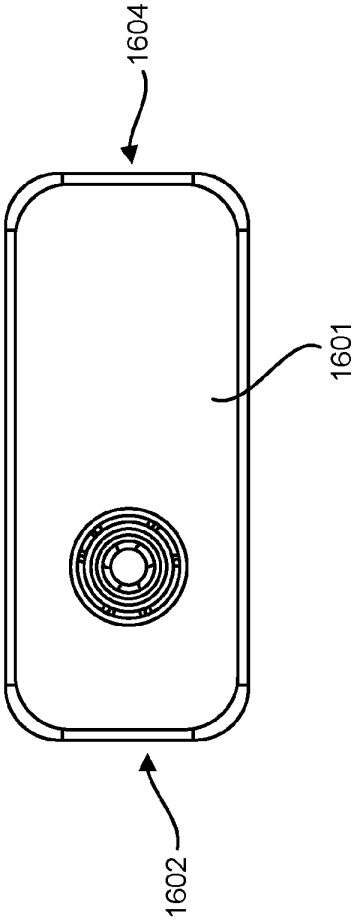


FIG. 16A

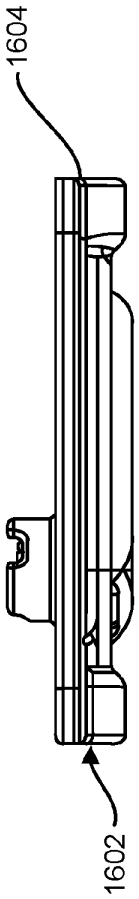


FIG. 16B

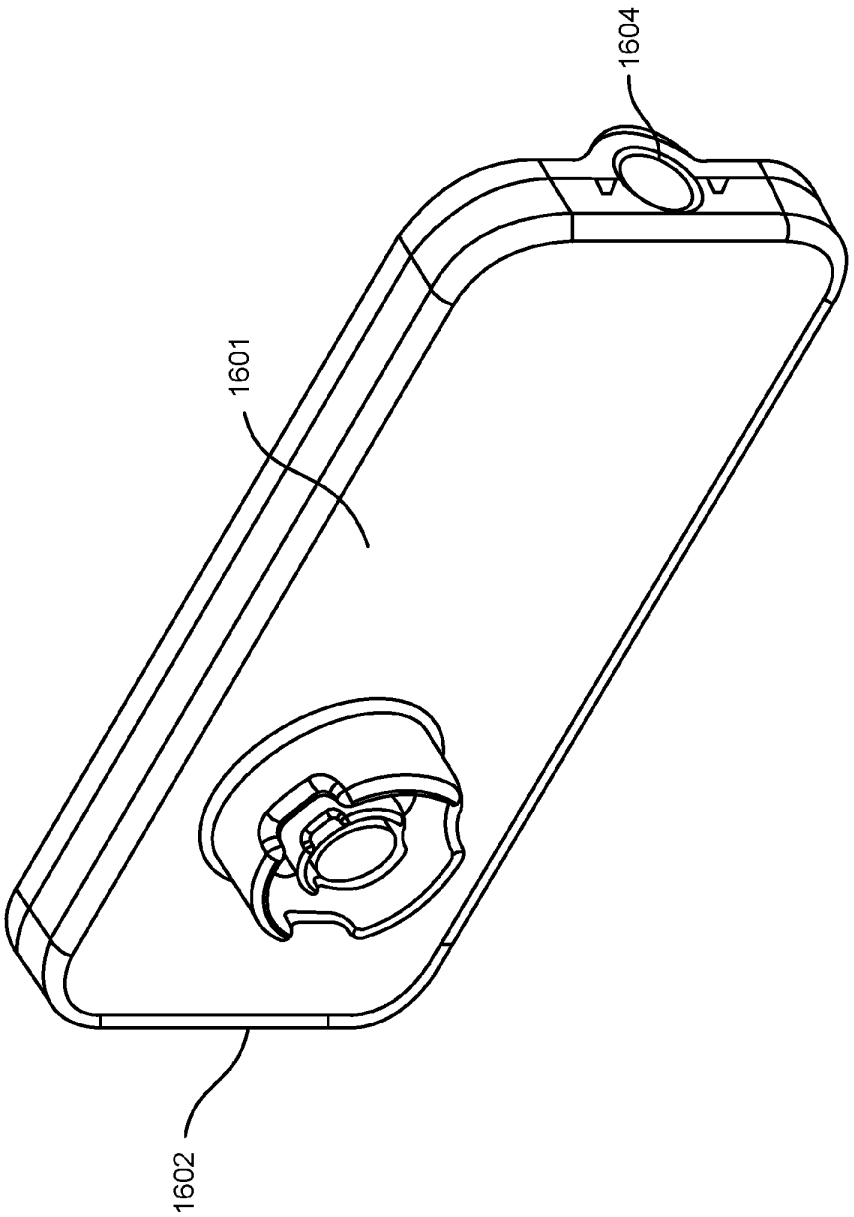


FIG. 16D

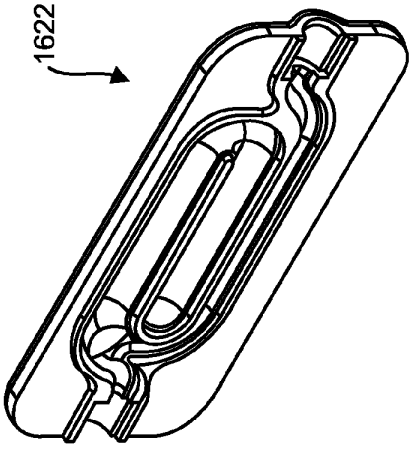


FIG. 17B



FIG. 17E

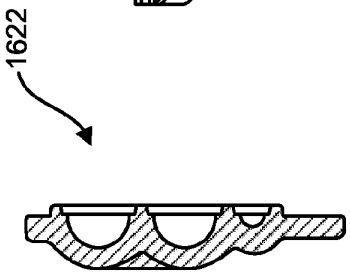


FIG. 17D

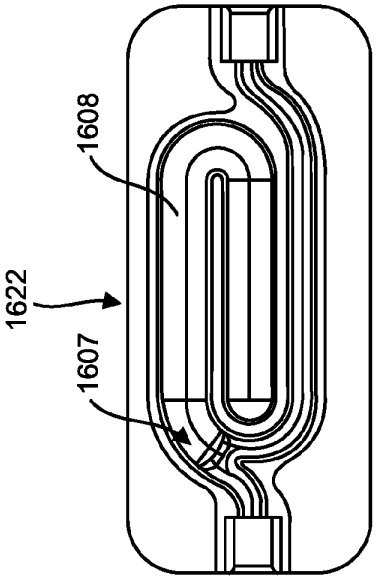


FIG. 17A

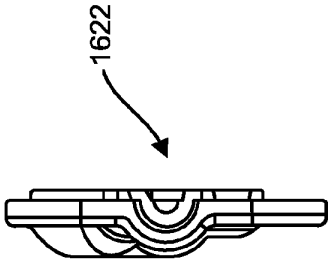


FIG. 17C

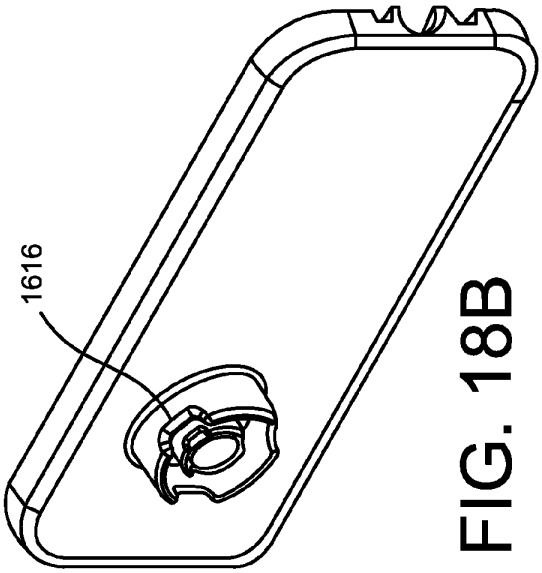


FIG. 18B

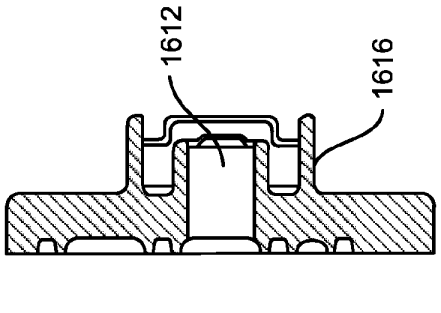


FIG. 18F

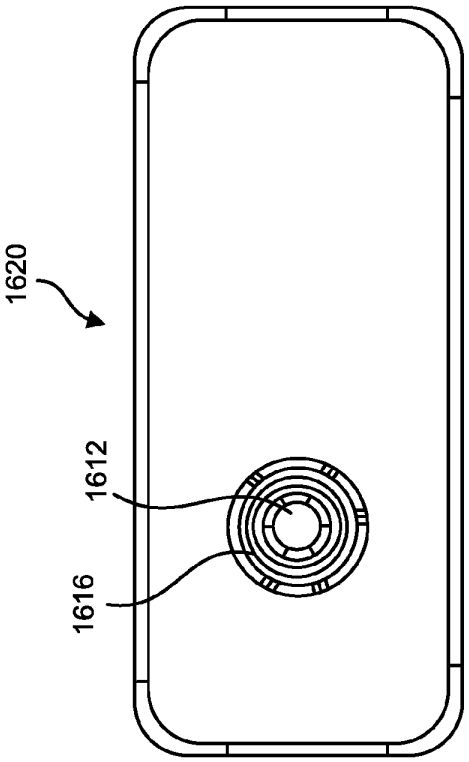


FIG. 18A

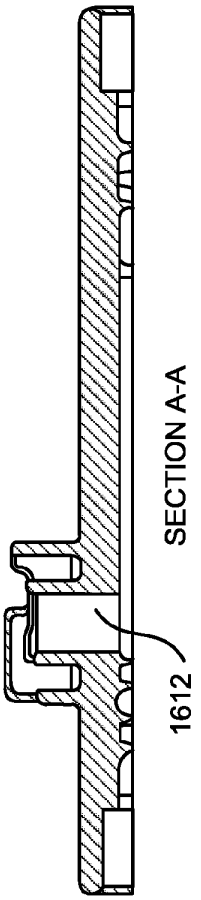


FIG. 18D

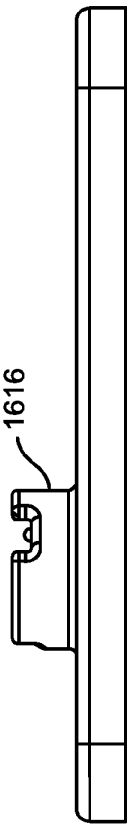


FIG. 18E

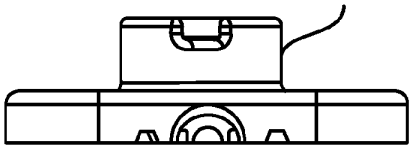


FIG. 18C

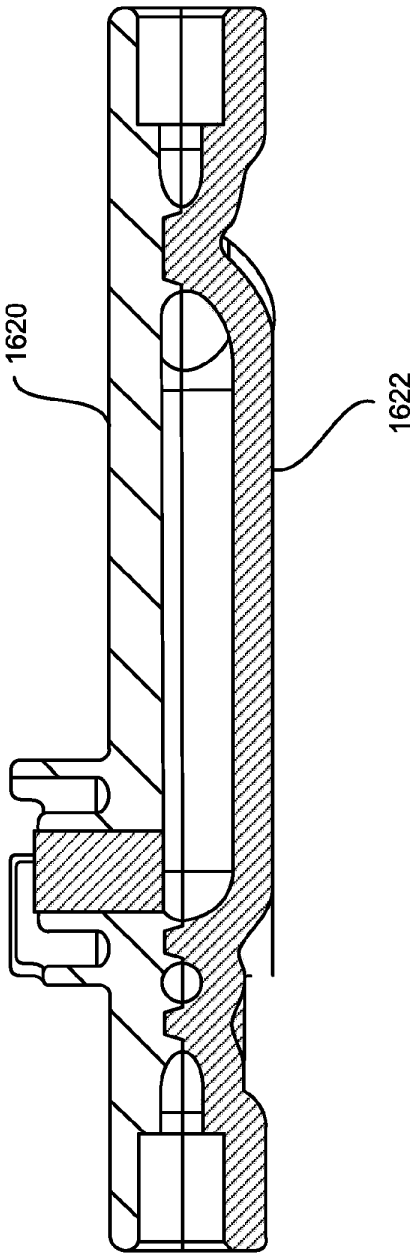


FIG. 19A

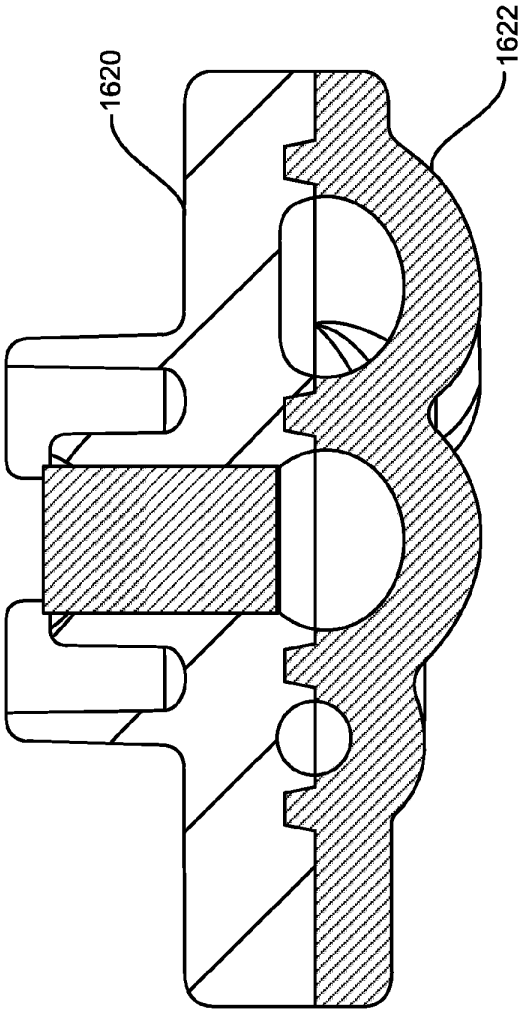


FIG. 19B

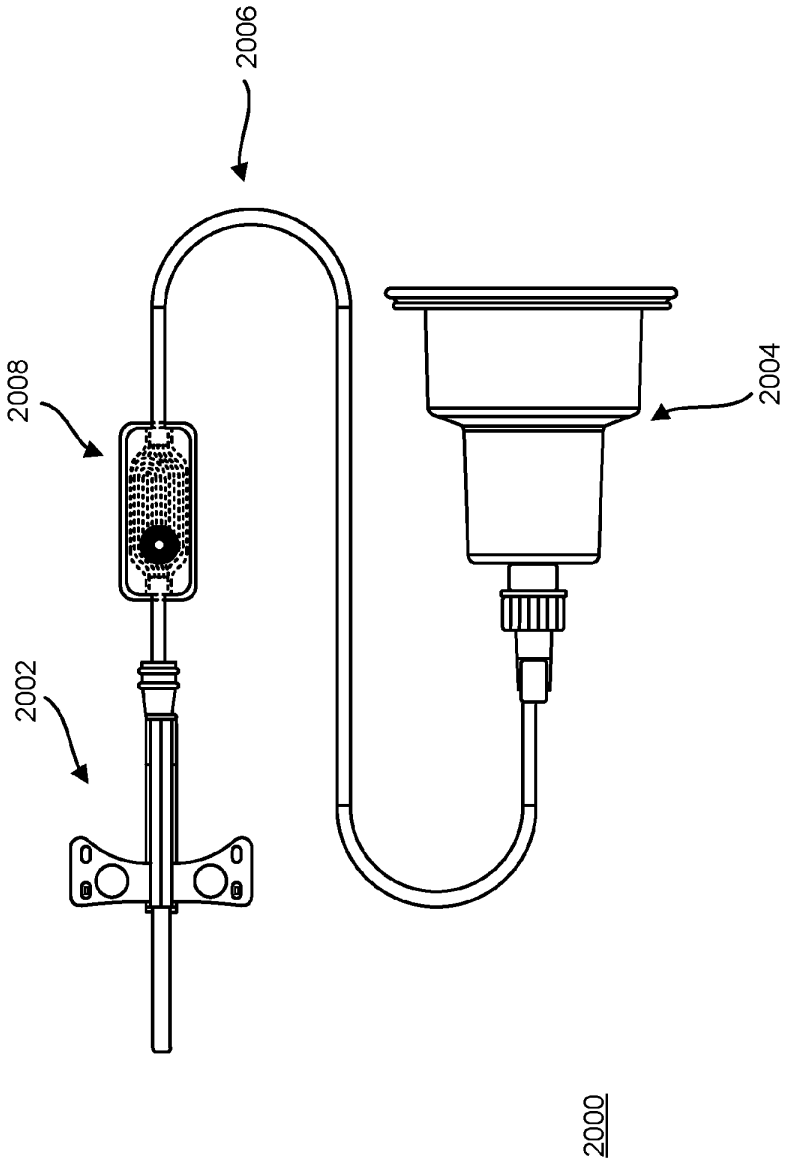


FIG. 20

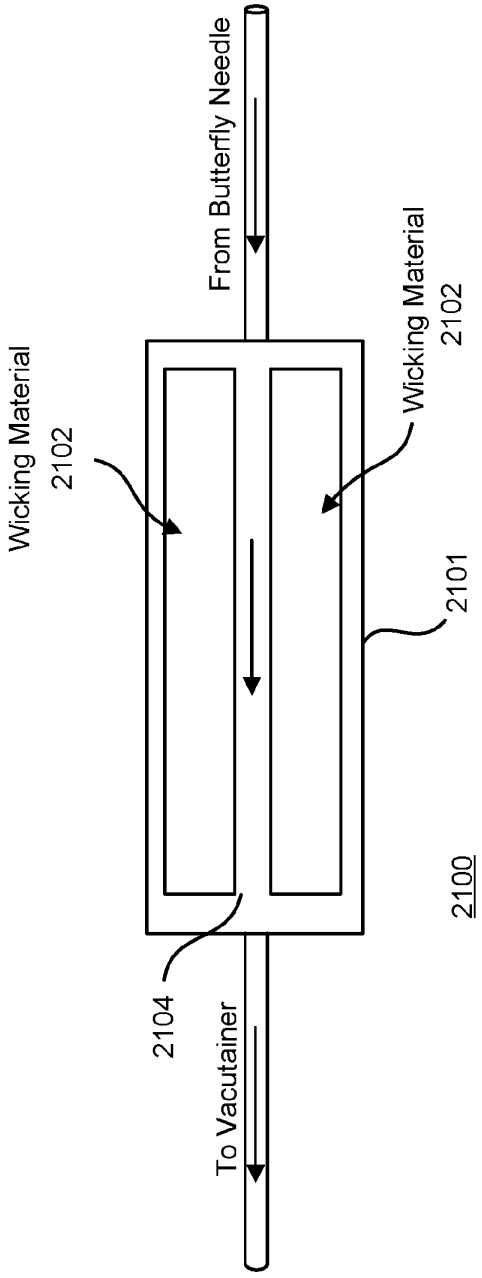

From Butterfly Needle
Wicking Material
2102
Wicking Material
2102
2101
2100
2104
To Vacutainer

FIG. 21

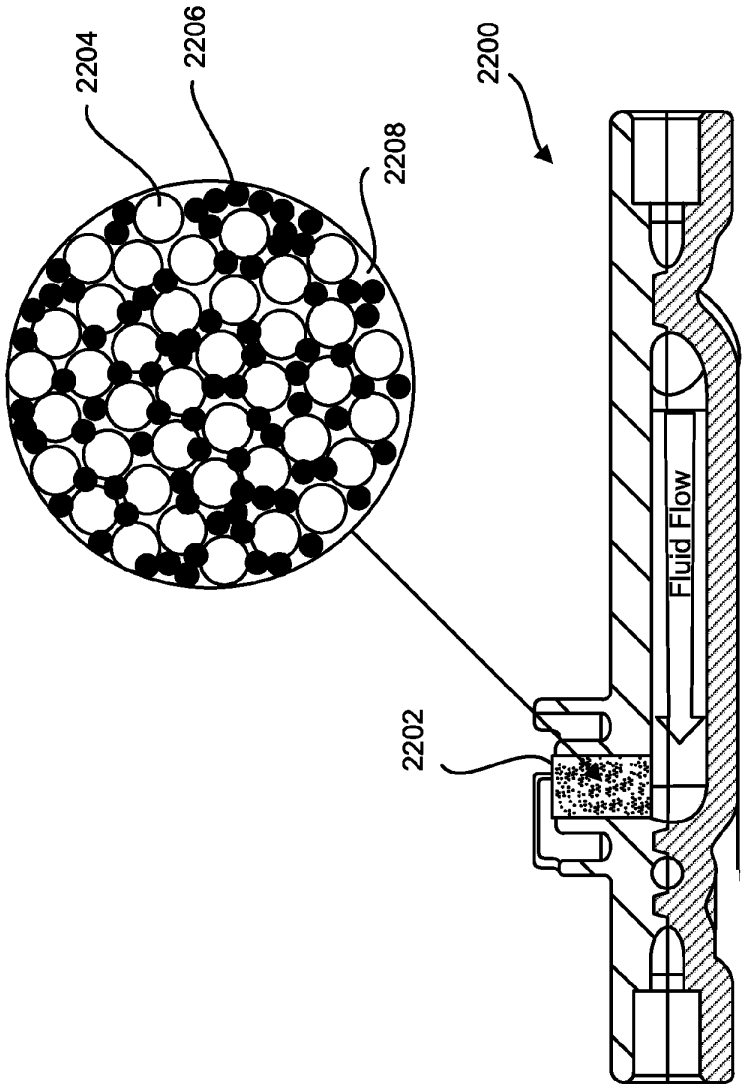


FIG. 22A

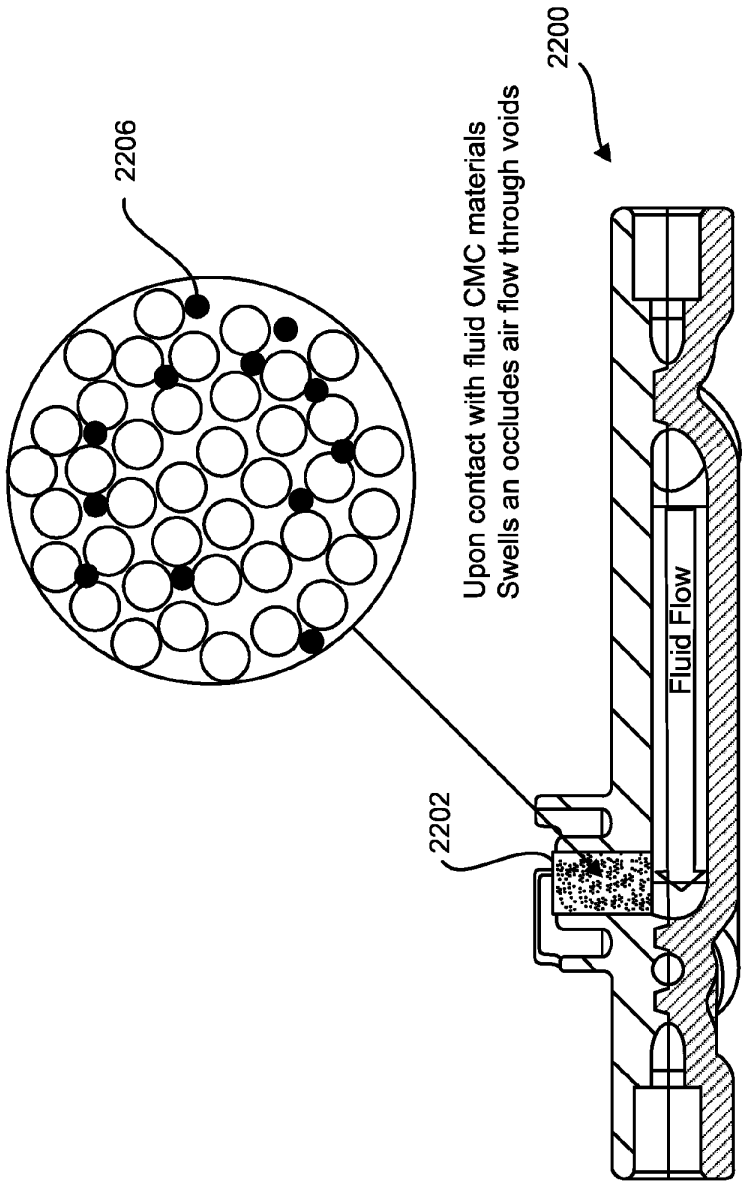

2200
2206
Upon contact with fluid CMC materials
Swells an occludes air flow through voids
Fluid Flow
2202

FIG. 22B

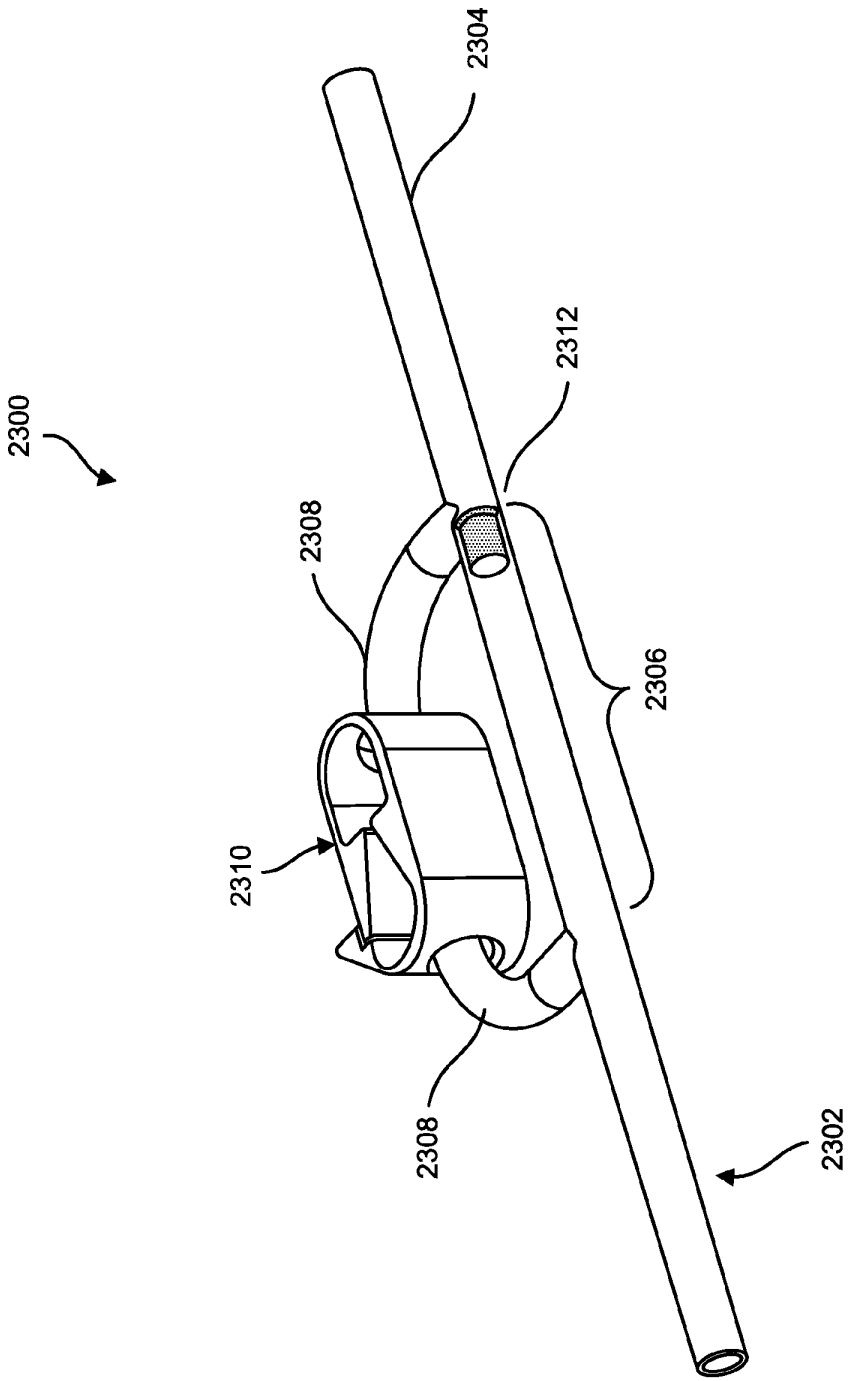


FIG. 23A

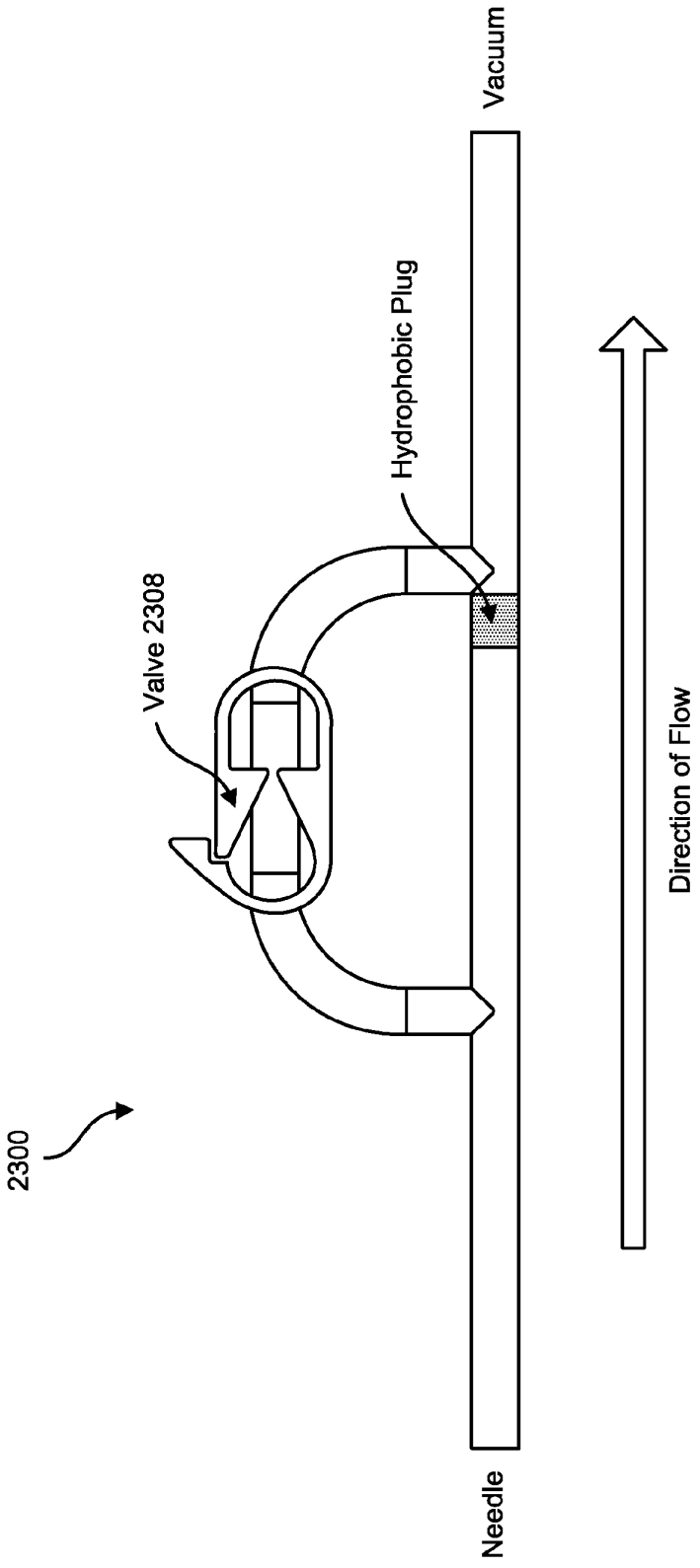

Vacuum
Hydrophobic Plug
Valve 2308
Direction of Flow
2300
Needle

FIG. 23B

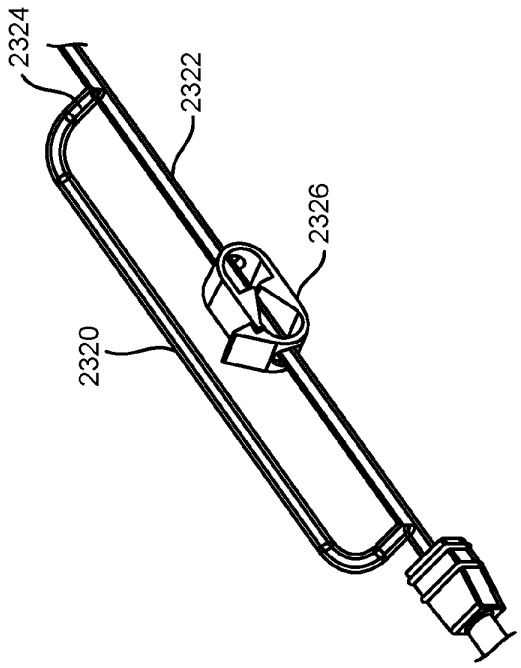


FIG. 23D

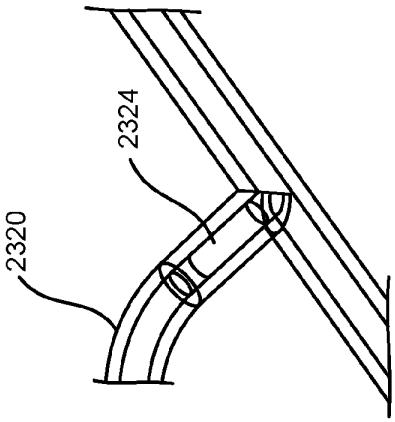


FIG. 23E

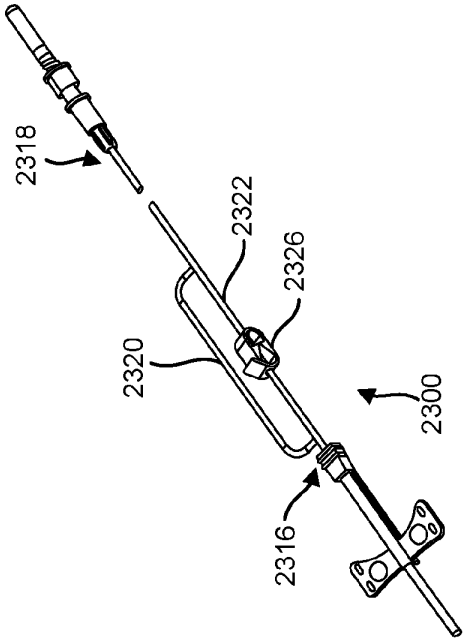


FIG. 23C

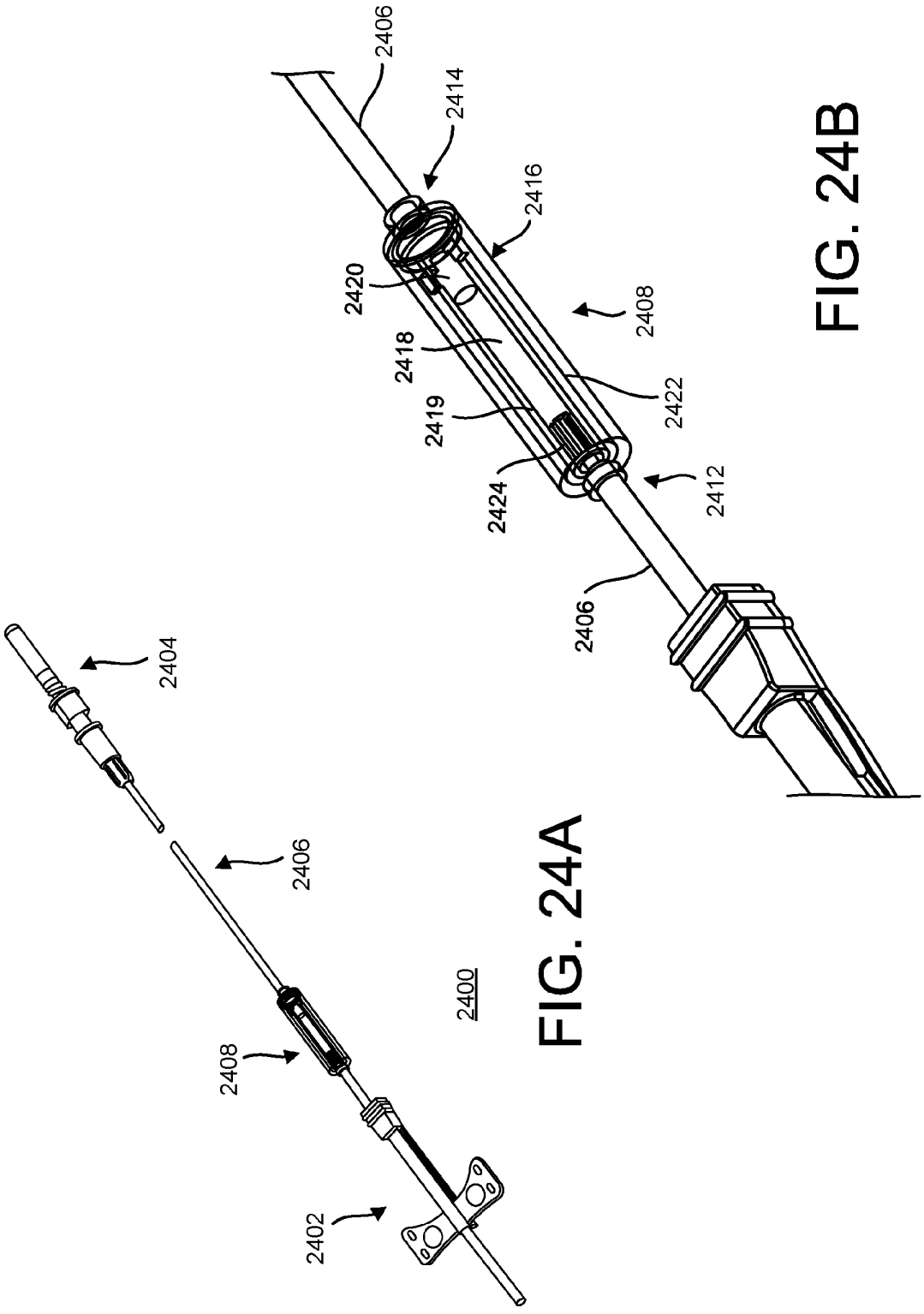


FIG. 24B

FIG. 24A

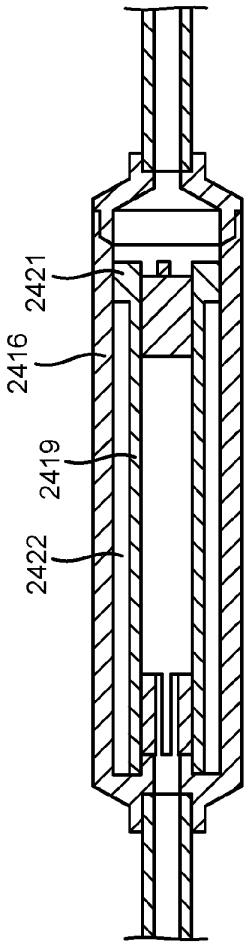


FIG. 24C

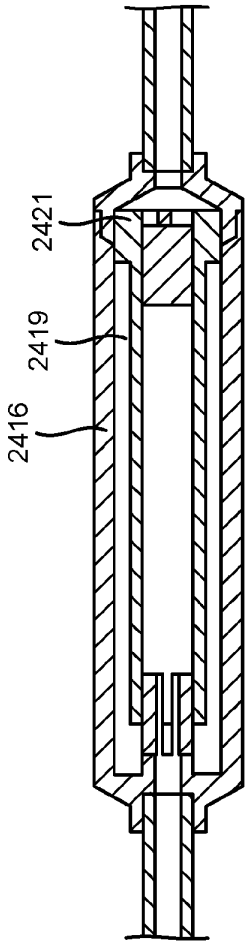


FIG. 24D

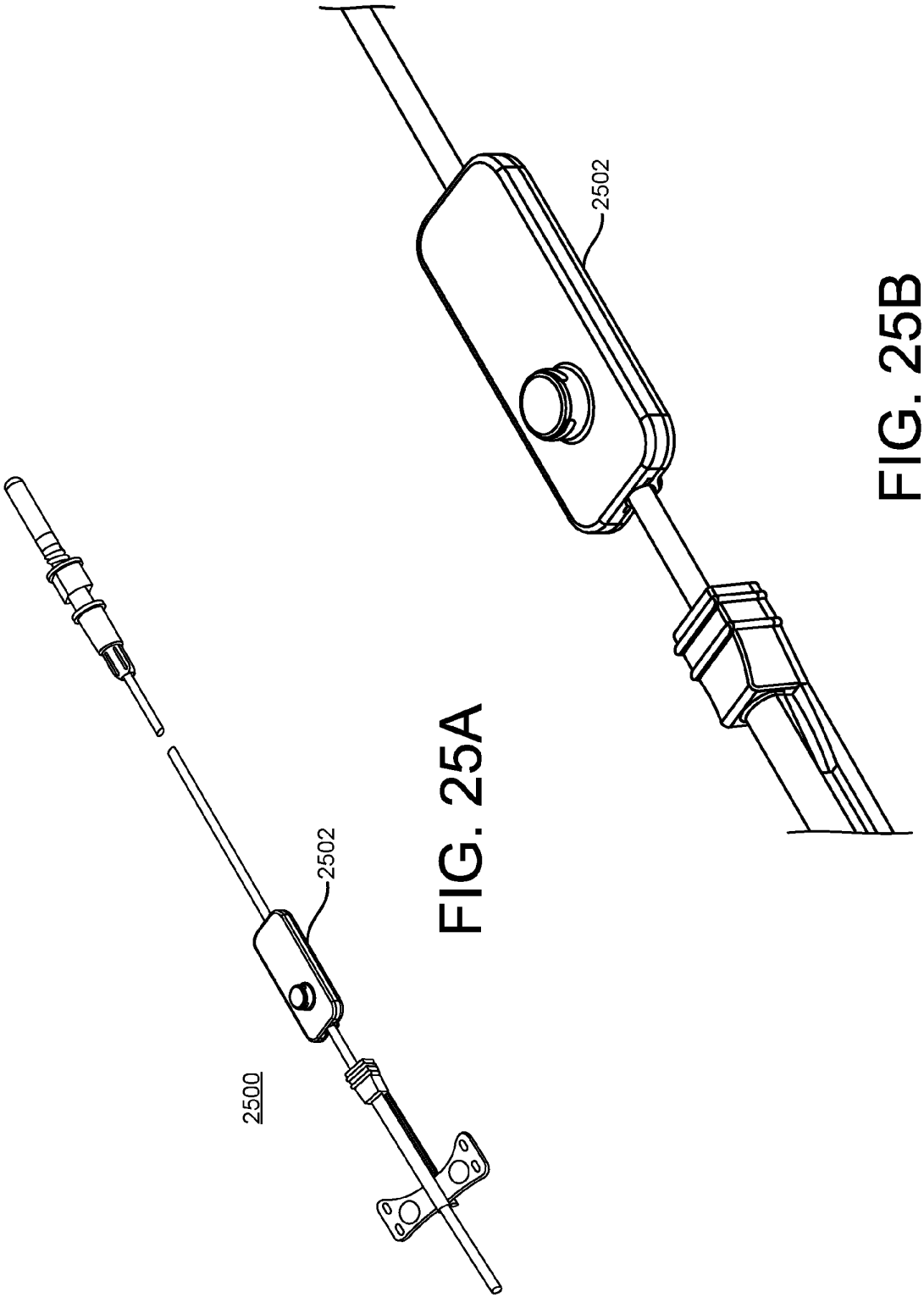


FIG. 25A

FIG. 25B

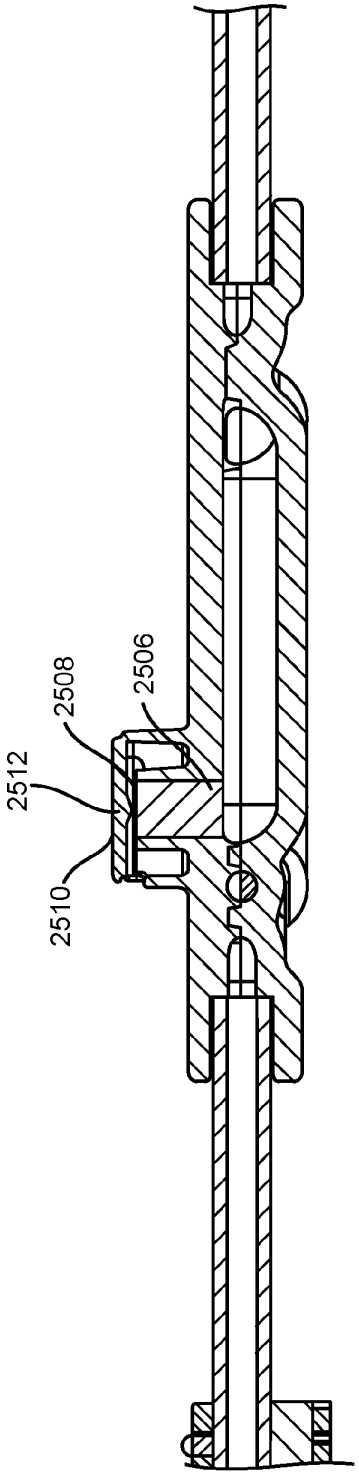


FIG. 25C

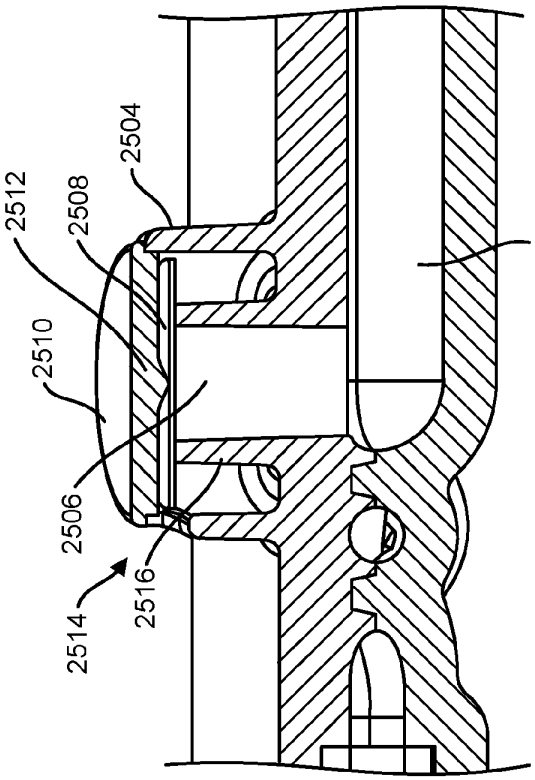


FIG. 25D

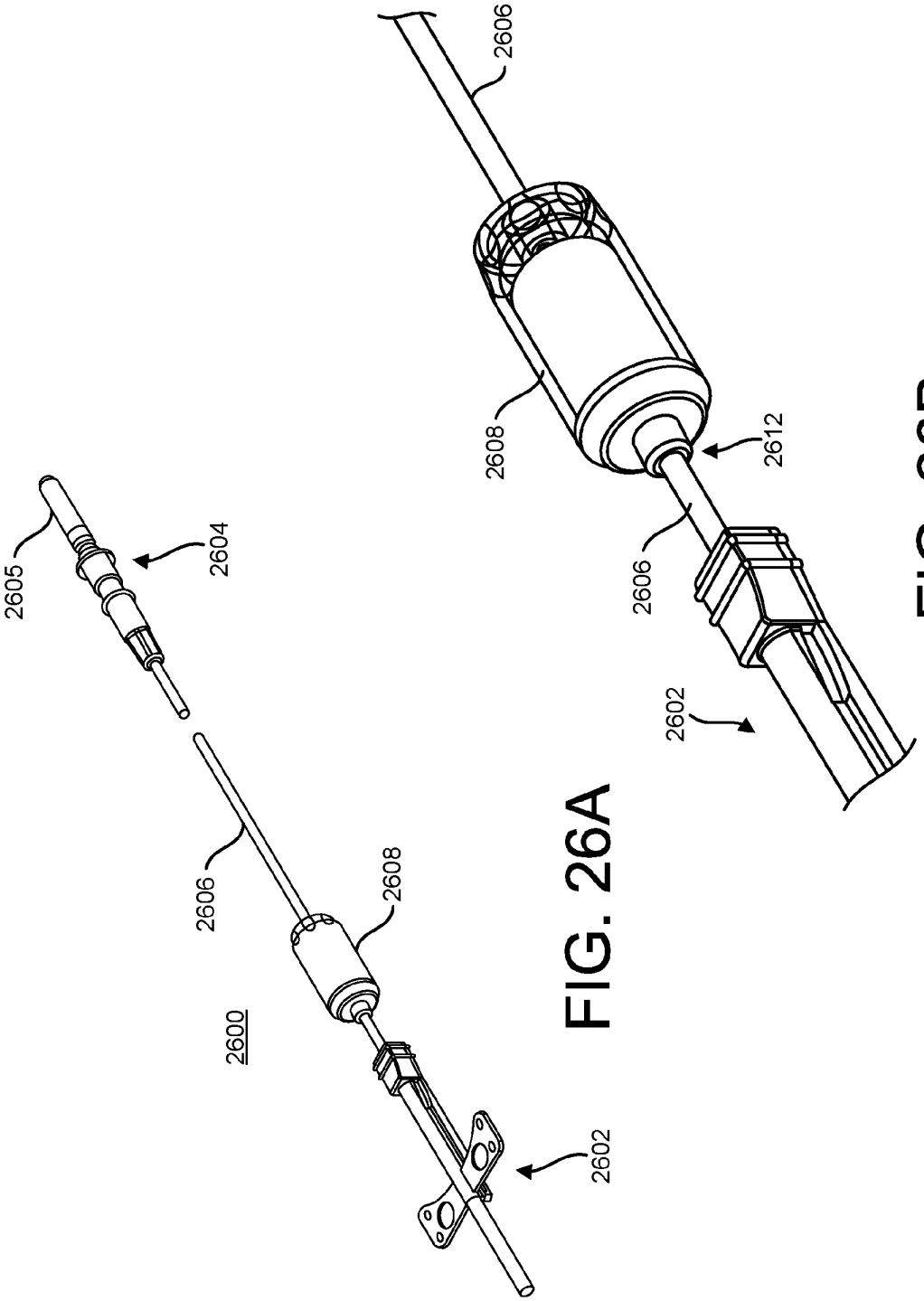


FIG. 26B

FIG. 26A

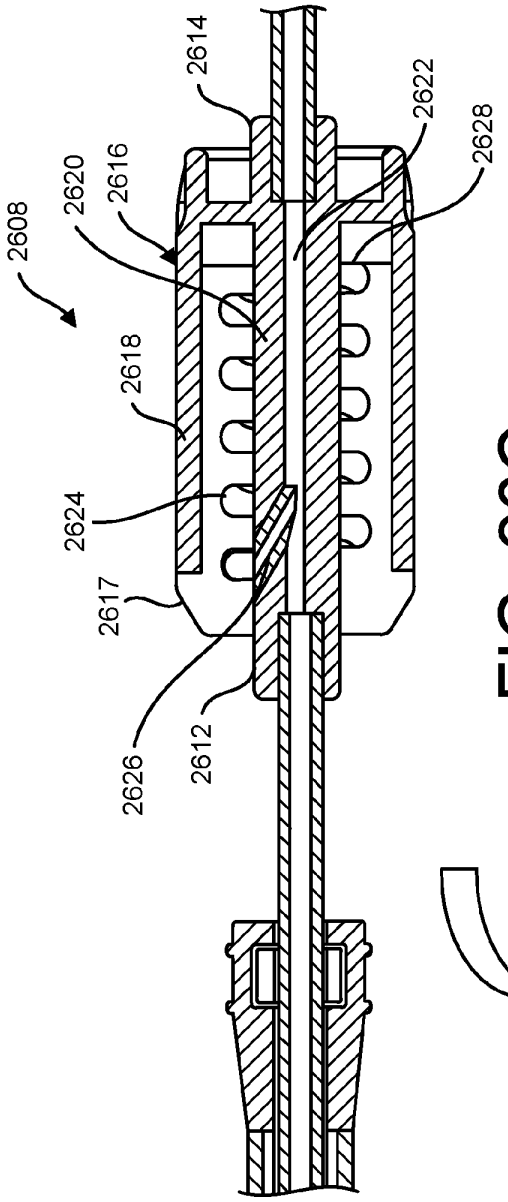


FIG. 26C

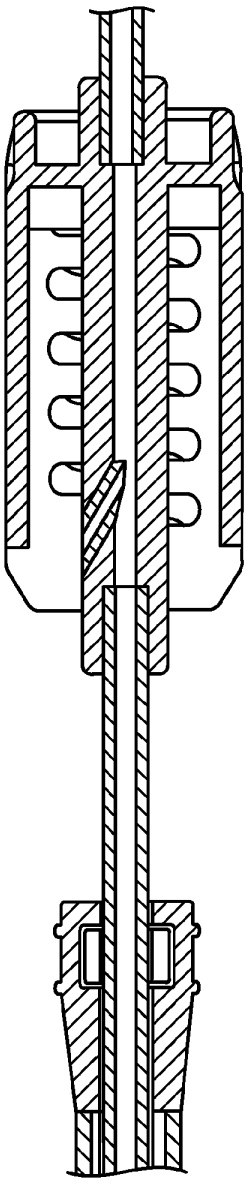


FIG. 26D

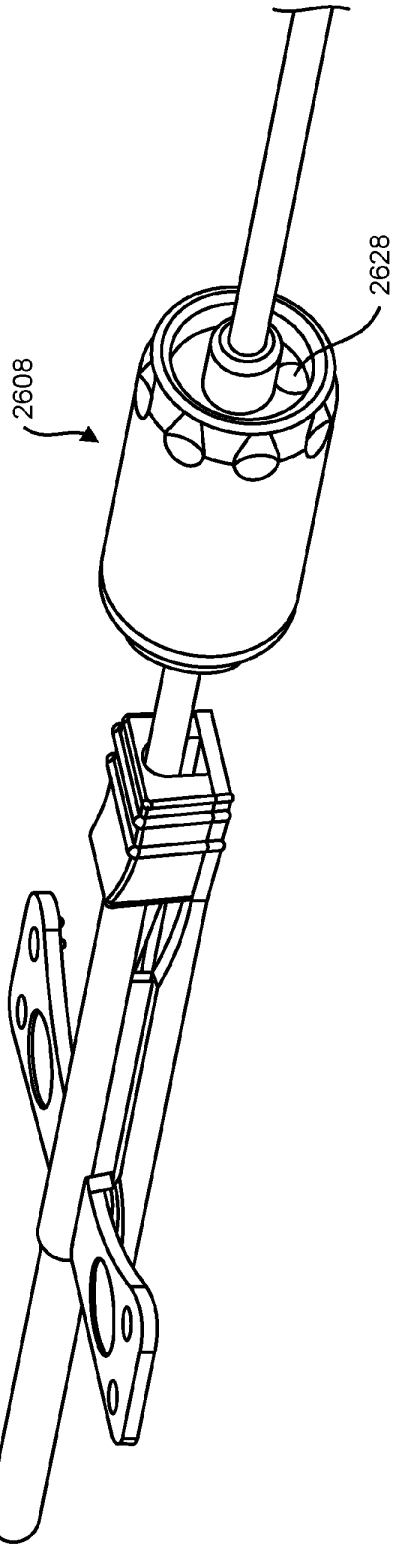


FIG. 26E

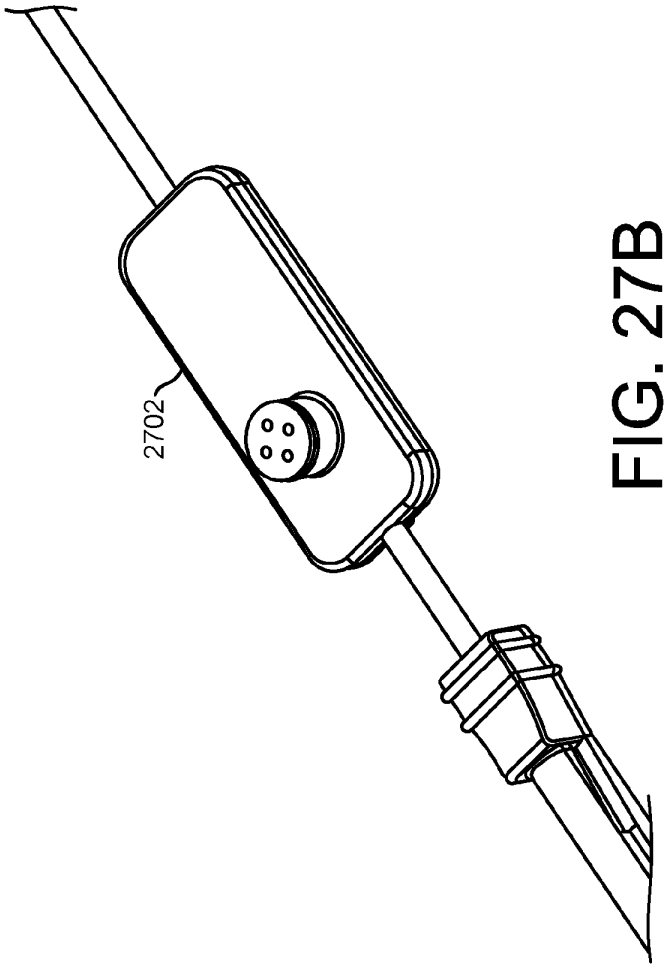


FIG. 27B

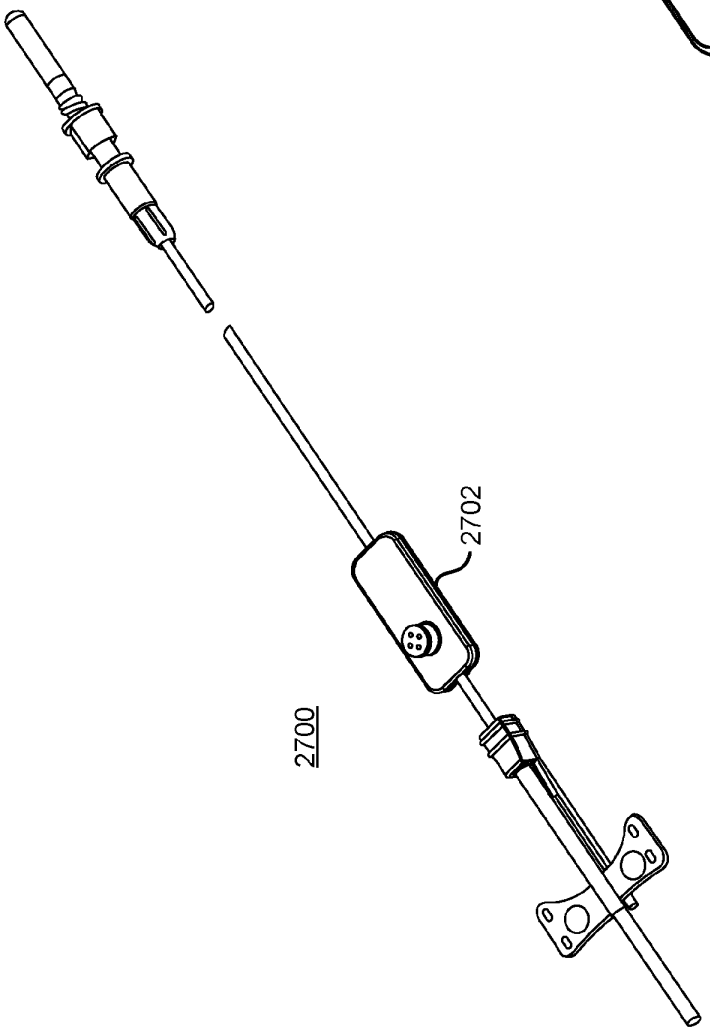


FIG. 27A

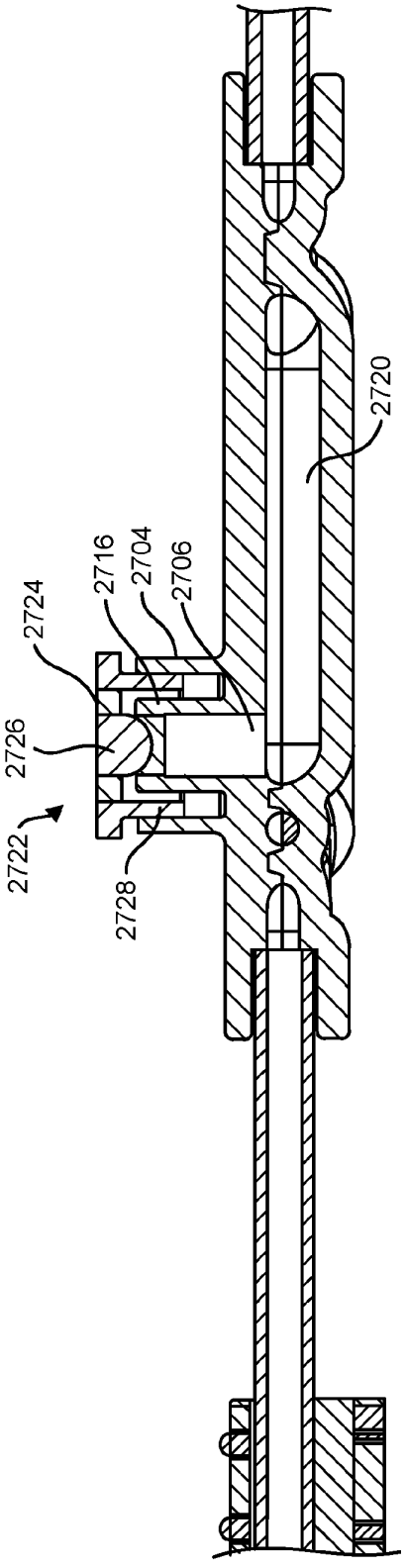


FIG. 27C

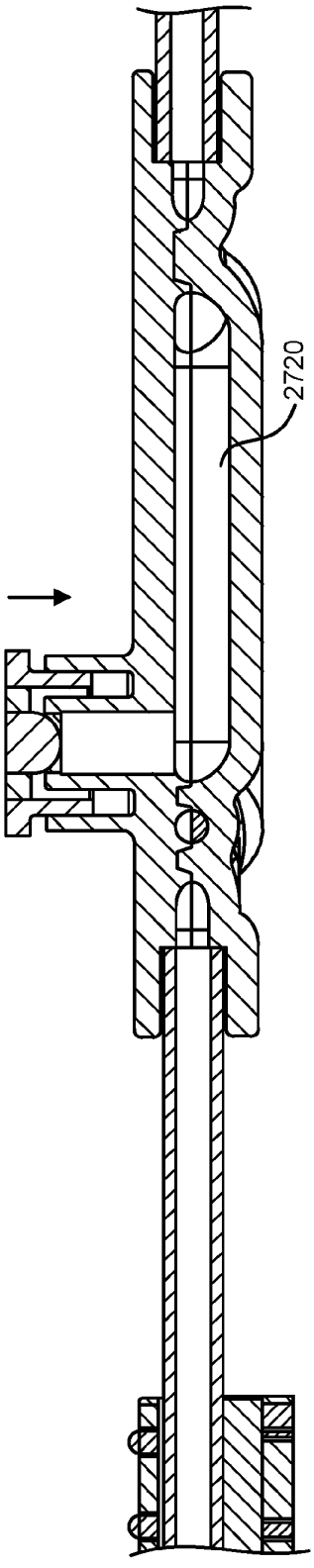


FIG. 27D

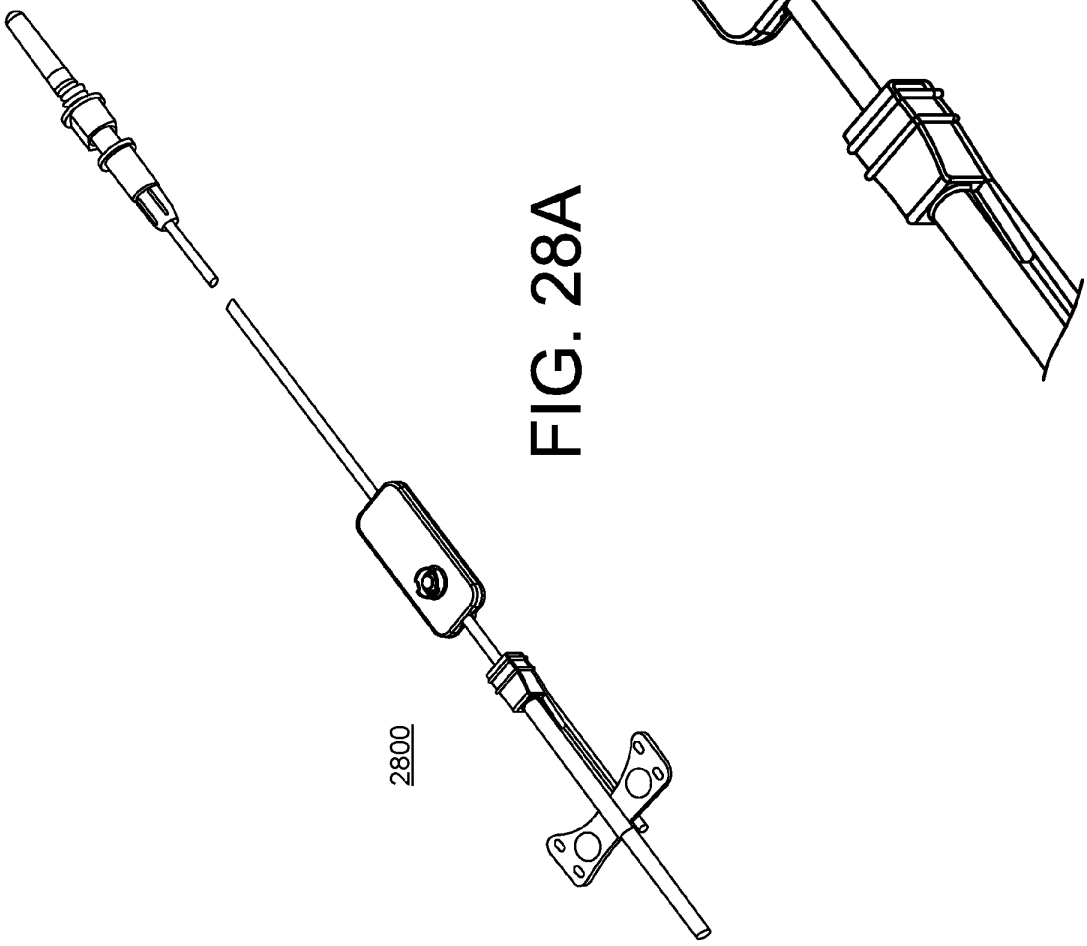


FIG. 28A

FIG. 28B

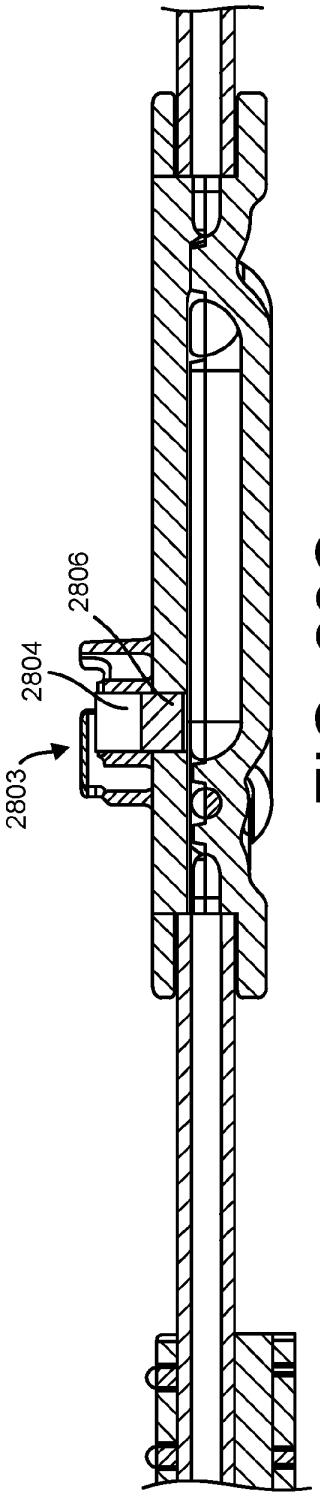


FIG. 28C

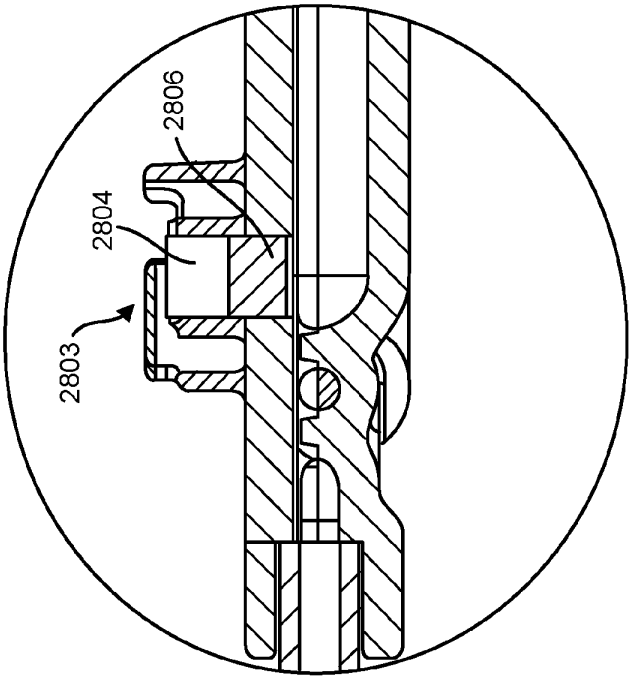


FIG. 28D

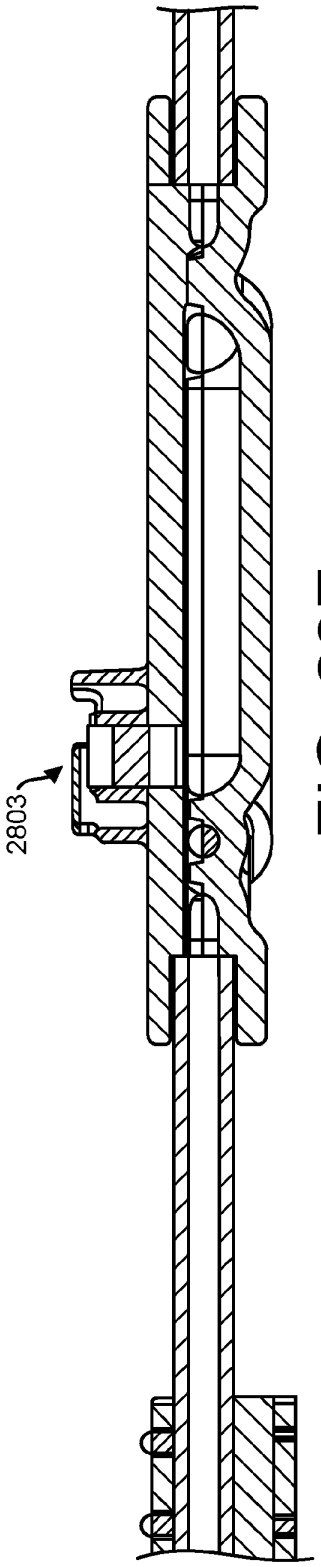


FIG. 28E

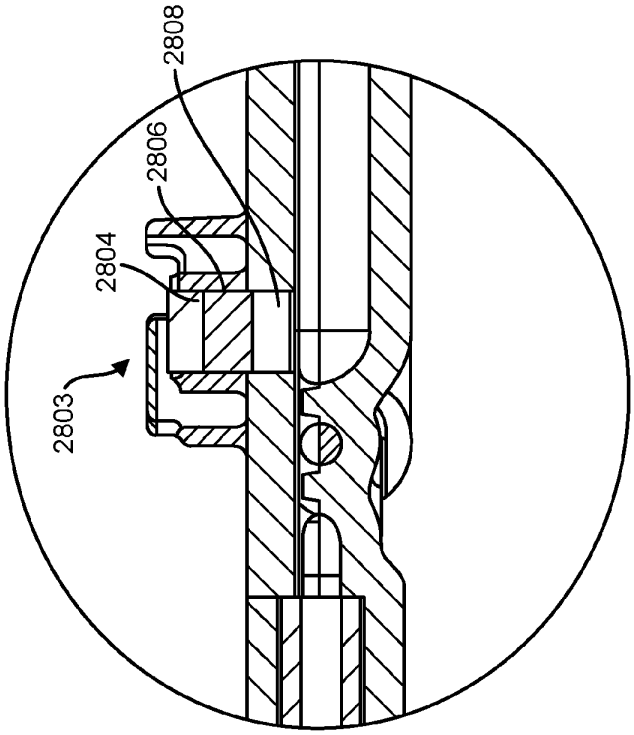


FIG. 28F

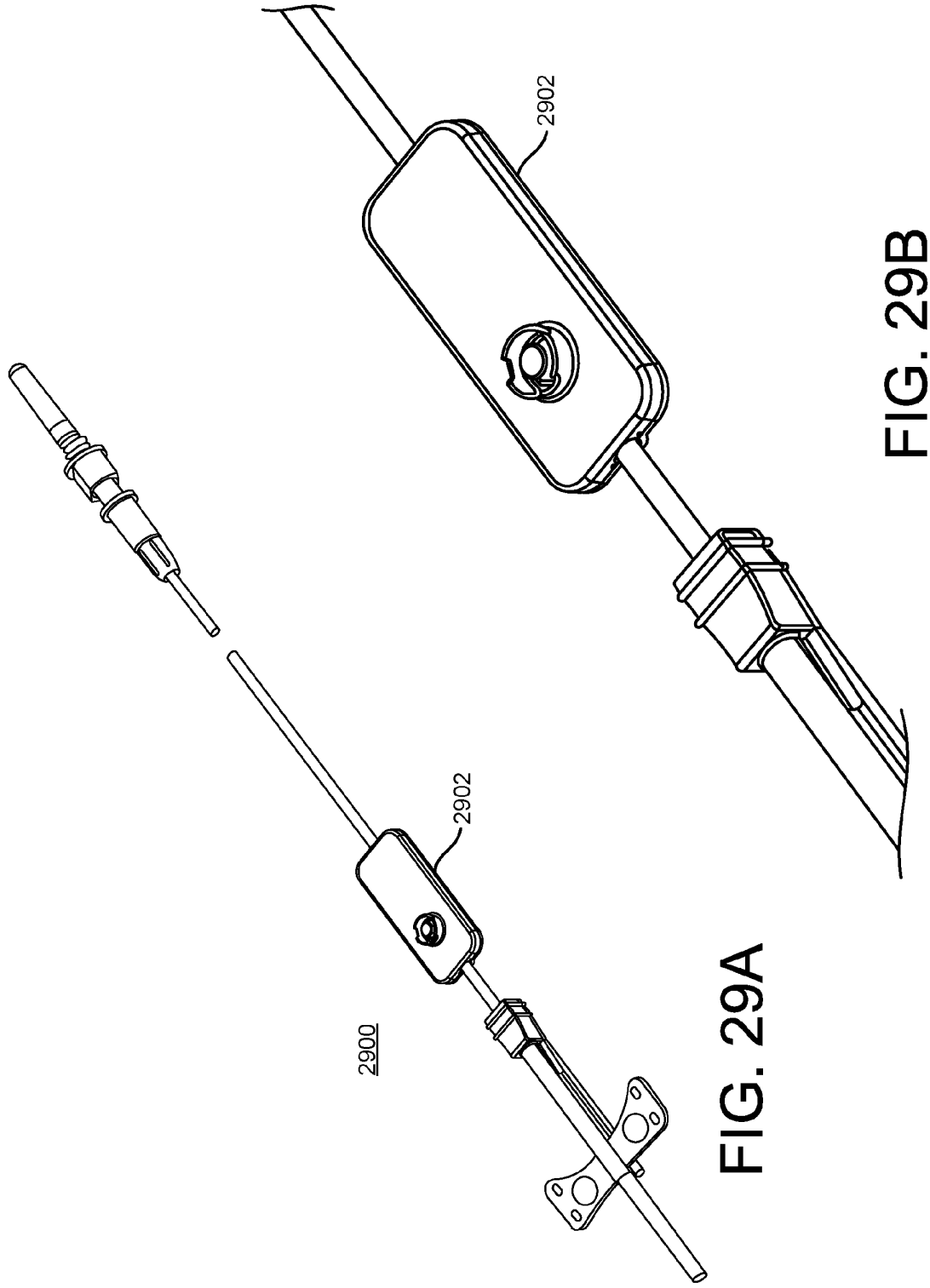


FIG. 29B

FIG. 29A

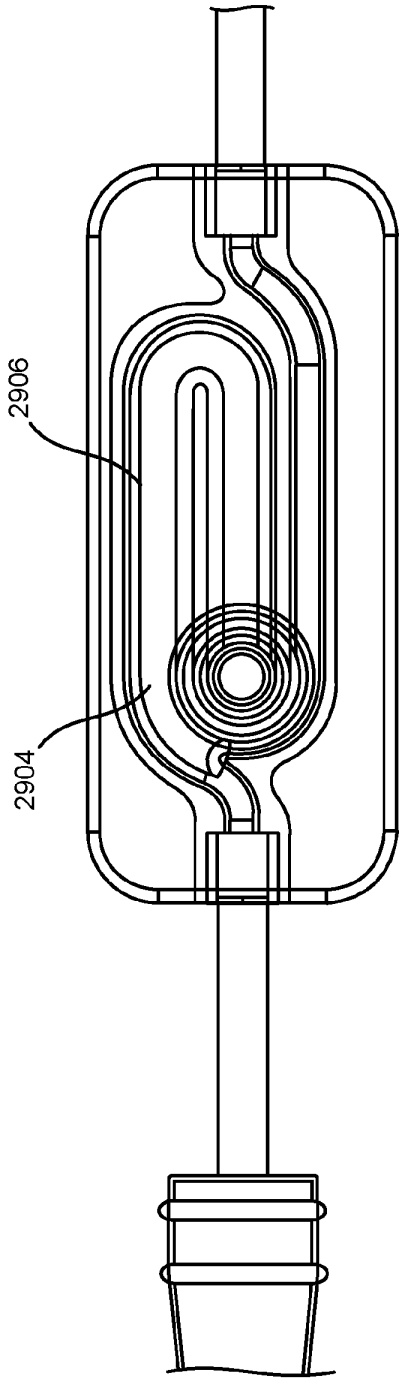


FIG. 29C

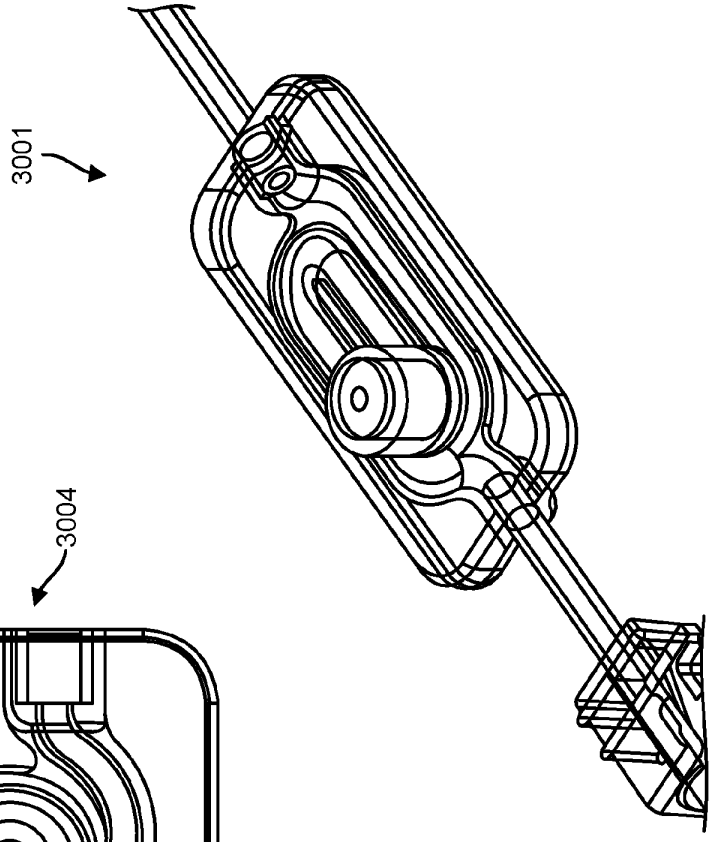


FIG. 30B

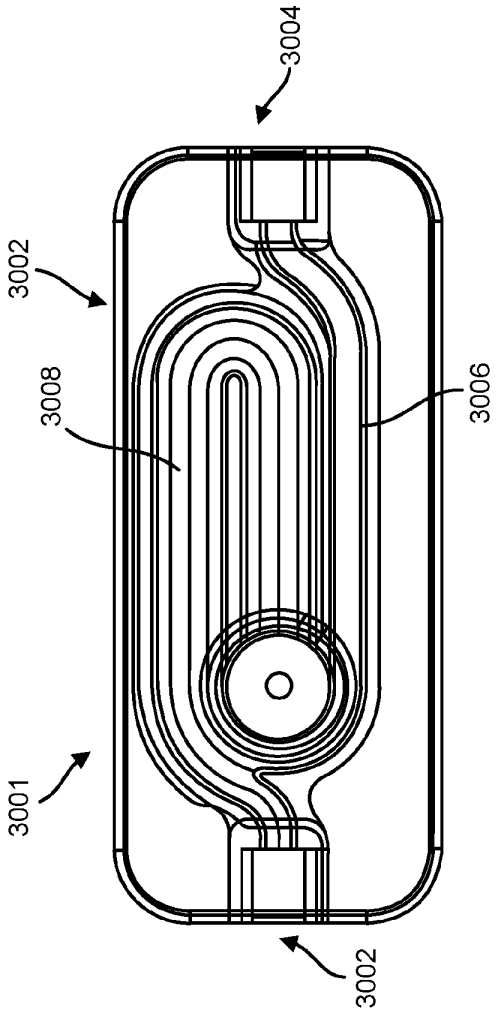


FIG. 30A

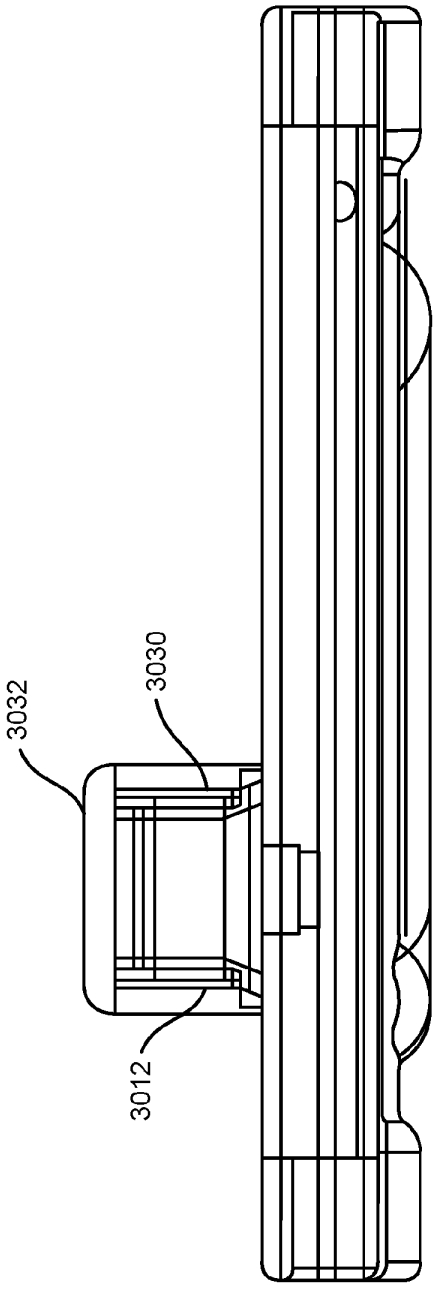


FIG. 30C

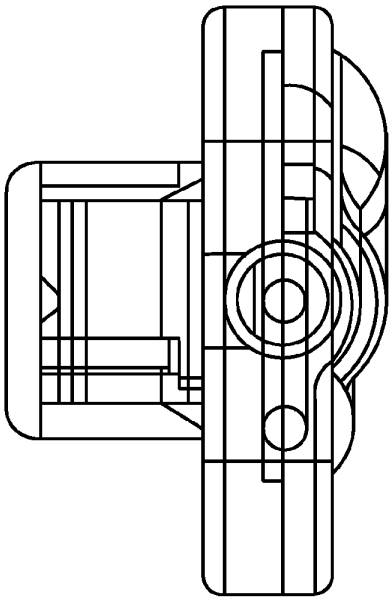


FIG. 30D

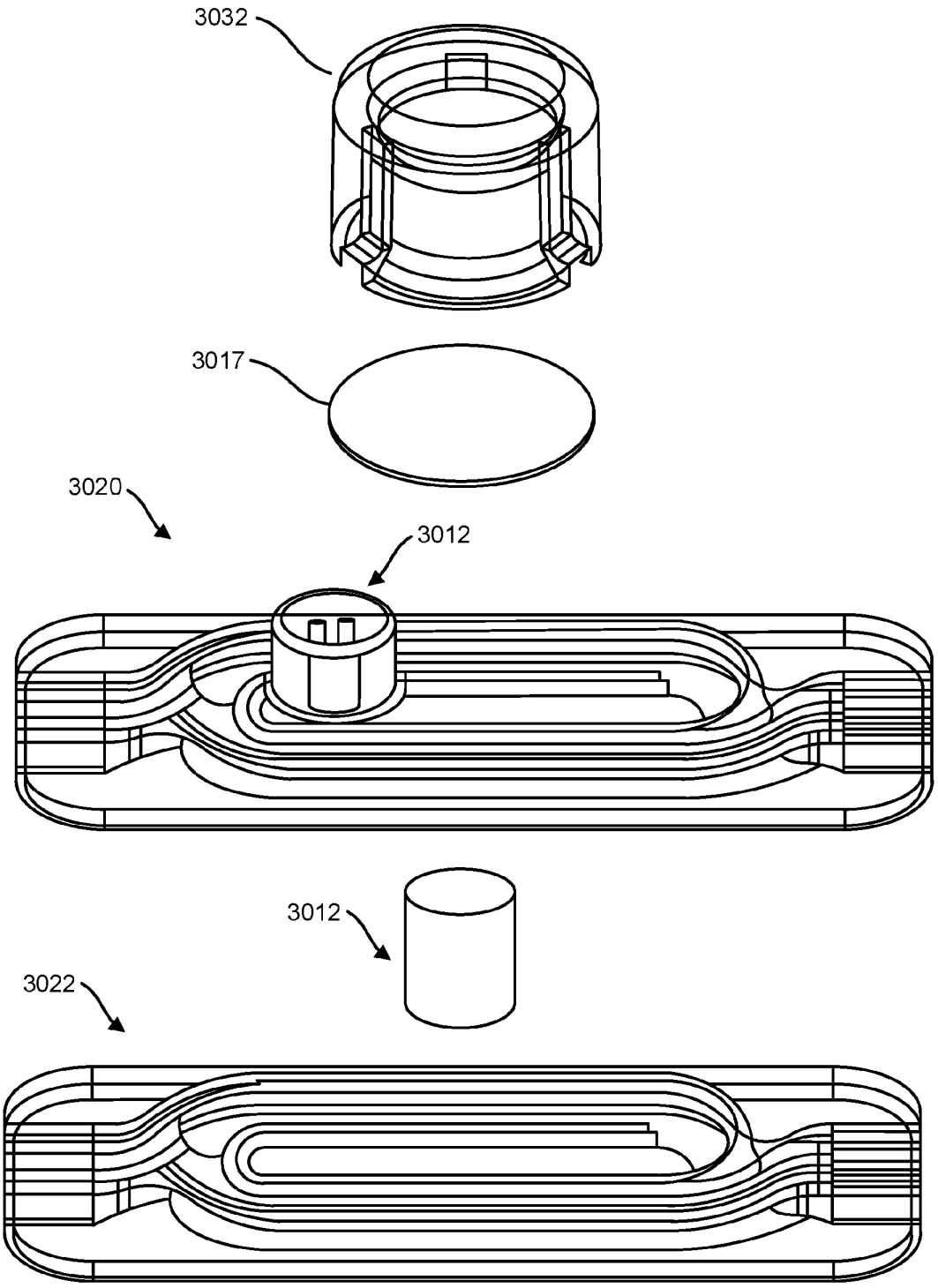


FIG. 30E

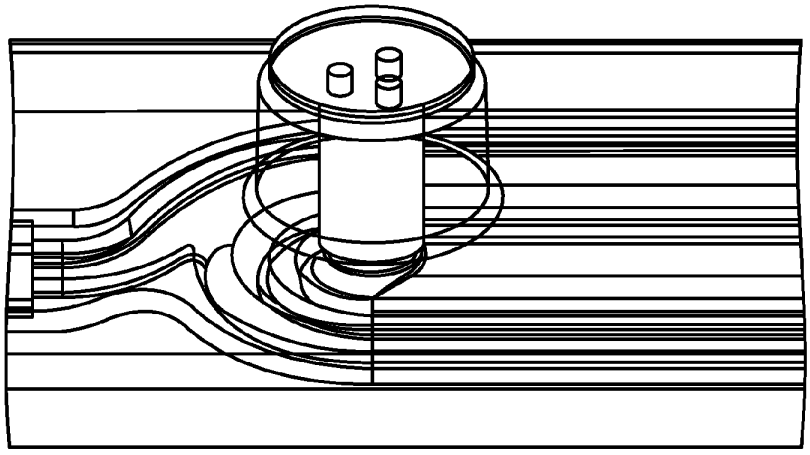


FIG. 30F

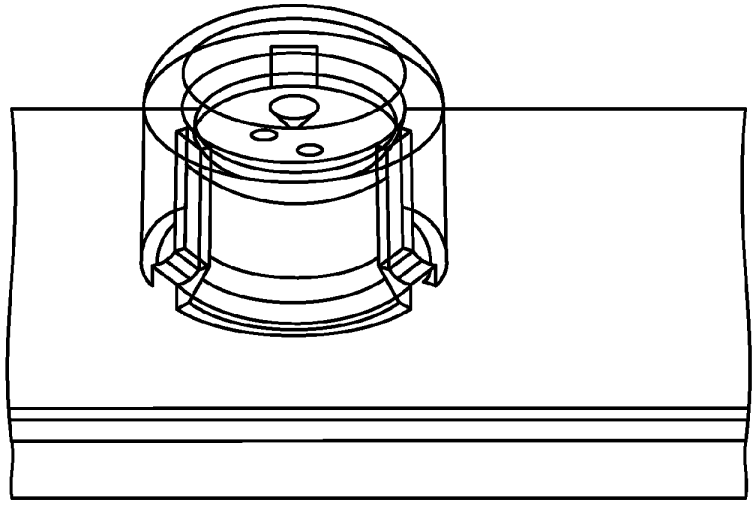


FIG. 30G

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.

* 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
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

1

Form PCT/ISA/210 (second sheet) (April 2005)

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

Form PCT/ISA/210 (continuation of second sheet) (April 2005)

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2017/068569

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2014039348 A1	06-02-2014	US 2014039348 A1	06-02-2014
		US 2016113560 A1	28-04-2016
		WO 2014022275 A1	06-02-2014
US 2014107564 A1	17-04-2014	EP 2906269 A1	19-08-2015
		US 2014107564 A1	17-04-2014
		US 2015367069 A1	24-12-2015
		WO 2014058945 A1	17-04-2014
US 4813433 A	21-03-1989	NONE	
US 2013317391 A1	28-11-2013	US 2013317391 A1	28-11-2013
		US 2015099996 A1	09-04-2015
		US 2015351678 A1	10-12-2015
WO 2013181352 A1	05-12-2013	AU 2013267448 A1	18-12-2014
		AU 2017216493 A1	07-09-2017
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		CN 104902817 A	09-09-2015
		CN 107736901 A	27-02-2018
		EP 2854643 A1	08-04-2015
		EP 3173021 A1	31-05-2017
		JP 6242386 B2	06-12-2017
		JP 2015519145 A	09-07-2015
		JP 2018034009 A	08-03-2018
		US 2014155781 A1	05-06-2014
		US 2015351679 A1	10-12-2015
		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)

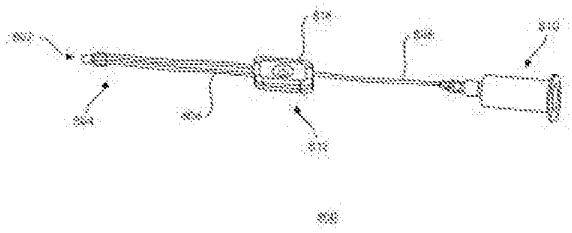
Classification: **- international:** ***A61B5/15; A61B5/153; A61B5/154; A61B5/157***
- cooperative: **A61B5/15003 (EP, US); A61B5/150213 (EP, US); A61B5/150221 (US); A61B5/150251 (EP, US); A61B5/150274 (EP, US); A61B5/150351 (US); A61B5/150755 (US); A61B5/150786 (US); A61B5/150946 (US); A61B5/150992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

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Literature display help

1 / 1 display

JP 2001-000424

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

Display format of the document display screen:
text display PDF display
primary literature | Correction/correction | PAJ

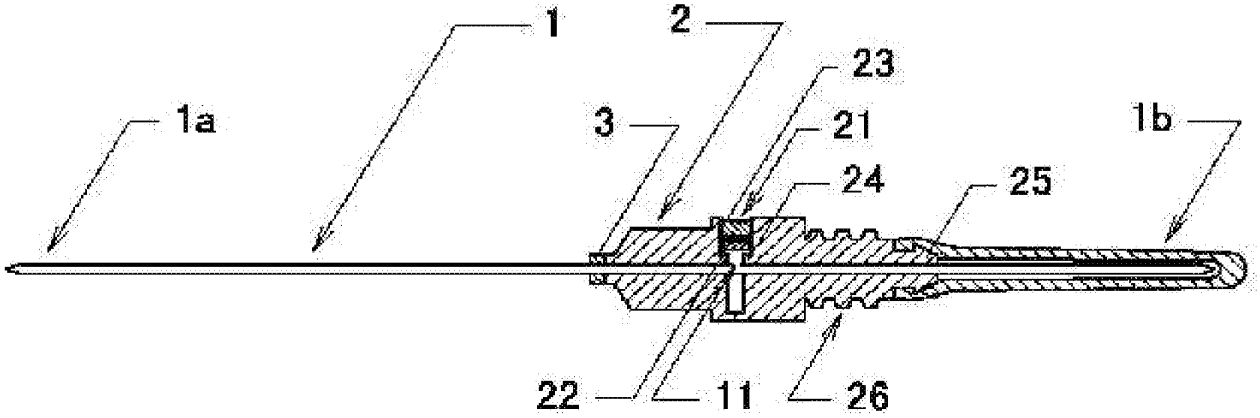
bibliography close

(19) [Country of issue] Japan Patent Office (JP)
(12) [Type of publication] Published patent publication (A)
(11) [Publication number] JP 2001-424 (P2001-424A)
(43) [Published date]] January 9, 2001 (2001.1.9)
(54) [Title of Invention] Blood collection needle
(51) [International Patent Classification 7th Edition]
A61B 5/15
[FI]
A61B 5/14 300 H
[Request for examination: Unclaimed
[Number of claims] 4
[Application form] OL
[Total number of pages] 3
(21) [Application number] Japanese Patent Application No. Hei 11-174400
(22) [Filing date] June 21, 1999 (1999.6.21)
(71) [Applicant]
[Identification number] 000135036
[Name] Nissho Co., Ltd.

(72) [Inventor]
[Name] Tsuguo Fujii
(72) [Inventor]
[Name] Suzuki Issei
[Theme code (reference)]
4C038
[F term (reference)]
4C038 TA06 UJ02 UJ06

wrap up close

(57) [Summary]
[Problem] To provide a blood collection needle that enables confirmation immediately after pu ncturing that the needle has definitely punctured a vein of a subject at the time of blood colle ction.
A needle tube (A) having a hole in at least a part of its side wall and having blade surfaces at both ends, and a passage provided so as to cover the hole and communicating between the o utside and the inside of the needle tube through the hole. an air-permeable, blood-impermea ble member (C) engaged with the open end of the passageway; and a needle tube support m ember (C) engaged with the needle tube support so as to seal one end of the needle tube. A b lood collection needle having a rubber-like cap (D) that is closed and a sealing member (E) th at is provided in the passage and can block the hole or the passage.



The scope of the claims open

What is claimed is
: 1. A needle tube (A) having a hole in at least a part of its side wall and having blade surface

s at both ends; an air-permeable blood-impermeable member (C) secured to the open end of the passageway, and one end of the needle tube so as to seal , a rubber-like cap (D) engaged with the needle tube support, and a sealing member (E) provided in the passage and capable of closing the hole or the passage.

2. The blood collection needle according to claim 1, wherein the passageway has a protrusion for locking the sealing member.

3. The blood collection needle according to claim 1, wherein the air-permeable blood-impermeable member is a swelling material.

4. The blood collection needle according to claim 1, 2 or 3, wherein the needle tube support is transparent or translucent.

detailed description open —

Description: BACKGROUND OF THE INVENTION

1.

Field of the Invention The present invention relates to a blood-collecting needle, and more particularly, one end of which is pierced into a blood vessel of a subject and the other end of which is communicated with a vacuum blood-collecting tube. , relates to a blood collection needle capable of collecting an amount of blood corresponding to the negative pressure in a vacuum blood collection tube. According to the blood collection needle of the present invention, it can be confirmed that one end has been punctured into the subject's vein before connecting the other end to the vacuum blood collection tube.

2.

Description of the Related Art Conventionally, when collecting blood using a vacuum blood collection tube, there has been a blood collection needle that can confirm that the needle has definitely punctured the vein of a subject, that is, so-called flashback, before attaching the vacuum blood collection tube. is proposed. As such a conventional blood collection needle, for example, JP-A-61-64234 discloses a housing having a front end portion, a rear end portion, and a sample collection chamber provided with a passage for communicating with the outside air; A blood collection needle is disclosed having a cannula extending from the rear end and a tablet that expands upon contact with blood and blocks communication with the atmosphere. However, with this blood collection needle, when a vacuum blood collection tube is attached, negative pressure is applied to the tablet, and outside air may flow into the blood collection needle.

[0003] Further, Japanese Patent Application Laid-Open No. 4-132541 discloses an elastic tip having a ventilation hole for communication between the inner cavity and the outside atmosphere, and an air-permeable filter provided at the outer opening of the ventilation hole. Also disc

losed are blood collection needles with translucent hubs or elastic tips that allow flashback to be seen. However, since the elastic tip of this blood collection needle is housed inside the bloo d collection needle holder and held by hand from above, it is very difficult to confirm flashback with the elastic tip. In addition, when one end is punctured into a subject's vein, blood that en ters the inside of the needle tube due to venous pressure fills the lumen of the elastic tip and then enters the vent hole. check flashbackIt takes time to do so. SUMMARY OF THE INVENTIO N The present invention has been made in view of the above circumstances

.

To provide a blood-collecting needle which does not impinge on the body and allows immediat e confirmation of flashback after one end of the needle is punctured into a vein. Means for Sol ving the Problems As a result of extensive studies, the inventors of the present invention have found that a hole is provided in the side wall of the needle tube, a passage is provided throug h the hole to allow communication between the outside and the inside of the needle tube, and a vacuum is provided

.

The present inventors have found that a blood collection needle provided with a mechanism fo r blocking the inside of the needle tube from the outside when the blood collection tube is atta ched solves the above problems, and arrived at the present invention.

[0006] That is, the present invention provides a needle tube (A) having a hole in at least a pa rt of its side wall and blade surfaces at both ends, a needle tube (A) provided so as to cover t he hole, and communicating the outside and the inside of the needle tube through the hole. a n air-permeable blood-impermeable member (C) secured to the open end of the passageway; and one end of the needle tube is sealed so as to seal the needle tube. A blood collection nee dle having a rubber-like cap (D) engaged with a support and a sealing member (E) provided i n the passage and capable of closing the hole or the passage.

DETAILED

DESCRIPTION OF THE INVENTION The present invention will now be described in detail with r eference to the drawings. FIG. 1 is a sectional view showing one embodiment of the blood coll ection needle of the present invention. The needle tube 1 is preferably made of stainless stee l. One end 1a is a blade surface and is formed so as to pierce the blood vessel of the subject, and the other end 1b is also a blade surface and is formed so as to be inserted into a vacuum blood collection tube (not shown).

[0008] A hole 11 is provided in the side wall of the needle tube 1 . The hole 11 may be provid ed in any part of the needle tube 1 as long as it is inside the needle tube support 2 . The need le tube 1 is provided with a transparent or translucent needle tube support 2 so as to cover th e hole 11 . The needle tube support 2 is hermetically fixed to the needle tube 1 on the one en d 1a side of the needle tube 1, for example, with an adhesive 3. As shown in FIG.

[0009] A passage 21 is formed in the needle tube support 2 to communicate the outside and t he inside of the needle tube 1 through the hole 11 . As long as the passage 21 communicates

with the outside, the open end to the outside may be provided anywhere. When the blade surf ace of one end 1a of the needle tube 1 is punctured into a vein of a subject through the passa ge 21, the blood that has entered the inside of the needle tube 1 enters the passage 21 throu gh the hole 11, and the blood that has entered the needle tube is removed. Flashback can be confirmed by viewing from the side of the support 2 .

A sealing member 22 is provided in the passage 21 . As the sealing member 22, plastic materi als such as polypropylene, Teflon (registered trademark) and silicon rubber can be used.It ma y be metal or ceramic such as. Further, in the passage 21, there is a gap between the sealing member 22 and the needle tube support 2 through which air and blood can pass.

An air-permeable, blood-impermeable member 23 is hermetically engaged with the open end of the passageway 21 to the outside of the needle tube 1 . This member 23 keeps the passag e 21 air-permeable and prevents the blood that has flowed in during blood collection from lea king to the outside. As the air-permeable and blood-impermeable member 23, a layered filter made of a polymer sintered body such as polypropylene or polyethylene is usually preferably used. It may be a membrane filter.

As shown in FIG. 2, when one end 1a of the needle tube 1 is punctured into the subject, the b lood that has flowed from the inside of the needle tube 1 through the hole 11 into the passag e 21 flows through the sealing member 22 and the needle tube support. It passes through the gap with the body 2 and is blocked by the air permeable blood impermeable member 23 . Afte r that, when the vacuum blood collection tube is attached to the other end 1b of the needle tu be 1, the negative pressure of the vacuum blood collection tube pulls the sealing member 22 t oward the needle tube 1 and closes the passage 21, as shown in FIG. As a result, negative pr essure is not directly applied to the air-permeable blood-impermeable member 23, so that a p redetermined amount of blood can be collected. Further, considering the sealing performance i nside the needle tube 1, it is more preferable that the passage 21 is provided with a protrusio n 24 for locking the sealing member 22 therein. As for the shape of the projection 24, in addit ion to the L-shaped cross section shown in FIG. etc.

As the air-permeable and blood-impermeable member 23, swelling substances such as acrylic copolymers, starch and gelatin can be used alone or in combination with other compounds. W hen one end 1a of the needle tube 1 is punctured into the subject, the air-permeable blood-im permeable member 23 expanded by the blood that has flowed in causes the sealing member 22 to pass directly into the needle tube 1 or as shown in FIG. 21 to block the hole 11 or the p assage 21. As a result, immediately after confirming the flash bag, the inside of the needle tu be 1part is sealed. Further, when the vacuum blood collection tube is attached, the negative p ressure of the vacuum blood collection tube further brings the sealing member 22 into close c ontact with the needle tube 1 or the convex portion 24, so that the inside of the needle tube 1 is more tightly sealed.

On the other end 1b side of the needle tube support 2, a rubber-like cap 4 that seals the blad e surface of the needle tube 1 is locked by a flange 25. As shown in FIG. Synthetic isoprene r

ubber, silicon rubber, or the like is used as the material of the rubber-like cap 4 . A threaded portion 26 is formed in the needle tube support 2, and the blood collection needle and the holder can be integrated by being screwed into the opening (not shown) of the holder. INDUSTRIAL APPLICABILITY The blood collecting needle of the present invention has a hole in a part of the side wall, so that flashback can be confirmed immediately after one end of the blood collecting needle is punctured into a vein

.

In addition, since it has a sealing member, there is no possibility that negative pressure will be applied to the air-permeable blood-impermeable member when the vacuum blood collection tube is attached.

Brief description of the drawing

open —

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 is a cross-sectional view showing a blood collection needle according to one embodiment of the present invention;

2 is an enlarged sectional view of a needle tube support portion of the blood collection needle of FIG. 1; FIG.

3 is an enlarged cross-sectional view of the needle tube support portion of the blood collection needle of FIG. 1 when the vacuum blood collection tube is attached; FIG.

FIG. 4 is an enlarged cross-sectional view of a needle tube support portion in another blood collection needle of the present invention;

[Description of Symbols]

1 Needle tube

11 Hole

2 Needle tube support

21 Passage

22 Sealing member

23 Air permeable blood impermeable member

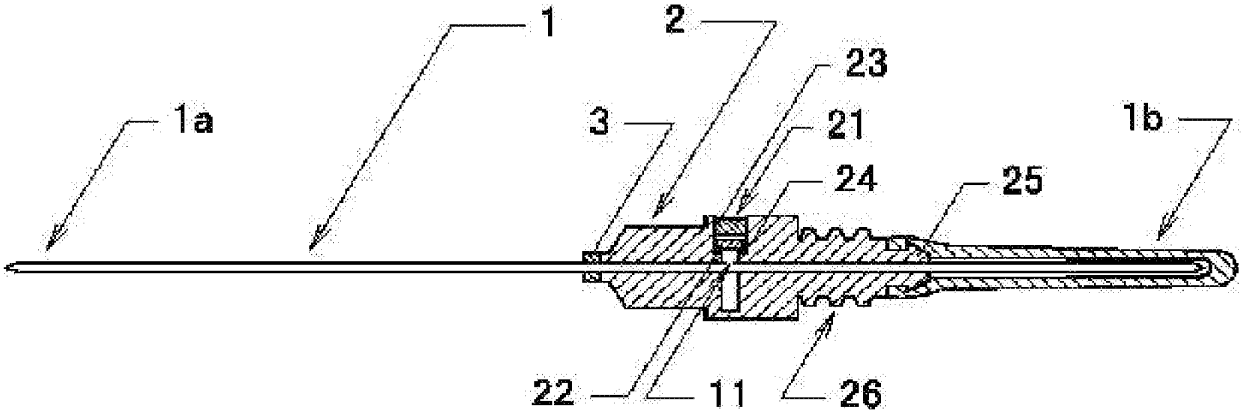
24 Convex portion

4 Rubber cap

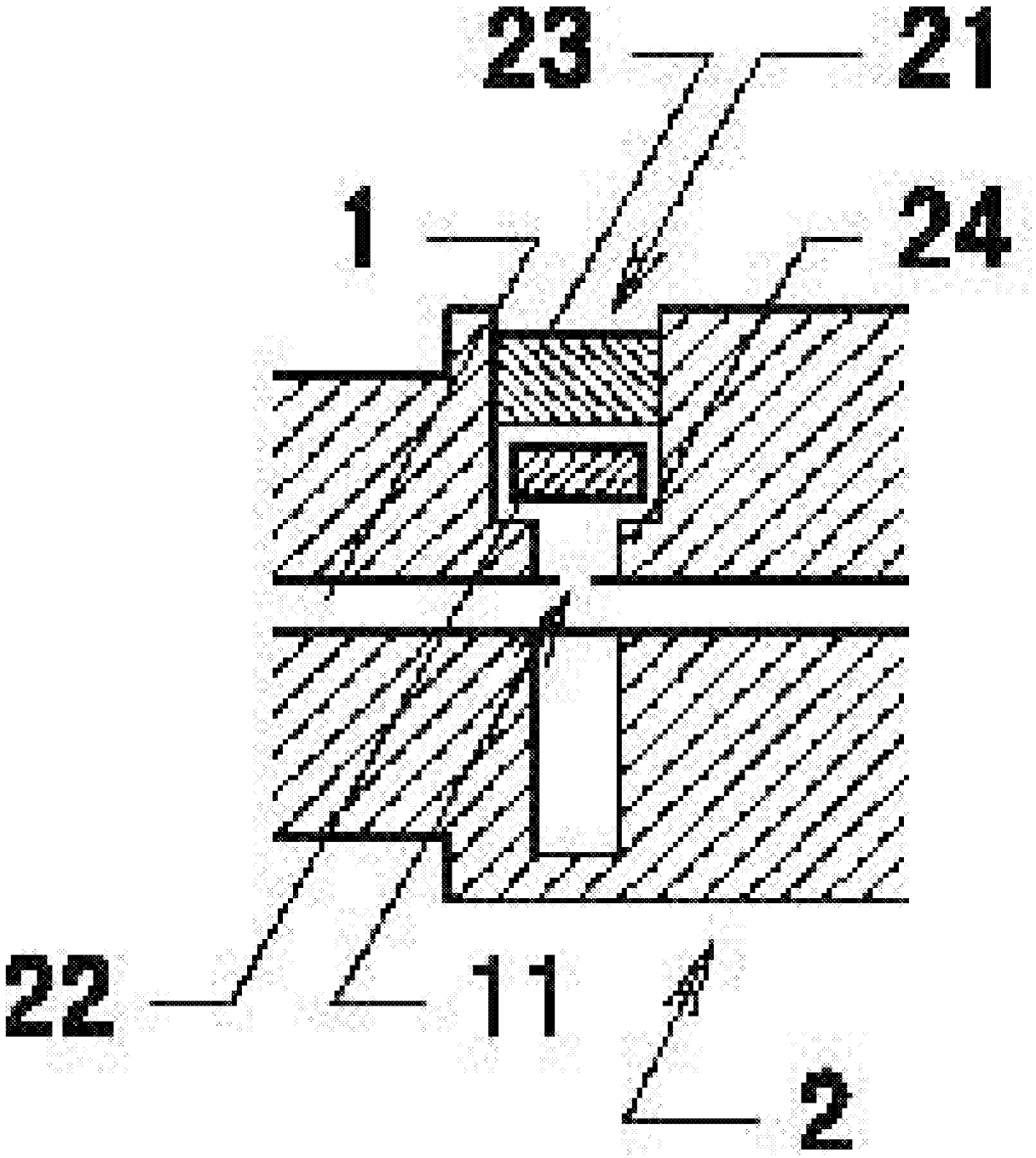
drawing

open —

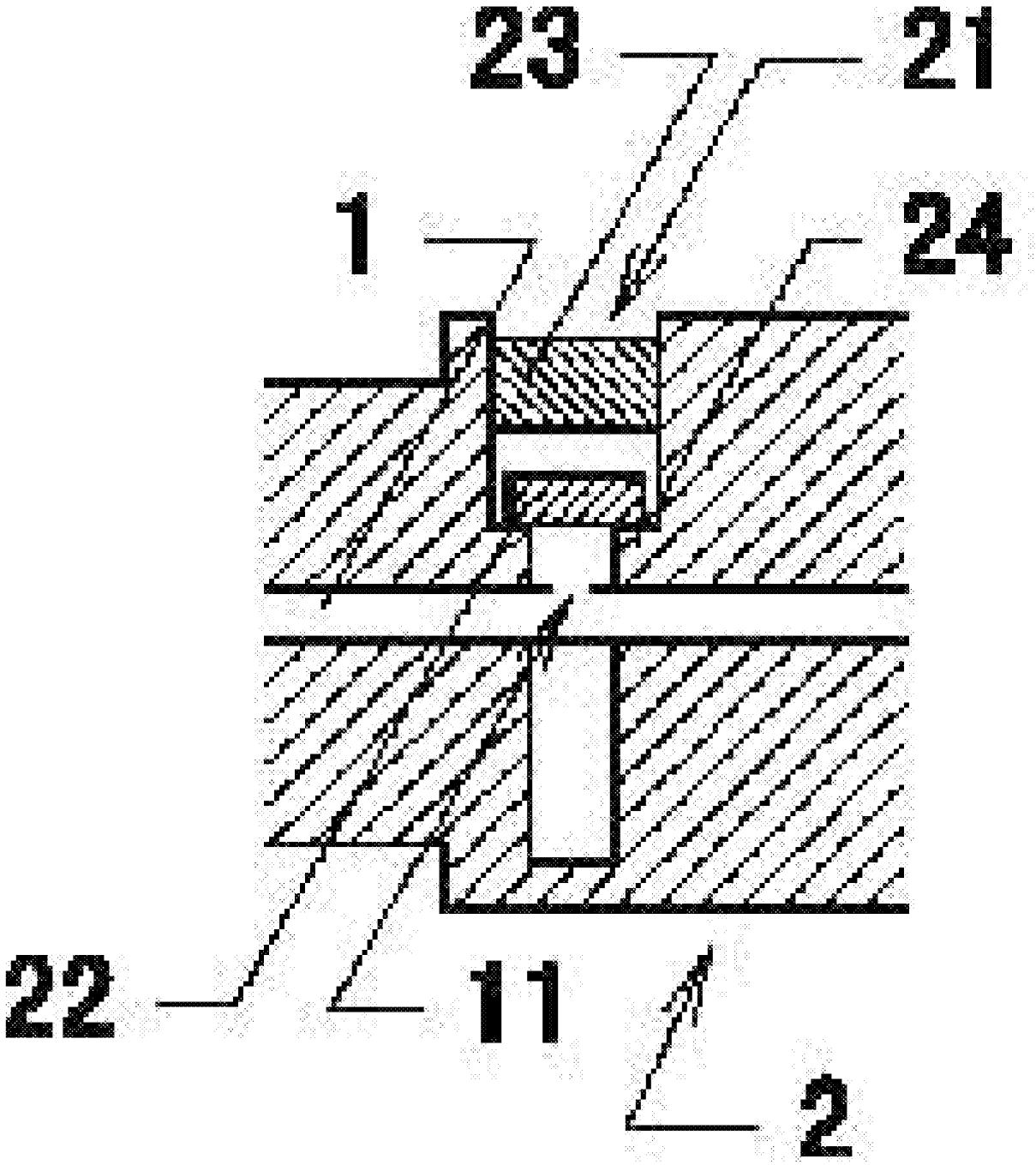
[Fig. 1]



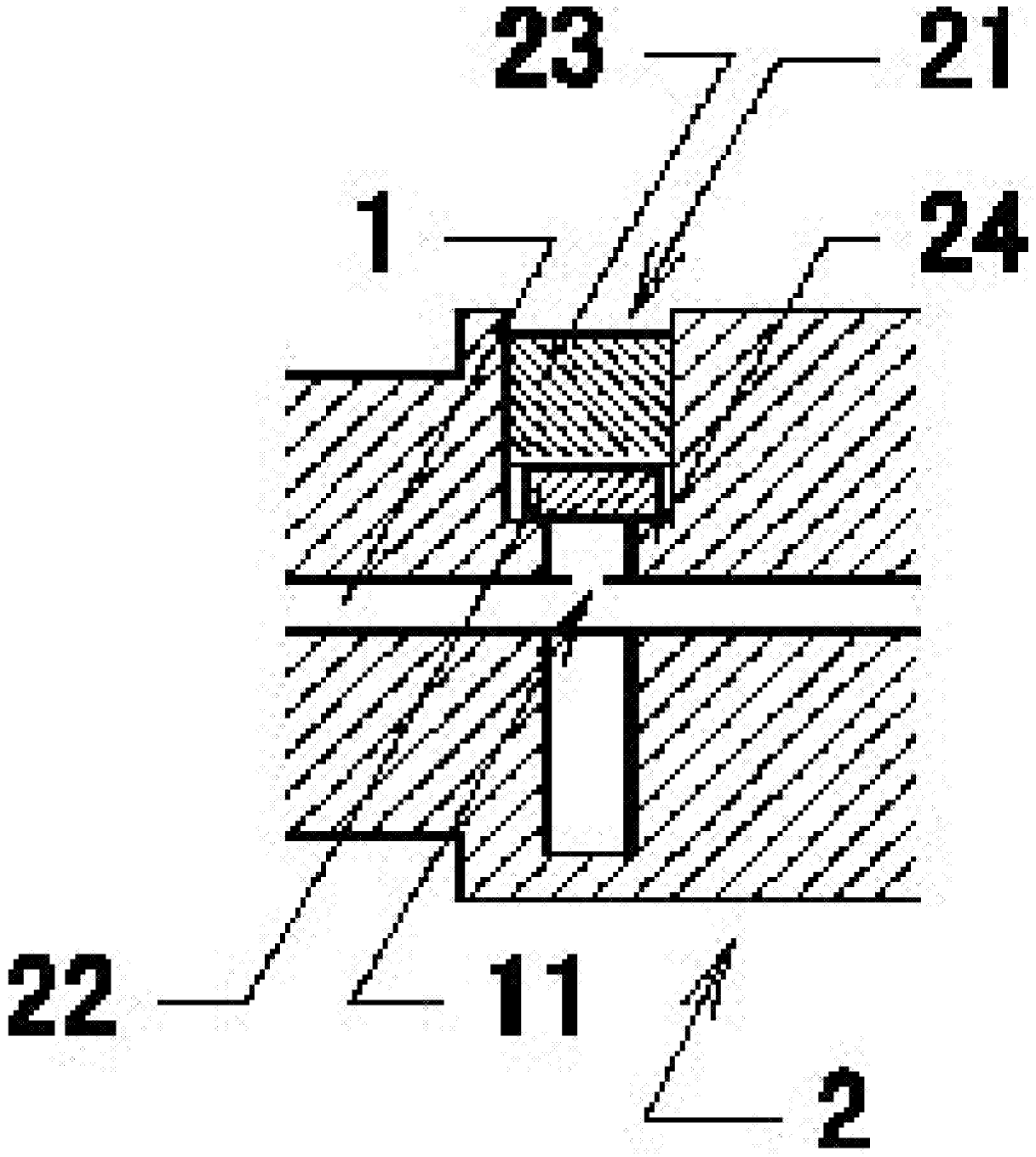
[Figure 2]



[Figure 3]



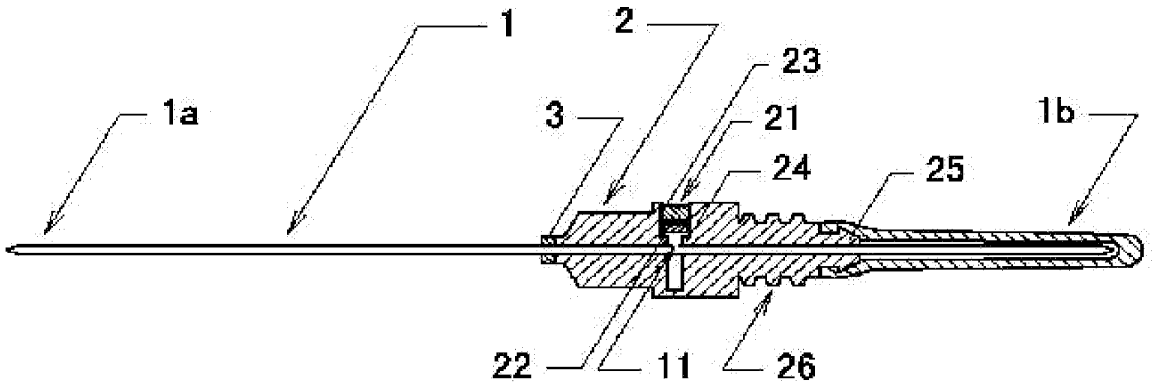
[Figure 4]



drawing open —

Representative drawing | 1 | 2 | 3 | Four

Magnify and Rotate



Representative drawing

1 / 1 display

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(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2001－424
（P2001－424A）
(43)公開日　平成13年１月９日(2001.1.9)

(51)Int.Cl.[7]	識別記号	ＦＩ	ﾃｰﾏｺｰﾄﾞ(参考)
Ａ６１Ｂ　5/15		Ａ６１Ｂ　5/14	３００Ｈ　４Ｃ０３８

審査請求　未請求　請求項の数４　ＯＬ　（全　３　頁）

(21)出願番号　特願平11－174400

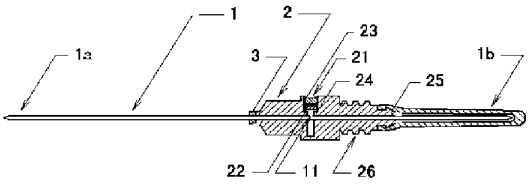
(22)出願日　平成11年６月21日(1999.6.21)

(71)出願人　000135036
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大阪府大阪市北区本庄西３丁目９番３号
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神奈川県大和市深見3211－17

Ｆターム(参考)　4C038 TA06 UJ02 UJ06

(54)【発明の名称】　採血針

(57)【要約】
【課題】採血時に針が確実に被検者の静脈に穿刺されたことを穿刺後、直ちに確認できる採血針を提供する。
【解決手段】側壁の少なくとも一部に孔を有し、両端が刃面である針管（Ａ）、該孔を覆うように設けられ、該孔を通じて外部と針管の内部とを連通した通路を備えた針管支持体（Ｂ）、該通路の外部への開放端に係止された空気透過性血液不透過性部材（Ｃ）、針管の一方の端を密封するように、前記針管支持体に係止されてなるゴム状キャップ（Ｄ）、および前記通路内に設けられ、前記孔あるいは通路を塞ぎ得る封止部材（Ｅ）とを有する採血針である。



【特許請求の範囲】
【請求項１】　側壁の少なくとも一部に孔を有し、両端が刃面である針管（Ａ）、該孔を覆うように設けられ、該孔を通じて外部と針管の内部とを連通した通路を備えた針管支持体（Ｂ）、該通路の外部への開放端に係止された空気透過性血液不透過性部材（Ｃ）、針管の一方の端を密封するように、前記針管支持体に係止されてなるゴム状キャップ（Ｄ）、および前記通路内に設けられ、前記孔あるいは通路を塞ぎ得る封止部材（Ｅ）とを有する採血針。
【請求項２】　通路が封止部材を係止する凸部を有する請求項１記載の採血針。
【請求項３】　空気透過性血液不透過性部材が膨潤物質である請求項１、または２記載の採血針。
【請求項４】　針管支持体が透明または半透明である請求項１、２、または３記載の採血針。
【発明の詳細な説明】
【０００１】
【発明の属する技術分野】本発明は採血針に関し、さらに詳細にはその一端を被検者の血管に穿刺し、他端を真空採血管内に連通させて、真空採血管内の負圧に応じた量の血液を採取できるようにした採血針に関する。本発明の採血針によれば、他端を真空採血管に連通させる前に一端が被検者の静脈に穿刺されたことを確認できる。
【０００２】
【従来の技術】従来から真空採血管による採血に際して、真空採血管を取り付ける前に、針が確実に被検者の静脈に穿刺されたこと、いわゆるフラッシュバックを確認できるような採血針が提案されている。このような従来の採血針としては、例えば、特開昭６１－６４２３４号公報には、前端部と後端部および外気と流通する通路を備えた試料収集室を有するハウジングと、その前端部および後端部から延設されたカニューレと、血液と接触して膨張し、外気との流通を遮断するタブレットを備えた採血針が開示されている。しかし、この採血針は、真空採血管を取り付けた時、タブレットに陰圧がかかるため、採血針内部に外気が流入するおそれがあり、既定の採血量が得られないことがある。
【０００３】また、特開平４－１３２５４１号公報には、弾性チップ内腔部と外部雰囲気とを連通させる通気孔を有し、該通気孔の外部口部に通気性フィルタを備えており、透明ないし半透明のハブまたは弾性チップによりフラッシュバックを確認できる採血針が開示されている。しかしながら、この採血針の弾性チップは、採血針ホルダー内部に収納され、しかも、その上から手で保持されるため、弾性チップによるフラッシュバックの確認は非常に困難である。また、一端を被検者の静脈に穿刺したときに静脈圧により針管内部に侵入した血液は、弾性チップ内腔部に充満したあと、通気孔に侵入する構造を有しているため、ハブによりフラッシュバックを確認するまでに時間を要する。
【０００４】
【発明が解決しようとする課題】本発明は上記事情に鑑みてなされたもので、真空採血管取り付け時、フィルタ部（以下、空気透過性血液不透過性部材と呼ぶ）に陰圧がかからず、採血針の一端が静脈に穿刺された後、直ちにフラッシュバックを確認できる採血針を提供することを目的とする。
【０００５】
【課題を解決するための手段】本発明者らは種々鋭意検討の結果、針管の側壁に孔を設け、その孔を通じて外部と針管内部とを連通させるような通路を設け、さらに真空採血管取り付け時に、針管内部を外部から遮断するような機構を設けた採血針が、上記課題を解決するものであることを見出し、本発明に到達した。
【０００６】すなわち本発明は、側壁の少なくとも一部に孔を有し、両端が刃面である針管（Ａ）、該孔を覆うように設けられ、該孔を通じて外部と針管の内部とを連通した通路を備えた針管支持体（Ｂ）、該通路の外部への開放端に係止された空気透過性血液不透過性部材（Ｃ）、針管の一方の端を密封するように、前記針管支持体に係止されてなるゴム状キャップ（Ｄ）、および前記通路内に設けられ、前記孔あるいは通路を塞ぎ得る封止部材（Ｅ）とを有する採血針である。
【０００７】
【発明の実施の形態】次に本発明を図面に基づいて詳細に説明する。図１は本発明の採血針の一実施例を示す断面図である。針管１はステンレス製であるのが好ましい。その一端１ａは刃面であり被検者の血管を刺すように形成されており、他端１ｂも刃面であり、真空採血管（図示せず）に差し込むように形成される。
【０００８】前記針管１の側壁には孔１１が設けられている。該孔１１は針管支持体２内であれば、針管１のどの部分に設けられていてもよい。該針管１には前記孔１１を覆うように、透明または半透明の針管支持体２が設けられる。該針管支持体２は針管１の一端１ａ側で、針管１と例えば接着剤３により密封的に固着されている。
【０００９】この針管支持体２内には、前記孔１１を通じて外部と針管１の内部とを連通した通路２１が形成されている。該通路２１は、外部と連通していれば、その外部への開放端はどこに設けられていてもよい。前記通路２１により、針管１の一端１ａの刃面を被検者の静脈に穿刺したとき、針管１内部に侵入した血液は、孔１１を通って前記通路２１に侵入し、侵入した血液を針管支持体２の側面から目視することで、フラッシュバックを確認することができる。
【００１０】前記通路２１内には、封止部材２２が設けられている。該封止部材２２としては、ポリプロピレン、テフロン（登録商標）およびシリコンゴムなどのプラスチック材料を使用することができるが、ステンレス

などの金属やセラミックであっても構わない。また通路２１内において、該封止部材２２と針管支持体２との間に空気及び血液が通過できる間隙を有している。

【００１１】前記通路２１の針管１外部への開放端には、空気透過性血液不透過性部材２３が密封的に係止されている。この部材２３により通路２１内の通気性を保ちながら、採血時に流入した血液は外部へ漏らすことがない。空気透過性血液不透過性部材２３としては、通常、ポリプロピレンやポリエチレンなどのポリマー焼結体からなる層状のフィルターが好適に使用されるが、ポリプロピレンやポリエチレンなどの疎水性樹脂からなる膜状のいわゆるメンブレンフィルターであってもよい。

【００１２】図２に示すように、針管１の一端１ａを被検者に穿刺したとき、針管１内部から孔１１を通って通路２１内に流入してきた血液は、封止部材２２と針管支持体２との間隙を通って、空気透過性血液不透過性部材２３で堰き止められる。その後、真空採血管を針管１の他端１ｂに取り付けると、図３に示すように、真空採血管の陰圧により封止部材２２が針管１に引き寄せられ、通路２１を塞ぐ。これにより、空気透過性血液不透過性部材２３に直接陰圧がかからないので、既定の採血量が得られる。また、前記通路２１は、内部に封止部材２２を係止する凸部２４を設けたものが、針管１内部の密封性を考慮するとより好ましい。凸部２４の形状としては、図１に示される断面がＬ字状であるものの他に、開放端に向かってテーパー状に広がるものや、通路２１の中間部で通路内方へ突出しているものなどが挙げられる。

【００１３】また、空気透過性血液不透過性部材２３としては、アクリル酸系共重合体、スターチおよびゼラチンなどの膨潤物質を、単独あるいは他の化合物と混合して使用することができる。針管１の一端１ａを被検者に穿刺したとき、流入してきた血液によって膨張した空気透過性血液不透過性部材２３は、封止部材２２を直接針管１に、あるいは図４に示すように通路２１内の凸部２４に押しつけ、孔１１または通路２１を塞ぐ。これにより、フラッシュバックを確認したあと、すぐに針管１内部が密封される。また、真空採血管取り付け時には、真空採血管の陰圧により、さらに封止部材２２は針管１、あるいは凸部２４に密着するので、針管１内部の密封性はより高くなる。

【００１４】針管支持体２の他端１ｂ側には、針管１の刃面を密閉的に覆うゴム状キャップ４がフランジ２５により係止されている。このゴム状キャップ４の材料としては、合成イソプレンゴムやシリコンゴムなどが採用される。また、この針管支持体２にはねじ部２６が形成されており、ホルダーの口部（図示せず）に螺合されることにより、採血針とホルダーを一体化させることができる。

【００１５】

【発明の効果】本発明の採血針は側壁の一部に孔を設けることにより、採血針の一端が静脈に穿刺された後、直ちにフラッシュバックを確認することができる。また、封止部材を有しているため、真空採血管取り付け時に、空気透過性血液不透過性部材に陰圧がかかるおそれがない。

【図面の簡単な説明】

【図１】本発明の一実施例の採血針を示す断面図である。

【図２】図１の採血針における針管支持体部分の拡大断面図である。

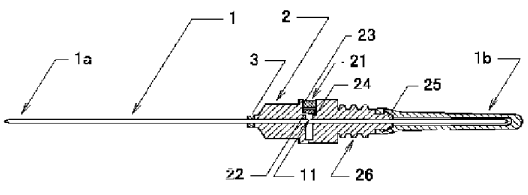
【図３】真空採血管取り付け時の、図１の採血針における、針管支持体部分の拡大断面図である。

【図４】本発明の他の採血針における、針管支持体部分の拡大断面図である。

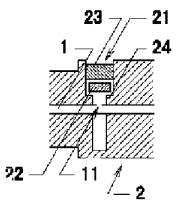
【符号の説明】

１　針管
１１　孔
２　針管支持体
２１　通路
２２　封止部材
２３　空気透過性血液不透過性部材
２４　凸部
４　ゴム状キャップ

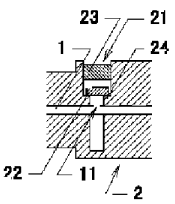
【図１】



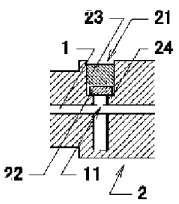
【図２】



【図３】



【図４】



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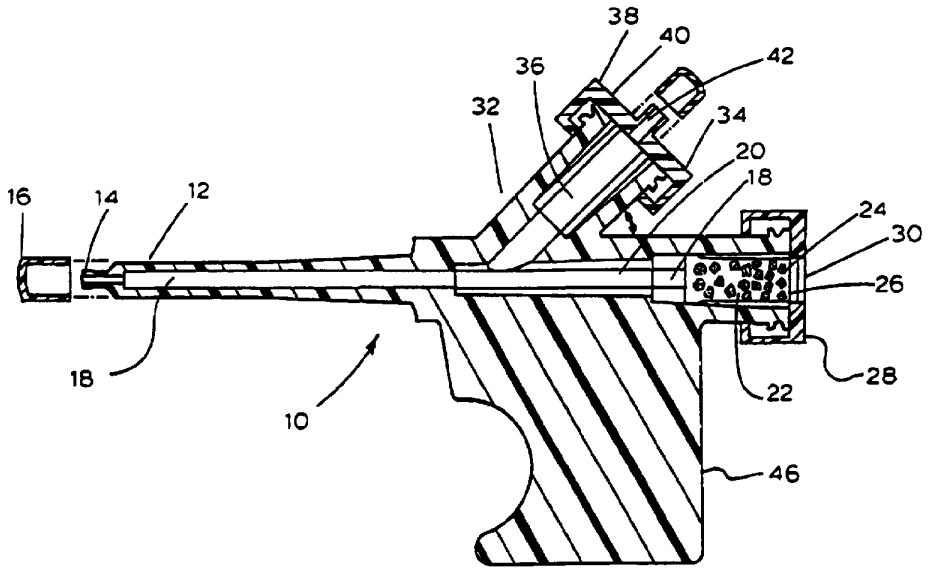
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(54) Title: CLOSED SYSTEM BLOOD SAMPLING DEVICE



(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.

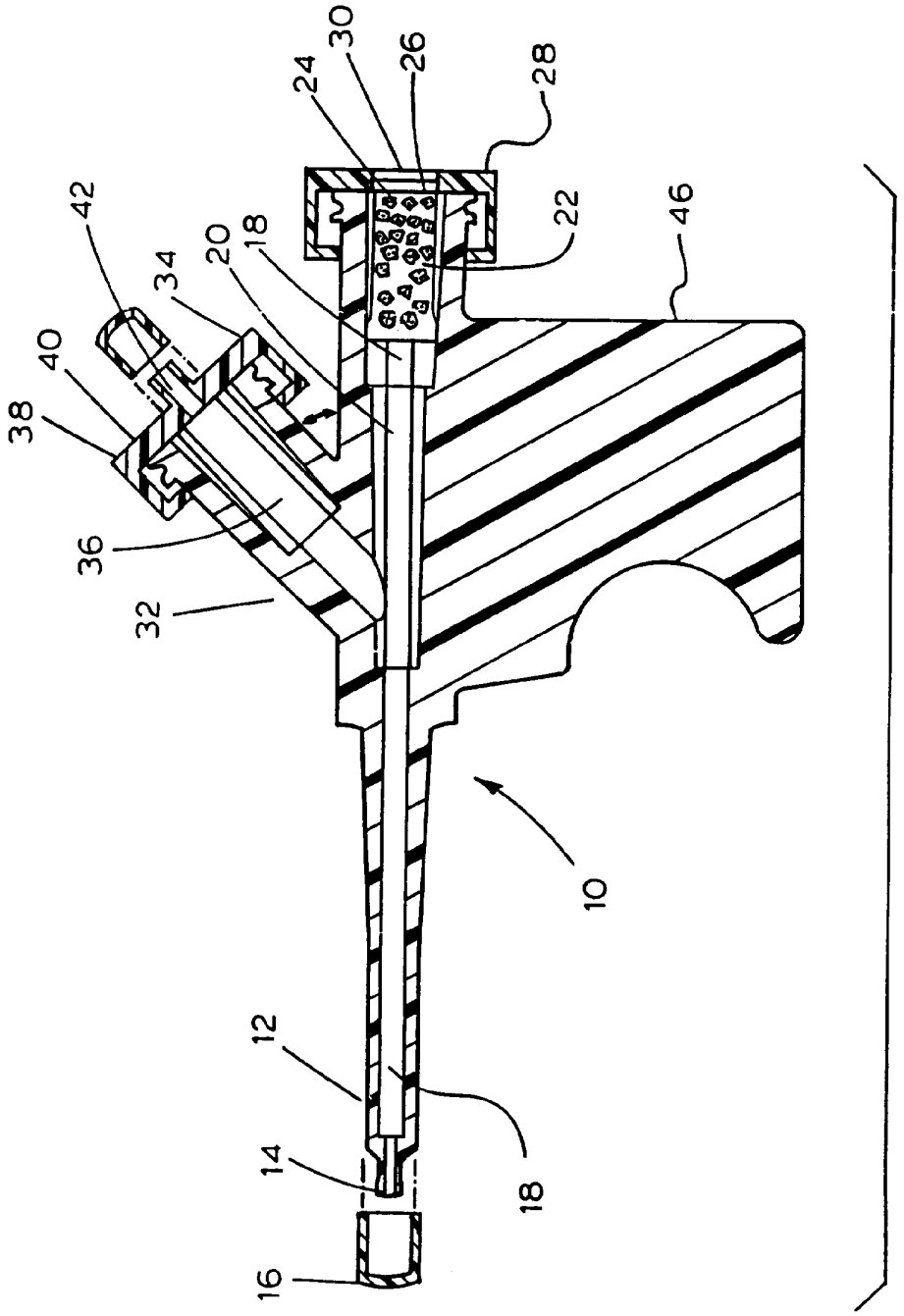


FIG. 1

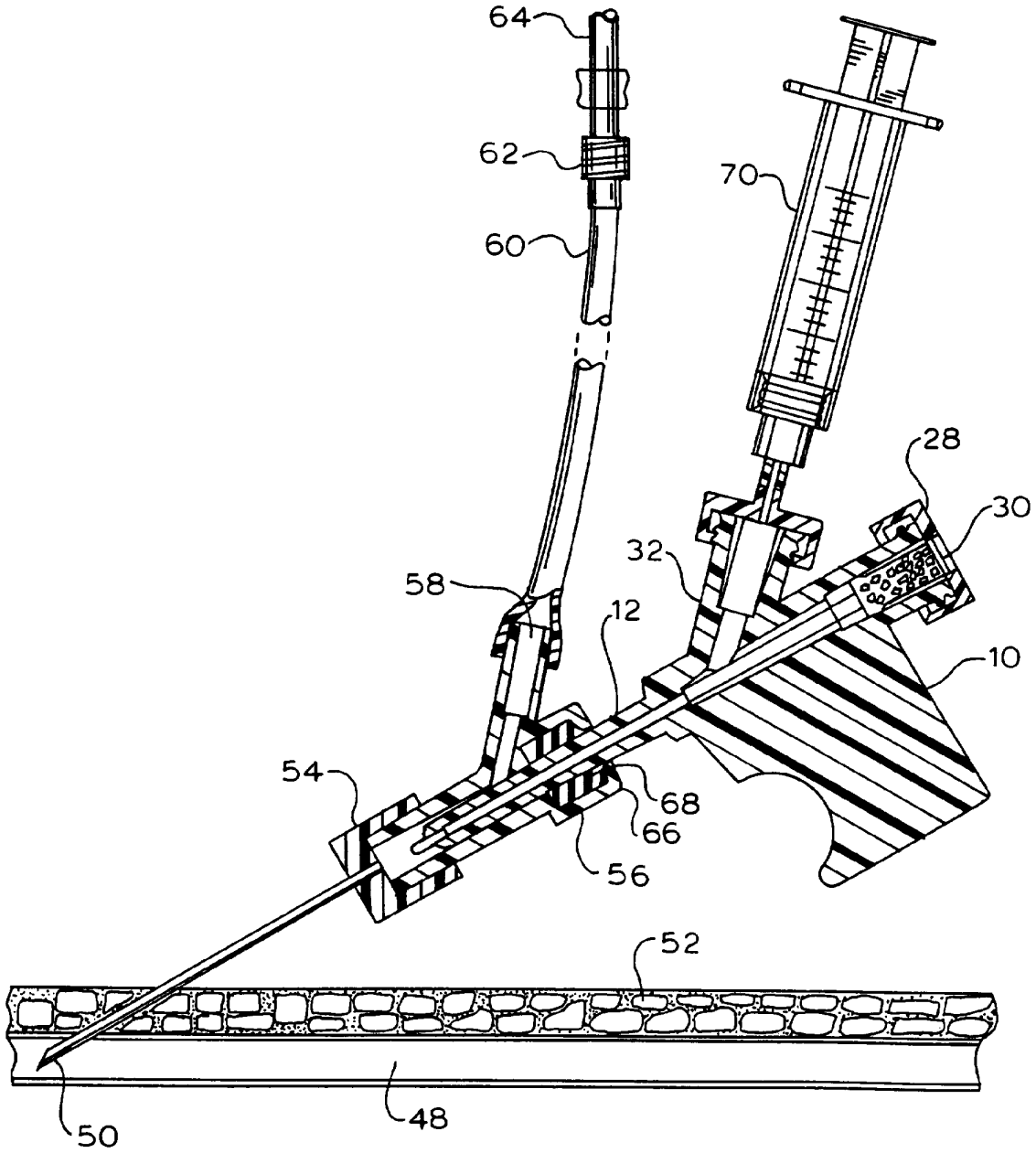


FIG. 2

SUBSTITUTE SHEET (RULE 26)

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)★

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	**FOR FURTHER ACTION**	see Form PCT/ISA/220 as well as, where applicable, item 5 below.
50828-501001WO		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/US2016/043709	22 July 2016 (22-07-2016)	24 July 2015 (24-07-2015)
Applicant		
CALLIOPE SOLUTIONS, INC.		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 5 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**
   a. With regard to the **language,** the international search was carried out on the basis of:
      [X] the international application in the language in which it was filed
      [ ] a translation of the international application into _____, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b))
   b. [ ] This international search report has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43.6*bis*(a)).
   c. [ ] With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. [ ] **Certain claims were found unsearchable** (See Box No. II)

3. [ ] **Unity of invention is lacking** (see Box No III)

4. With regard to the **title,**
   [X] the text is approved as submitted by the applicant
   [ ] the text has been established by this Authority to read as follows:

5. With regard to the **abstract,**
   [ ] the text is approved as submitted by the applicant
   [X] the text has been established, according to Rule 38.2, by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority

6. With regard to the **drawings,**
   a. the figure of the **drawings** to be published with the abstract is Figure No. 15C
      [X] as suggested by the applicant
      [ ] as selected by this Authority, because the applicant failed to suggest a figure
      [ ] as selected by this Authority, because this figure better characterizes the invention
   b. [ ] none of the figures is to be published with the abstract

Box No. IV Text of the abstract (Continuation of item 5 of the first sheet)

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.

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.

* 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 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

2

Form PCT/ISA/210 (second sheet) (April 2005)

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

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
		US 2012330187 A1	27-12-2012
JP H08257018 A	08-10-1996	NONE	
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
		JP 4914601 B2	11-04-2012
		JP 2006150083 A	15-06-2006
		US 2006129064 A1	15-06-2006
US 4056101 A	01-11-1977	NONE	
US 2013317391 A1	28-11-2013	US 2013317391 A1	28-11-2013
		US 2015099996 A1	09-04-2015
		US 2015351678 A1	10-12-2015

Information on Search Strategy - Pilot phase (see OJ 2015, A86)
The type of information contained in this sheet may change during the pilot for improving the usefulness of this new service.

Application Number
PCT/US2016/043709

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

APPLICANT: CALLIOPE SOLUTIONS, INC.

IPC CLASSIFICATION: A61B5/15, A61B5/153, A61B5/154

EXAMINER: Schultz, Ottmar

CONSULTED DATABASES: EPODOC, WPI, COMBI, TXT+

CLASSIFICATION SYMBOLS DEFINING EXTENT OF THE SEARCH:

IPC:

CPC: A61B5/15003, A61B5/150213, A61B5/150389, A61B5/150473, A61B5/150572, A61B5/153, A61B5/154

FI/F-TERMS:

KEYWORDS OR OTHER ELEMENTS FEATURING THE INVENTION:
See claims.

EPO FORM P04A42

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US2016/043709	22.07.2016	24.07.2015

International Patent Classification (IPC) or both national classification and IPC
INV. A61B5/15 A61B5/153 A61B5/154

Applicant
CALLIOPE SOLUTIONS, INC.

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☒ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

Name and mailing address of the ISA:	Date of completion of this opinion	Authorized Officer
European Patent Office Gitschiner Str. 103 D-10958 Berlin Tel. +49 30 25901 - 0 Fax: +49 30 25901 - 840	see form PCT/ISA/210	Schultz, Ottmar Telephone No. +49 30 25901-0

Form PCT/ISA/237 (Cover Sheet) (January 2015)

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of:

   ☒ the international application in the language in which it was filed.

   ☐ a translation of the international application into , which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1 (b)).

2. ☐ This opinion has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43*bis*.1(a))

3. ☐ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, this opinion has been established on the basis of a sequence listing:

   a. ☐ forming part of the international application as filed:

      ☐ in the form of an Annex C/ST.25 text file.

      ☐ on paper or in the form of an image file.

   b. ☐ furnished together with the international application under PCT Rule 13*ter*.1(a) for the purposes of international search only in the form of an Annex C/ST.25 text file.

   c. ☐ furnished subsequent to the international filing date for the purposes of international search only:

      ☐ in the form of an Annex C/ST.25 text file (Rule 13*ter*.1(a)).

      ☐ on paper or in the form of an image file (Rule 13*ter*.1(b) and Administrative Instructions, Section 713).

4. ☐ In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that forming part of the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

5. Additional comments:

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	2, 6, 7, 11, 14
	No:	Claims	1, 3-5, 8-10, 12, 13, 15-20
Inventive step (IS)	Yes:	Claims	6, 14
	No:	Claims	1-5, 7-13, 15-20
Industrial applicability (IA)	Yes:	Claims	1-20
	No:	Claims	

2. Citations and explanations

see separate sheet

Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

+++++

Reference is made to the following document:

D1: WO 2011/162772 A1 (CLEARVIEW PATIENT SAFETY TECHNOLOGIES LLC [US]; FISCHEL LLOYD [US]; BR) 29 December 2011.

+++++

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

+++++

1 INDEPENDENT CLAIMS 1, 8, 17

1.1 Claims 8 seeks to define a blood sequestration device by being connected with a blood sampling pathway having a patient needle and a sample collection device whereby said blood sampling pathway does not form part of the claimed blood sequestration device.

This would only be the case if e.g. claim 8 defined e.g. "A system of a blood sequestration device and a blood sampling pathway having a patient needle and a sample collection device, whereby the blood sequestration device is connected with the blood sampling pathway, said blood sequestration device comprising...".

The technical features and the related definitions of the blood sampling pathway can therefore not be used to render the subject-matter of claim 8 either novel or inventive.

Since the intended limitation does not belong to the subject-matter claimed, namely the blood sequestration device, this said limitation leads to uncertainty with regard to the actual protection sought, contrary to the requirements of Article 6 PCT.

The same reasoning applies, mutatis mutandis, to the subject-matter of the corresponding independent claim 17, which therefore is also considered not meeting the requirements of Article 6 PCT.

1.2 The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claim 1 is not new in the sense of Article 33(2) PCT. The reason is the following:

Document D1 discloses (the references in parenthesis applying to this document) in figure 15 all the features of independent claim 1, namely:

"A blood sequestration device (see figure 15) comprising;

an inlet port (see ref. sign 117 "well");

an outlet port (see ref. sign 330 "sleeve connector");

a sequestration chamber (see ref. sign 117 "guide tube aperture") connected with the inlet port, the sequestration chamber having a vent (see ref. sign 117 "venting member") comprising an air permeable blood barrier;

a sampling channel (see the channel formed in the sleeve connector 330) having a proximal end connected with the inlet port and a distal end connected with the outlet port; and

a housing (see ref. sign 116 "guide tube") that houses and defines the inlet port, the outlet port, the sequestration chamber, and the sampling channel".

1.3 The same reasoning applies, mutatis mutandis, to the subject-matter of the corresponding independent claims 8 an 17, which therefore are also considered not new (Article 33(1) and (2) PCT).

2 DEPENDENT CLAIMS 2-7, 9-16, 18-20

2.1 Dependent claims 2 to 5, 7, 9 to 13, 15, 16 and 18 to 20 do not contain any features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of novelty (Article 33(2) PCT) and/or inventive step (Article 33(3) PCT), the reasons being as follows:

As far as the features of these said dependent claims are not already explicitly anticipated by document D1 (for further details, see the relevant passages as cited in the International Search Report and in the above-mentioned paragraph 1), these features would be chosen by a person skilled in the art simply by routine trial and error or these said features are at least generally known by a person skilled in the art either to be one of several straightforward possibilities from which this said person would select or to be regarded by this said person as a normal design option and thus would not add any inventive merit to the subject-matter of the these said dependent claims.

2.2 The features of dependent claims 6 and 14 in combination with the features of any claim to which these said claims refer, seem neither to be known from, nor rendered obvious by, the available prior art.

+++++

Re Item VII

Certain defects in the international application

+++++

1 The independent claims are not in the two-part form in accordance with Rule 6.3(b) PCT with those features known in combination from the prior art (e.g. one of the documents cited in the International Search Report) being placed in the preamble (Rule 6.3(b)(i) PCT) and with the remaining features being included in the characterising part (Rule 6.3(b)(ii) PCT).

2 Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in the documents cited in the International Search Report is not mentioned in the description, nor are at least some of these documents identified therein.

3 The features of the claims are not provided with reference signs placed in parentheses (Rule 6.2(b) PCT).

+++++

Re Item VIII

Certain observations on the international application

+++++

Claims 8 seeks to define a blood sequestration device by being connected with a blood sampling pathway having a patient needle and a sample collection device whereby said blood sampling pathway does not form part of the claimed blood sequestration device.

This would only be the case if e.g. claim 8 defined e.g. "A system of a blood sequestration device and a blood sampling pathway having a patient needle and a sample collection device, whereby the blood sequestration device is connected with the blood sampling pathway, said blood sequestration device comprising...".

The technical features and the related definitions of the blood sampling pathway can therefore not be used to render the subject-matter of claim 8 either novel or inventive.

Since the intended limitation does not belong to the subject-matter claimed, namely the blood sequestration device, this said limitation leads to uncertainty with regard to the actual protection sought, contrary to the requirements of Article 6 PCT.

The same reasoning applies, mutatis mutandis, to the subject-matter of the corresponding independent claim 17, which therefore is also considered not meeting the requirements of Article 6 PCT.

+++++

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	**FOR FURTHER ACTION**	see Form PCT/ISA/220 as well as, where applicable, item 5 below.
KURIN3PCT		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/US2017/068569	27 December 2017 (27-12-2017)	27 December 2016 (27-12-2016)
Applicant		
KURIN, INC		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 4 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**
   a. With regard to the **language,** the international search was carried out on the basis of:
      [X] the international application in the language in which it was filed
      [ ] a translation of the international application into _____, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b))
   b. [ ] This international search report has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43.6*bis*(a)).
   c. [ ] With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. [ ] **Certain claims were found unsearchable** (See Box No. II)

3. [ ] **Unity of invention is lacking** (see Box No III)

4. With regard to the **title,**
   [X] the text is approved as submitted by the applicant
   [ ] the text has been established by this Authority to read as follows:

5. With regard to the **abstract,**
   [X] the text is approved as submitted by the applicant
   [ ] the text has been established, according to Rule 38.2, by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority

6. With regard to the **drawings,**
   a. the figure of the **drawings** to be published with the abstract is Figure No. 30B
      [ ] as suggested by the applicant
      [ ] as selected by this Authority, because the applicant failed to suggest a figure
      [X] as selected by this Authority, because this figure better characterizes the invention
   b. [ ] none of the figures is to be published with the abstract

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:	PCT
see form PCT/ISA/220	WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43*bis*.1)
	Date of mailing *(day/month/year)* see form PCT/ISA/210 (second sheet)
Applicant's or agent's file reference see form PCT/ISA/220	**FOR FURTHER ACTION** See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US2017/068569	27.12.2017	27.12.2016

International Patent Classification (IPC) or both national classification and IPC
INV. A61B5/15 A61B5/153 A61B5/154 A61B5/157

Applicant
KURIN, INC

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☒ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

Name and mailing address of the ISA:	Date of completion of this opinion	Authorized Officer
European Patent Office Gitschiner Str. 103 D-10958 Berlin Tel. +49 30 25901 - 0 Fax: +49 30 25901 - 840	see form PCT/ISA/210	Nielsen, Michael Telephone No. +49 30 25901-0

Form PCT/ISA/237 (Cover Sheet) (January 2015)

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of:

   ☒ the international application in the language in which it was filed.

   ☐ a translation of the international application into , which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1 (b)).

2. ☐ This opinion has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43*bis*.1(a))

3. ☐ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, this opinion has been established on the basis of a sequence listing:

   a. ☐ forming part of the international application as filed:

      ☐ in the form of an Annex C/ST.25 text file.

      ☐ on paper or in the form of an image file.

   b. ☐ furnished together with the international application under PCT Rule 13*ter*.1(a) for the purposes of international search only in the form of an Annex C/ST.25 text file.

   c. ☐ furnished subsequent to the international filing date for the purposes of international search only:

      ☐ in the form of an Annex C/ST.25 text file (Rule 13*ter*.1(a)).

      ☐ on paper or in the form of an image file (Rule 13*ter*.1(b) and Administrative Instructions, Section 713).

4. ☐ In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that forming part of the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

5. Additional comments:

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-20
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-20
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-20
	No:	Claims	

2. Citations and explanations

see separate sheet

Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

In light of the documents cited in the international search report, it is considered that the invention as claimed in the independent claims meets the criteria mentioned in Article 33 (1) PCT, i.e. it appears to be novel, to involve an inventive step and to be industrially applicable.

Prior art: Blood drawing devices capable of isolating a pre-sample in order to minimize the risk of contamination of the main sample. Well known concept, see any of the documents cited in the search report.

Problem: As in the prior art to minimize the risk of contamination of blood drawn from a patient.

Solution: The pre-sample chamber (sequestration chamber) having **the specific vent** as defined in the independent claims 1, 8 and 15.

None of the cited documents hint to said specific solution in order to solve said problem. Contribution to the art.

Claims 2-7, 9-14 and 16 to 20 are dependent on one or more independent claims whose subject-matter is considered as being new and inventive, as discussed above, and as such said dependent claims also meet the requirements of the PCT with respect to novelty and inventive step.

Re Item VII

Certain defects in the international application

1). The independent claims are not in the two-part form in accordance with Rule 6.3(b) PCT.

2). The features of the claims are not provided with reference signs placed in parentheses (Rule 6.2(b) PCT).

3). Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art (see search report) is not mentioned in the description, nor are these documents identified therein.

4). Upon entering the regional phase via the European Patent Office, the requirements of Rule 43(2) EPC should be observed.

Information on Search Strategy - Pilot phase (see OJ 2015, A86)
The type of information contained in this sheet may change during the pilot for improving the usefulness of this new service.

Application Number
PCT/US2017/068569

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

APPLICANT: KURIN, INC

IPC CLASSIFICATION: A61B5/15, A61B5/153, A61B5/154, A61B5/157

EXAMINER: Nielsen, Michael

CONSULTED DATABASES: WPI

CLASSIFICATION SYMBOLS DEFINING EXTENT OF THE SEARCH:

IPC:

CPC: A61B5/15003, A61B5/150213, A61B5/150251, A61B5/150389, A61B5/150488, A61B5/150992, A61B5/153, A61B5/150274, A61B5/1535, A61B5/1545, A61B5/157

FI/F-TERMS:

KEYWORDS OR OTHER ELEMENTS FEATURING THE INVENTION:

EPO FORM P04A42

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.

* 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
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

1

Form PCT/ISA/210 (second sheet) (April 2005)

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

Form PCT/ISA/210 (continuation of second sheet) (April 2005)

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2017/068569

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2014039348 A1	06-02-2014	US 2014039348 A1	06-02-2014
		US 2016113560 A1	28-04-2016
		WO 2014022275 A1	06-02-2014
US 2014107564 A1	17-04-2014	EP 2906269 A1	19-08-2015
		US 2014107564 A1	17-04-2014
		US 2015367069 A1	24-12-2015
		WO 2014058945 A1	17-04-2014
US 4813433 A	21-03-1989	NONE	
US 2013317391 A1	28-11-2013	US 2013317391 A1	28-11-2013
		US 2015099996 A1	09-04-2015
		US 2015351678 A1	10-12-2015
WO 2013181352 A1	05-12-2013	AU 2013267448 A1	18-12-2014
		AU 2017216493 A1	07-09-2017
		CA 2875118 A1	05-12-2013
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		CN 107736901 A	27-02-2018
		EP 2854643 A1	08-04-2015
		EP 3173021 A1	31-05-2017
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		US 2014155781 A1	05-06-2014
		US 2015351679 A1	10-12-2015
		WO 2013181352 A1	05-12-2013

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

Vox Sanguinis (2002) **83**, 13–16
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ORIGINAL PAPER

Diversion of first blood volume results in a reduction of bacterial contamination for whole-blood collections

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Vox Sanguinis

Background and Objectives In a previous study we established a reliable setpoint for the prevalence of bacteria in whole blood. In the present study we investigated the possible preventive effect, of diversion of the first 10 ml of a blood donation, on the bacterial contamination rate.

Materials and Methods To divert the first 10 ml of a whole-blood donation, we used a special five-bag system equipped with a Composampler® device. After venepuncture, the first 10 ml of a donation was sampled into a vacutainer tube. This was followed by the collection of the whole-blood unit. The extra bag allowed direct sampling of the final donation in a closed system for BacT/Alert. Whole-blood samples were taken after storage (2–14 h at 20 °C) and subsequent mixing. BacT/Alert culture bottles were incubated until positive, or for 7 days if negative. Confirmation and identification of positive cultures was performed according to internationally recognized standard reference methods.

Results The prevalence of bacteria in whole blood, as determined by using standard collection techniques, was 0·35% (95% confidence interval 0·27–0·44%, n = 18 257). After diversion of the first 10 ml this value was significantly lower: 0·21% ($P < 0·05$, 95% confidence interval 0·12–0·35%, n = 7087). Most strikingly, a reduction in the frequency of staphylococcal species was observed ($P < 0·02$, reduction from 0·14 to 0·03%).

Conclusions Diversion of the first 10 ml of blood was shown to contribute significantly to a reduction in the prevalence of superficial skin bacteria in whole-blood units. In our opinion, blood collection systems should be adapted to use the first 10–30 ml of a whole-blood donation for testing purposes.

Received: 15 November 2001, revised 1 March 2002, accepted 2 March 2002

Key words: bacteria, collection, diversion, reduction, whole blood.

Introduction

Since the implementation of programmes for reducing the contamination of the blood supply by blood-borne viruses, transfusion-transmitted bacterial infections (TTBI) have become one of the major hazards of blood transfusion. Sazama [1] estimated that 10% of blood transfusion-associated deaths are caused by bacterial contamination of the transfused product.

In the last decade, increased attention has been given to the prevention of possible systematic contamination during the collection (i.e. by disinfection) and preparation stages (i.e. closed systems, by the use of sterile-docking devices, etc.) of blood components. Reliable data on the frequency of bacterial contamination of donated whole blood, used for component preparation, is needed in order to validate the occurrence of systemic contamination, or to evaluate measures taken to decrease contamination. Recently, we showed that 0·34% of whole blood units were contaminated with bacteria [2]. That

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KUR-MAG-DE003803

study compromised a number of units tested, resulting in a narrow 95% confidence interval (CI) of 0·27–0·44%.

Because the majority of bacteria involved in TTBI are skin organisms, it is probable that contamination is introduced during venepuncture. Investigators have speculated that a skin-plug is punched out by the needle during phlebotomy [3,4]. Therefore, one of the suggested measures to reduce the bacterial contamination of whole-blood collections is diversion of the first volume of whole blood collected [4]. Olthuis *et al.* [5] were the first to show that for apheresis collections, the first 10 ml had a higher rate of bacterial contamination than the next two aliquots of 10 ml. Recently, Wagner *et al.* [6] showed the effectiveness of the diversion approach in an *in vitro* model system. Bruneau *et al.* [7] showed that the first aliquot (15-ml) of whole blood collected has a higher contamination rate than the second aliquot, without testing the final whole-blood unit collected.

We investigated, under routine blood bank conditions, whether diversion of the first 8–10 ml of whole blood from the primary collection container reduced the degree of bacterial contamination in the final whole-blood collection.

Materials and methods

Blood collection

Whole blood (500 ± 50 ml) was collected under standardized blood bank conditions in four-bag Compoflex CPD/SAGM systems (Fresenius Hemocare, NPBI International, Emmer-Compascuum, the Netherlands), with an additional fifth bag. These blood-collection systems were designed and validated [2] for use in this particular study (see Fig. 1). They allow both diversion of the whole blood (by Composampler) and sampling in a closed system, with the only aseptic handling being the transfer (in a laminar airflow cabinet) of a sample from the final donation to anaerobic and aerobic culture bottles (BacT/Alert; Organon Teknika, Boxtel, the Netherlands).

At all different collection sites of the De Meierij and CLB Sanquin Blood Banks, standardized methods for disinfection (double-swab method with isopropyl alcohol swabs), blood collection and storage were used. After venepuncture, an EDTA-vacutainer tube (nominal volume 10 ml; Becton-Dickinson, Franklin Lakes, NJ) was filled via the Composampler device (the mean collected volume was 9·8 ml with ≈ 1 ml of anticoagulant derived from the tube between the needle and the Composampler), followed by filling of the primary collection bag utilizing a clamp on the line before the Composampler. The only difference between the Blood Banks was the storage time on butane-diol cooling plates [8] (Fresenius Hemocare/NPBI International) between collection and sampling for BacT/Alert (2–3 h in Group A; De Meierij Blood Bank, and overnight in Group B; CLB Blood Bank). Butane-diol cooling plates were used to rapidly cool down the blood to 20 °C (within 2 h) and to hold the blood at this temperature during subsequent storage [8].

Automated microbe-detection system

Sampling was performed as described previously [2]. Both aerobic and anaerobic culture bottles were inoculated with a 10-ml sample of whole blood under aseptic conditions in a laminar airflow cabinet, using the integrated sampling

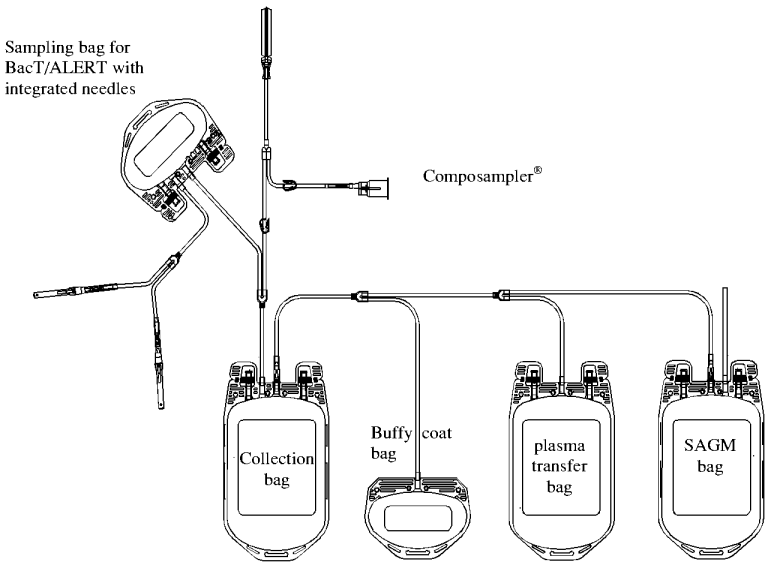


Fig. 1 Special five-bag Compoflex® blood-collection system, consisting of a conventional four-bag system with an additional BacT/ALERT sampling bag (the fifth bag) containing integrated transfer needles and equipped with a Composampler® to allow vacutainer sampling.

KUR-MAG-DE003804

needle of the extra sampling bag. Culture bottles were incubated at 35 °C in the BacT/Alert® system (an automated microbial detection system, based on the colorimetric detection of CO_2 [9]) until flagged positive, or for 7 days if negative. Subculture and identification of positive flagged bottles was performed as described previously [2].

Statistical analysis

Statistical analysis was performed using the computer program INSTAT 2·03 (GraphPad Software, San Diego, CA). The difference in proportions between the two groups was analysed using a one-sided χ^2-test (one-sided because of the hypothesis that diversion would lower the contamination rate). *P*-values of < 0·05 were considered significant. Confidence intervals (CI) were calculated according to Fleiss [10].

Results

Degree of bacterial contamination

In group A (sampling within 3 h after collection of whole blood), a total of 3405 units was collected and tested by using the BacT/ALERT® system. Out of these 3405 units, seven were culture positive, i.e. 0·21% (95% CI: 0·09–0·44%). In group B (sampling after overnight storage) in total 3682 units were collected and tested. In this group eight units were culture positive, i.e. 0·22% (95% CI: 0·10–0·45%). No significant difference was found between the two test groups (χ^2-test, $P = 0·48$). Combining these results, in total 7087 units of whole blood were tested (Table 1), with a bacterial contamination rate of 0·21% (95% CI: 0·12–0·35%). Using our standard collection method without diversion of the first 10 ml of sample, the prevalence was 0·35% (18 257 units tested [2]), which is significantly different (χ^2-test, one-sided because of the hypothesis that diversion would reduce the contamination rate; $P = 0·044$). Except for the diversion step, the collection procedures were similar for both studies. Furthermore, the distribution over the year of the collections for both studies was similar (to avoid seasonal effects).

Table 1 Summarized results of both studies

	Diversion of the first 10 ml	Standard, whole-blood collections [2]
Donations tested	*n* = 7087	*n* = 18 257
Positive cultures	*n* = 15	*n* = 63
Contamination rate[a]	0·21%	0·35%
95% CI of rate[b]	0·12–0·35%	0·27–0·44%

[a]Significant difference, $P < 0·05$ (χ^2-test; one-sided).
[b]Difference between the rates, (95% CI): 0·133 (–0·02 to 0·29).

Table 2 Differentiation of positive samples

	Diversion of the first 10 ml	Standard, whole-blood collections [2]
Resident skin flora		
Staphylococcus[a,b]	2 (0·03)	25 (0·14)
Propionibacterium[c]	10 (0·14)	27 (0·15)
Micrococcus	0	1 (0·01)
Diphteroids, *Corynebacterium* spp	0	5 (0·03)
Transient skin flora		
Bacillus	0	3 (0·02)
Gemella morbillorum	1 (0·01)	0
Klebsiella pneumoniae	1 (0·01)	0
(Upper) Gastrointestinal flora		
Streptococcus bovis	1 (0·01)	0
Peptostreptococcus	0	1 (0·01)
Not identified[d]	0	1 (0·01)

Values are expressed as absolute numbers per series (% prevalence).
[a]Coagulase-negative isolates, i.e. no occurrence of *Staphylococcus aureus*. Isolates were mainly *Staphylococcus epidermidis*.
[b]Significant difference, $P = 0·015$.
[c]Mainly *Propionibacterium acnes*.
[d]Growth curve in the BacT/ALERT was suggestive for *Propionibacterium*.
Resident skin flora: bacteria normally living on the skin. Transient skin flora: bacteria normally present in the air, but transient on skin. Gastrointestinal flora: bacteria normally present in the (upper) gastrointestinal system.

Identification of positive samples

Table 2 shows the bacterial species isolated from the subcultures derived from the BacT/ALERT® bottles that were flagged as positive. When the first 10 ml of blood was diverted, the majority of bacteria cultured were *Propionibacterium* spp, i.e. common skin flora. One isolate of *Streptococcus bovis* was found; this bacterial species is not normally part of the resident skin flora and therefore may have been transient skin flora that was not removed during the pre-bleed hygiene procedures. An examination of the donor from whom an isolate of *Klebsiella pneumoniae* was recovered revealed that the donor had no clinical signs of infection, and no blood products from this donation were used for transfusion. Culture results from both the red cell concentrate and the plasma from this donation were negative. Six months later a whole-blood sample from this donor was found to be culture negative.

The rate of contamination with *Staphylococcus* spp was significantly lower in the series tested after diversion of the first 10 ml of the blood donation ($P = 0·015$), whereas the contamination rate for *Propionibacterium* spp was similar (Table 2). Contamination rates for diphteroids and *Bacillus* spp were lower after diversion of the first 10 ml of the blood donation, but not significantly so.

KUR-MAG-DE003805

Discussion

In this study, under routine blood bank conditions diversion of the first 10 ml of whole blood was shown to significantly reduce the rates of bacterial contamination of final whole-blood units. Although previous studies by Wagner *et al.* [6] (using an *in vitro* model system) and Bruneau *et al.* [7] (with culture of diverted samples), strongly suggested that diversion of an initial blood sample would be effective in reducing skin contaminants in the collected unit, our study is the first to prove this for whole-blood collections.

A rather unexpected finding was the specific reduction of contamination with *Staphylococcus* spp upon diversion of the first 10 ml of sample, whereas contamination with *Propionibacterium* spp was similar, regardless of whether or not the first 10 ml of sample was diverted. A possible explanation for this might be that venepuncture, rather than coring skin plugs (which are transferred into the diverted volume, and include both superficial and intrinsic bacteria), results in skin flaps that do not become transferred into the diverted volume. Superficial skin bacteria such as *Staphylococcus* spp might be rinsed from the skin flaps by the initial diverted volume, whereas bacteria such as *Propionibacterium* spp (which colonize the deeper skin layer, the sebaceous glands and hair roots) are eluted from the flap during prolonged flow and thus are still able to enter the collected unit.

Compared to *Staphylococcus* spp, *Propionibacterium* spp are slow growing, yielding a positive signal in the BacT/Alert between 5 and 6 days after culture. Because culture in the BacT/Alert is carried out under optimal conditions with respect to medium composition and temperature, it is probable that *Propionibacterium* will rarely reach critical levels in platelet concentrates during the standard storage time of 5 days. Based on the findings of the present study, the effect of diversion on the actual frequency of (stored) erythrocyte and platelet concentrates containing sufficient bacteria to cause health problems might be greater than expected.

It is unknown whether the origin of the *Strep. bovis* and *K. pneumoniae* contaminants was the upper gastrointestinal tract of the donor, as these bacteria can easily be part of transient skin flora not removed from either the donor or phlebotomist during the pre-bleed hygiene procedures.

To prevent waste of collected whole blood, the initial diverted volume could be used for test purposes and, based on the results of Wagner *et al.* [6] and Bruneau *et al.* [7], a volume larger than 10 ml (current tests need ≈ 25 ml) could only be beneficial in terms of the final contamination rate. However, our diversion system cannot easily be used to fill several tubes without affecting the integrity of the closed system, because the Composampler membrane is no longer intact after its first use. Therefore, as long as clotting of the test sample is prevented, the collection system used by Bruneau *et al.* [7] might be an alternative.

Using whole blood as a source material for platelet components, the theoretical prevalence of bacteria in pooled platelet concentrates, composed of five single-donor units, would still be considerable (≈ 1%), despite the reduced contamination rate of whole blood. Therefore, in addition to diversion of the first volume during blood collection, all platelet concentrates should be tested for bacterial contamination in order to increase the safety of the blood supply.

In conclusion, the rate of bacterial contaminants in whole-blood units could be reduced by diversion of the first 8–10 ml of collected volume, especially with respect to contamination with *Staphylococcus* spp, commonly considered to be superficial skin flora.

Acknowledgements

This study was supported by Organon Teknika (Boxtel, the Netherlands) and Fresenius HemoCare/NPBI International (Emmer-Compascuum, the Netherlands). The authors would also like to thank all donors, donor assistants and technicians involved in this study.

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Bacterial Contamination of Blood Components

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INTRODUCTION

Allogeneic blood for transfusion is a potential source of infection by a variety of known and unknown transmissible agents. Since the 1980s, with the recognition of human immunodeficiency virus contamination of the blood supply, only a blood supply with a zero risk to recipients has been politically acceptable (67). This approach has led to the concept of "creeping precautionism" in the blood supply (46). The precautionary principle has grown out of the environmental movement. Briefly, it states ". . .where there are threats of serious or irreversible damage to the environment, lack of full scientific certainty should not be used as a reason for postponing cost-effective measures to prevent environmental degradation. . ." (46). To this end, astounding reductions in the viral risk of allogeneic blood has been accomplished (27). However, a number of transfusion safety measures have been implemented to achieve this level of safety, despite relatively poor cost-effectiveness, in order to assuage the public's fears (32).

Given the reduction of viral transmission via allogeneic blood, the low but known risk of bacterial contamination has emerged as the greatest residual threat of transfusion-transmitted disease (Fig. 1).

TRANSFUSION-TRANSMITTED BACTERIAL INFECTION OF RED CELLS

Each year, approximately 13,898,000 units of red cells or whole blood are transfused in the United States alone (1). This equates to one unit being transfused every 2.3 s. Despite this large number, sepsis associated with the transfusion of bacterially contaminated red cell blood components is generally regarded as a very rare event. From 1976 through September 1998, 26 fatalities thought to be secondary to contaminated whole blood or red cells were reported to the U.S. Food and Drug Administration (FDA) (36). Thus, approximately one red cell-related death per year has been reported. The majority of deaths reported to the FDA involved *Yersinia enterocolitica*. The highest reported incidence of *Y. enterocolitica* contamination was reported in New Zealand, with an incidence rate of 1 in

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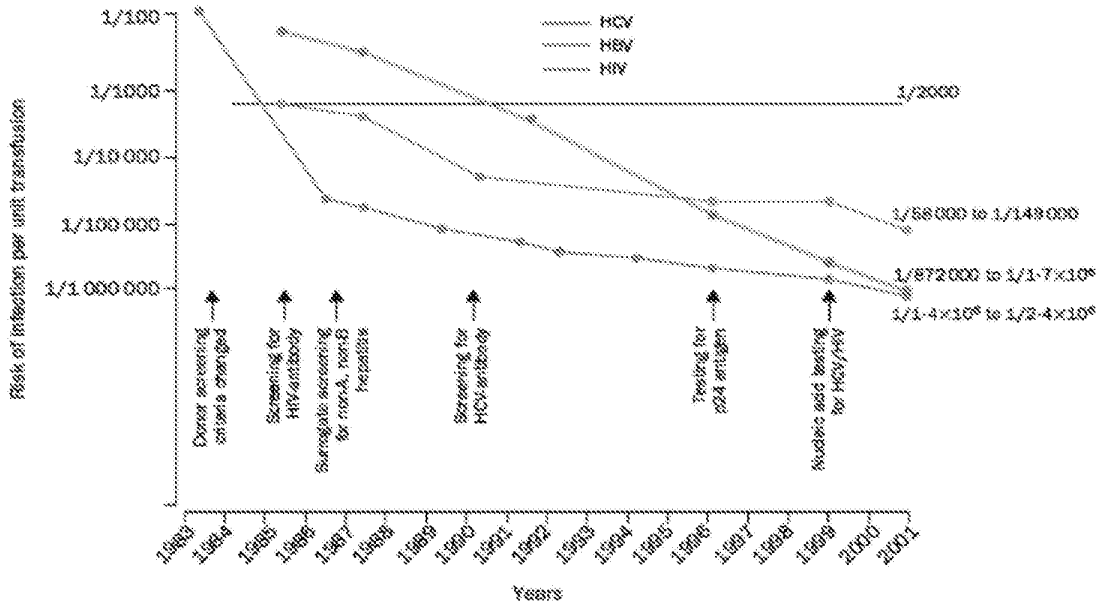


FIG. 1. Risk of infectious disease transmission per unit transfused by year, 1983 to 2001. Reprinted from reference 27 with permission of the publisher.

65,000 and a fatality rate of 1 in 104,000 red cell units transfused (59). Unrecognized cases, underreporting, and regional variation may account for observed differences in this incidence.

Interestingly, more recent passive reporting studies of bacterially contaminated red cells from the United States, France, and the United Kingdom that caused symptoms of infection show a relative paucity of *Yersinia* cases (Table 1) (35, 51, 57). Of the reported deaths, one was due to a coagulase-negative

TABLE 1. Organisms isolated from red cells implicated in transfusion-associated infections[a]

Organism	No. of contaminated units in:			Total no.
	United States	United Kingdom	France (29 isolates, 25 implicated units)	
Gram positive				
Coagulase-negative staphylococci	2 (1)	2	3	7 (1)
Streptococcus spp.			4[d]	4
Staphylococcus aureus			2[b]	2
Enterococcus faecalis			1[c]	1
Bacillus cereus			2	2
Propionibacterium acnes			1	1
Subtotal	2 (1 or 50%)	2 (0 or 0%)	13 (0 or 0%)	17 (1 or 6%)
Gram negative				
Serratia liquifaciens	2 (2)	1	2 (1)	5 (3)
Serratia marcescens	1			1
Yersinia enterocolitica		1 (1)	1	2 (1)
Enterobacter spp.			1 (1)	1 (1)
Acinetobacter spp.			5 (1)[b]	5 (1)
Pseudomonas spp.			2 (1)	2 (1)
Escherichia coli			3[c]	3
Klebsiella pneumoniae			1	1
Proteus mirabilis			1	1
Subtotal	3 (2 or 67%)	2 (1 or 50%)	16 (4 or 25%)	21 (7 or 33%)
Total	5 (3 or 60%)	4 (1 or 25%)	29 (4 or 14%)	38 (8 or 21%)

[a] Summary of organisms identified in the BACON, SHOT, and BACTHEM studies (35, 51, 57). Numbers and percentages of fatalities are given in parentheses.
[b] In one case, *S. aureus* and *A. baumannii* were both isolated from the implicated bag.
[c] In one case, *E. faecalis* and *E. coli* were both isolated from the implicated bag.
[d] In two cases, two isolates of *Streptococcus* were isolated from the implicated bag. Of the eight reported fatalities, seven (87.5%) were due to gram-negative organisms.

TABLE 2. Organisms implicated in infections associated with platelet transfusions[a]

Organism	No. of contaminated units in:			Total no.
	United States	United Kingdom	France	
Gram positive				
Bacillus cereus	1	4 (1)	2	7 (1)
Coagulase-negative staphylococci	9	6 (1)	5	20 (1)
Streptococcus spp.	3 (1)	2		5 (1)
Staphylococcus aureus	4	2 (1)		6 (1)
Propionibacterium acnes			3	3
Subtotal	17 (1 or 6%)	14 (3 or 21%)	10 (0 or 0%)	41 (4 or 10%)
Gram negative				
Klebsiella spp.			2 (1)	2 (1)
Serratia spp.	2 (2)		1 (1)	3 (3)
Escherichia coli	5 (1)	2 (1)	1	8 (2)
Acinetobacter spp.			1	1
Enterobacter spp.	2 (1)	1 (1)	1	4 (2)
Providencia rettgeri	1 (1)			1 (1)
Yersinia enterocolitica	1			1
Subtotal	11 (5 or 45%)	3 (2 or 67%)	6 (2 or 33%)	20 (9 or 45%)
Total	28 (6 or 21%)	17 (5 or 29%)	16 (2 or 13%)	58 (11 or 19%)

[a] Summary of organisms identified in the BACON, SHOT, and BACTHEM studies (35, 51, 57). Numbers and percentages of fatalities are given in parentheses.

Staphylococcus strain and seven were due to a variety of gram-negative organisms (including *Serratia liquefaciens* in three cases). These organisms are all capable of growth at 1 to 6°C. Sepsis associated with the transfusion of red cells contaminated with gram-negative bacteria is typically severe and rapid in onset. Patients frequently develop high fever (temperatures as high as 109°F have been observed) and chills during or immediately following transfusion. From 1987 to February 1996, 20 recipients of *Yersinia*-infected red cells were reported to the Centers for Disease Control (S. T. Cookson, M. J. Arduino, S. M. Aguero, W. R. Jarvis, and the *Yersinia* Study Group, Program Abstr. 36th Intersci. Conf. Antimicrob. Agents Chemother., abstr. 237, 1996). Twelve of the 20 recipients died, and the median time to death was only 25 h. Of the seven who developed disseminated intravascular coagulopathy, six died.

Prospective bacterial cultures of whole blood or red cells, however, have shown a much higher incidence of bacterial contamination (2 to 4 per 1,000 units); however, the organisms commonly cultured are *Staphylococcus* or *Propionibacterium* spp., which generally proliferate poorly during storage at 1 to 6°C (4).

TRANSFUSION-TRANSMITTED BACTERIAL INFECTION OF PLATELETS

Each year, within the United States approximately 4 million platelet units are transfused (1×10^6 single-donor apheresis platelets and 3 million whole-blood-derived platelet concentrates) (1). This equates to one platelet unit being transfused every 8 s. Unlike red cell or whole-blood components, which are stored at 1 to 6°C, platelets are stored at 20 to 24°C to preserve function and survival. Such storage makes them an excellent growth medium for a broad spectrum of bacteria. Multiple aerobic-culture surveillance studies have demonstrated that 1 in 1,000 to 2,000 platelet units are bacterially contaminated (4). Thus, 2,000 to 4,000 bacterially contaminated units would be expected to be transfused per year. Estimates of the fraction of cases that result in patient symptoms have been as low as 1 in 10 cases. However, in the only study that has prospectively cultured platelets that were transfused, eight culture-positive but Gram stain-negative platelet pools that were bacterially contaminated resulted in symptoms in three patients (37.5%) [A. Dykstra, G. Hoeltge, M. Jacobs, J. Miller, R. Domen, and R. Yomtovian, Transfusion 38(Suppl.): 104S, 1998]. Notably, six Gram stain-positive pools (which would be expected to have had the highest bacterial load) were interdicted and never transfused.

Thus, clinical sepsis would be expected in at least 1 in 10 to 2 in 5 contaminated transfusions (200 to 1,600 cases). National passive-reporting studies from the United States, the United Kingdom, and France (Table 2) suggest that one-fifth to one-third would result in death (40 to 533 deaths per year) (35, 51, 57). This translates to a risk of death from a transfusion of a bacterially contaminated platelet unit of between 1 in 7,500 and 1 in 100,000. Clinical observations from university hospitals actively pursuing suspected cases of platelet-related sepsis confirm these estimates. Ness et al. from Johns Hopkins University, reported a fatality rate of 1 in 17,000 with pooled whole-blood-derived platelets and 1:61,000 with single-donor-apheresis-derived platelets (48). Similarly, University Hospitals of Cleveland observed a fatality rate of 1 in 48,000 per random platelet unit (21). The French BACTHEM study documented a fatality rate due to bacterially contaminated platelets of 7 per 10^6 (1 in 140,000) (51).

From 1976 through September 1998, 51 fatalities thought to be secondary to contaminated platelets were reported to the U.S. FDA (36). Gram-negative organisms accounted for the majority of deaths (59.7%). Similarly, passive surveillance studies from the United Kingdom, the United States, and France show that gram-positive organisms were implicated in 41 (71%) of 58 of cases but gram-negative organisms (mostly members of the *Enterobacteriaceae*) account for the majority (9 [82%] of 11) of the fatalities (Table 1) (35, 51, 57).

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Clinical Presentation

Clinical sequelae of the infusion of bacterially contaminated platelets are variable and may be acute or delayed (contributing to missed diagnoses). Ironically, the majority (85%) of platelets are transfused to patients in the medical oncology, hematology, pediatric hematology/oncology, and bone marrow transplantation settings, all typically immunosuppressed patients (61). A study of platelet transfusions in autologous bone marrow transplant patients found that 1 in 2,000 units of platelet concentrates associated with a febrile episode (within 24 h of transfusion) were linked to bacterially contaminated platelets (16). Of the 10 patients known to have received a bacterially contaminated unit, 4 experienced septic shock.

Because of the severity of the patient's underlying disease and the variability in presentation and timing, sepsis resulting from bacterially contaminated platelets may go unrecognized. For example, an outbreak of *Salmonella enterica* serovar Choleraesuis sepsis in seven patients was traced to one repeat platelet donor, subsequently found to have occult chronic osteomyelitis (52). One patient died, and two had long-term recurrences of *Salmonella* sepsis. The time to the onset of illness ranged from 5 to 12 days (mean, 8.6 days). In many cases, the platelet-related bacterial sepsis is discovered only in retrospect. Investigations of two *Serratia liquefaciens*-contaminated red cell units led to platelet products from the whole-blood donations and to the recognition of an associated septic death in one recipient and bacteremia in the other recipient (53).

TRANSFUSION-TRANSMITTED BACTERIAL INFECTION OF PLASMA AND CRYOPRECIPITATE

Cell-free products such as plasma and cryoprecipitate are stored frozen and thus are rarely associated with contamination. However, in some cases *Pseudomonas cepacia* and *P. aeruginosa* have been cultured from cryoprecipitate and plasma thawed in contaminated water baths.

SOURCES OF CONTAMINATION

Gram-positive skin commensals such as *Staphylococcus epidermidis* and *Bacillus cereus* are the organisms most often recovered from donated blood (and implicated in bacterial contamination of platelets). Such contamination is thought to occur principally during phlebotomy, as a result of incomplete disinfection and/or skin core removal (including skin appendages where the skin disinfectants may not penetrate) by the collection needle (25). These organisms typically do not grow at 1 to 6°C but survive and multiply readily at the platelet storage temperature of 20 to 24°C.

In the case of gram-negative bacterial contamination, asymptomatic donors with transient bacteremia are presumed to be responsible for most cases of contamination. For example, in the case of *Y. enterocolitica* contamination of red cells, implicated donors typically are found to have elevated antibody titers (immunoglobulin M or G) to *Y. enterocolitica*, implying a recent infection (38, 39, 60).

An outbreak of *Serratia marcescens* contamination of red cells in Denmark and Sweden (29, 30) was thought to involve the manufacturing process since the sterile bag sets were autoclaved and put in a clean but not sterile outer plastic package. It was thought that *S. marcescens* present in the dust in the factory contaminated the outside of the containers and that in the presence of moisture and a nutrient (the plasticizer diethylhexyl phthalate) the bacteria proliferated and gained entry into the bag (58).

In rare cases, unusual circumstances have been identified as the source of bacterial contamination. For example, a donor with a pet boa constrictor, who reported fever and bloody diarrhea treated with antibiotics 13 days prior to his donation, was linked to *Salmonella enterica* platelet sepsis in two patients (33). Scarring or dimpling of the venipuncture site (due to prior donations) can result in recessed pits that are difficult to adequately sterilize (3). A repeat single donor with a "dimpled" venipuncture site resulted in four cases of gram-positive bacterial platelet sepsis in recipients (3). Another unusual association was made between one donor in a platelet pool and the death of a leukemic recipient from septic shock. The contaminating organism was identified as *C. perfringens* and was thought to originate from a donor who had two young children and frequently changed their diapers (42). As stated above, an outbreak of *S. enterica* serovar Choleraesuis platelet sepsis in seven patients at the National Institutes of Health Clinical Center was traced to a repeat platelet donor with an occult osteomyelitis (52). However, in most cases the source of the bacterial contamination remains unidentified.

METHODS TO REDUCE THE RISK OF POST-TRANSFUSION SEPSIS

There are multiple strategies to reduce transfusion-related bacterial infection. The various approaches can be grouped into four major categories: avoidance, bacterial detection, bacterial elimination, and growth inhibition.

Avoidance

Donor screening. Screening of donors to detect a possible risk of infection or transient bacteremia (e.g., from recent dental procedures) is routinely performed. However, questioning about symptoms suggestive of infection are often problematic; for example, gastrointestinal symptoms have not been a specific predictor (13% of donors have had gastrointestinal symptoms in the previous 30 days) (28). Such questioning also lacked sensitivity, since only 13 of 20 donors associated with *Y. enterocolitica*-contaminated red blood cells recalled a history of gastrointestinal symptoms (38, 39, 60; Cookson et al., Prog. Abstr. 36th ICAAC, 1996).

Skin preparation. Skin disinfection reduces the skin bacterial load (65), but a sterile venipuncture cannot be guaranteed due to inaccessibility of organisms present in sebaceous glands and hair follicles; organisms present in skin fragments may be drawn into the component bag (25). Multiple studies have evaluated skin disinfection in the context of blood donation (25, 26, 43). A summary of the effectiveness of some of the more commonly used skin disinfection methods is given in Table 3 (43). In general, either iodine or povidone iodine are used. In donors with allergies to iodine, chlorhexidine or double isopropyl alcohol skin disinfection is employed. The differ-

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TABLE 3. Percentage and mean count of donors with bacteria after skin disinfection[a]

No. of CFU/plate	% of contaminated donors after disinfection with:			
	Povidone iodine × 2	IPA[b] and iodine	IPA × 2 (sponge)	IPA × 2 (swab)
0	39	79	0	29
≤10	57	93	69	50
≤100	75	100	86	68
≤1,000	96	100	97	89
Mean count	175	3	161	237

[a] Data are from reference 43.
[b] IPA, isopropyl alcohol.

ence noted in Table 3 for two different isopropyl alcohol scrubs was attributed to the abrasive nature of the sponge used in one of the preparations.

Diversion of the initial blood draw. Several studies have demonstrated the partial effectiveness of diverting the first 10 to 30 ml of blood from the initial collection. A study performed with 22,000 samples of donated blood by the Red Cross in The Netherlands, in which the first 10 ml of donor blood was diverted from the primary bag, showed that 16 of the first 5-ml aliquots were bacterially contaminated while only 2 of the second 5-ml aliquots were positive after culture (19). A second study in France showed that removal of the first 10 ml of donor blood was associated with a significant decrease in bacterial contamination (18,263 collections with 0.39% contamination compared with 7,115 collections with 0.21% contamination; $P < 0.05$) (12).

Such methods are most effective with respect to skin contaminants (12, 19). However, it has been said that "one should not be diverted by diversion," since most fatal cases of bacterial contamination involve gram-negative organisms and thus would not minimized by diversion. Interestingly, the addition of a diversion bag to whole-blood collections in the United States has been initially complicated by hemolysis with certain sample tubes (from Pall, East Hills, N.Y.) and dilution of the sample with anticoagulant (from Baxter, Round Lakes, Ill), requiring redesign of both diversion systems (data presented at the HHS Advisory Committee on Blood Safety and Availability, Washington, D.C.; http://www.hhs.gov/bloodsafety/pastmeetings.html#n).

Apheresis versus whole-blood-derived platelet concentrates. Therapeutic doses of platelets can be obtained from two sources. Platelets can be collected from a donor by the use of an automated cell separator (apheresis); such collections can yield one to three therapeutic doses. Alternatively, platelets can be obtained from whole-blood donations (whole blood platelet concentrates [WBPCs]); however, a therapeutic dose requires the pooling of four to six WBPCs. Current estimates suggest that 69% of all therapeutic doses of platelets transfused in the United States are apheresis derived (1). Usage varies considerably by country.

Since bacterial contamination may result from a contaminated venipuncture or an asymptomatic bacteremic donor, it would be expected that pooled platelet products would be associated with a higher risk of contamination than a single donor product. From 1986 to 1998, the incidence of septic events related to platelets at Johns Hopkins University Hospital decreased from 1 in 4,818 to 1 in 15,098 as the hospital went from transfusing 51.7% to 99.4% single-donor apheresis units (48). The overall clinical sepsis rate was approximately 1 in 2,500 for WBPC pools and 1 in 13,400 for single-donor apheresis transfusion. The related mortality rate was approximately 1 in 17,000 for WBPC pools and 1 in 61,000 for single-donor apheresis platelets. It was concluded that the use of single-donor apheresis platelets is a simple means of reducing septic platelet transfusion reactions. Similarly, the University Hospitals of Cleveland have monitored the contamination rates of both single-donor and whole-blood-derived concentrates [A. Dykstra, M. Jacobs, and R. Yomtovian, Transfusion **38**(Suppl.):104S, 1998]. The rate of bacterial contamination of apheresis-derived platelets was 1 in 2,184. While the rate for random-donor platelets was similar at 1 in 1,861, random-donor platelet concentrates in a pool of six units would be expected to result in a contamination rate of 1 in 310.

Bacterial Detection

Timing of detection. Culture studies performed both on red cell units and platelets have shown that culture on the day of collection invariably misses bacterially contaminated units that would possibly achieve dangerous levels of overgrowth during storage of the blood components [5a, 10; M. A. Blajchman, A. Ali, P. Lyn, L. Bardossy, and H. Richardson, Transfusion 7(Suppl.):7S, 1997]. This is in contrast to viral contamination of blood components, in which the virus or the immune response to the virus (antibodies) is detected from a sample obtained at the time of donation. Bacterial contamination of blood components generally requires time for the organisms to proliferate before being detectable in a small representative sample of the product. Therefore, knowledge of the growth characteristics of bacteria in blood components is essential before one considers implementation of a detection strategy (Fig. 2 and 3).

Growth characteristics of 165 platelet units inoculated (to 1 to 50 or 1,000 CFU/ml) within 1 day of collection with one of the following: *B. cereus*, *P. aeruginosa*, *K. pneumoniae*, *S. marcescens*, *S. aureus*, and *S. epidermidis* showed that after 1 day of storage all samples of *B. cereus*, *P. aeruginosa*, and *K. pneumoniae* had concentrations of ≥10 CFU/ml (the level of detection), while only 71.4 and 84.2% of the *S. marcescens* and *S. aureus* samples were at concentrations of ≥10 CFU/mL (10). By day 3 of storage, all units inoculated with *B. cereus*, *P. aeruginosa*, *K. pneumoniae*, *S. marcescens*, and *S. aureus* contained $\geq 10^5$ CFU/ml. Units contaminated with *S. epidermidis* showed slower and more varied growth.

Bacterial culture. Although there are a variety of automated and semi-automated systems, only two are FDA cleared for quality control of bacterial culture in platelets in the United States. The first is an automated liquid culture system (BacT/ALERT; bioMérieux, Durham, N.C.) that uses broth bottles with a colorimetric sensor which changes color as a consequence of increasing CO_2 produced by bacterial proliferation. The machine monitors both the rate of change of the colorimetric sensor and the absolute color change of the sensor. Generally, one aerobic (and in some cases one aerobic and one anaerobic) bottle is inoculated with 4 ml of the platelet product. This system is not completely closed, since a needle is used

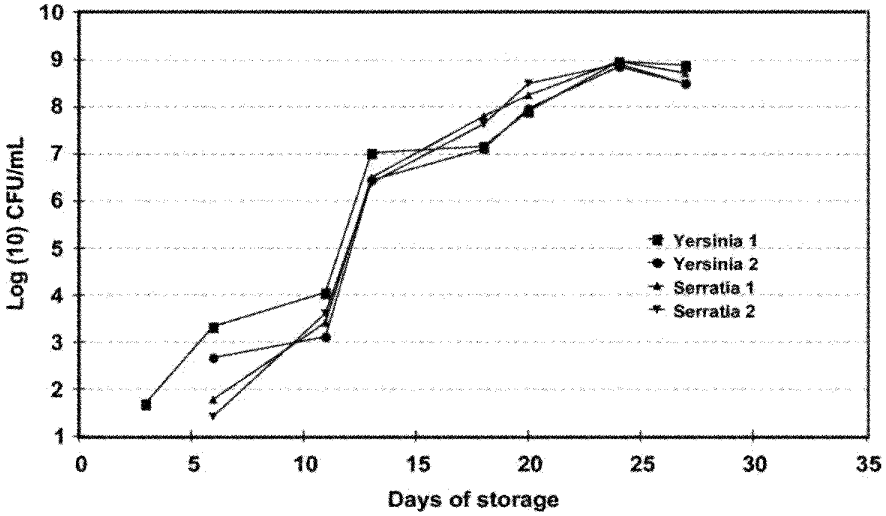


FIG. 2. Growth curves of four units of AS-3 red blood cells inoculated with *S. liqueifaciens* (two units inoculated to 4.2 CFU/ml) and *Y. enterocolitica* (two units inoculated to 11.6 CFU/ml) (5a). Bacteria were not detectable by culture until days 3 to 6. Isolates were from strains actually implicated in post-red-blood-cell-transfusion sepsis (the isolates were kindly provided by M. Arduino, Centers for Disease Control and Prevention, Atlanta, Ga.).

to inoculate the bottles. It has been extensively validated by tests with a wide range of potentially contaminating organisms (7, 8, 11, 44). The method reliably detects contamination of platelets inoculated to 10 CFU/ml and in many cases to ≤5 CFU/ml (e.g., *B. cereus*, *S. marcescens*, *C. perfringens*, *S. epidermidis*, *S. pyogenes*, *E. coli*, *K. pneumoniae*, *S. aureus*, and viridans streptococci) in 12 to 26 h. *Propionibacterium acnes* (which is of questionable clinical significance in this setting) required longer incubations. Recently, our laboratory completed an 11-month pilot program in which we cultured 2,397 apheresis-derived platelets on day 2 of storage (collection day = day 0) and again at the time of issue (or following outdate: days 6 to 8) (6). This study involved the inoculation of 9,588 bottles; one "machine" false-positive bottle (negative subculture, Gram stain, and repeat culture), and one inadvertent contamination false-positive bottle (*Propionibacterium* sp.) were detected. Thus, the overall false-positive rate was 2 in 4,794 samplings (0.04%, or 1 in 2,397 samplings) or 2 in 9,588 bottles (0.02% or 1 in 4,794 bottles). During this period, we successfully interdicted three apheresis-derived units (one collection) contaminated with *S. epidermidis* but were unable to prevent the transfusion of four apheresis units contaminated

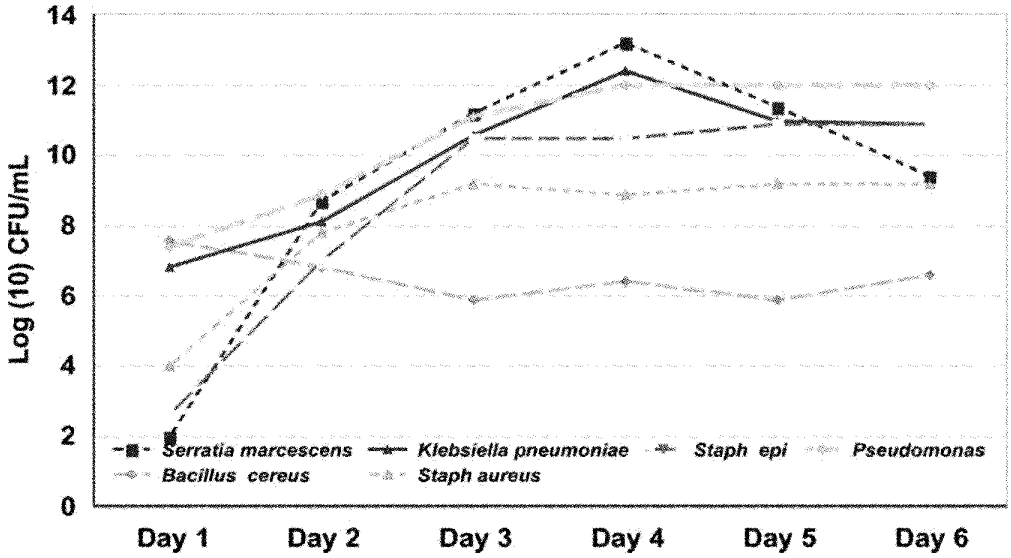


FIG. 3. Growth curves of six bacteria species (*S. marcescens*, $n = 7$; *K. pneumoniae*, $n = 21$; *S. epidermidis*, $n = 21$; *Pseudomonas* sp., $n = 15$; *B. cereus*, $n = 9$; *S. aureus*, $n = 22$) in 95 platelet units. All bacteria were inoculated on day zero at 10–50 CFU/ml (10).

TABLE 4. Summary of recent experiences with culturing of apheresis-derived platelets at three large blood centers[a]

Center	No. (rate) of results[b]		
	True positive	False positive	No. tested
New York Blood Center	5 (1/4,101)	5 (1/4,101)	20,506
Florida Blood Services	6 (1/1,790)	5 (1/2,147)	10,737
Puget Sound Blood Center	5 (1/1,800)	15 (1/600)	8,999
Total	16 (1/2,515)	25 (1/1,610)	40,242

[a] http://www.hhs.gov/bloodsafety/pastmeetings.html#n.
[b] True positive = positive bottles in which an organism was identified and a repeat sample from the bag or a retention sample also contained the same organism. False positive = positive bottles that contained no organism (machine false positive) or from which the organism could not be reisolated from the original bag or a retained sample.

with *Propionibacterium* sp., for which the culture bottles were reactive after 6 days of incubation. Thus, the overall true-positive rate was 7 of 2,397 apheresis units (0.29%), with a true-positive rate for aerobic organisms of 3 of 2,397 (0.13% or 1 of 799 units) and an anaerobic true-positive rate of 4 of 2,397 (0.17% or 1 of 599 units). Within our facility, transition from a research setting to a clinical microbiology laboratory has resulted in a higher false-positive (laboratory contamination) rate of 0.6% per unit (with one aerobic and one anaerobic bottle) (unpublished data). More recent experience from three large blood centers is included in Table 4.

The second culture system is the Pall Bacterial Detection System (BDS) (49). Sampling is obtained so as to maintain an effectively closed system. Approximately 5 to 6 ml of leukocyte-reduced platelet-rich plasma is removed from the bag and passed through a filter that removes residual white cells and platelets but allows approximately 50% of the bacteria (variable by organism) and plasma to pass into an incubation bag. The incubation bag holds 2 to 3 ml and contains sodium polyanethol sulfonate, which facilitates the growth of gram-negative organisms by inhibiting both complement and plasma lysosomal enzymes and by antagonizing the action of growth-retarding lipoproteins normally present in plasma. The incubation bag is then incubated at 35°C for at least 24 h before the oxygen concentration of the bag's headspace is measured with an oxygen analyzer. A decrease in the oxygen concentration to 19.5% or lower is an indication of bacterial growth. Thus, this system does not detect obligate anaerobic organisms. Leukocyte-reduced platelets challenged with 10 known platelet contaminants at doses of 100 to 500 CFU/ml were detected at a rate of 96.5% at 24 h and 100% at 30 h (49). External validation studies have shown lower than expected sensitivity for *S. epidermidis* and *S. agalactiae* [K.-A. T. Nguyen, T. Yamamoto, and N. Hirschler, Transfusion **43**(Suppl.):S63-030K, 2003; H. C. Pleasant, G. A. Geele, and M. P. Holub, Transfusion **43**(Suppl.):S62-030K, 2003 (abstract)]. Most recently, an enhanced version of this system has been cleared by the FDA, it includes modifications to the configuration (with removal of the filter, which removed some bacteria), and the incubation bag now contains a platelet-aggregating agent and tryptic soy medium to enhance the sensitivity and decrease the incubation time (http://www.pall.com/BDS.asp??noleftnav).

Less sensitive methods of detection such as Gram or Wright stains or the use of glucose and pH determination (in some case with multireagent strips) are used for rapid detection of bacteria in platelet components prior to transfusion. However, the overall sensitivity is only 10^6 to 10^7 CFU/ml (13, 62, 63, 66). Werch et al., from the M. D. Anderson Cancer Center, reported on the screening of 3,093 platelet concentrates, in which they found that multireagent strips for 30 bags had glucose levels or pH outside of the reference range (63). Two of these platelet units were culture positive for *B. cereus*. This screening method resulted in 1 unit per 110 being wasted but prevented two patients from receiving contaminated platelets.

Molecular biology techniques. Because of the high sensitivity and specificity and the rapidity of obtaining results, molecular biological approaches are theoretically appealing for the detection of contaminating organisms in blood components. One such approach is the use of a nonamplified chemiluminescence-linked universal bacterial rRNA probe (5, 9). This technique was shown to detect four bacterial species in the range of 10^4 to 10^5 CFU/ml. In some cases, *S. aureus* was detected at levels as low as 10^2 to 10^3 CFU/ml. Other investigators have pursued the use of PCR-based amplification for a limited number of organisms (56).

However, bacterial DNA contamination of nucleotide amplification reagents (particularly the bacterially derived enzymes) and laboratory materials and the presence of bacterial DNA sequences commonly found in human blood complicate the usefulness of universal bacterial amplification techniques (22, 45, 47). It also remains to be seen if complex molecular biology techniques could be successfully deployed to a wide range of transfusion services.

Detection systems recently approved in Europe. Recently, two bacterial detection systems were approved in Europe. The Scansystem (Hemosystem, Marseilles, France) involves a 70-min solid-phase laser cytometry. In a few studies, the Scansystem detected 11 organisms in the range of 10 to 10^3 CFU/ml [P. Morel, M. Deschaseaux, X. Bertrand, C. Naegelen, and D. Talon, Transfusion **43**(Suppl.):SP13, 2003]. Positive samples require a technologist to perform a microscopic confirmation.

A second "rapid" method recently approved detects bacteria by using dielectrophoresis (Cell Analysis, Slough, United Kingdom). Platelet concentrates inoculated with six organisms at concentrations of 10^3 to 10^5 CFU/ml were detected after 30 min of dielectrophoresis by image analysis as they were released from the electrodes when the electric field was discontinued [C. P. McDonald, R. Smith, J. Colvin, S. Robbins, J. Barbara, W. Betts, R. Anthony, K. Chan, A. Brown, and K. Gregory, Transfusion **41**(Suppl.):S119-040H, 2001].

Detection systems under development. Currently, there are at least three other rapid-detection systems under development. Genpoint (Oslo, Norway) has developed a unique system that uses paramagnetic particles to concentrate bacteria (BUGS'n BEADS) coupled with a PCR for highly conserved DNA. The target sensitivity of this assay is 1,000 CFU/ml, and the total time is 2.5 h. Immunetics, Inc. (Cambridge, Mass.) is developing a 96-well 1-h enzyme immunoassay which employs proteins and derived peptides that bind to the peptidoglycan component of the bacterial cell wall. Preliminary results suggest a sensitivity of 10^3 to 10^4 CFU/ml (or lower) for a variety of organisms [L. A. Beausang and A. Levin, Transfusion

43(Suppl.):20A, 2003; D. Kagan, and A. E. Levin, Transfusion 41(Suppl.):S118-040H, 2001]. Verax Biomedical (Worcester, Mass.) is developing an immunoassay embodied in a lateral-flow format. Preliminary results suggest a sensitivity of 10^3 to 10^4 CFU/ml for a variety of organisms [F. Kenny, C. Woodbury, M. Pelak, J. Weinberg, and J. A. Hall, Transfusion 43(Suppl.):10A, 2003].

Implementation of detection systems: problems and considerations. (i) Platelet concentrates and prestorage pooling. Bacterial detection of whole-blood-derived platelet concentrates presents logistical problems for systems that do not allow the prestorage pooling of platelet concentrates (e.g., United States, Canada, and Hong Kong). In Europe, whole-blood-derived buffy coat platelets are prepooled prior to storage; this allows for the culturing of platelets by the methods described above. If prepooling is not allowed, culturing of each individual platelet sample is generally not thought to be practical due to the loss of volume from each bag required per culture and the high cost of culture for each individual bag. In the absence of prepooling, many centers have chosen or are contemplating the use of less sensitive bacterial detection strategies such as Gram stains or glucose or pH measurement (or the use of multireagent strips) (2).

(ii) Anaerobic organisms. Anaerobic organisms such as *Propionibacterium* sp. can be identified in platelets; however, it is not known whether anaerobic organisms such as propionibacteria are clinically significant since growth in the aerobic environment of platelet storage is slow and not favorable. Although a few cases of *Propionibacterium*-contaminated units have been infused into patients, no long-term sequelae have been reported (6, 40, 55). Debate continues as to the value of an anaerobic culture in this context. It is worth noting that some aerobic organisms or isolates (e.g., viridans streptococci) can be more rapidly detected in an anaerobic culture system (7, 8, 11).

(iii) Potential for reduced shelf-life. Some centers have chosen to incubate platelet cultures for 12 to 24 h prior to release. This has in many cases led to a decrease in the available shelf-life of the platelets. Given that the current platelet products have a shelf-life of only 5 days (and that, for 1 to 2 days, such products are not available, pending completion of viral testing), any further reduction in available shelf-life can impact inventory control and hospital supply.

(iv) Use of noncleared detection systems. Use of non-FDA-cleared detection systems (e.g., alternative automated culture systems) would at a minimum require internal validation. Examples of validation of detection systems are available in the literature (7, 8, 11, 44, 49). Patent issues currently preclude certain companies from actively pursing this market. Use of a non-FDA-cleared device for bacterial quality control of platelets, when cleared devices are available, may place an institution at higher legal risk should a patient die after receiving bacterially contaminated platelets.

Bacterial Elimination

Pathogen reduction technologies. Continued efforts to create a "zero-risk" blood supply have led to various pathogen reduction technologies. A variety of photoactive sensitizers have been investigated for use in the reduction of viruses, bacteria, and parasites.

The best studied of these methods is the use of amotosalen HCL (S-59), a synthetic psoralen combined with a photochemical treatment process that causes permanent cross-links in DNA and RNA (INTERCEPT Platelet System; Baxter Healthcare Corp., Round Lake, Ill.) (41, 64). However, organisms capable of spore formation may be resistant to photochemical inactivation (34). The SPRINT trial, a multi-center phase III trial, has evaluated the hemostatic effectiveness of S-59 pathogen-inactivated platelets. Treated platelets were found to be as effective as conventional platelets for the prevention and treatment of bleeding; however, the treated platelets resulted in a lower post-transfusion platelet response, resulting in the need for 35% more platelets to support transfusion-dependent patients (18, 41). Concerns also remain regarding mutagenicity and teratogenicity associated with such technologies.

Growth Inhibition

The addition of antibiotics to blood components has been considered but has not been adopted due to the added risk of drug reactions (trading one infrequent reaction for another) and the potential for the development of antibiotic resistance if small amounts of antibiotics were infused with every transfusion (31).

THE PROSPECT OF SEVEN-DAY STORAGE WITH DETECTION

Currently, within the United States platelet storage is limited to 5 days due to the fear of bacterial overgrowth during storage at 20 to 24°C. In 1983, platelet storage in the United States was extended to 7 days; however, in 1986 the FDA shortened the outdate to 5 days following reports of bacterial sepsis with older units (65). With the prospect of bacterial detection, the possibility of an extended shelf-life is being reconsidered. European reports have described the use of bacterial culturing of platelets on days 1 to 3 of storage in order to extend the shelf-life of platelets to 7 days, thereby reducing the number of outdates [M. Ollgaard, I. Albjerg, and J. Georgen, Vox Sang. 74(Suppl. 1):1126, 1998; D. Vuetic, J. Taseki, B. Balint, and V. Mirovic, Vox Sang. 80(Suppl. 1):P371, 2000]. Within the United States, premarket multicenter studies (or possibly postmarket studies) are currently under discussion to provide data that may allow the extension of storage to 7 days. It would be expected that the cost of culturing would be mitigated by the savings obtained by the extension of platelet storage time (20). For example, in Denmark, when bacterial culture was implemented in 1997, it was anticipated to be cost neutral if the outdating could be reduced from 18 to 8% by extending the storage time to 7 days (24). The actual outdating rate decreased to 3 to 6%.

CONCLUSIONS

Regulatory oversight in the United States and Canada has generally concentrated on new emerging threats such as West Nile virus (leading to nationally mandated efforts to screen the

blood supply with West Nile virus nucleic acid testing). However, there is no similar mandate in these countries for bacterial screening. To place these risks into some perspective, in 2002 23 transfusion-transmitted cases of West Nile virus were identified in the United States (50). Of these 23 recipients, 7 died, but only 5 of these deaths were associated with West Nile virus meningoencephalitis. During the same period, 17 deaths from bacterial contamination of blood components were reported to the FDA (14). Contaminated apheresis-derived platelets and pooled platelets were the products most often implicated. Gram-negative bacteria were the causative agents in the majority of these fatalities. It is perplexing that similar (or greater) government emphasis has not been placed on the detection of bacteria.

In blood banking and transfusion medicine, our paramount concern is to improve transfusion safety for patients, in our attempt to achieve a zero-risk blood supply. Unlike other recent threats (existing or theoretical) to blood safety, the movement for reducing bacterial contamination has come from the blood-banking and the transfusion medicine community. In this case, voluntary accrediting agencies such as the American Association of Blood Banks and the College of American Pathologists have taken the lead by developing standards to reduce the risk of bacterial contamination of blood components (17, 23). Our patients deserve no less.

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Closed Blood Conservation Device for Reducing Catheter-Related Infections in Children After Cardiac Surgery

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Abstract

Background Arterial catheters are potential sources of nosocomial infection.

Objective To investigate use of a closed blood conservation device in preventing catheter-related bloodstream infections in children after cardiac surgery.

Methods Children with an indwelling arterial catheter after cardiac surgery were randomly assigned to 2 groups: a control group with a conventional 3-way stopcock in the catheter system and an interventional group with the conservation device in the catheter system. Catheter tips, catheter intraluminal fluid, and blood samples obtained from the catheter and peripherally were cultured for microbiological analysis. RESULTS Intraluminal fluid contamination was significantly lower (P = .03) in the interventional group (3 of 147 catheters) than in the control group (10 of 137 catheters). The 2 groups did not differ significantly in the rate of tip colonization (9 of 147 vs 12 of 137, P = .40) or in the number of catheter-related bloodstream infections (0 of 147 vs 2 of 137, P = .21).

Conclusion Use of a closed blood conservation device could decrease the incidence of catheter-related contamination of intraluminal fluid.

This article has been designated for CNE credit. A closed-book, multiple-choice examination follows this article, which tests your knowledge of the following objectives:

1. Describe closed blood conservations devices
2. Identify the key findings of the study and implications on preventing catheter-related bloodstream infections in pediatric patients
3. Discuss the indications for use in the pediatric intensive care unit

Arterial catheters are routinely used in critically ill patients for continuous monitoring of arterial blood pressure and for obtaining blood samples for arterial blood gas analysis. Catheter-related bloodstream infections (BSIs) are a common and serious complication of intravascular catheters and are associated with increased morbidity, mortality, length of hospital stay, and medical costs.[1–5] Although previous studies[6–8] indicated a low risk for infections associated with use of arterial catheters, recent studies[9–11] showed that the risk for arterial catheter–related infection was high, comparable to the risk associated with short-term use of central venous catheters. Compared with adult patients, children are more susceptible to nosocomial infection, and catheter-related BSI is considered the most common nosocomial infection in pediatric intensive care units (PICUs).[12] Prevention of catheter-related BSI in PICU patients with multiple intravascular catheters has become a top priority.

Catheter-related BSI is the most common nosocomial infection in PICUs.

Unlike central venous catheters, arterial catheters have an open-loop design that allows backflow of blood into the pressure tubing. This backflow and frequent blood sampling are now considered the 2 major causes of catheter-related BSI.[13–15] Keeping the arterial catheter system closed could be an effective method to decrease the risk of catheter-related BSI. Several investigators have reported that the risk for blood contamination could be minimized for both central venous[14,16–18] and arterial[13,19] catheters in adult patients when closed-loop systems were used.

The venous arterial blood management protection (VAMP) device (Edwards Lifesciences Corporation) is a needleless closed-loop blood sampling system. The device has been introduced into clinical practice to eliminate discarding of blood during blood sampling.[20] Besides reducing blood loss, use of a VAMP device may also reduce the risk for catheter-related BSI by keeping the arterial catheter system closed. Oto et al[21] reported that the risk for contamination of intraluminal fluid in adult patients could be decreased by adding a VAMP device to the arterial catheter system. However, the potential benefit of using this type of device to prevent catheter-related BSI in children is still not well recognized. The objective of our study was to investigate the effect of a VAMP device in reducing the occurrence of catheter-related BSI in children after cardiac surgery.

Materials and Methods

Setting and Sample

The study was approved by the appropriate ethical committee, and informed written consent was obtained from patients' parents. The study sample consisted of children who had undergone open heart surgery and were admitted to the PICU. Patients were included if they were less than 12 years old, were expected to stay more than 48 hours in the PICU, and had an arterial catheter inserted. Patients were excluded if they were expected to stay less than 48 hours or die during the study period, had an apparent infection before admission to the PICU, had the arterial catheter removed within 48 hours of surgery, or had confirmed diagnosis of non–catheter-related infection (eg, pulmonary or surgical site infection). All arterial catheters were inserted in the operating room or reinserted in the PICU. Aseptic technique was used for all insertions, and all patients received prophylactic antibiotics for 48 hours after surgery.

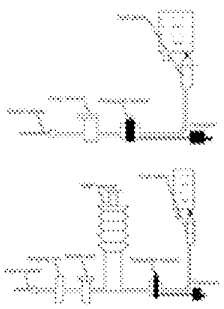
Samples and Randomization

A 2-sided test for randomized control trials indicated that for 80% power and $\alpha = .05$, a sample size of at least 130 patients in each group was needed. During the study period, each patient was randomly allocated to 1 of 2 groups by using a sealed-envelope method. The control group had a conventional 3-way stopcock system in the catheter, and the interventional group had a VAMP Plus device in the catheter. Both groups were followed up until removal of the arterial catheter, discharge from the PICU, or death.

The Figure shows the components of the blood sampling systems in the 2 groups. In the control group, the heparin cap of the 3-way stopcock was removed and a sterile syringe was inserted into the stopcock port after the port was cleaned with iodine swabs. After about 5 mL of blood was obtained, the first syringe was removed and another sterile syringe was inserted into the stopcock port for obtaining the required amount of blood. Then, the 5 mL of blood in the first syringe was injected back into the patient through the arterial catheter, and the stopcock port was cleaned again with iodine swabs. Finally, a new sterile heparin cap was reconnected to the 3-way stopcock, and the mixture of heparin and physiological saline in the flush device was infused into the arterial catheter system. Throughout the entire process, the heparin cap was off, leaving the 3-way stopcock port open to the outside. Also, 2 sterile syringes were needed, and blood obtained with the first syringe was injected back into the patient.

Figure

Schematic diagrams of the conventional 3-way stopcock arterial catheter system (top, control group) and the venous arterial blood management protection (VAMP, Edwards Life-Sciences) system (bottom, VAMP group). In



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the conventional 3-way stopcock system, key components are an arterial catheter, a 3-way stopcock capped with a sterile heparin cap, a pressurized reservoir, a transducer, and a continuous flush device containing a solution of heparin (6.25 IU/mL) in physiological saline. In the VAMP system, the 3-way stopcock is replaced by a VAMP device, a needleless closed-loop blood-sampling system, including a sampling port, a shutoff valve, and a closed-loop blood reservoir.

In the VAMP group, the inner cylinder of the blood reservoir was pulled back until blood passed the sample port and filled half of the blood reservoir, and then the shutoff valve was closed. The sampling port was disinfected twice with iodine swabs, an arterial blood collection syringe (Becton, Dickinson and Company) with an attached blood collection cap (VMP400, Edwards Life-sciences Corporation) was inserted into the sampling port, and the required blood sample was obtained. After collection of the blood sample, the syringe was removed and the sample port was disinfected with iodine swabs. Finally, the shutoff valve was opened, and the blood in the reservoir and the mixture of heparin and physiological saline in the flush device were reinjected into the patient. Throughout the entire process, no parts of the arterial catheter system were removed and the system was completely closed.

During the study period, each patient had an arterial catheter device in place for at least 48 hours. The heparin-saline solution in the flush device was replaced every 24 hours. Other components of the systems (including transducer, continuous flush device, and the tubing) were replaced at 96-hour intervals.[22] All medical personnel were strictly trained in the blood-sampling procedure and routine care of the arterial catheter system. The arterial catheter was removed if it was no longer necessary, the patient had signs of catheter-related BSI, or complications related to use of the catheter occurred.

Keeping the arterial catheter system closed is an effective method of decreasing the risk of catheter-related BSI.

Microbiological Analysis

The differential time to positivity between cultures of blood from the catheter and cultures of peripheral blood is a simple and reliable tool for diagnosis of catheter-related BSI.[23] Samples of blood from the arterial catheter and samples of peripheral blood were cultured simultaneously when a patient's temperature was greater than 38.5°C (101.3°F) and were monitored continually. A diagnosis of catheter-related BSI was made when cultures of the catheter blood became positive for microbial growth 2 hours earlier than did cultures of peripheral blood and cultures of both samples had the same microorganisms.

Arterial catheter tips were cultured after removal of the catheters. A 5-cm segment of the catheter (or the entire short catheter) was placed into a sterile tube and cultured by using a roll plate technique.[24] Colonization of a tip was defined as a growth of 15 or more colony-forming units in a semiquantitative culture.

Intraluminal fluid from both arterial catheter systems was also cultured. After aseptic removal of the arterial catheter, sampling port, and transducer, a sterile syringe containing 10 mL of sterile physiological saline was inserted at the proximal connection of the transducer, and the saline was injected into the arterial catheter. In the catheters with the VAMP device, the 10 mL of saline was also used to flush the VAMP reservoir. Finally a 10-mL aliquot of the mixture of saline and intraluminal fluid was drained into a sterile culture bottle and cultured in trypticase soy broth for 7 days at 37°C (98.6°F). The cultures were examined daily; if the broth was cloudy, standard laboratory subculturing was performed.

Data Collection

Patient demographic data included age, sex, and score on the Acute Physiology and Chronic Health Evaluation II at PICU admission. Data on the arterial catheters included the location of the catheter, date of insertion, site of any reinsertion, and final date of removal. Data on cultures of catheter tips, intraluminal fluid from the catheter, and samples of blood obtained simultaneously from the catheter and peripherally also were noted.

Statistical Analysis

Statistical analysis was performed by using SPSS, version 16.0 (IBM SPSS). Quantitative variables were expressed as means and standard deviations unless stated otherwise and were compared by using a *t* test or the Mann-Whitney test. Categorical data were compared between groups by using χ^2 analysis or the Fisher exact test. Logistic regression analysis was used to evaluate the direct relationship between arterial catheter–related infection and patients' demographic or catheter characteristics. A bidirectional hypothesis was applied, and a *P* less than .05 was considered significant.

Results

Characteristics of the Patients and the Arterial Catheters

From March 2010 to December 2012, 260 children were enrolled in the study. A total of 12 patients were excluded because of death (3 patients), confirmed pulmonary infection (7 patients), or removal of the arterial catheter within 48 hours after surgery (2 patients). The final sample consisted of 248 children and 284 placements of an arterial catheter. The VAMP group included 128 patients with 147 arterial catheters inserted. The control group consisted of 120 patients with 137 arterial catheters inserted. The median duration of insertion for both groups was 7 days. The 2 groups did not differ significantly in age, sex, score on the Acute Physiology and Chronic Health Evaluation II, insertion site of the arterial catheter, and length of time the catheter was in place (Table 1).

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Table 1

Basic characteristics of patients in the venous arterial blood management protection (VAMP) and control groups

Microbiological Analysis

Intraluminal fluid contamination was significantly lower (*P*=.03) in the interventional group (3 of 147 catheters) than in the control group (10 of 137 catheters). The 2 groups did not differ significantly in the rate of colonization of the catheter tip (9 of 147 vs 12 of 137; *P*=.40) or in the number of catheter-related BSIs (0 of 147 vs 2 of 137; *P*=.21; Table 2). Logistical regression analysis indicated that the incidence of colonization of the catheter tip was significantly related to both the length of time the catheter was in place (odds ratio, 0.737; 95% CI, 0.580–0.936; *P*=.01) and the score on the Acute Physiology and Chronic Health Evaluation II (odds ratio, 0.879; 95% CI, 0.781–0.989; *P*=.03). Contamination of intraluminal fluid was also significantly associated with the length of time the catheter was in place (odds ratio, 0.506; 95% CI, 0.350–0.731; *P*<.001), and use of the VAMP device was a strong predictor of a decrease in the risk for contamination of intraluminal fluid (odds ratio, 0.069; 95 CI, 0.013–0.592; *P*=.01; Table 3).

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Table 2

Results of microbiological analysis of the 2 types of arterial catheter systems

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Table 3

Risk factors associated with the occurrence of catheter tip colonization and intraluminal fluid contamination

Microorganisms Identified

In the VAMP group, all colonization of catheter tips and contamination of intraluminal fluid was caused by coagulase-negative staphylococci. In the control group, various species of microorganisms were detected, but coagulase-negative staphylococci were still the most common bacteria found in the arterial catheter systems. Table 4 indicates microorganisms identified for each group.

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Table 4

Results of microbiological analysis of the 2 types of arterial catheter systems

Discussion

Arterial catheters are commonly used for hemodynamic monitoring and for collecting samples of arterial blood. Previously, the risk for infection associated with use of arterial catheters was considered low.[6–8] The 2002 guidelines[22] of the Centers for Disease Control and Prevention even commented that arterial catheters had a "low infection risk" and were "rarely associated with bloodstream infection." However, in a prospective study[25] of 212 intensive care unit patients with placement of both arterial and central venous catheters, the cumulative incidence of catheter-related BSI for arterial catheters was 7.7%, comparable to an incidence of 9.4% for central venous catheters (P=.45). Several studies[9–11] confirmed that risk for infection associated with arterial catheters was similar to the risk associated with central venous catheters. Thus, prevention of catheter-related BSI has become an important issue in medical practice. Effective methods to minimize the risk of arterial contamination or infection include use of a rigorous aseptic technique for placement of the catheter, selection of an optimal site for the catheter, prompt removal of any unnecessary catheter, and keeping the catheter system closed.[13,19,21,26]

Coagulase-negative staphylococci are the most common bacteria found in arterial catheter systems.

Unlike adult patients, children in the intensive care unit are more susceptible to nosocomial infection. Because most studies[13,21] on catheter-related BSI were done in adults, we investigated the effect of using a VAMP device in the management of critically ill children. Although we found no significant difference between the VAMP group and the control group in colonization of catheter tips or occurrence of catheter-related BSI, contamination of intraluminal fluid was significantly lower in the group with the VAMP device. This result is similar to the findings of Oto et al[21] and Crow et al.[13] Oto et al found that catheter-related contamination of intraluminal fluid decreased from 8.4% for an arterial catheter system with a conventional 3-way stopcock to 1.8% when an arterial catheter with a VAMP device was used (P=.03). Crow et al reported that the incidence of contamination of intraluminal fluid was lower with a closed blood-sampling system (7%) than with a 3-way stopcock system (61%).

As mentioned earlier, frequent opening of the arterial catheter system for blood sampling and backflow of blood into the pressure tubing are 2 important causes of catheter-related BSI.[13–15] When the conventional 3-way stopcock system is used, frequent acquisition of blood samples through the open arterial catheter system, reinjection of blood into the artery, and the inevitable presence of residual blood within the stopcock port could lead to a high risk for microbial contamination of the catheter. In contrast, an arterial catheter system with a VAMP device is a completely closed infusion system. No part of the VAMP system must be opened when a blood sample is obtained, so no pathway exists for transfer of microorganisms to intravascular fluid

Although microbial contamination of intraluminal fluid was significantly lower in the VAMP group than in the control group in our study, use of the VAMP system did not decrease the incidence of colonization of catheter tips. This result agrees with the findings of Oto et al,[21] who observed no significant difference (P=.48) in the rate of colonization of catheter

tips: 7.3% in the test group and 10.3% in the control group. We can only speculate that the reason for this result in our study is the short length of time the catheters were in place and a relatively low rate of colonization of catheter tips. Researchers[7,27,28] have reported that colonization of catheter tips may be more closely related to the insertion site of the arterial catheter and the length of time the catheter is in place than to the catheter system. In our study, further logistic regression analysis indicated that the length of time the catheter was in place was an important factor in the colonization of catheter tips, and we found no significant difference between the 2 groups in the length of time the catheter was in place. Meanwhile, the rate of colonization of catheter tips in our study was relatively low. In a study by Thorpe and Thomas,[29] the contamination rate was higher than the rate in our investigation for both a blood conservation system (30%) and a traditional 3-way stopcock system (37%). Infections of short-term catheters (those in place <10 days) are due mainly to microbial colonization of the skin around the insertion site.[21] In our study, the microorganisms detected on the catheter tips (median time in place, 7 days) in both groups were mostly coagulase-negative staphylococci, organisms primarily found on the skin.

The occurrence of catheter-related BSI for arterial catheters did not differ significantly between the 2 groups in our study. We identified 2 instances of catheter-related BSI in the control group and no instances in the VAMP group. Although no conclusion can be made about the direct effect of a VAMP device in preventing catheter-related BSI in arterial catheter systems, we speculate that use of a VAMP device could lower the risk for catheter-related BSI in children. Because of the unique closed-loop design, use of a VAMP device has obvious advantages in children, especially children who have had heart surgery who require repeated blood sampling and continuous blood pressure monitoring. Use of a VAMP device could prevent microbial contamination of intraluminal fluid and save the blood normally discarded when blood samples are obtained for blood gas analysis. Because children, especially infants, are more susceptible than adults to nosocomial infections such as catheter-related BSI in the intensive care unit,[12,30,31] a small step forward in preventing catheter-related BSI could be highly beneficial for patients in the PICU. Our results did not directly prove the effect of a VAMP device in reducing catheter-related BSI in children after cardiac surgery, but the VAMP device could be still used as part of "bundle care" for use of intravascular catheters to minimize the risk of catheter-related contamination.

The VAMP device could be used as part of "bundle care" for use of intravascular catheters to minimize the risk of catheter-related contamination.

Limitations

Our investigation had several major limitations. First, the study was done at a single center and with a limited study cohort. Further large-scale, well-designed, randomized control trials are needed to verify the validity of our results. Second, although we tried to ensure equal treatment of both groups with the blood-sampling technology and routine care, physicians and nurses were aware of the device, and they might have been more careful or cautious with patients in the VAMP group. In addition, with the semiquantitative method described by Maki et al,[24] only the external surface of a catheter tip is sampled, and the VAMP device might prevent internal colonization better than it prevents external colonization because the device forms a closed system. The quantitative catheter segment culture technique reported by Cleri et al[32] might be a more suitable method for investigating the effect of a VAMP device on colonization of catheter tips.

Conclusion

In conclusion, compared with the conventional 3-way stopcock device, use of a VAMP device could decrease the incidence of arterial catheter–related contamination of intraluminal fluid. The VAMP device may be an effective method of preventing catheter-related BSI in the PICU. CCN

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Footnotes

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Doing It Right the First Time: Quality Improvement and the Contaminant Blood Culture

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The aim of the project was to determine whether the rate of contaminant blood cultures could be reduced by using a team of dedicated phlebotomists. Comparisons were made between adult patients requiring blood cultures for suspected bacteremia on medical and surgical units before and after the introduction and withdrawal of a dedicated blood culture team. The results showed that a significant reduction in the contaminant blood culture rate was achieved by the blood culture team ($P < 0.001$; χ^2 test). Therefore, in our experience, the rate of contaminant blood cultures can be reduced in a teaching hospital by using a team of dedicated phlebotomists. Calculations made with our data and those published by others suggest that cost savings from reducing false-positive blood cultures are greater than the cost of the blood culture team.

The costs of correcting a defective product often exceed the costs of designing a system to avoid producing a defect (5). For hospitals, these costs are not only monetary but also carry a burden of human suffering. The contaminant blood culture can be regarded as a "defective product." The cost of correcting this defect far exceeds the cost of repeating the blood culture itself (2, 6). Contaminant blood cultures are common events in teaching hospitals (1, 2, 10). They are associated with increased length of stay, inappropriate administration of antibiotics, and use of further testing (2, 6), resulting in more than 50% greater total hospital charges (2).

Standards published by the American Society of Microbiology indicate that the rate of blood culture contamination should not exceed 3% (8). Nevertheless in many teaching hospitals the contamination rate exceeds 6% (2, 10). A recent publication suggested that this could be reduced to less than 4% by using a different method of skin preparation (10). In our institution the contamination rate reported to our quality assessment and improvement committee was 4.7%, and this was identified as an opportunity for improvement.

When quality concerns occur, there is a natural tendency to blame the line worker (3). For many teaching hospitals, the line worker who collects blood for culture is usually an intern or resident. Our initial effort was to educate the house staff on proper performance and provide guidelines for appropriate test use. Despite this effort, the contamination rate remained the same. To achieve a quality improvement breakthrough, we questioned the system rather than blaming the line worker. We hypothesized that our house staff had numerous clinical responsibilities and could not possibly dedicate the time and energy required to perform the process of collecting blood for culture without the result being a contamination rate that is unacceptable. We instituted a trial of a blood culture team (BCT) consisting of dedicated phlebotomists. We hypothesized that this would lead to a significant reduction in the rate of contaminant blood cultures. Published data (2) indicated that saving the true costs of contaminant blood cultures would make this initiative economically advantageous. The subsequent quality improvement would pay for the cost of the program, confirming the contention of industry consultants that for some goals quality is free (4). We report a significant reduction in the rate of blood culture contamination achieved by a team of dedicated phlebotomists ($P < 0.001$; χ^2 test).

MATERIALS AND METHODS

Patient population. The New York Hospital Medical Center of Queens is an acute-care community hospital with 487 beds. There are independent medical and surgical residency programs. The patient units chosen for this study were adult general medical and surgical care units. All patients on these units requiring a blood culture for suspected bacteremia during the study periods were included. No consents were obtained, and patients were not informed of this study. Institutional review board approval was not deemed necessary.

Study design. A BCT consisting of three full-time phlebotomists was established. Blood samples for culture were collected by the BCT after orders were written by house staff or attending physicians by a standardized protocol based on methods published previously (9). Briefly, a commercially available skin preparation kit (prep kit) with isopropanol and tincture of iodine (Cepti-seal blood culture prep kit II; Mediflex Hospital Systems, Overland Park, Kans.) was used according to the manufacturer's specifications, and two sets of blood samples for culture were collected from separate sites of each patient. Each was inoculated into one anaerobic and one aerobic culture bottle (BACTEC NR 7A and 6A, respectively; Becton-Dickinson Diagnostic Systems, Sparks, Md.). Blood samples were collected by house staff when the BCT was not available to the patient care unit.

The house staff were educated in proper technique by conventional methods (alcohol and povidone-iodine swabs), but no attempt was made to verify their use. Commercial prep kits were not available to the house staff initially. These were made available on one patient unit after the BCT was withdrawn and the house staff was educated regarding their use. This was done to evaluate the effect of the commercial prep kit.

Blood cultures were evaluated by using BACTEC NR-660 (Becton-Dickinson Diagnostic Systems). Blood cultures were considered contaminated if microorganisms derived from common skin flora were cultured: *Corynebacterium* spp., *Bacillus* spp., *Propionibacterium* spp. (e.g., *Propionibacterium acnes*), and coagulase-negative staphylococci.

The presence of coagulase-negative staphylococci was closely monitored since it may represent true infection. Culture sets in which only one of four bottles or two of four bottles (one set) were positive were analyzed. Coagulase-negative staphylococci present in three of four and four of four bottles were not considered contaminants for the purposes of this study to avoid including true positives.

The following criteria were used in combination to confirm contamination for cultures positive for coagulase-negative staphylococci: (i) subsequent (and often prior) cultures were negative and (ii) physician review of the medical record indicated that contamination was present.

Two patient care units (designated units A and B) were selected for sequential

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TABLE 1. Comparison of blood culture collection techniques by house staff and phlebotomy team (BCT)

Blood culture collection technique	Unit A			Unit B		
	Duration of study (mo)	No. of contaminated cultures/total no. of cultures (%)[a]	*P* value	Duration of study (mo)	No. of contaminated cultures/total no. of cultures (%)	*P* value
A. House staff without prep kits	3	24/287 (8.4)	<0.001[b]	2	15/312 (4.8)	<0.001[b]
B. BCT with prep kits	6	11/956 (1.2)	<0.001[c]	3	8/799 (1.0)	
C. House staff with prep kits	3	10/208 (4.8)				

[a] For comparison of techniques A and C, $P = 0.173$.
[b] Comparison of techniques A and B.
[c] Comparison of techniques B and C.

introduction of the BCT. Unit A was a large, busy general medical floor and was heavily weighted toward emergency admissions. This area had been noted in the past to have a high rate of blood culture contamination. Unit B consisted of a smaller general medical floor and a general surgical floor. Historically, the rate of blood culture contamination on unit B was similar to that for the institution as a whole. Blood culture data were collected for 3 months prior to the introduction of the BCT on unit A and for 2 months prior to the introduction of the BCT on unit B. Data were collected for a subsequent 6 months for unit A and 3 months for unit B after the introduction of the BCT. The BCT was then withdrawn from unit A and the commercial prep kits made available to the house staff, who were instructed to use them according to specifications. Data were then collected for 3 subsequent months for unit A.

Statistical methods. The Mantel-Haenszel chi-square test was performed with True Epistat software (Epistat Services, Richardson, Tex.) on an International Business Machines Corporation-compatible desktop computer. Two-tailed *P* values were used.

RESULTS

Effects of BCT and commercial skin prep. The results of studies examining the effects of the BCT and the commercially available skin prep are presented in Table 1 and are displayed graphically in Fig. 1. Unit A had a high baseline rate of blood culture contamination (8.4%), a rate that exceeded that seen in the hospital as a whole (4.7%; unpublished data). This high rate was thought to be due to the character of the unit, a busy, high-turnover, general medical floor heavily weighted toward emergency admissions, and the effect that this had on the house staff workload. Unit B had a lower baseline rate of contamination of blood cultures (4.8%), and this result was similar to that for the whole institution. After the introduction of a BCT, the rate of contamination decreased significantly for unit A to 1.2% ($P < 0.001$; χ^2 test) and decreased significantly for unit B to 1% ($P < 0.001$; χ^2 test). When the BCT was withdrawn from unit A, commercial blood culture kits with isopropanol and tincture of iodine were supplied and the house staff were educated in their use. Despite the use of the prep kits, there was a significant increase in the contamination rate to 4.8% compared to that observed with the BCT, 1.2% ($P < 0.001$; χ^2 test). The performance of the house staff on unit A did exhibit a trend toward improvement with the use of the commercial prep kits compared to that at the baseline (4.8 versus 8.4%), but this was not statistically significant ($P = 0.173$; χ^2 test). Others have found significant improvements with improved methods of skin preparation (9, 10).

Calculations of economic benefits. Data establishing the true consequences of false-positive blood cultures have been published by Bates et al. (2). The median hospital charges for patients with false-positive blood cultures were reported to be more than 50% greater than those for similar patients with true-negative blood cultures. This was accounted for by increased length of stay and increases in pharmacy and laboratory charges, with an increase in total median charges of more $4,000 per patient. In our hospital, costs account for greater than 98% of charges. If we assume a 50% increase in actual hospital costs and average diagnosis-related group charges of approximately $5,000, then each contaminant blood culture costs our institution $2,500. If we accept this conservative estimate, then the following calculation can be made. For unit A, over 6 months, 11 of 956 cultures of blood collected by the BCT with a commercial skin prep kit were contaminated. Without blood collection by the BCT and with the use of the commercial skin prep kit, 4.8%, or 45 contaminant blood cultures, would have been expected. This represents elimination of 34 contaminant cultures or a calculated savings of $85,000. The cost of the BCT, with three full-time equivalent salaries and benefits, for 6 months was $45,000. The savings resulting from this improvement, $40,000, does not include further cost reductions that the BCT achieved simultaneously on unit B, which were also substantial, as well as other productive work that the team performed (collection of blood at appropriate intervals for determination of antibiotic levels for patients on aminoglycosides). More than 14,000 blood culture sets were collected in our institution for the year 1994. We would predict that at least 650 sets would have been contaminated on the basis of an institutional contamination rate of 4.7%. A reduction of the contamination rate to 1.2% would eliminate more than 480 contaminant cultures, with potential savings of $1,200,000.

DISCUSSION

Our data have indicated that a significant reduction in the rate of contaminant blood cultures was achieved in two patient care units by a BCT using commercial prep kits ($P < 0.001$) compared to the results obtained by house staff. Improved

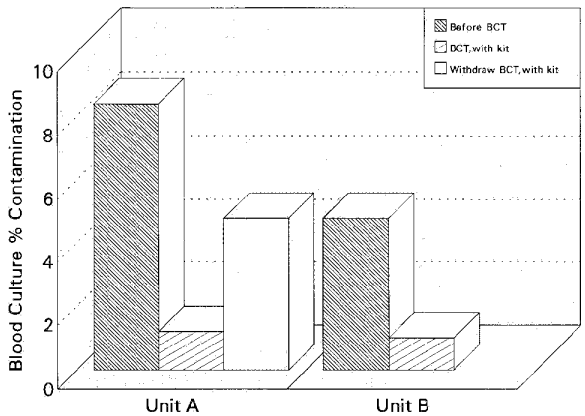


FIG. 1. Effect of BCT and commercial prep kits on rate of blood culture contamination.

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results occurred when house staff used a commercial prep kit, although the difference from the baseline data was not statistically significant ($P = 0.173$; χ^2 test). Others have shown that significant benefits result from improved methods of skin preparation (9, 10). The trend that we observed would corroborate those reports. Conservative estimates of the cost savings achieved by reductions in contaminant blood cultures indicated that the BCT was economically advantageous.

Quality can be defined for some products as conformance to specifications measured by the number of defects divided by the number of opportunities to produce a defect (7). The contaminant blood culture is an easily measured example of a defect produced by a process within a hospital. Unfortunately, the implications of producing this defect are not merely economic. Human suffering results from the increased use of diagnostic testing and additional hospital days with treatment with unnecessary antibiotics. Improving quality in hospital settings is a valid goal, regardless of cost. Nevertheless, pressures to reduce costs from consumers and government exist independently of consideration of quality. In other industries, when the cost of error is calculated, it is clear that improving quality by designing systems to reduce the production of defects results in substantial savings (7). Calculations made by using our results and those reported by others (2) indicate that this is the case for contaminant blood cultures.

Quality improvement can reduce costs in medicine as well as in other industries. Incentives to do so are already present. Organizations that harness the tools of quality improvement theory should be well equipped to meet this challenge. An appropriate goal for hospitals is to control costs by improving quality. To do otherwise risks the substantial achievements of generations of physicians and scientists.

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(Acta Anaesth. Belg., 2005, 56, 283-285)

New Closed IV Catheter System

A. VAN ZUNDERT

The insertion of peripheral intravenous (IV) lines is an extremely common procedure, practiced on approximately four out of five hospitalised patients. Issues are being raised concerning the hygienic aspects of the injection port of peripheral ported catheters (1, 2, 3).

Recently the choice of IV catheters has improved both patient care and the protection of caregivers.

We report here on our experience with IV catheters. In the past, our hospital used the BD Venflon™ (BD Infusion Therapy AB, Helsingborg, Sweden), followed by the BD Venflon Pro™. Recently we began using the BD Safelon Pro™ and most recently we have introduced the BD Nexiva™ (Fig. 1). The latter is a completely closed IV catheter system (Table 1).

A peripheral catheter is usually less than or equal to 7.5 cm in length, uses stainless steel needles and a plastic cannula, is limited to short-term or single-dose administration and should deliver therapy into peripheral veins without causing infection, leakage or extravasations. In the Netherlands, ported catheters are very popular, but its disadvantages include blood spilling and the risk of inadvertent prick accidents. An optimal peripheral IV catheter (Table 2) should reduce complications including phlebitis, thrombosis, haematoma formation at the puncture site as well as infiltration and rarely tissue necrosis. Additionally an ideal catheter should provide protection to the user against sharps injury and have advanced engineering to ensure ease of use (clearly visible and rapid flashback ; flexible and needle-less access ; and easy maintenance). Safety and comfort for the patient must be non-negotiable features.

Multi-lumen port access catheters provide many of the advantages of a central venous catheter. The inclusion of an additional port on the catheter itself (the 'ported' catheters used frequently in Europe), the attachment of a stopcock or, most cleverly, the use of an extension tubing (either attached or integral to the catheter) with multiple ports are current approaches to making peripheral catheters 'multi-access'.

The BD Nexiva™ integrated IV catheter system has many of these advanced features. It includes a safety IV catheter, an extension tubing with Y-connection or integrated stopcock and a BD Q-Syte™ needle-less access system. The Q-Syte™ can be accessed with Luer Lok (screw-on) or Luer Slip (tapered) syringes. The former may give a more secure connection. However the latter are perfectly acceptable : giving Luer Slip syringes a $^{1}/_{4}$ turn may ensure that no disconnection occurs. Regardless of the connector used, it is very important that the Q-Syte™ be cleaned with an antiseptic solution (and allowed to dry) before any device is inserted. The catheter itself is made of Vialon™ (BD Infusion Therapy, Sandy Utah, USA), biomaterial, a special designed medical grade polyurethane reducing phlebitis significantly (4, 5, 6). The two soft wings come with holes which allow for suturing, if needed. However, most peripheral catheter insertions require no suturing.

Not surprisingly, this integrated IV catheter system requires some modifications in insertion technique in comparison to the conventional IV catheter. Place the index finger on the push tab, the middle finger on the soft wing and thumb on the septum. The primary flashback is observed through the notch in the tip of the needle as soon as the needle tip enters the vein. While threading the catheter, secondary flashback is observed in the extension tubing. At this point the tourniquet is released. As long as the catheter is in the vein, there is continued blood flow in the extension tubing all the way to the vent plug where the blood stops. This avoids unnecessary blood contact. While withdrawing the needle from the catheter, the soft wings should be fixated by pressing a finger on one of them. Upon

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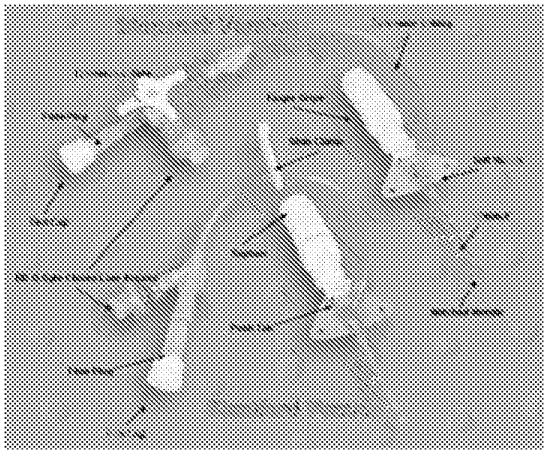


Fig. 1. — The new integrated completely closed IV catheter system (BD Nexiva™). Shown are two versions : the top one has a three-way valve to which the Q-Syte™ is attached ; the bottom one, with the Q-Syte™ closed Luer Lok access. Both devices have a flow plug for venting out the air during insertion. Advantages of both versions include avoidance of needlestick injuries and blood contact.

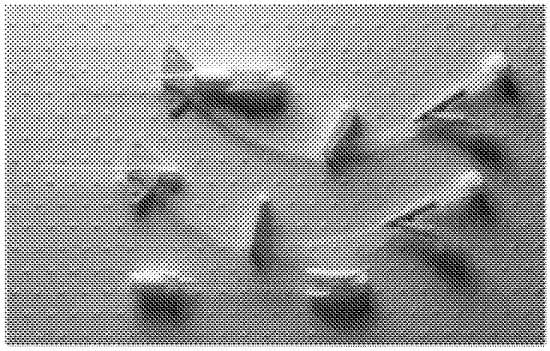


Fig. 2. — Non-activated (top) and activated (bottom) versions of the BD Nexiva™.
The white portion (catheter body) is used for gripping the device. Once inserted into the vein, the catheter body is withdrawn completely and the needle is automatically sheathed (see lower picture), thus protecting from accidental needle stick injuries.

Table 1

Characteristics of IV needles

	Ported IV cannula	Integrated valve	Needle tip protection	Integrated extension line
BD Venflon™	Yes	No	No	No
BD Venflon Pro™	Yes	No	No	No
BD Safelon Pro™	Yes	No	Yes	No
BD Nexiva™	No	Yes	Yes	Yes

Table 2

Advantages of new IV cannula over previous IV catheters

- rapid reliable blood flashback via notched needles
- reduced pain to patient*
- lower infection and thrombotic risks**
- simplicity in dressing, resistant to snagging
- needle-less access to ports
- more closed to bacterial entry
- reduced needlestick risk
- minimal blood exposure for the user

* a function of many factors including : the sharpness and geometry of the needle tip, the gauge of the catheter, the nature of the plastic in the catheter, the skill and speed of the inserter and the skill at preparing and distracting the patient.

** a function of many factors including : the catheter material, the agent and procedure used to prepare the skin, the drug injected, the post-insertion site care and the sterility of infusions given.

withdrawal, the needle tip is automatically shielded thus protecting the healthcare worker from needlestick injuries.

Once the needle is withdrawn and has been shielded it cannot be inserted into the cannula again. Furthermore, the hub, after needle withdrawal, cannot be accessed by any device (e.g. syringe, tubing, plug). At this point, the extension line has to be clamped before removing the vent plug and either connecting the infusion line or flushing and attaching the white cap. The three-way stopcock version (Fig. 1) does not have a clamp. The valve serves this function.

Our experience with the new BD Nexiva™ integrated IV catheter system is limited to hundred insertions ; but so far it has been positive. We have found that the grip on the catheter is designed in such a way as to make vein access quite easy. Confirmation that one is in, is provided via a clear primary flashback. Patients seem to experience less pain due to its sharp needle. Once withdrawn, the needle tip is covered automatically thus protecting the patient and the caregiver from needlestick injuries. The flat soft wings are simple to dress with Tegaderm™ (3M Health Care, St. Paul, USA). An IV line can be attached immediately to the side port without need for additional extension tubing or administration sets. Instead of a 'ported' access, the BD Nexiva™ has a BD Q-Syte™ access. This is a

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needle-less valve containing silicone and can also be used to attach another IV line, administer medication or blood withdrawal. There are additional convenience features. The flat profile of the BD Nexiva™ IV catheter allows dressing to cover it smoothly without wrinkling or binding up. Therefore it is less likely to catch on objects in the environment.

There are two features of BD Nexiva™ that could be improved. In few occasions, secondary flashback (via extension line) stops too early, leaving a gap in the tubing containing air. This can be solved by aspirating the remaining air from the tubing. The BD Q-Syte™ is not a one-way valve, so that backflow is possible if a syringe is attached. The BD Nexiva™ stopcock version solves this issue.

In conclusion, our experience with the BD Nexiva™ peripheral IV catheter indicates that it provides better IV access to peripheral veins, with less pain to patients and with rapid and clearly visible primary and secondary flashback of blood. By having all the add-ons (valve, extension tube, stopcock) already integrated into the device, infection risk should be reduced. Above all this IV cannula prevents needlestick and blood exposure, which is a dramatic improvement in an era where risks of infections are increasingly due to blood exposure.

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REVIEW Open Access

Blood conservation devices in critical care: a narrative review

Catherine Page*, Andrew Retter and Duncan Wyncoll

Abstract

Anaemia is associated with inferior outcomes in critically ill patients. It is difficult to prevent and is treated commonly with the transfusion of packed red cells. However, transfusion to augment oxygen delivery has not been shown to consistently offer a survival advantage when the haemoglobin concentration exceeds 7 g/dL. Several studies point to inferior outcomes when patients are transfused. Observational studies have confirmed that critically ill patients have frequent blood draws as part of their routine daily care. Cumulatively large volumes of blood are frequently taken, which contribute significantly towards the development of anaemia. Reducing iatrogenic blood loss may reduce the risk of developing anaemia and possibly the need for transfusion. Blood conservation devices may help to achieve this goal. The integration of blood conservation devices into routine care has been relatively slow in critical care. This review summarises the current evidence base and confirms that blood conservation devices do reduce the volume of iatrogenic blood loss. In the most recent studies, these devices have been shown to reduce transfusion requirements even in those intensive care units that follow a restrictive transfusion strategy.

Keywords: Critical care, Blood conservation devices, Anaemia, Transfusion

Review

Introduction

Anaemia and the transfusion of allogenic red blood cells (RBC) are common in the critically ill [1,2]. Observational studies indicate that almost 90% of patients become anaemic by the third day of intensive care unit (ICU) admission [3]. Anaemia is associated with poor patient outcomes, especially amongst those patients with cardiovascular disease [4-7]. Current guidelines strongly support policies of restrictive transfusion, but despite this 40% of ICU patients still receive transfused blood, accounting for approximately 8% of the national blood supply in the UK [8].

Multiple pathogenic mechanisms contribute towards the development of anaemia in critically ill patients. RBC life span is reduced, and there is decreased production of erythropoietin and a blunted marrow response to its action [9]. Hepcidin synthesis is greatly increased in inflammation, trapping iron in macrophages, decreasing plasma iron concentrations, and causing iron-restricted erythropoiesis [10]. In addition to this cytokine milieu, repeated phlebotomy makes a very significant contribution. In one study, weekly blood loss due to phlebotomy was reported to be between 340 to 660 ml [11]. The SOAP study reported a positive correlation between organ dysfunction and the number of blood draws ($r = 0.34$; $P < 0.001$) and the total volume drawn ($r = 0.28$; $P < 0.001$) [1].

Given the high prevalence of anaemia and its detrimental consequences, it appears intuitive to transfuse patients with RBCs in an attempt to restore oxygen delivery and mitigate tissue dysoxia. However, the administration of blood is subject to increased scrutiny. Although the risks related to transfusion, such as infection, febrile, allergic and haemolytic transfusion reactions, transfusion-related acute lung injury, and transfusion-associated circulatory overload are very low, concern remains about adverse outcomes associated with blood transfusion [12]. There also is now greater appreciation of the less recognized risks of transfusion relating to RBC storage effects and to the immunomodulatory effects of RBC transfusion [13]. Critically ill patients are likely to be more at risk of the immunosuppressive and microcirculatory complications of blood cell transfusions than the general population. It is due to these risks that minimising the use of blood

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transfusions in the critically ill has become such an important topic. One of the most significant findings during the past decade has been that using transfusions to augment oxygen delivery within the critically ill has not been shown to offer a survival advantage when the haemoglobin (Hb) concentration exceeds 7 g/dL [14]. The strongest evidence guiding transfusion policy in adult critically ill patients comes from the Transfusion Requirements In Critical Care (TRICC) study (Hebert et al., 1999) [15]. Patients with Hb ≥90 g/l were randomized to either the "liberal" group (transfusion trigger of <100 g/l) or the "restrictive" group (transfusion trigger of <70 g/l). The restrictive group received 54% fewer units of blood and 33% received no blood transfusions in the ICU, whereas all of the liberal group received transfusions. Overall, there was a nonsignificant reduction in 30-day mortality for the restrictive group. Significantly, those critically ill patients <55 years and patients with an APACHE score <20, the risk of death at 30 days was significantly lower with the restrictive strategy. For patients aged <55 years, those in the restrictive group had a 5.7% mortality vs. 13% for those in the liberal group (95% confidence interval (CI) for the absolute difference 1.1–13.5%; $P = 0.028$) [14].

The results of the TRICC study have now been corroborated by three recent studies. The Transfusion Requirements After Cardiac Surgery (TRACS) study found no difference in a composite end-point of 30-day mortality and severe comorbidity in cardiac patients prospectively randomized to a liberal or restrictive transfusion strategy [16]. The "FOCUS" study of restrictive transfusion in high-risk patients after hip surgery also showed no difference in mortality or morbidity in the group assigned to the restrictive transfusion strategy [17]. Most recently Villaneuva published the first study examining restrictive transfusion in acute upper gastrointestinal bleeding. There was improved survival in patients with variceal and peptic ulcer bleeding and decreased rates of rebleeding in patients randomized to a lower transfusion threshold [18]. In summary, the most recent literature consistently shows no advantage in transfusing against a liberal transfusion strategy. A restrictive approach to transfusion now is supported by national guidelines [15].

Therefore, the key to conserving RBC transfusions within critical care is by modifying transfusion practice, but this seems difficult to implement. In-line blood conservation devices, which eliminate the need for "discarded" blood when taking blood draws from central and arterial lines, offer a simple solution to try and reduce the need for RBC transfusion. In a survey of members of the Society of Critical Care Medicine in the United States, most agreed that blood conservation devices are useful in preventing anaemia [19]. There is evidence that phlebotomy volumes can be reduced by the use of in-line blood conservation devices. Despite their potential benefits, a survey in 2001 found that only 18% of adult ICUs in England and Wales use blood conservation devices [20]. The reasons for this are not clear but may relate to the cost or a lack of evidence that such devices reduce transfusion requirements.

In recent years, evidence has been published that supports the use of blood conservation devices. This review explores the contribution of phlebotomy to the development of anaemia in the critically ill and examines the role that blood conservation devices may have in its prevention. We searched PubMed looking for articles published on blood conservation devices. The studies identified are summarized in Table 1. The authors reviewed the literature with a particular emphasis on four questions.

1. Is there evidence that blood conservation devices reduce the volume of blood taken from critically ill patients?
2. Does the use of a blood conservation device have an impact on patients' transfusion requirements?
3. Do blood conservation devices have an effect in reducing the number of catheter-related blood stream infections?
4. Are blood conservation devices cost-effective?

Is there evidence that blood conservation devices reduce the volume of blood taken from critically ill patients?

The SOAP study examined phlebotomy practice in 1,136 patients, suggesting a mean blood loss due to phlebotomy of about 41 ml/day/patient [1]. This equates to approximately 280 ml per week; the volume of a unit of packed red cells ranges from 280 to 340 ml. Routine blood tests and arterial blood gas sampling are the commonest interventions in critically ill patients with arterial blood gases accounting for almost 40% of blood drawn from ventilated patients [19]. Patients with arterial catheters are phlebotomized twice as often, and have a threefold increase in blood loss compared with patients who do not have intra-arterial access [29]. The mean frequency of blood draws varies from 5 to more than 24 samples per day [30], with a correlation between the severity of illness and the number of blood draws [1,25,31]. The total volume of diagnostic blood taken is a significant independent predictor of subsequent transfusion [32]. Thus, the sickest patients are at the greatest risk of iatrogenic anaemia and allogenic transfusion.

Conventional arterial line systems require that an initial blood sample be removed to "clear the line". This initial volume is discarded, so that a second sample of undiluted blood can then be obtained. The fraction of "discarded" blood is a major contributory factor in the anaemia of critical illness. The volume of discarded blood typically varies from 2-10 ml. Only the dead space volume of the arterial line is required to be cleared,

Table 1 Current studies relating to the use of blood conservation devices in critical care

Study and year of publication	Design	Outcome
Silver - 1993 [11]	Prospective, randomized crossover comparing the Safedraw device and conventional arterial line.	31 patients enrolled, study period 7 days. Over 7-day period, the control group had a larger blood discard volume by an average of 156.8 ml ($p < 0.001$).
Peruzzi - 1993 [21]	Prospective, randomized, controlled trial comparing the VAMP system to control.	100 patients enrolled, mean study period 4 days. Total volume of blood discarded significantly lower in the VAMP group (19.4 ml vs. 103.5 ml, $p < 0.001$). Hb decreased by 1.4 g/dL in the control vs. 1 g/dL in the VAMP group (p = nonsignificant). Transfusion requirements similar in both groups –no transfusion protocol.
Peruzzi - 1996 [22]	Prospective, randomized trial comparing microbial contamination between the VAMP and Safedraw device.	40 patients studied for an average of 3 days. No difference in contamination rates between the two devices. No catheter-related infections
Thorpe - 2000 [23]	Prospective, randomized trial comparing VAMP device to conventional arterial line.	100 patients followed for 15 days. No significant difference in Hb concentration or transfusion requirements between the two groups. Mean Hb remained >10 throughout study - no transfusion protocol.
MacIsaac - 2003 [24]	Randomized, unblinded, control trial comparing VAMP to control.	160 patients, mean study period 3 days. Total volume of blood discarded significantly lower in the VAMP group (1 ml vs. 62 ml, $p < 0.001$). No significant change in Hb concentration between groups but unadjusted for transfusion. Fewer patients transfused within VAMP group (17 vs. 30 $p = 0.04$)- no transfusion protocol
Mahdy - 2009 [25]	Prospective, randomized, unblinded controlled clinical study. Comparing VAMP plus paediatric vials to control plus adult vials.	39 patients, study period 3 days Total volume of blood discarded significantly less in the VAMP group (0 ml vs. 25 ml, $p < 0.001$) No statistical difference in fall of Hb concentration (0.79 vs. 1.3 g/dL, $p = 0.09$) - no patient required transfusion.
Rezende - 2010 [26]	Prospective, randomized, controlled trial comparing transfusion rates and Hb loss between VAMP system and control.	127 patients followed for 14 days. Smaller decline in Hb within the VAMP group ($p = 0.03$) - no difference in transfusion rate; transfusion threshold 7 g/dL.
Mukhopadhyay - 2010 [27]	Before and after intervention study assessing the impact of a restrictive transfusion strategy when comparing VAMP to control.	250 patients followed for 28 days or until discharge from ICU. Smaller decline in Hb within the VAMP group (1.44 vs. 2.13 g/dL, $p = 0.02$) VAMP group required less transfusions (0.068 vs. 0.131 units/patient/day, $p = 0.02$); transfusion threshold of 7.5 g/dL.
Oto - 2011 [28]	Prospective, randomized study comparing bacterial contamination between VAMP and control.	216 patients followed for a median of 4 days. No statistically significant change in tip colonization between the two groups. No catheter-related infections.

which is actually closer to 2 ml. Closed blood sampling devices (blood conservation devices), where return of the initial discarded sample occurs, can help to reduce the volume of blood "lost". The most common closed arterial system used within the UK is the VAMP (venous-arterial management protection) device produced by Baxter Healthcare, although there are other manufacturers with similar devices. These devices allow blood and flush solution to be drawn into a reservoir distal to the sampling port. Blood is then collected at the sampling port without being diluted with the flush solution. The blood held in the reservoir is reinfused into the patient. It can be used on both arterial and central venous lines and can be accessed with a blunt needle [23]. An image of the system is shown in Figure 1.

During the past 20 years, a number of trials have shown that the use of a blood conservation device can reduce the volume of blood taken from critically ill patients. Silver and colleagues demonstrated that an average of 49 ml less blood was lost per patient per day, and

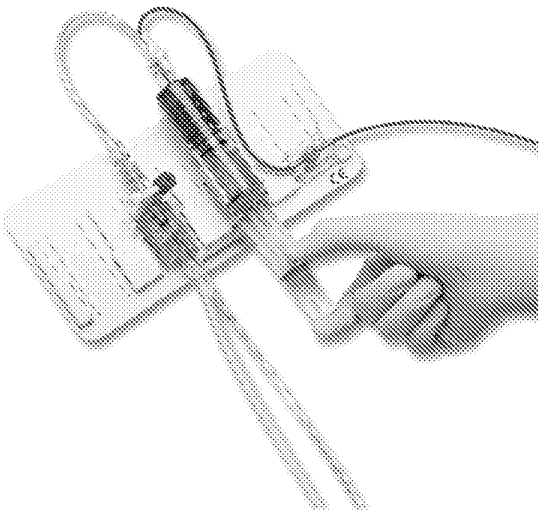


Figure 1 Edwards VAMP system. The port to the right of the image is the sampling port, which is accessed by a needless device. The middle syringe is the reservoir where the previous "discarded" blood is held before being reinfused back into the patient. Picture submitted with permission from Edwards Lifesciences Ltd.

that during a 7-day period an average of 340 ml of blood were saved per patient by using a blood conservation device [11]. A prospective, randomized, controlled trial by Peruzzi showed a marked reduction in the volume of blood discarded daily: 96 ml in the conventional arm compared with 5 ml in patients with the conservation device during the mean study period of 4 days. Although the mean Hb concentration remained consistently higher in the conservation device group, statistical significance was not reached until 9.5 days of ICU care [21].

Thorpe et al. reported the fall in Hb levels during 7 days between the VAMP device and a control group in 102 patients. No significant difference was seen in Hb levels during the 7-day stay; however, their study was small and no data were provided regarding the amount of blood draws taken or volume of phlebotomy between the two groups [23]. MacIsaac published a larger randomized, controlled trial involving 160 patients. The blood conservation device group lost significantly less blood for diagnostic testing (63 ml vs. 133 ml for controls), but the study failed to demonstrate a significant fall in Hb levels between admission and discharge when comparing the two groups [24]. Mahdy reported a small unblinded, randomized, controlled trial comparing the use of a VAMP system plus paediatric bottles against a standard arterial line system plus adult phlebotomy bottles in 39 patients. As expected, there was a statistically significant difference in terms of the volume of blood taken for analysis over the first 72 hours: 15 ml compared with 45 ml [25].

In summary, in all trials the volume of blood taken for diagnostic testing between the blood conservation devices and control groups was significantly less; however, only in the larger trials did this result in a reduced rate of fall in Hb. This could be explained by the small numbers and short study periods, the frequent exclusion of patients receiving renal replacement therapy, and those admitted with a primary bleeding issue. Ironically, it would seem likely that these "excluded patients" may actually be the most at risk of anaemia and might benefit most from a blood conservation device.

Does the use of a blood conservation device have an impact on patient transfusion requirements?

Before 2010, no study provided unequivocal evidence that a blood conservation system reduced transfusion requirements in critically ill patients [21,23,25]. In 2003, MacIsaac et al. published a prospective randomized, unblinded, controlled trial (n = 80) that examined the influence of the VAMP system on anaemia in ICU patients. They demonstrated a statistically significant reduction in transfusion requirements within the VAMP group. Because this was not their primary end point and because no transfusion triggers were set, the results need to be interpreted with caution.

Chant published a retrospective chart review of 155 patients in a medical-surgical ICU that had a greater than 30-day ICU stay [33]. This study found that of patients transfused, daily phlebotomy volume was significantly higher. The unit had a relatively low Hb transfusion trigger of 7.7 g/dL after day 21. They concluded even that small increases in daily phlebotomy volumes were associated with a doubling of the chances of being transfused after day 21.

Mukhopadhyay et al. in 2010 undertook the largest study to date of the VAMP system [27]. They performed a before and after study to investigate whether the use of a blood conservation device in the presence of a standardized, restrictive, transfusion practice could reduce the number of units transfused per patient per day. They showed both a smaller drop in Hb levels between admission and discharge in the intervention group, and most importantly that the use of a blood conservation device was independently associated with lower RBC transfusions (control group 0.13 units vs. active group 0.068 units RBC/patient/day, $p = 0.02$). In most patients, a transfusion threshold of 7.5 g/dL was used, but in 23.8% of the control and 29% of the active group patients were transfused above the threshold. This is very much in keeping with routine clinical practice where clinicians, especially treating patients with significant coronary disease, find it difficult to comply with restrictive transfusion thresholds.

The authors suggested that a blood conservation system is of maximal benefit in patients with higher APACHE II scores, those receiving renal replacement therapy, initial low admission Hb, and longer ICU stays [27]. Interestingly both the ICU (38% vs. 21%) and hospital (53% vs. 30%) mortality in the control group was significantly higher ($P = 0.001$). These findings must be interpreted with care, because the study was not a randomized, controlled trial and mortality was not the primary or secondary endpoint. Nevertheless, even after adjusting for all other variables, mortality in the intervention group remained significantly less.

In summary, of the six studies looking at the impact of blood conservation devices on the rates of transfusion, only one study has shown a positive impact leading to reduced blood product support. However, the majority of studies to date have not incorporated a standardised transfusion threshold, and some studies report patients being transfused at levels as high as 10 g/dL. Therefore, no definitive conclusions can be drawn, but the most recent results are interesting and encouraging.

Do blood conservation devices have an effect in reducing the number of catheter-related blood stream infections?

Although infection is most frequently associated with venous lines, arterial catheterisation also leads to catheter-related bloodstream infection secondary to fluid stagnation and manipulation of the device. When the system is opened for blood sampling, there is a small risk of microbial contamination. In theory, closed blood conservation device systems reduce this risk by minimising access through open sampling ports [28].

Oto et al. reported a prospective randomized study comparing contamination resulting from the use of the VAMP system or a 3-way stopcock that had been in use for >24 hours within the radial artery. Of 216 patients, there was a statistically significant difference in the colonisation of intraluminal fluid (test device 2/109 vs. 9/107 in the control group). There was no difference in colonisation of the tip between the two groups and no arterial catheter-related blood stream infections seen in either group. In both groups the incidence of tip contamination was related to time in situ and frequency of accesses [28]. Similar trends have been observed in other studies during a 7-day period where more lines were colonised in the control group (37/99) compared with the VAMP system (29/96) [23]. These studies confirm earlier findings that suggest blood conservation devices can be used without concern of exacerbating infectious processes [22].

Are blood conservation devices cost effective?

As yet, there is no published data on the cost-effectiveness of these in-line blood conservation devices. However, given that the typical acquisition costs are only marginally above standard transducer systems (approximately 15 Euros for a 72-hour system) and given that blood in Europe is typically approximately 150 Euros per unit, at worst their introduction is likely to be cost neutral. It is difficult to quantify financial savings from the potential patient benefits of reducing transfusion requirements related to subsequent improvements in outcome (reduced mortality/length of stay, etc.) from limiting the effects of "harmful blood". The systems are simple to use and limited training is required.

Conclusions

Only a small number of studies have examined the utility of blood conservation devices. Their advantages are appealing with a reduced risk of needle stick injuries and splashes to staff, along with reduced blood wastage through routine phlebotomy. The literature consistently reports that patients lose less blood when blood conservation devices are used. This combined with a trend towards a reduction in transfusion requirements when blood conservation devices are used alongside restrictive transfusion triggers is encouraging. However, they are only one part of good blood practice. The most effective blood conservation strategies remain the simplest and likely least costly, most importantly complying with restrictive RBC transfusion guidelines and avoidance of excessive testing. In reality, these remain the hardest to implement. Practice is starting to change with increased awareness of the most recent literature and new national guidelines to help support physicians in their decisions surrounding transfusions. We feel that increasing compliance to restrictive transfusion practice by actively auditing against the national guidelines should be encouraged within critical care units. Additionally reducing the number of blood draws is a continuing issue within the critical care community. It is difficult to form guidelines as the requirements for each individual patient will vary on a day-to-day basis. Improved education on the impact phlebotomy has on iatrogenic anaemia, limiting the use of order sets, and improved guidance from senior members of the critical care team towards the junior doctors and nursing staff who frequently are the team members who order the bloods can help to try and change practice. However, from our experience critical care units continue to take high number of blood draws and it would seem sensible to use a blood conservation device that limits discarded blood whilst units continue to try and change their own transfusion practice. If these interventions are combined, there is the potential to reduce significantly iatrogenic anaemia and any adverse consequences of transfusion.

Abbreviations

VAMP: Venous arterial blood management protection; ICU: Intensive care unit; RBC: Red blood cell; Hb: Haemoglobin.

Competing interests
The authors declare that they have no competing interests.

Authors' contributions
Dr. DW developed the initial idea and plan for the review, and edited the document. Dr. CP and Dr. AR were primarily responsible for the literature search and writing the initial draft of the article. All authors read and approved the final manuscript.

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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.

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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), bacterioides 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.

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KUR-MAG-DE004886

Bibliographic data: DE7203008 (U) — 1972-05-10

Combined blood withdrawal and transfusion appts - for obtaining blood plasma by plasmaphaeresis

Inventor(s):

Applicant(s): IMMUNO AG FUER CHEM-MED PROD

Classification: **- international:** ***A61B5/15; A61M1/02; A61M5/14;*** (IPC1-7): A61M1/00
- cooperative: **A61M1/0236 (EP, US); A61M5/14 (EP, US)**

Application number: DE19720003008U 19720127

Priority number(s): AT19710009545 19711105

Also published as: AT310345 (B) BE841642 (Q) DE2203858 (A1) DE2203858 (B2) DE2203858 (C3) more

Abstract not available for DE7203008 (U)
Abstract of corresponding document: DE2203858 (B2)

Combined blood withdrawal and re-transfusion appts. is intended for obtaining large quantites of plasma by means of plasmaphaeresis; the blood is removed through is needle implanted in a vein and collected in the recipient which is partly filled with an anticoagulation agent. The recipient is taken out of the system and is centrifuged to separate the plasma from the erythrocytes, w which are retained in the recipient. After washing the latter free from plasma, they are made into a suspension in physiological sodium chloride soln. and transfused back to the patient. While this treatment is in progress, a slow current of sodium chloride soln. is infused into the patient from recipient, through the tube and the drop-counting chamber. The recipient, after the process mentioned above, is attached to the connector of the tube. Sodium chloride is transferred to the recipient to form the suspension of the erythrocytes. The suspension is then infused into the patient. The appts., is simple to handle and has the great advantage that the donor is protected because a blood sample can be taken at any moment through the connector to avoid any confusion of blood groups during the plasmaphaeresis.

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DESCRIPTION DE7203008U

[0001]

13 IMMUNO

[0002]

17 Public limited company for chemiscli-medizirii sclie

[0003]

21 Products Vienna (Austria.

22)

[0004]

26 Combined blood collection and infusion device

[0005]

30 Plasmapheresis is used to obtain large quantities of plasma. This is a method in which blood is taken from the donor using a suitable blood-sucking device into a container partially filled with an anticoagulant, after which the container is centrifuged.

33 The plasma which is left over after centrifugation is sucked off and the container with the erythrocytes is connected to an infusion device after it has been suspended in physiological saline solution and the erythrocytes are infused into the donor via the venipuncture needle which is still in the donor's vein.

37 This process is repeated once when performing a so-called double plasmapheresis.

[0006]

41 The infusion devices previously used for plasmapheresis contained a drip chamber

[0007]

45 connecting line leading from a storage vessel to the single or double plasmapheresis bag and this has a further connecting line to the venipuncture needle. The devices for double plasmapheresis contained two

[0008]

51 ■■ió. koi.i

[0009]

55 the corresponding connection lines to the venipuncture needle, which are also inextricably connected to the bags. This inextricable connection between the two bags and the venipuncture needle makes it more difficult and expensive to manufacture and use the devices and does not permit any variation in the work program.

59 E.g., it is not possible to collect centrifuged plasma in a reservoir without the bag intermediate stations. Wolters it is not possible with the known double bag devices to repeat the process of collection and reinfusion more than once, because in practice it is impossible in the device to be produced efficiently, which contains more than four bags which are inseparably connected to one another and to the venipuncture needle by means of corresponding connecting lines.

[0010]

67 The invention aims to avoid the disadvantages and difficulties described and consists in a blood collection and infusion device which has a reservoir for an infusion liquid, a connecting line leading via a drip chamber from the reservoir to the venipuncture needle and a further connection from the venipuncture needle to a blood reservoir, that the blood container provided with one or more connection points can be interchangeably connected to a line branching off from the connecting line between the reservoir and the venipuncture needle, which line is preferably provided with a shut-off element.

[0011]

77 The blood container can be designed as a single-chamber bag or as a two-chamber bag and can advantageously consist of flexible, transparent plastic material.

[0012]

82 As a result of the detachable connection of the ulutbehltex-s with the other parts of the device, the manufacture of the container is simpler and cheaper; the work program can be varied and modified in any way.

85 It is thus possible, after the contents of the blood container have been centrifuged, to convey the plasma into a second bag connected to the first bag or into another storage container.

87 It is also possible to repeat the process of removal and infusion not just twice but as often as you like, which z.

89 B. is essential in leukocytopheresis and thrombocytopheresis, in which cases the process is to be repeated up to 10 times.

91 Throughout the manipulation, the venipuncture can be left in the donor's vein

[0013]

95 The subject of the invention is explained in more detail using an exemplary embodiment in the drawing.

97 1 denotes the reservoir for an infusion liquid, with which the line 2 leading to the drip chamber 3 can be connected.

99 h

100 is a shut-off device in this line.

101 A branch piece 5, which is also a shut-off device

102 H

103 y

104 has, carries a coupling piece 6, which is connected to the blood container in the reinfusion phase in a manner to be described later.

106 From the drip chamber 3 leads the line 7, which is also a shut-off device

107 c"

108 has, to the venipuncture needle 8.

109 According to the invention, the line 9 branches off from this connecting line between the reservoir and the venipuncture needle and again has a shut-off element 4

111 nl

112 has and a coupling piece 10 has.

113 The blood container 11 designed as a single-chamber bag can be releasably connected to the line 9 via the attachment piece 12 and the coupling piece 10. The bag is preferably made of flexible and transparent plastic material

116 lk

117 are closable removal openings of the bag

[0014]

121 designated.

122 An embodiment of the invention consists in the fact that the bag 11 is connected to the bag 16, which is otherwise constructed in the same way, by means of a vesicle line; in this case, the blood container is designed as a two-chamber bag

[0015]

128 The function of the device is the following: After connecting the container 1 to the line 2, with the shut-off elements 4 and 4'' open and the shut-off element s 4'' and 4Ml closed, the system is completely filled with physiological before inserting the venipuncture needle into the vein, avoiding air bubbles Saline solution filled. Then the shut-off element 4M in the line 7 is closed and the venipuncture needle inserted into the vein is connected to the B^ätsl 11 by connecting the coupling piece 10 to the attachment 12, the shut-off element 4Mt is opened and blood collection begins.

135 After the desired amount of blood has been removed, the shut-off element 4''' is closed and the container 11 is separated from the system.

137 Now another bag is connected to the coupling piece 10.

138 Then, with the shut-off element 4 still open, the shut-off element 4'' is opened and a slow flow of physiological saline solution is infused into the donor's vein.

140 After removal from the system, the bag 11 is centrifuged and the supernatant plasma is separated from the sediment and collected.

142 The sediment remains in the blood bag 11 .

143 In the next phase, the shut-off device 4n in the line 7 is closed, the blood bag 11 is connected to one of the connectors 13 or 14 with the coupling piece 6 of the line 5, 4'' is closed. 41 is opened and physiological saline solution is transferred into the bag 11 until a infusable suspension of erythrocytes in the physiological saline is formed.

147 Then the obturator 4 is

[0016]

151 closed, kopened and the suspension infused into the vein. The process can be repeated as often as desired, whereby, as mentioned earlier, the blood container can be designed either as a single or as a double bag.

154 As can be seen, the device is easy to use; Compared to the known devices, it also has the further great advantage that, to protect the donor during the plasmapheresis procedure, the blood group of the donor can be checked at any time by taking a blood sample at the coupling piece 10 in order to avoid mixing up the blood group when the erythrocytes are reinfused.

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CLAIMS DE7203008U

1.

13 * Uc/n sayings t

2.

17 1. Combined blood collection and infusion device for carrying out single and multiple plasma.phereses or leukocyto- and thrombocytophereses, with a reservoir for an infusion liquid, a connecting line leading via a drip chamber from the storage vessel to the venipuncture needle and a further connection from the Venipuncture needle to a blood reservoir, characterized in that the blood reservoir (II), which is provided with one or more connection points, can be interchangeably connected to a line (9) branching off from the connecting line (7) between the reservoir (1) and the venipuncture needle (8), which is preferably equipped with a shut-off element (kn1) is provided, can be connected.

3.

28 2, Combined blood collection and infusion device according to Claim 1, characterized in that the blood container (II) is designed as a single-chamber bag or as a two-chamber bag and preferably consists of flexible, transparent plastic material.

DEUTSCHES GEBRAUCHSMUSTER

Bekanntmachungstag: 10. 5. 1972

A61m 1-00 7203008
30k 1-02
AT 27.01.72
Pr 05.11.71 Österreich A9545-71
Bez: Kombiniertes Blutabnahme- und Infusionsgerät.
Anm: Immuno Aktiengesellschaft für chemisch-medizinische Produkte, Wien;
Vtr: Glawe, R., Dr.-Ing.; Delfs, K., Dipl.-Ing.; Moll, W., Dipl.-Phys. Dr. rer.nat; Pat.-Anwälte, 8000 München und 2000 Hamburg;

tbm

Bitte beachten: Zutreffendes ankreuzen; stark umrandete Felder freilassen!

An das
Deutsche Patentamt
8000 München 2
Zweibrückenstraße 12

Ort: München
Datum: 26. Januar 1972
Eig.Zeichen: A 54

(Bitte freilassen!)

9 D 1/4 B

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Immuno Aktiengesellschaft für chemisch-medizinische Produkte, 122o, Wien, Industriestr. 72, Österreich

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A1 10

Vertreter:
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Kombiniertes Blutabnahme- und Infusionsgerät

9

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(Reihenfolge: Anmeldetag, Land, Aktenzeichen; Kästchen 1 ankreuzen)
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(Reihenfolge: 1. Schaustellungstag, amtl. Bezeichnung und Ort der Ausstellung mit Eröffnungstag; Kästchen 2 ankreuzen)

1 X
2

5. November 1971, Österreich, A 9545/71

05.11.71 OEA 9545-71

6

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Anlagen: (Die **angekreuzten Unterlagen** sind **beigefügt**)

- Ein weiteres Stück dieses Antrags — 1. X
- Eine Beschreibung — 2. X
- 2 Stück mit 2 Schutzanspruch(en) — 3. X
- 1 Satz Aktenzeichnungen mit 1 Blatt — 4. X
- zwei gleiche Modelle
- Vertretervollmacht — 5. X
- Prioritätsbescheinigung

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Von diesem Antrag und allen Unterlagen wurden Abschriften zurückbehalten.

Raum für Gebührenmarken — (bei Platzmangel auch Rückseite benutzen)

7203008 10.5.72

(Patentanwalt)

I M M U N O
Aktiengesellschaft für
chemisch-medizinische
Produkte
Wien (Österreich)

Kombiniertes Blutabnahme- und Infusionsgerät

Zur Gewinnung großer Plasma-Mengen wird die Plasmapherese angewendet. Dies ist eine Methode, bei der dem Spender mittels eines geeigneten Abnahmegerätes Blut in ein mit einem gerinnungshemmenden Mittel teilweise gefüllten Behälter abgenommen wird, worauf der Behälter zentrifugiert wird. Das nach dem Zentrifugieren überstehende Plasma wird abgesaugt und der Behälter mit den Erythrocyten wird nach Aufschwemmen mit physiologischer Kochsalzlösung an ein Infusionsgerät angeschlossen und die Erythrocyten werden über die noch in der Vene des Spenders befindliche Venenpunktionsnadel dem Spender infundiert. Dieser Vorgang wird bei Durchführung einer sogenannten Doppelplasmapherese einmal wiederholt.

Die für Plasmapheresen bisher verwendeten Infusionsgeräte enthielten eine über eine Tropfkammer führende Verbindungsleitung von einem Vorratsgefäß zum Einfach- oder Doppelplasmapheresebeutel und dieser besitzt eine weitere Verbindungsleitung zur Venenpunktionsnadel. Die Geräte für Doppelplasmapheresen enthielten zwei

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miteinander unlösbar verbundene Blutabnahmebeutel mit den entsprechenden, ebenfalls mit den Beuteln unlösbar verbundenen Verbindungsleitungen zur Venenpunktionsnadel. Diese unlösbare Verbindung der beiden Beutel und der Venenpunktionsnadel untereinander erschwert und verteuert die Herstellung und Handhabung der Geräte und erlaubt keinerlei Variation im Arbeitsprogramm. Z.B. ist es nicht möglich, zentrifugiertes Plasma ohne die Beutelzwischenstationen in einem Vorratsbehälter zu sammeln. Weiters ist es mit den bekannten Doppelbeutelgeräten nicht möglich, den Vorgang der Abnahme und Reinfundierung mehr als einmal zu wiederholen, weil es in der Praxis unmöglich ist, ein Gerät rationell herzustellen, welches mehr als vier, durch entsprechende Verbindungsleitungen unlösbar miteinander und mit der Venenpunktionsnadel verbundene Beutel enthält.

Die Erfindung bezweckt die Vermeidung der geschilderten Nachteile und Schwierigkeiten und besteht bei einem Blutabnahme- und Infusionsgerät, welches einen Vorratsbehälter für eine Infusionsflüssigkeit, eine über eine Tropfkammer führende Verbindungsleitung vom Vorratsgefäß zur Venenpunktionsnadel und eine weitere Verbindung von der Venenpunktionsnadel zu einem Blutbehälter aufweist, darin, daß der mit einer oder mehreren Anschlußstellen versehene Blutbehälter austauschbar an eine von der Verbindungsleitung zwischen Vorratsbehälter und Venenpunktionsnadel abzweigenden Leitung, die vorzugsweise mit einem Absperrorgan versehen ist, anschließbar ist.

Der Blutbehälter kann als Einkammerbeutel, oder als Zweikammerbeutel ausgebildet sein und vorteilhaft aus flexiblem transparentem Kunststoffmaterial, bestehen.

6

Infolge der lösbaren Verbindung des Blutbehälters mit den übrigen Teilen des Gerätes ist die Herstellung des Behälters einfacher und billiger; das Arbeitsprogramm kann in beliebiger Weise variiert und modifiziert werden. So ist es möglich, nach Zentrifugieren des Inhaltes des Blutbehälters das Plasma in einen mit dem ersten Beutel verbundenen zweiten Beutel oder in einen sonstigen Vorratsbehälter zu fördern. Es ist ferner möglich, den Vorgang der Abnahme und Infusion nicht nur zweimal sondern beliebig oft zu wiederholen, was z.B. wesentlich ist bei der Leukozyto- und Thrombozytopherese, in welchen Fällen der Vorgang bis zu 10 mal zu wiederholen ist. Während der gesamten Manipulation kann die Venenpunktionsnadel in der Vene des Spenders verbleiben.

Der Erfindungsgegenstand ist an einem Ausführungsbeispiel in der Zeichnung näher erläutert. Mit 1 ist der Vorratsbehälter für eine Infusionsflüssigkeit bezeichnet, mit dem die zur Tropfkammer 3 führende Leitung 2 verbindbar ist. 4 ist ein Absperrorgan in dieser Leitung. Ein Abzweigstück 5, welches ebenfalls ein Absperrorgan 4' aufweist, trägt ein Kupplungsstück 6, welches in später noch zu beschreibender Weise mit dem Blutbehälter in der Reinfusionsphase verbunden wird. Von der Tropfkammer 3 führt die Leitung 7, die ebenfalls ein Absperrorgan 4" aufweist, zur Venenpunktionsnadel 8. Von dieser Verbindungsleitung zwischen Vorratsbehälter und Venenpunktionsnadel zweigt erfindungsgemäß die Leitung 9 ab, die wieder ein Absperrorgan 4"' aufweist und ein Kupplungsstück 10 besitzt. Der als Einkammerbeutel ausgebildete Blutbehälter 11 ist über das Ansatzstück 12 und das Kupplungsstück 10 lösbar mit der Leitung 9 verbindbar. Der Beutel besteht vorzugsweise aus flexiblem und transparentem Kunststoffmaterial. Mit 13 und 14 sind verschließbare Entnahmeöffnungen des Beutels

bezeichnet. Eine Ausführungsform der Erfindung besteht darin, daß der Beutel 11 durch eine Verbindungsleitung 15 mit dem sonst in gleicher Weise ausgebildeten Beutel 16 verbunden ist; in diesem Fall ist der Blutbehälter also als Zweikammerbeutel ausgebildet.

Die Funktion des Gerätes ist die folgende: Nach Verbinden des Behälters 1 mit der Leitung 2 wird bei geöffneten Absperrorganen 4 und 4" und geschlossenen Absperrorganen 4' und 4"' das System vor Einführen der Venenpunktionsnadel in die Vene unter Vermeidung von Luftblasen vollständig mit physiologischer Kochsalzlösung gefüllt. Dann wird das Absperrorgan 4" in der Leitung 7 geschlossen und die Venenpunktionsnadel in die Vene eingeführt. Dann wird durch Verbinden des Kupplungsstückes 10 mit dem Ansatzstück 12 der Beutel 11 angeschlossen, das Absperrorgan 4"' geöffnet und die Blutabnahme beginnt. Nach Entnahme der gewünschten Blutmenge wird das Absperrorgan 4"' geschlossen und der Behälter 11 vom System abgetrennt. Nun wird ein weiterer Beutel an das Kupplungsstück 10 angeschlossen. Sodann wird bei noch offenem Absperrorgan 4 das Absperrorgan 4" geöffnet und ein langsamer Fluß von physiologischer Kochsalzlösung in die Vene des Spenders infundiert. Der Beutel 11 wird nach Abnahme vom System zentrifugiert und das überstehende Plasma von dem Sediment getrennt und gesammelt. Im Blutbeutel 11 bleibt das Sediment übrig. In der nächsten Phase wird das Absperrorgan 4" in der Leitung 7 geschlossen, der Blutbeutel 11 mit einem der Anschlußstücke 13 oder 14 mit dem Kupplungsstück 6 der Leitung 5 verbunden, 4" geschlossen, 4' geöffnet und physiologische Kochsalzlösung in den Beutel 11 übergeführt, bis eine infundierbare Suspension von Erythrocyten in der physiologischen Kochsalzlösung gebildet ist. Dann wird das Absperrorgan 4 ge-

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schlossen, 4" geöffnet und die Suspension in die Vene infundiert. Der Vorgang kann beliebig oft wiederholt werden, wobei, wie früher erwähnt, der Blutbehälter entweder als Einfach- oder als Doppelbeutel ausgeführt sein kann. Wie ersichtlich, ist das Gerät einfach zu bedienen; es hat gegenüber den bekannten Geräten auch noch den weiteren großen Vorteil, daß zum Schutz des Spenders während der Plasmapheresеprozedur jederzeit die Blutgruppe des Spenders durch Entnahme einer Blutprobe beim Kupplungsstück 10 kontrolliert werden kann, um eine Verwechslung der Blutgruppe bei der Reinfusion der Erythrocyten zu vermeiden.

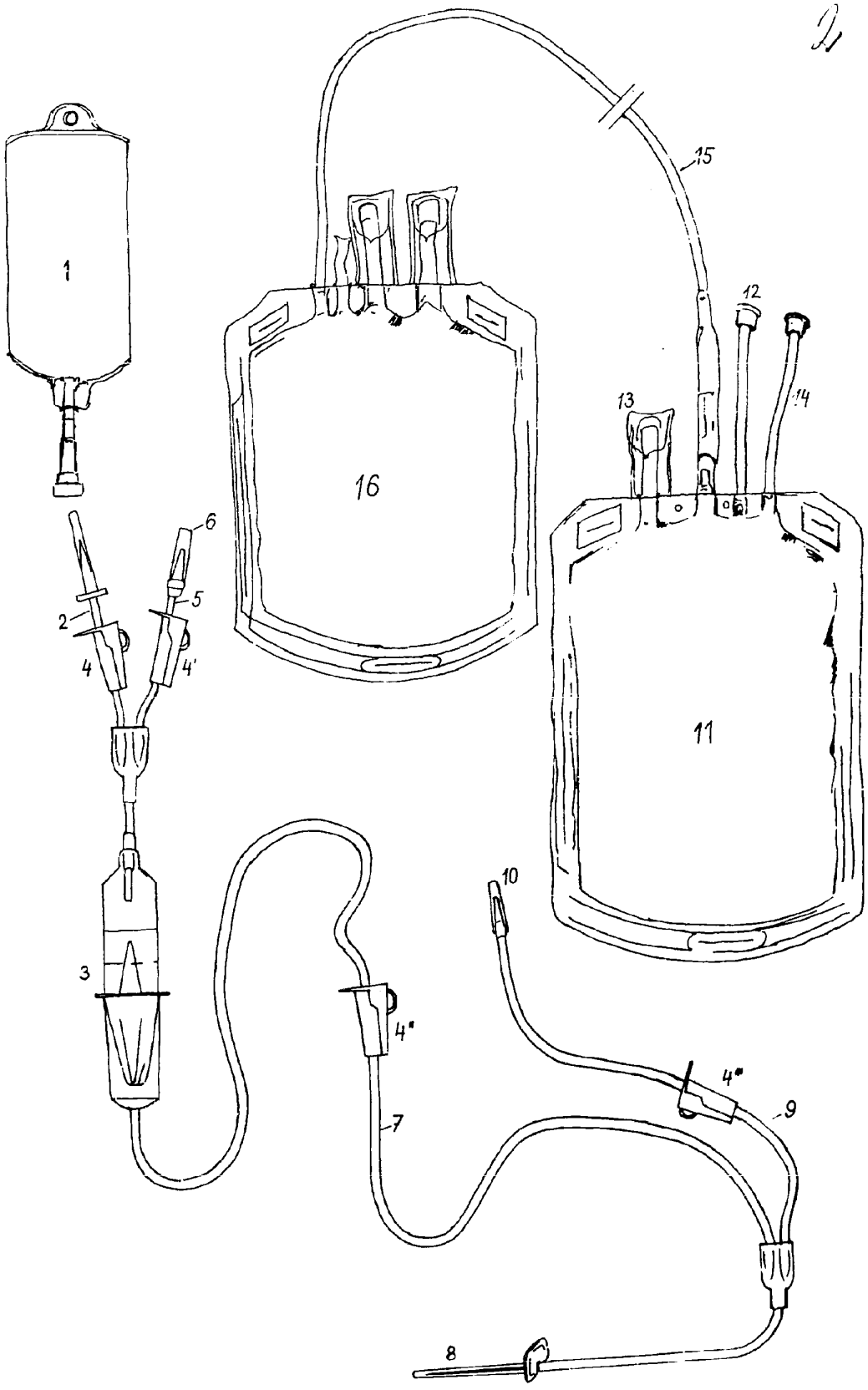
3

Patentansprüche:

1. Kombiniertes Blutabnahme- und Infusionsgerät zur Durchführung von Einfach- und Mehrfachplasmapheresen bzw. von Leukozyto- und Thrombozytopheresen, mit einem Vorratsbehälter für eine Infusionsflüssigkeit, einer über eine Tropfkammer führenden Verbindungsleitung vom Vorratsgefäß zur Venenpunktionsnadel und einer weiteren Verbindung von der Venenpunktionsnadel zu einem Blutbehälter, dadurch gekennzeichnet, daß der mit einer oder mehreren Anschlußstellen versehene Blutbehälter (11) austauschbar an eine von der Verbindungsleitung (7) zwischen Vorratsbehälter (1) und Venenpunktionsnadel (8) abzweigenden Leitung (9), die vorzugsweise mit einem Absperrorgan (4''') versehen ist, anschließbar ist.

2. Kombiniertes Blutabnahme- und Infusionsgerät nach Anspruch 1, dadurch gekennzeichnet, daß der Blutbehälter (11) als Einkammerbeutel oder als Zweikammerbeutel ausgebildet ist und vorzugsweise aus flexiblem transparentem Kunststoffmaterial besteht.

7203008 10.5.72



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Espacenet

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CLOSED SYSTEM BLOOD SAMPLING DEVICE

Inventor(s): DESECKI VINCENT C; BROWNE GLENNIE ± (DESECKI, VINCENT, C, ; BROWNE, GLENNIE)

Applicant(s): BAXTER INT [US] ± (BAXTER INTERNATIONAL INC)

Classification: **- international:** ***A61B5/15;*** (IPC1-7): A61M5/00
- cooperative: **A61B5/15003 (EP, US); A61B5/150213 (EP, US); A61B5/150259 (EP, US); A61B5/150992 (EP, US); A61B5/155 (EP, US)**

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Abstract of WO9605875 (A1)

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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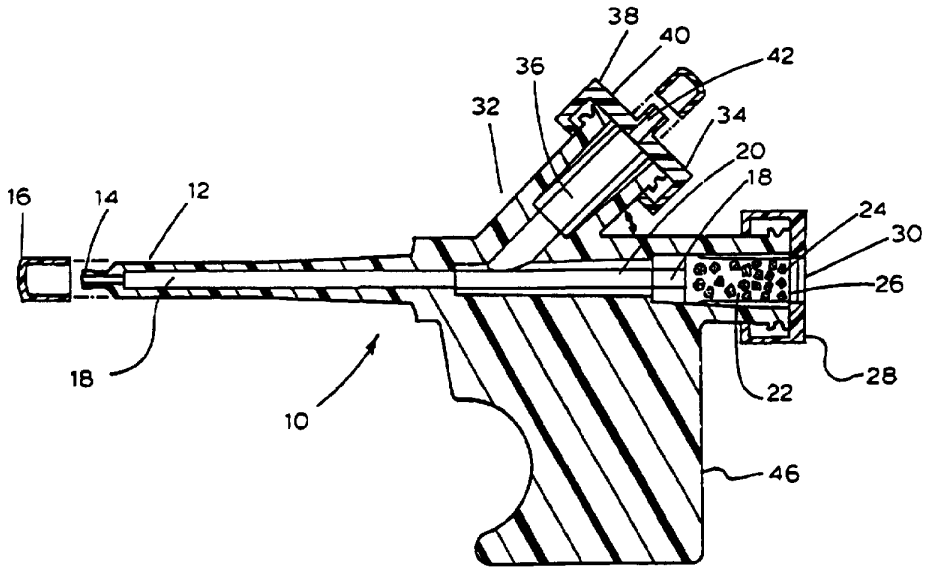
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(57) Abstract

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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CS	Czechoslovakia	**LU**	Luxembourg	**TG**	Togo
CZ	Czech Republic	**LV**	Latvia	**TJ**	Tajikistan
DE	Germany	**MC**	Monaco	**TT**	Trinidad and Tobago
DK	Denmark	**MD**	Republic of Moldova	**UA**	Ukraine
ES	Spain	**MG**	Madagascar	**US**	United States of America
FI	Finland	**ML**	Mali	**UZ**	Uzbekistan
FR	France	**MN**	Mongolia	**VN**	Viet Nam
GA	Gabon				

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.

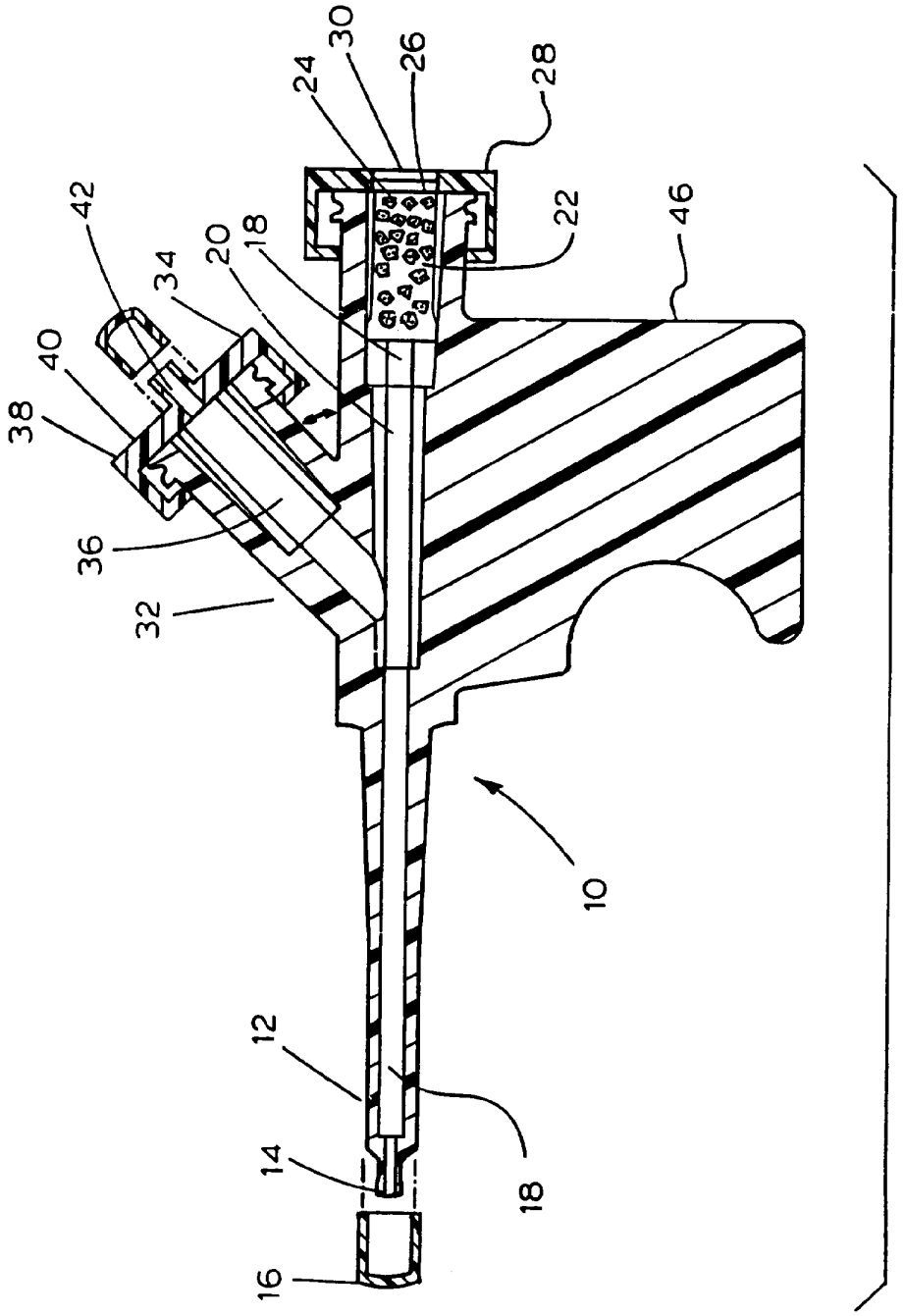


FIG. 1

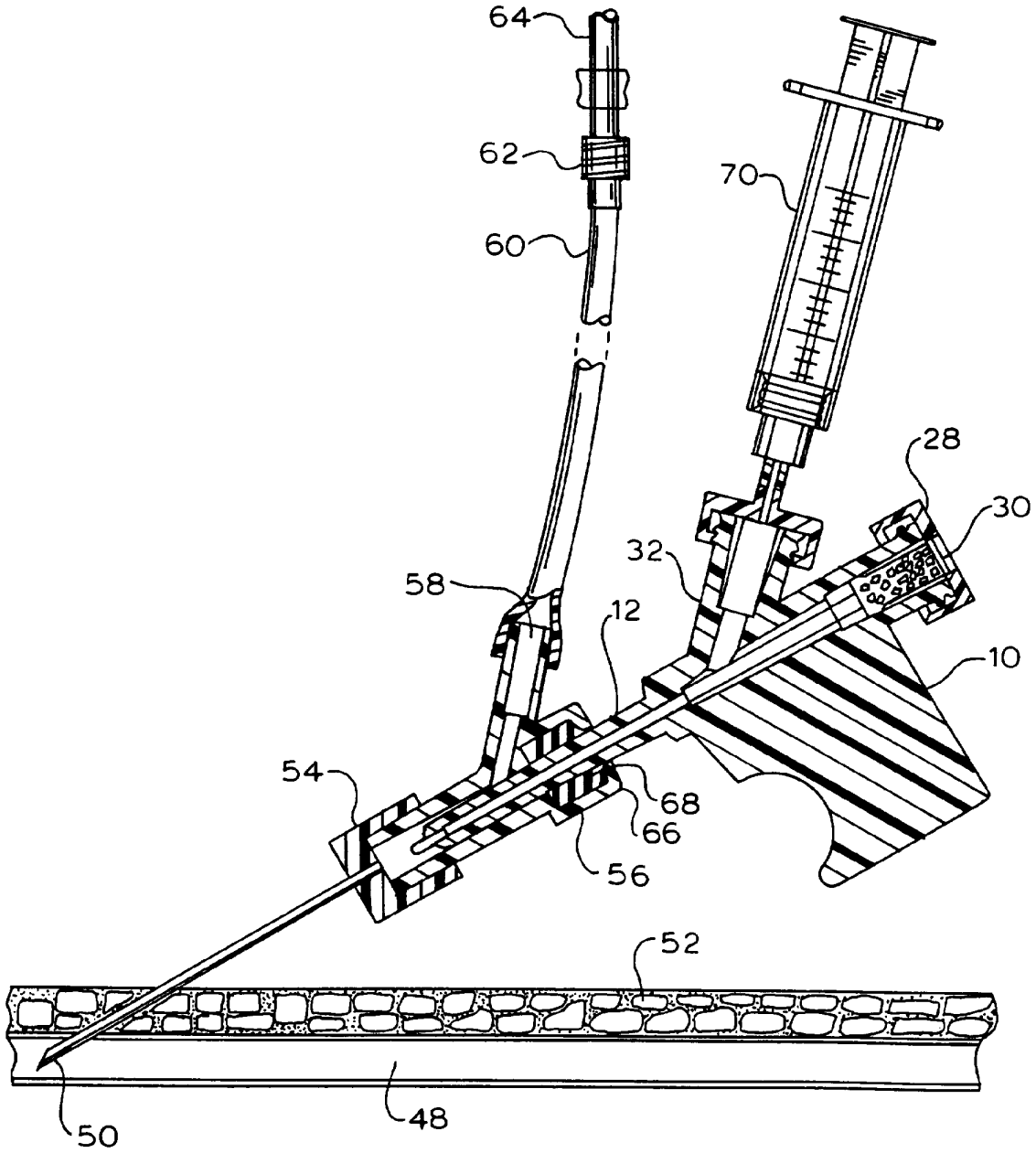


FIG. 2

SUBSTITUTE SHEET (RULE 26)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US95/10702

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) :A 61M 5/00
US CL : 604/122

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 604/122, 35, 125, 126, 128, 256, 258, 283, 284
128/ 760, 762, 767, 768

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

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

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X -- Y	US, A, 4,531,937 (Yates) 30 July 1985, See Entire Reference	1-7,9-15 --- 8,16

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be part of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E"	earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search 08 DECEMBER 1995	Date of mailing of the international search report 04 JAN 1996
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No.	Authorized officer SAM RIMELL Telephone No. (703) 308-0858

Form PCT/ISA/210 (second sheet)(July 1992)★

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29 April 2020

Examination report No. 1 for standard patent application

Griffith Hack
GPO Box 4164
Sydney NSW 2001
Australia

Your reference	P108089.AU
Application number	2016297849
Applicant name	Kurin, Inc.
Earliest priority date	24 July 2015

Final date for acceptance:	**29 April 2021**
Date of this report:	29 April 2020
Examination request date:	11 December 2019

Dear Griffith Hack,

Your application has been examined under *section 45 of the Patents Act 1990*. I consider that this application does not meet the requirements of the Act because there are issues with the application that are explained in the report details.

You have **12 months** from the date of this report to overcome all my objection(s) otherwise this application will lapse.

You will also need to pay any annual continuation fees that apply. Your next continuation fee is due on **22 July 2020**.

NOTE: There is a current postponement of acceptance in place. If you overcome all other objections before the expiration of that postponement, the Commissioner will only accept the application at that time if you have filed a clear and unambiguous statement requesting the withdrawal of that postponement. Otherwise, a further adverse report will be issued.

Details of this patent application can be viewed on AusPat, our Australian patent search database.

Yours sincerely,

Morris Ark
Section: MXT - MIXED TECHNOLOGY
Phone: (612) 6210 8487

Report details

Basis of the report

In examining this application I have considered:

- the PCT pamphlet as originally filed

Summary of novelty, inventive step and patentable subject matter

	Satisfy requirements?	*Claim numbers*
Novelty/inventive step	**Yes**	NONE
	No	1-20
Patentable subject matter	**Yes**	1-20
	No	NONE

Detailed objections on issues that have been identified

Documents cited or considered relevant

D1 : WO 2011162772 A1 (CLEARVIEW PATIENT SAFETY TECHNOLOGIES, LLC et al.) 29 December 2011 [1]
Category: **X** Claims: 1-20

[1] Cited in WO 2017019552

Special categories of cited documents:

X: The claimed invention cannot be considered novel under *subsection 7(1)* in light of the document and/or cannot be considered to involve an inventive step under *subsection 7(2)* of the Act in light of the common general knowledge considered together with the document.

Novelty and inventive step

1 The invention defined in **claims 1, 8 and 17** are not novel (and do not involve an inventive step) when compared with the following prior art document **D1**.

Regarding **claim 1**, **D1** discloses a blood sequestration device (Fig. 15; item 10) comprising;

> an inlet port (100); an outlet port (330); a sequestration chamber connected with the inlet port (117), the sequestration chamber having a vent (160) comprising an air permeable blood barrier (Para [0042]); a sampling channel (130) having a proximal end connected with the inlet port and a distal end connected with the outlet port; and a housing (116) that houses and defines the inlet port, the outlet port, the sequestration chamber, and the sampling channel.

Claims **8 and 17** define a blood sequestration device with a similar scope to claim 1, only differing by the additional features of a blood sampling pathway or blood sampling system

connected to said device. **D1** also discloses a blood sampling pathway or system connected to the blood sequestration device (Fig. 23; patient needle 184, connected to inlet 100).

Furthermore, appended **claims 2-7, 9-16, 18-20** are not considered to make any patentable contribution over the teachings of the cited document **D1** or are common general knowledge in the art or workshop improvements and which therefore cannot contribute to providing novelty or an inventive step. For example, **D1** discloses features of **claims 2, 11, 20** of the air permeable blood barrier sealing upon contact with blood (Para [0081], [0085]). Features of dependent **claim 3** are considered matters of workshop improvement over **D1**. It would be obvious to the person skilled in the art that a sequestration channel be implemented to improve transport of blood to the sequestration chamber.

END OF REPORT

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	**FOR FURTHER ACTION**	see Form PCT/ISA/220 as well as, where applicable, item 5 below.
KURIN3PCT		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/US2017/068569	27 December 2017 (27-12-2017)	27 December 2016 (27-12-2016)
Applicant		
KURIN, INC		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 4 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**
   a. With regard to the **language,** the international search was carried out on the basis of:
      [X] the international application in the language in which it was filed
      [ ] a translation of the international application into _____, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b))
   b. [ ] This international search report has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43.6*bis*(a)).
   c. [ ] With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. [ ] **Certain claims were found unsearchable** (See Box No. II)

3. [ ] **Unity of invention is lacking** (see Box No III)

4. With regard to the **title,**
   [X] the text is approved as submitted by the applicant
   [ ] the text has been established by this Authority to read as follows:

5. With regard to the **abstract,**
   [X] the text is approved as submitted by the applicant
   [ ] the text has been established, according to Rule 38.2, by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority

6. With regard to the **drawings,**
   a. the figure of the **drawings** to be published with the abstract is Figure No. 30B
      [ ] as suggested by the applicant
      [ ] as selected by this Authority, because the applicant failed to suggest a figure
      [X] as selected by this Authority, because this figure better characterizes the invention
   b. [ ] none of the figures is to be published with the abstract

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US2017/068569	27.12.2017	27.12.2016

International Patent Classification (IPC) or both national classification and IPC
INV. A61B5/15 A61B5/153 A61B5/154 A61B5/157

Applicant
KURIN, INC

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☒ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

Name and mailing address of the ISA:	Date of completion of this opinion	Authorized Officer
European Patent Office Gitschiner Str. 103 D-10958 Berlin Tel. +49 30 25901 - 0 Fax: +49 30 25901 - 840	see form PCT/ISA/210	Nielsen, Michael Telephone No. +49 30 25901-0

Form PCT/ISA/237 (Cover Sheet) (January 2015)

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of:

   ☒ the international application in the language in which it was filed.

   ☐ a translation of the international application into , which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1 (b)).

2. ☐ This opinion has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43*bis*.1(a))

3. ☐ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, this opinion has been established on the basis of a sequence listing:

   a. ☐ forming part of the international application as filed:

      ☐ in the form of an Annex C/ST.25 text file.

      ☐ on paper or in the form of an image file.

   b. ☐ furnished together with the international application under PCT Rule 13*ter*.1(a) for the purposes of international search only in the form of an Annex C/ST.25 text file.

   c. ☐ furnished subsequent to the international filing date for the purposes of international search only:

      ☐ in the form of an Annex C/ST.25 text file (Rule 13*ter*.1(a)).

      ☐ on paper or in the form of an image file (Rule 13*ter*.1(b) and Administrative Instructions, Section 713).

4. ☐ In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that forming part of the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

5. Additional comments:

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-20
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-20
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-20
	No:	Claims	

2. Citations and explanations

see separate sheet

Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

In light of the documents cited in the international search report, it is considered that the invention as claimed in the independent claims meets the criteria mentioned in Article 33 (1) PCT, i.e. it appears to be novel, to involve an inventive step and to be industrially applicable.

Prior art: Blood drawing devices capable of isolating a pre-sample in order to minimize the risk of contamination of the main sample. Well known concept, see any of the documents cited in the search report.

Problem: As in the prior art to minimize the risk of contamination of blood drawn from a patient.

Solution: The pre-sample chamber (sequestration chamber) having **the specific vent** as defined in the independent claims 1, 8 and 15.

None of the cited documents hint to said specific solution in order to solve said problem. Contribution to the art.

Claims 2-7, 9-14 and 16 to 20 are dependent on one or more independent claims whose subject-matter is considered as being new and inventive, as discussed above, and as such said dependent claims also meet the requirements of the PCT with respect to novelty and inventive step.

Re Item VII

Certain defects in the international application

1). The independent claims are not in the two-part form in accordance with Rule 6.3(b) PCT.

2). The features of the claims are not provided with reference signs placed in parentheses (Rule 6.2(b) PCT).

3). Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art (see search report) is not mentioned in the description, nor are these documents identified therein.

4). Upon entering the regional phase via the European Patent Office, the requirements of Rule 43(2) EPC should be observed.

Information on Search Strategy - Pilot phase (see OJ 2015, A86)
The type of information contained in this sheet may change during the pilot for improving the usefulness of this new service.

Application Number
PCT/US2017/068569

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

APPLICANT: KURIN, INC

IPC CLASSIFICATION: A61B5/15, A61B5/153, A61B5/154, A61B5/157

EXAMINER: Nielsen, Michael

CONSULTED DATABASES: WPI

CLASSIFICATION SYMBOLS DEFINING EXTENT OF THE SEARCH:

IPC:

CPC: A61B5/15003, A61B5/150213, A61B5/150251, A61B5/150389, A61B5/150488, A61B5/150992, A61B5/153, A61B5/150274, A61B5/1535, A61B5/1545, A61B5/157

FI/F-TERMS:

KEYWORDS OR OTHER ELEMENTS FEATURING THE INVENTION:

EPO FORM P04A42

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.

* 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

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Date of the actual completion of the international search	Date of mailing of the international search report
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Name and mailing address of the ISA/	Authorized officer
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INTERNATIONAL SEARCH REPORT

International application No
PCT/US2017/068569

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

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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

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2017/068569

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Hazards of Bacterial Contamination of Blood Products

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SUMMARY

Post-transfusion bacterial sepsis is infrequent. It is, however, associated with a high mortality due to septic shock. This reflects the release of endotoxin from gram negative bacteria. Lesser transfusion reactions are usually under-reported. These are frequently caused by gram positive bacteria. Gram positive species such as staphylococci and other skin surface organisms may be cultured from platelets stored at room temperature. Typically, gram negative "psychrophyllic" species which survive storage at 4°C are cultured from stored refrigerated blood implicated in transfusion reactions. These include Yersinia enterocolitica, Pseudomonas fluorescens *etc. Bacterial contamination of the blood supply can occur via an endogenous or an exogenous source. Endogenous donor bacteraemia due to* Y.enterocolitica *may be asymptomatic or may follow an episode of gastroenteritis. Exogenous infections occur through some defect in the usual collection practice. Transfusion-acquired syphilis is now extremely uncommon. In the third world, beside the need for effective screening for viral pathogens, infections with protozoa, in particular plasmodia, trypanosoma and leishmania remain a major obstacle to ensuring safe blood supplies. Prevention of transfusion reactions demands rigorous attention to details of collection, storage, reissuing and infusion of blood products, as well as prompt treatment, testing and reporting of suspected reactions.*

Key Words: TRANSFUSION: reaction, post-transfusion bacterial sepsis, bacterial contamination, Yersinia enterocolitica, Pseudomonas fluorescens, Pseudomonas, Trypanosomiasis

In recent years attention has focused on the likelihood of transmission of viral pathogens such as HIV, HTLV-I, hepatitis B and C via blood transfusion. By contrast, reactions following transfusion of bacterial pathogens are less well recognised. These may however be acutely life-threatening with a mortality of up to 25%. From 1975 to 1989, 14 fatal transfusion-related events were reported to the United States Food and Drug Authority (FDA).[1] When all blood products were considered (red blood cells, platelets and plasma) 24 fatal events were reported in a similar time period (1976-85).[2] Although non-fatal events are more frequent, these often are under-reported, estimates of 1-7/1000 having been quoted.[1]

Transfusion of contaminated blood may cause septic shock. This may in part be due to massive release of endotoxin from gram-negative bacteria. Nausea and vomiting, fevers, chills, tachycardia and hypotension can occur during or following transfusion.

Numerous bacteria have been incriminated in post-transfusion sepsis. Of 36 bacteria causing clinical sepsis after red cell transfusion,[3] the most frequently isolated bacteria were *Yersinia enterocolitica* (17) and *Pseudomonas fluorescens* (10). Other bacteria included other pseudomonads (3), enterobacter, flavobacteria (2), *Treponema pallidum* (2) and *Campylobacter jejuni*. A similar group of organisms were seen following platelet and plasma transfusions, i.e. pseudomonas, serratia and enterobacter species. However gram-positive bacteria, such as *Streptococcus pyogenes*, *Staphylococcus aureus* and *Staphylococcus epidermidis*, have also been not infrequently cultured in episodes of clinical sepsis after platelet transfusions,[2,3] (vide infra).

It is possible to divide transfusion reactions into those originating from an endogenous source (donor bacteraemia or parasitaemia) or an exogenous source (surface colonisation or contamination).

ENDOGENOUS BACTERIA (AND PROTOZOA)

Donor bacteraemia may occur in several settings.

Bacteraemia may occur during chronic or low-grade infections, usually unrecognised by the patient. Examples include osteomyelitis, endocarditis and specific diseases such as syphilis and brucellosis. A case report documents a donor with salmonella osteomyelitis who transmitted salmonella to seven

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platelet recipients.[4] Subacute parasitic infections with plasmodia (malaria) and with trypanosoma (Chagas' disease) are frequent causes of blood transfusion transmission in the tropics and in South America.

Bacteraemia may follow recovery from an episode of bacterial gastroenteritis, particularly after infection with *Yersinia enterocolitica* and salmonella sp.[5,6] In a review of seven cases of yersinia transfusion reactions, four patients had preceding diarrhoea within four weeks of transfusion and one had concomitant diarrhoea. However, two patients gave no history of diarrhoeal symptoms. Asymptomatic bacteraemia was usual at the time of donation.

Transient bacteraemia may follow procedures such as dental work. The bacteraemia is usually of a very short duration, not exceeding 30 minutes, unless endocarditis ensues. In such instances the micro-organisms comprise oral streptococci and anaerobes. These are generally of lesser virulence and are unlikely to survive refrigeration compared with gram-negative bacteria.

EXOGENOUS BACTERIA

In this instance bacteria enter blood through some defect in the usual collection practice. Most commonly contamination occurs through inadequate skin preparation.[1,3,7] Less frequently bacteria may colonise collection tubing as occurred in an outbreak of serratia infection.[8] Contamination may occur during storage. An episode of sepsis due to *Pseudomonas cepacia* followed port contamination after the thawing of platelets in a water bath.[9]

A review of UK reports of exogenous post-transfusion sepsis documented 14 episodes between 1980-89.[10] Of these, ten were due to "environmental" pseudomonads (eight were *Pseudomonas fluorescens*) and eight of the ten patients died. Of the many organisms that may colonise skin surfaces, pseudomonas species, serratia, flavobacteria etc, are notable in that they can survive paltry disinfection or may actually be present in the disinfectant solution. These gram-negative isolates are associated with more severe transfusion reactions compared with gram-positive species such as coagulase-negative staphylococci and viridans streptococci.

The increase in notification of bacterial infections is paralleled by the increase in demand for platelet transfusion. Storage at room temperature enhances bacterial proliferation. In many cases bacteria are grown on culture without clinical disease: in these the bacteria are usually skin saprophytes such as pro-*Pionibacterium acnes* or corynebacterium species, often referred to as "diphtheroids". However any of a large number of both gram-positive and negative organisms have been isolated in episodes of sepsis.

Following refrigeration most gram-positive bacteria will not survive. Moreover these are often present in low number and are usually destroyed by host defences—complement, lysosyme and other opsonins. By contrast, gram-negative, psychrophilic (cold-loving) bacteria will survive refrigeration.

PSYCHROPHILIC BACTERIA

Bacteria can be divided into thermophiles growing at $>50°C$, mesophiles, and psychrophiles capable of growth at $<5°C$. The latter organisms prefer growth at room temperature but will survive refrigeration. At 5°C metabolism is significantly reduced and growth occurs at a slow linear rate. After prolonged storage, between one and three weeks, there is sufficient build-up of bacteria or endotoxin to cause a severe transfusion reaction. Alternately once blood is rewarmed these organisms will re-establish their usual logarithmic growth within two to four hours.[1] Metabolic enzymes with optimal activity at room temperature will be switched on. This highlights the need for proper storage and transportation of blood.

The psychrophile most commonly associated with transfusion reactions is *Yersinia enterocolitica*. Other species encountered include enterobacter, klebsiella species, pseudomonas species especially *P. fluorescens* and *P. putida*, and *E. coli*.

Yersinia enterocolitica

Yersinia belongs to the enterobacteriaceae and is a facultative anaerobe. It is usually a zoonotic organism and is transmitted to humans via the food chain, especially from contaminated pork as well as from water and milk. Yersinia lacks siderophores necessary to scavenge iron when bound to transferrin. As they require exogenous free iron, their growth and virulence is enhanced in the presence of iron overload states such as haemachromatosis, cirrhosis and following the use of desferrioxamine.

Gastroenteritis is the usual presentation of yersinia infection. When bacteraemia occurs, symptoms may range from endotoxic shock to an asymptomatic carrier state. Numerous examples of yersinia blood transfusion infection have been reported including several from Australia.[1-3,5,10-16] Diarrhoea may precede blood donation by 8-30 days, however yersinia is rarely cultured from the donor's stool. A rise in yersinia antibodies can however be detected in the donor. In most reports transfused blood had been stored for more than three weeks prior to transfusion.

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OTHER BACTERIA

Treponema pallidum

Transfusion-acquired syphilis is now uncommon both due to donor screening and due to reduced disease prevalence. One should note a rise in syphilis in the United States more recently. Storage at 4°C will inactivate *T. pallidum.*[3] However transmission may occur following transfusion of fresh blood products.

PARASITES (PROTOZOA)

Plasmodia which parasitise red blood cells, and trypanosoma and leishmania which parasitise reticulo-endothelial cells can all be transmitted by blood transfusion. These are important in tropical and subtropical areas of the world, and in perspective the scale of the problem of transmission of protozoa overshadows our concern with bacterial infection. Over three thousand cases of transfusional malaria occur yearly. However the true incidence is considerably higher.

Trypanosoma cruzi (Chagas' disease) is endemic in Central and South America. Twenty million people are believed to be infected, and at least twenty thousand cases of Chagas' disease are acquired through blood transfusion yearly. There is a 15-20% infection rate following transfusion of blood from an infected but asymptomatic donor. Such donors are potentially infective for life. In Brazil, 0.4% crystal violet, which is trypanosomocidal, is added to stored blood for transfusion. Several reports of transfusion-associated acute trypanosomiasis have now been reported from non-endemic areas (USA, Canada).[17-19] One in a thousand residents of Los Angeles are seropositive. Serology is available in special circumstances.

Leishmania donovani is a protozoan organism transmitted by sandflies. Leishmania species have been detected in blood from more than twenty US army personnel who served in the Middle East during Operation Desert Storm.[20] In response to this donations of blood have been recently deferred from this group until 1993.

PREVENTION OF TRANSFUSION REACTIONS

Blood donors should be questioned rather than asked to tick boxes. Specific details of recent medical procedures, dental work, febrile illnesses, tattooing etc. should be sought. Whether patients with recent abdominal pain and/or diarrhoea should be excluded from blood donation remains a vexed question. Patient description of recent symptoms is very likely to be influenced by the manner of questioning. A detailed patient assessment of recent gastrointestinal symptoms could lead to considerable wastage of blood products.

Collection of blood requires detailed attention to antisepsis. Patients with scarred phlebotomy sites may require exclusion.

Blood should be visually inspected prior to transfusion. The presence of haemolysis and the presence of any particulate matter may indicate contamination. Bacteriological screening of blood has been recommended by some.[3] However considering the low frequency of bacterial transfusion reactions this is likely to have a low yield, be expensive and lead to discarding of blood falsely culture-positive.

Blood that has been stored at room temperature for more than 30 minutes is recommended for rejection for re-use. This has recently been questioned.[1] It has been suggested that two hours may be more practicable and less wasteful, in view of the lag period before bacterial growth is re-established after warming to room temperatures. However the safety margin for error may be reduced by such eased restrictions which may lead to even longer periods during which blood is held at room temperature in operating theatres.[16] If these blood units are then returned and re-used they be more likely to be associated with transfusion reactions by virtue of storage for more than 21 days and prolonged periods of time at room temperature.

Storage of blood in ward refrigerators should not occur. These may have poor temperature regulation, may be used for other purposes and consequently be frequently opened and closed.

Prolonged infusions of blood for greater than four hours should be avoided.

Platelets are held at room temperature for up to seven days. Recently this period was reduced from seven to five days in the United States.

MANAGEMENT OF BACTERIAL TRANSFUSION REACTIONS

In the case of a suspected bacterial transfusion reaction, the specimen being transfused should be gram stained. Both donor and recipient bloods should be cultured, as should any related blood products. Any residual blood should be refrigerated promptly. Syphilis serology can be subsequently tested on donor blood.

Broad spectrum antibiotics should be started quickly. The choice of antibiotic may be determined by gram stain result. In its absence, broad spectrum gram-negative antibiotic cover should be provided. Antibiotics of choice would include anti-pseudomonal penicillins, timentin, piperacillin, or the third generation cephalosporins such as cefotaxime or ceftriaxone. Initially these should be combined with an aminoglycoside such as gentamicin, at least until the presence of a pseudomonas species infection is excluded.

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Espacenet

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Blood collection set with an expanded internal volume

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Classification: **- international:** ***A61B5/154; A61B5/155***
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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.

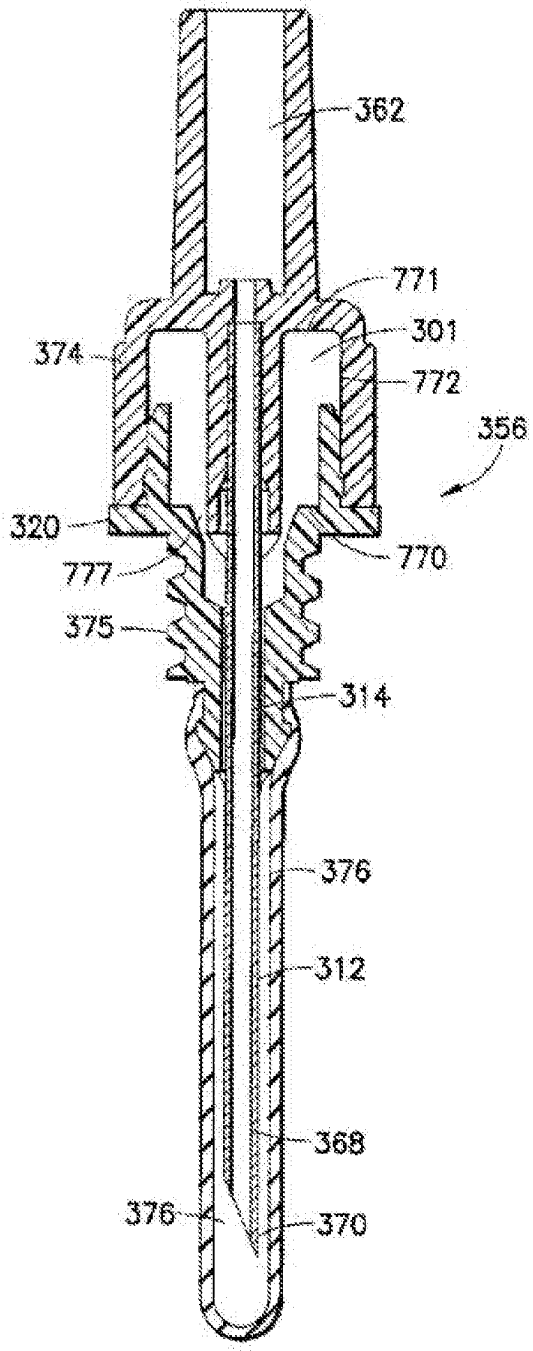


FIG.4

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(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.

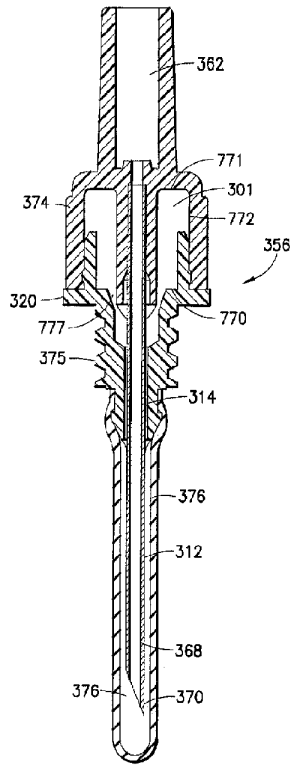


FIG.4

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.

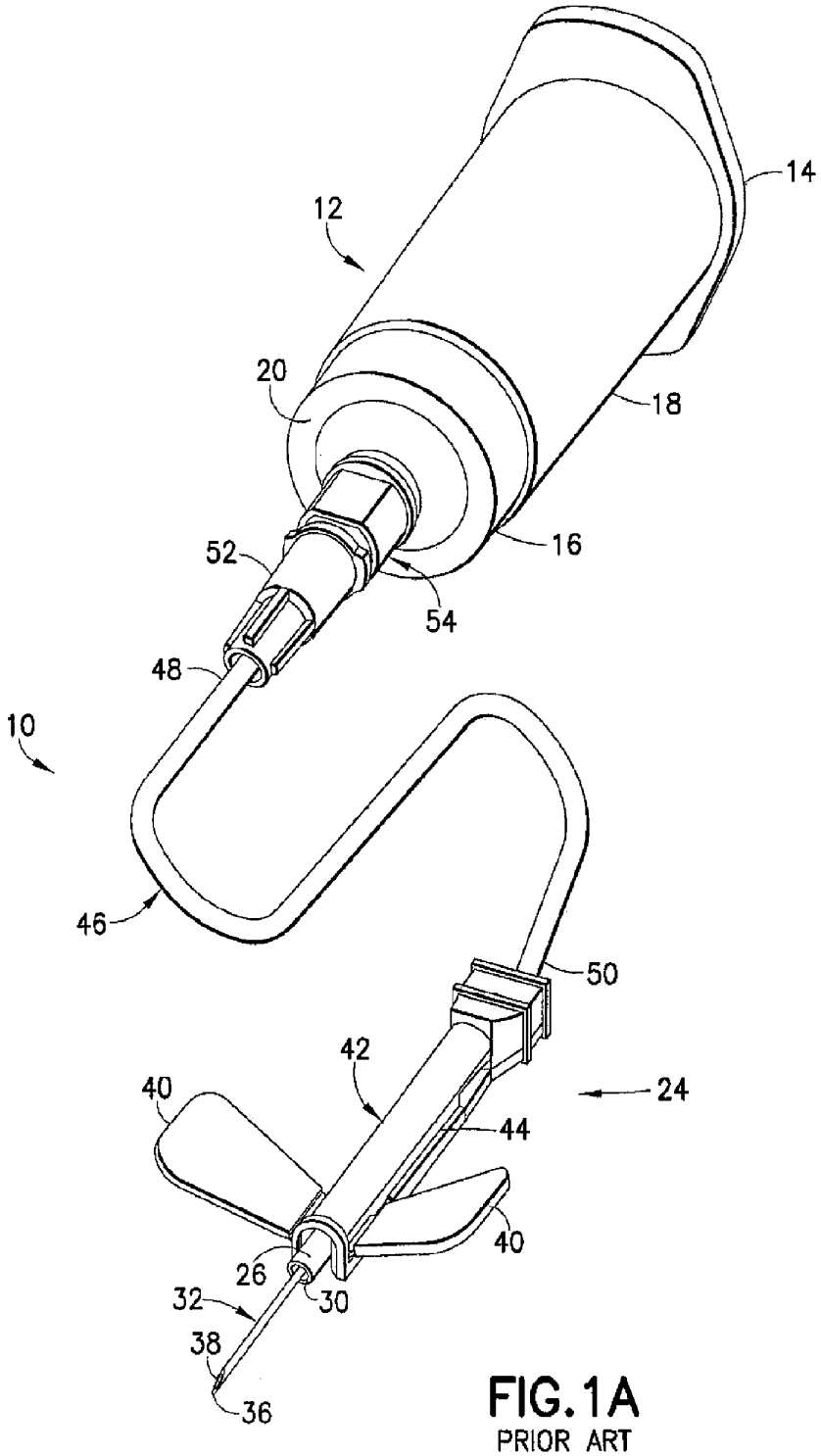


FIG. 1A
PRIOR ART

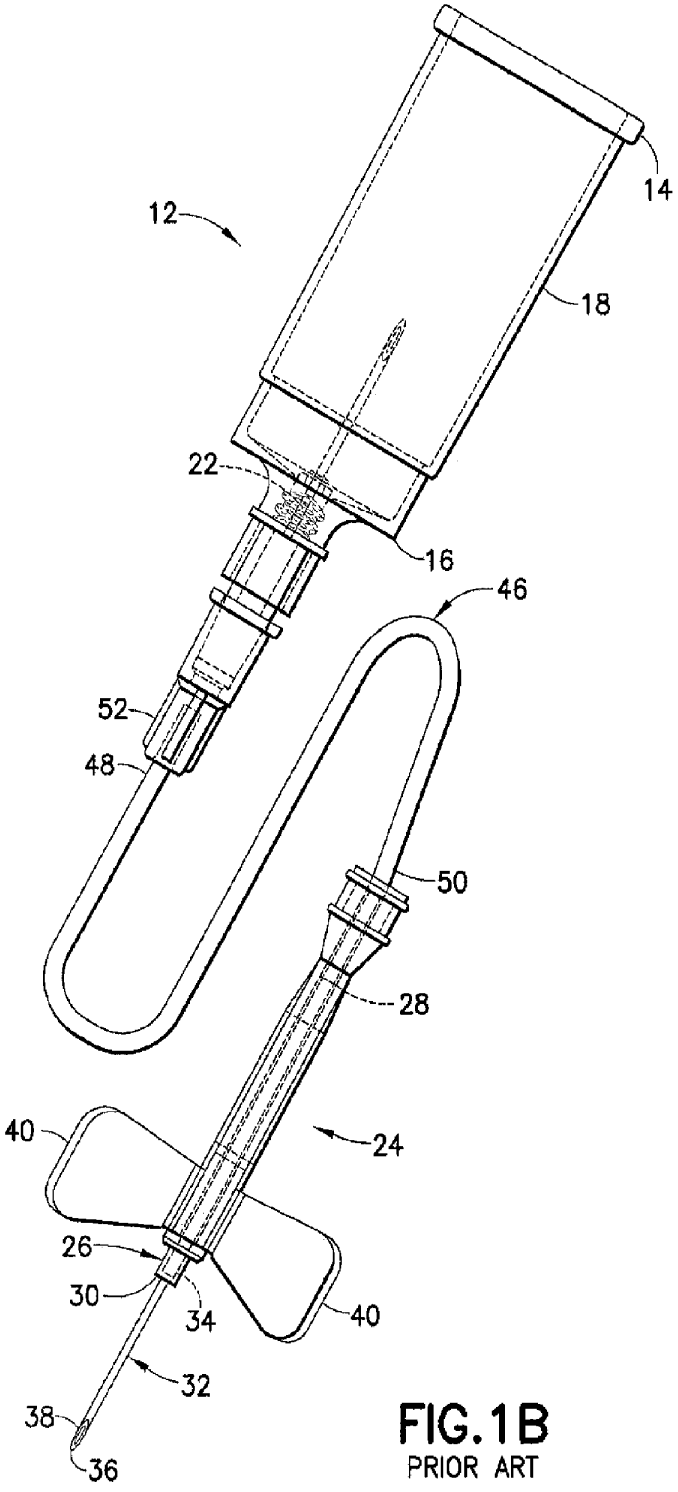


FIG.1B
PRIOR ART

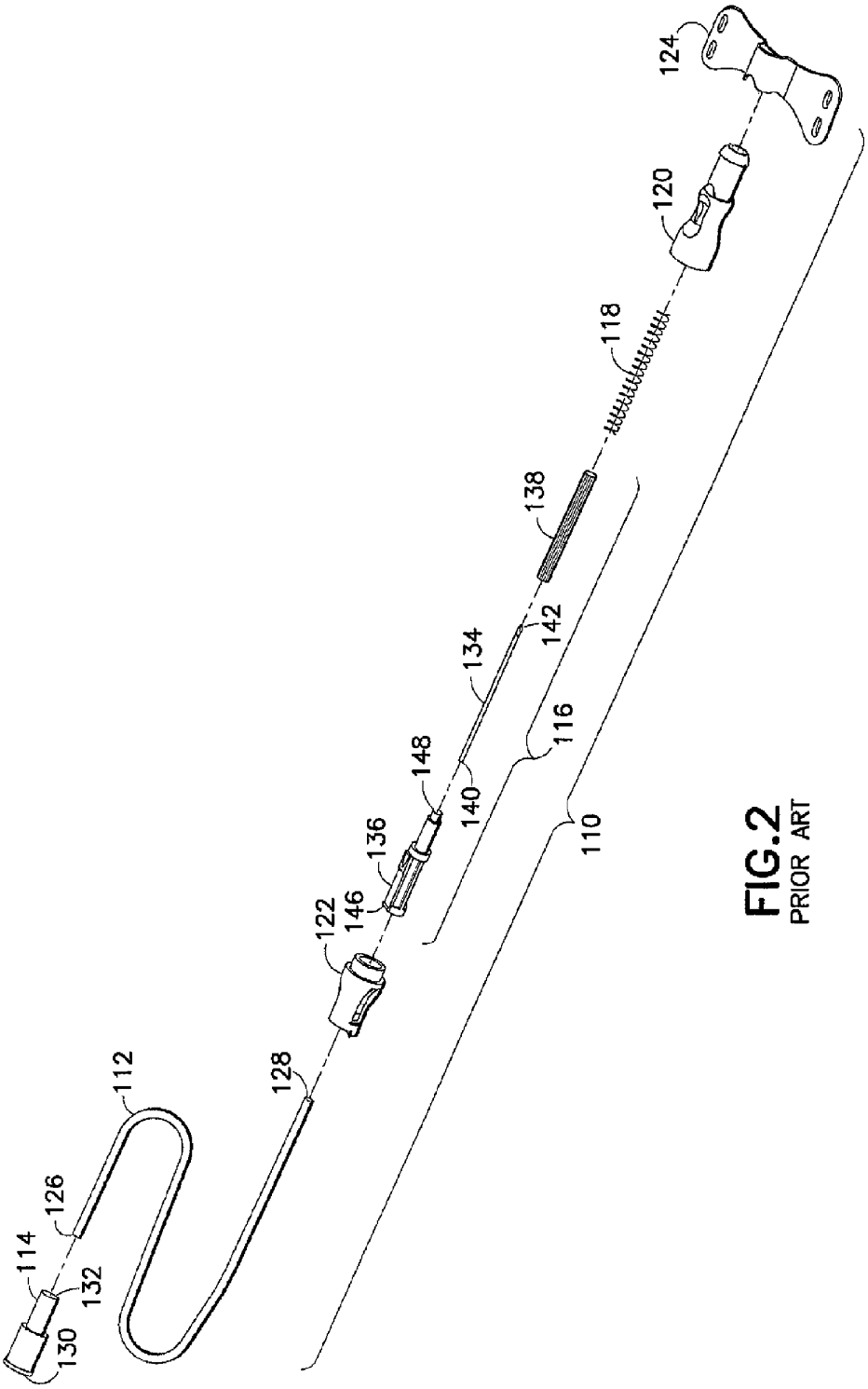


FIG.2
PRIOR ART

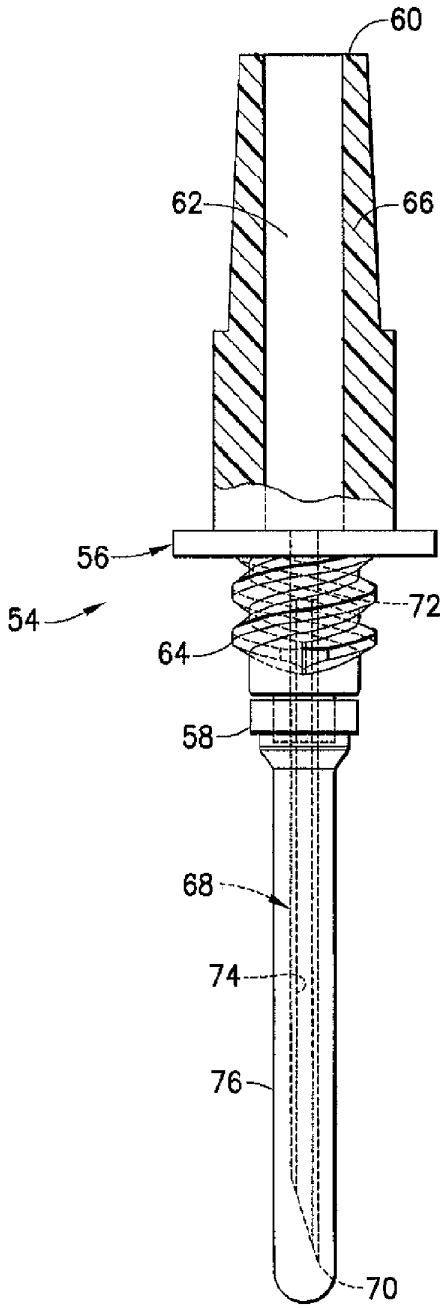


FIG.3
PRIOR ART

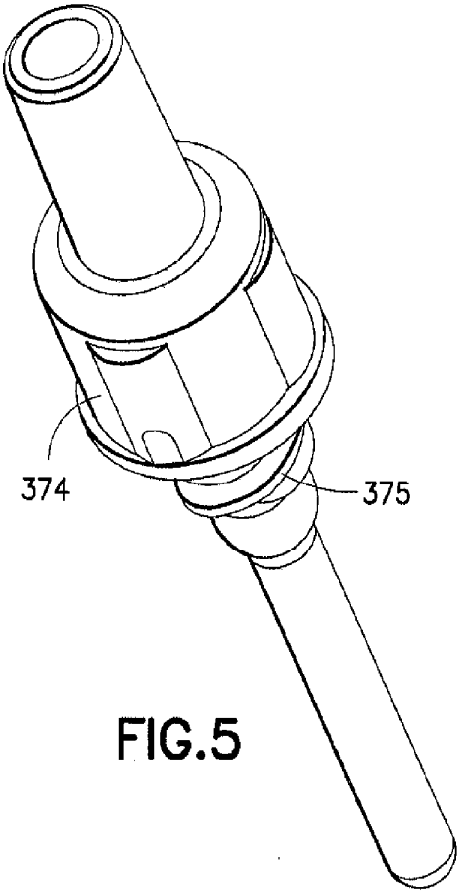

374
375

FIG.5

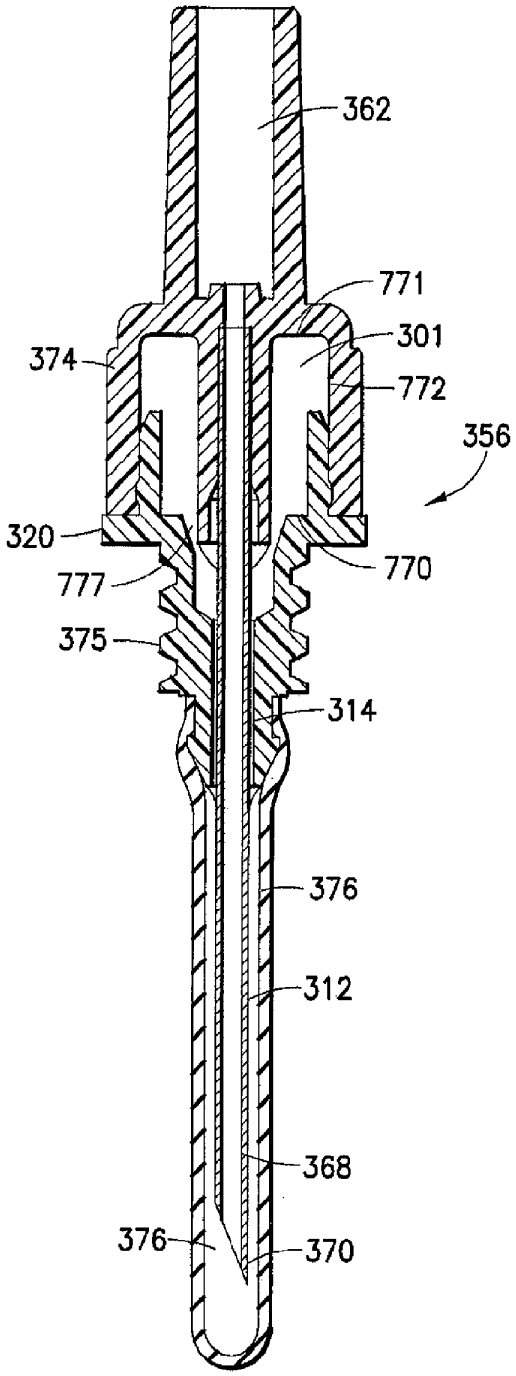

362
771
301
374
772
356
320
770
777
375
314
376
312
368
376
370

FIG.4

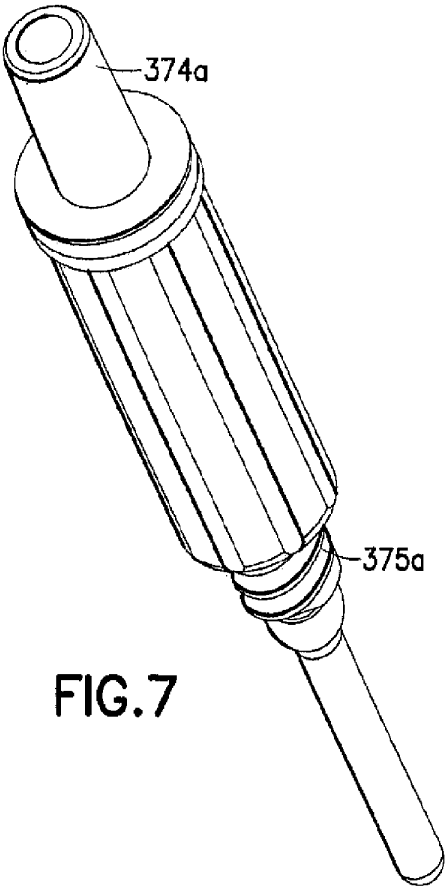

374a
375a

FIG.7

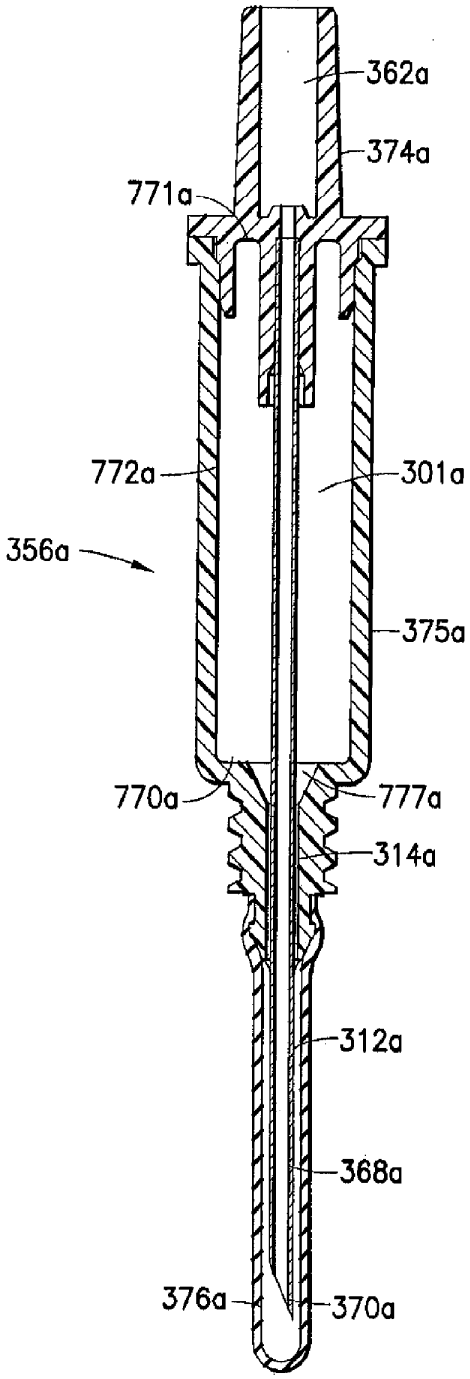

362a
374a
771a
772a
301a
356a
375a
770a
777a
314a
312a
368a
376a
370a

FIG.6

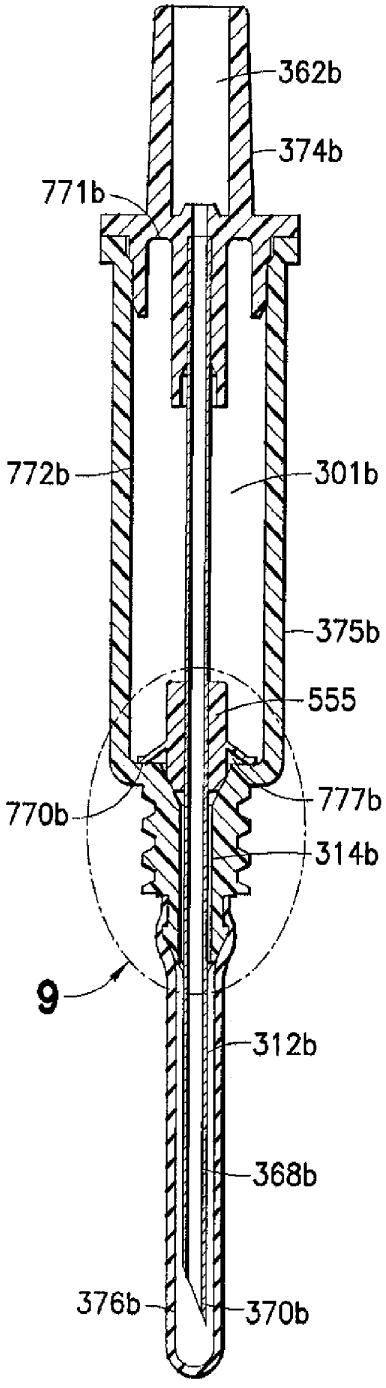

362b
374b
771b
772b
301b
375b
555
770b
777b
314b
9
312b
368b
376b
370b

FIG.8

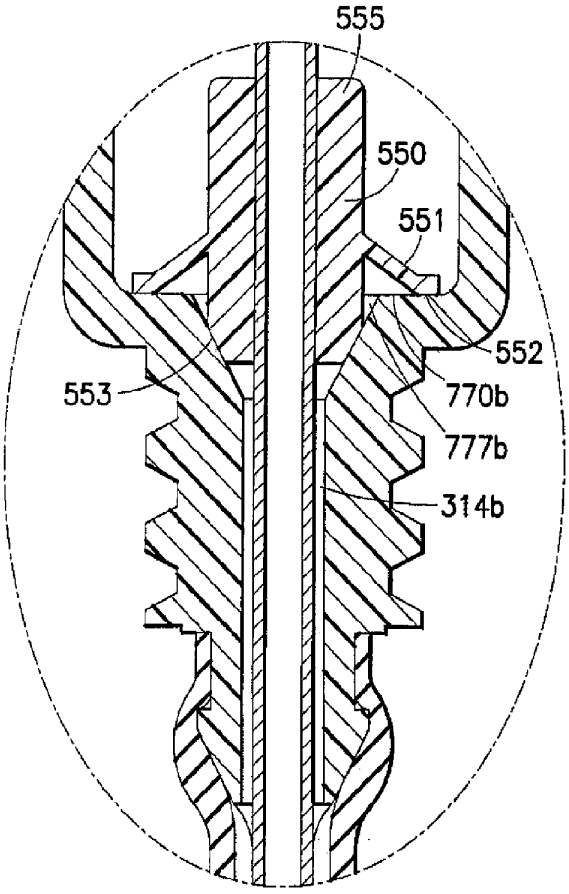

555
550
551
552
553
770b
777b
314b

FIG.9

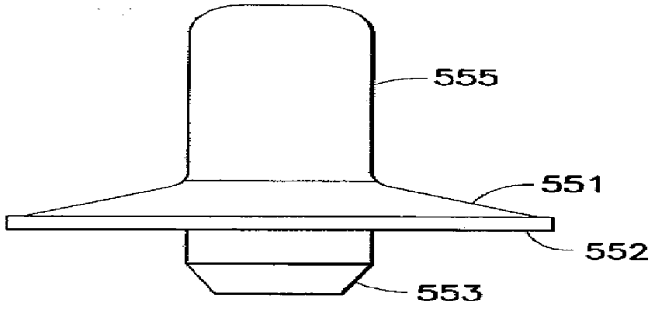


FIG. 10

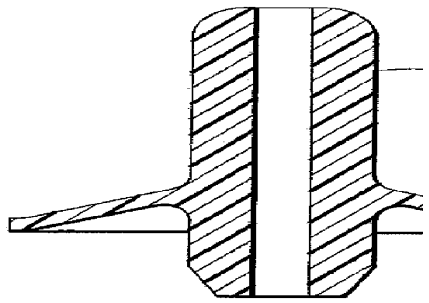


FIG. 12

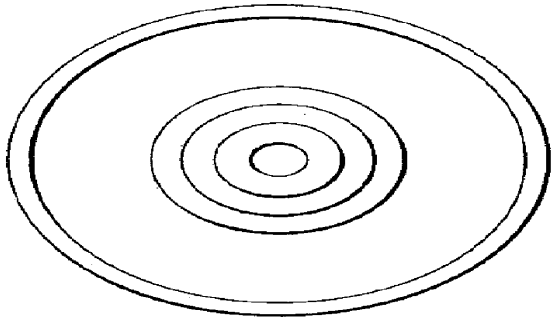


FIG. 11

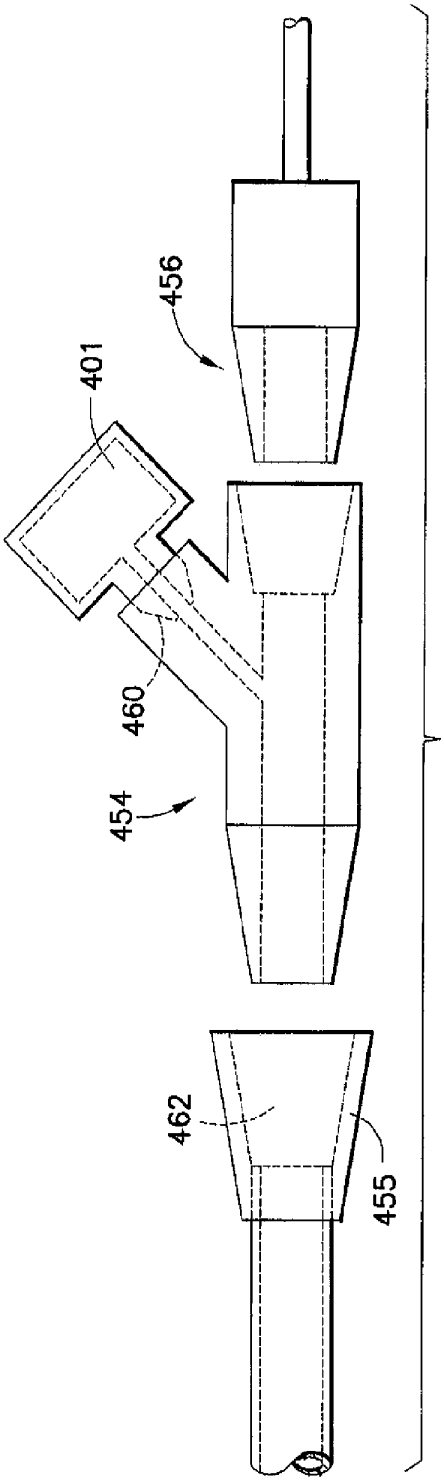


FIG.13

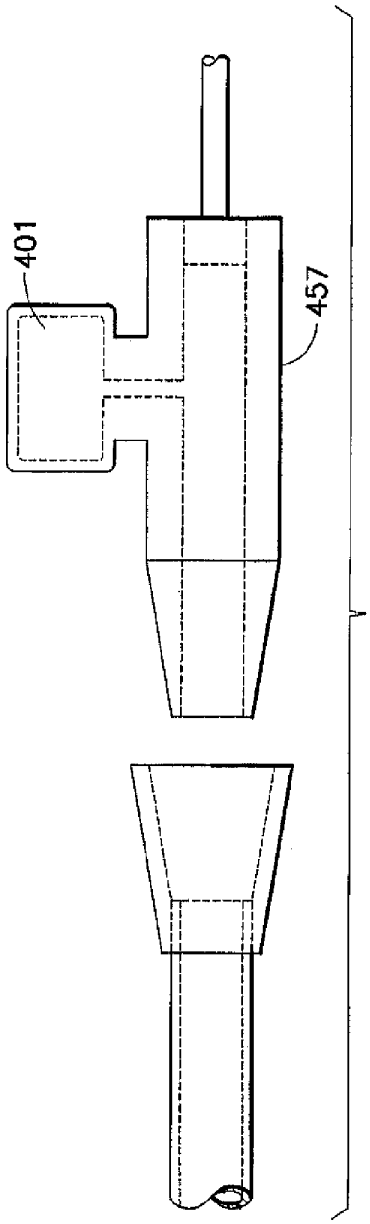


FIG.14

European Patent Office

EUROPEAN SEARCH REPORT

Application Number
EP 05 11 1371

DOCUMENTS CONSIDERED TO BE RELEVANT

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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
Y : particularly relevant if combined with another document of the same category
A : technological background
O : non-written disclosure
P : intermediate document

T : theory or principle underlying the invention
E : earlier patent document, but published on, or after the filing date
D : document cited in the application
L : document cited for other reasons

& : member of the same patent family, corresponding document

EPO FORM 1503 03.82 (P04C01)

ANNEX TO THE EUROPEAN SEARCH REPORT ON EUROPEAN PATENT APPLICATION NO. EP 05 11 1371

This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report. The members are as contained in the European Patent Office EDP file on
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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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BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE AND METHOD

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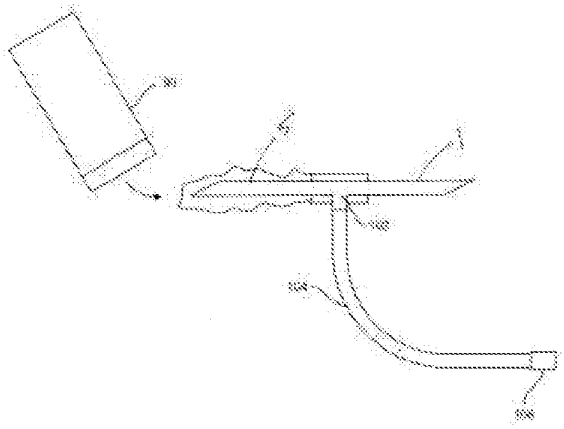
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Application number: CA20162993646 20160722 Global Dossier

Priority number(s): US201562196797P 20150724 ; US201562238636P 20151007 ; US201662318194P 20160404 ; US201615140448 20160427 ; US201615140443 20160427 ; WO2016US43709 20160722

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Abstract of CA2993646 (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.

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(54) Titre : SYSTEME D'OPTIMISATION D'ECHANTILLON DE SANG ET DISPOSITIF ET PROCEDE DE SEQUESTRATION DE CONTAMINANTS DU SANG

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

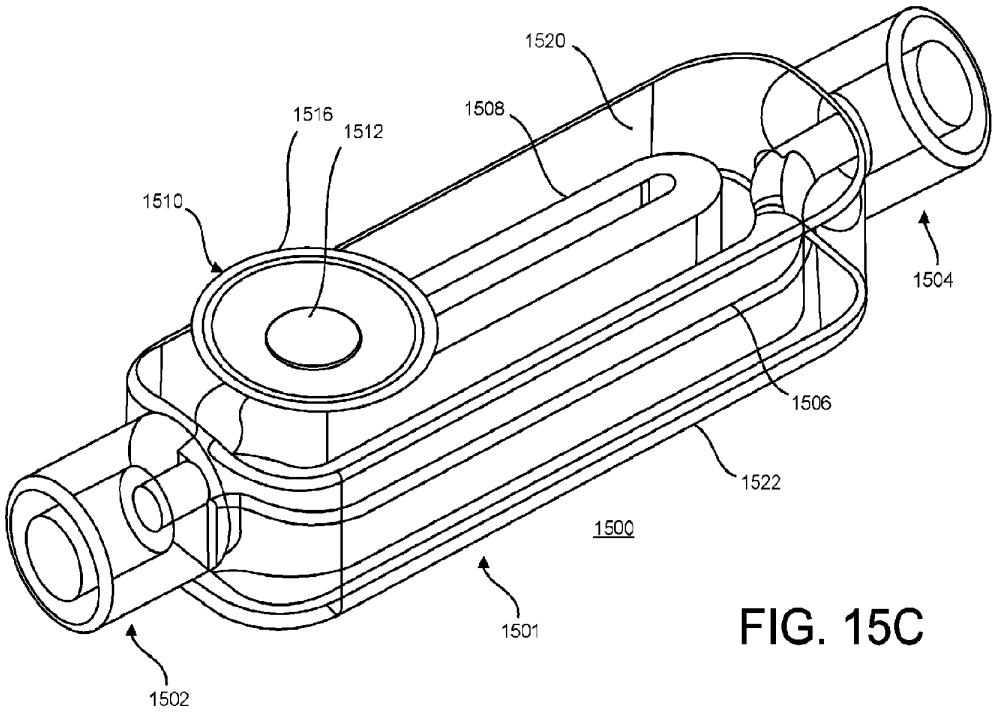


FIG. 15C

(57) Abrégé/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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(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.

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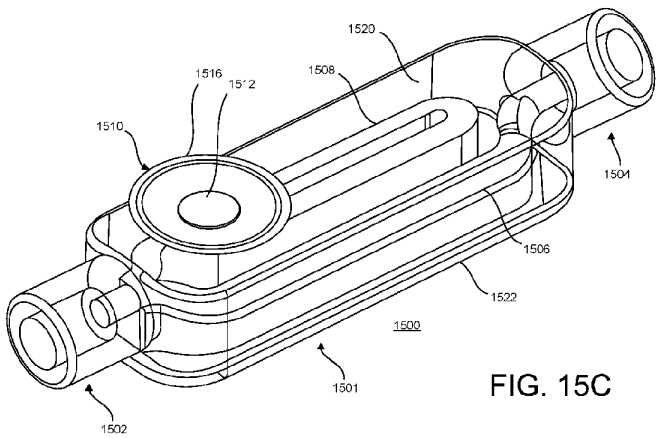


FIG. 15C

(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.

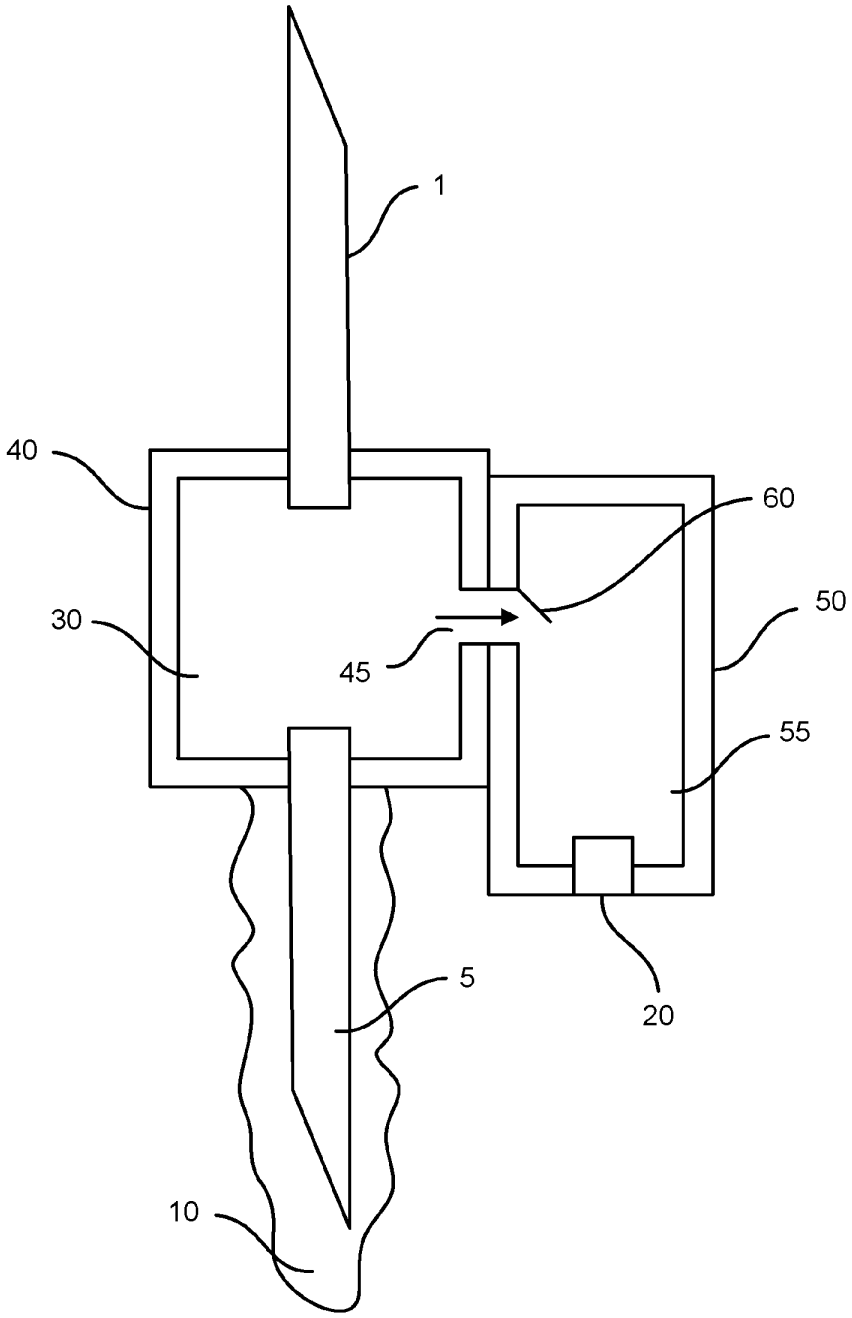


FIG. 1

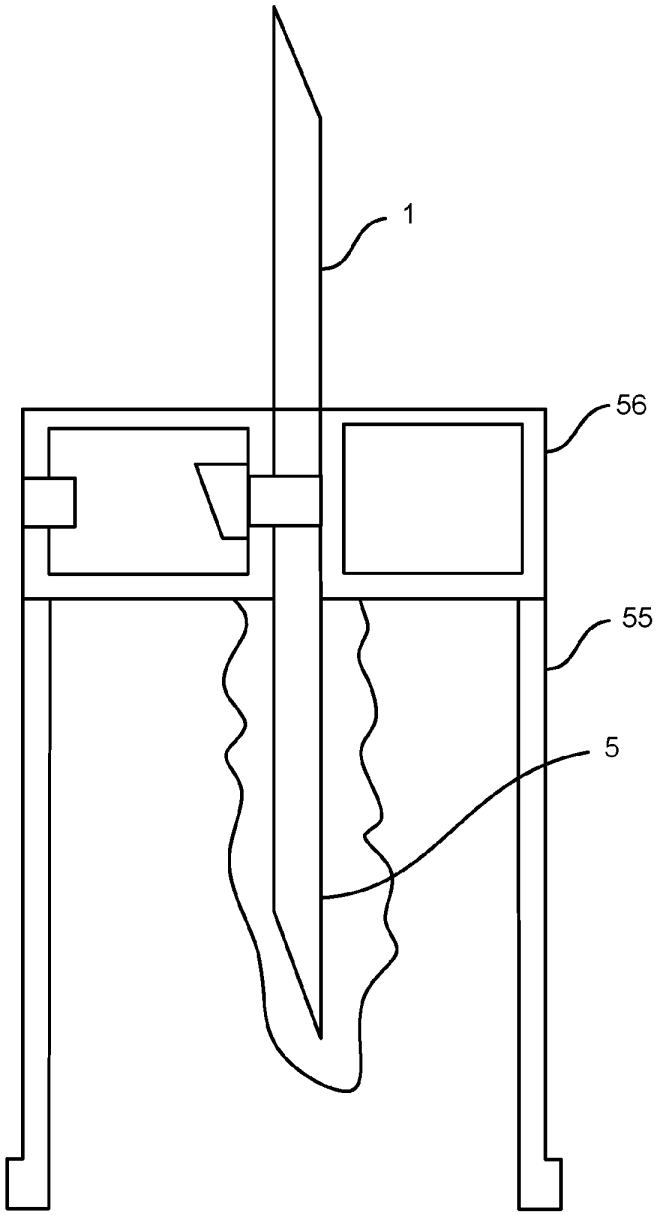


FIG. 2

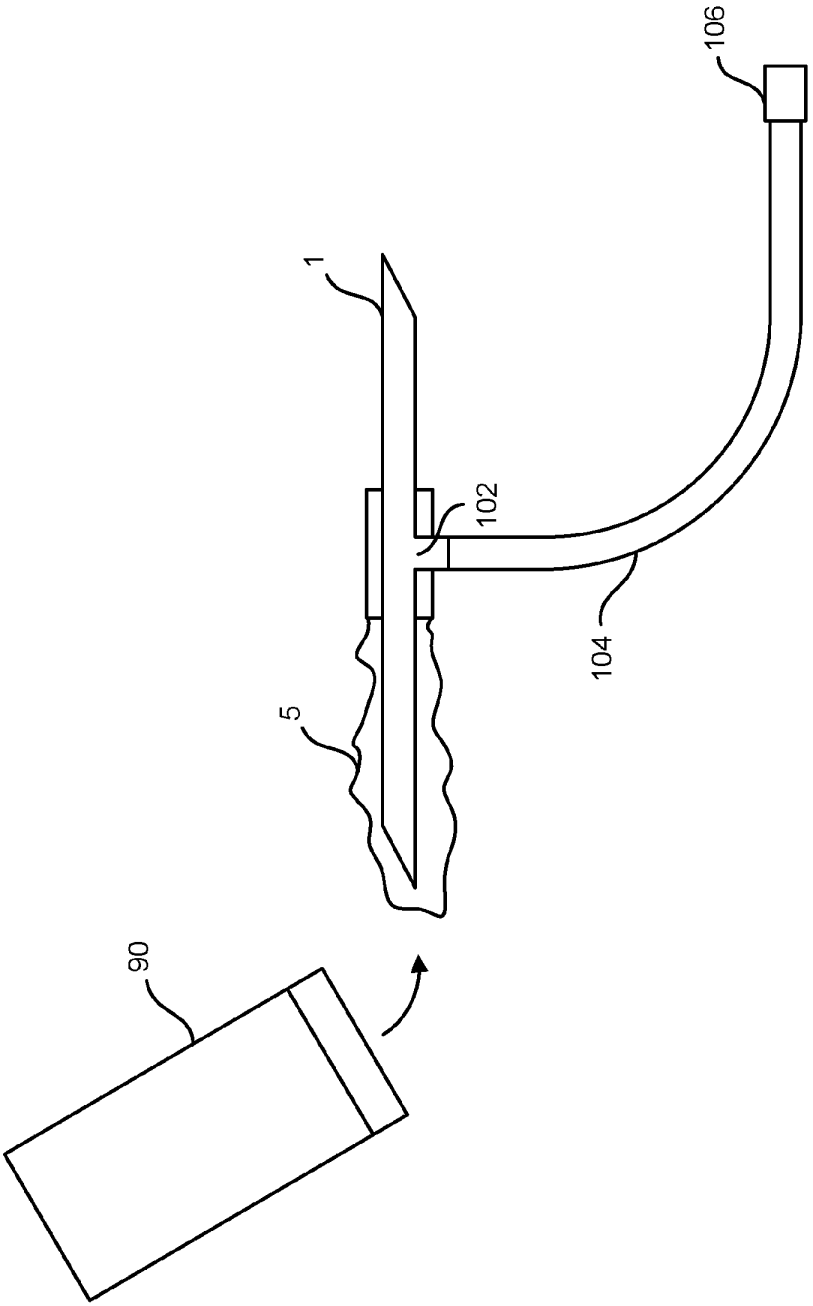


FIG. 3

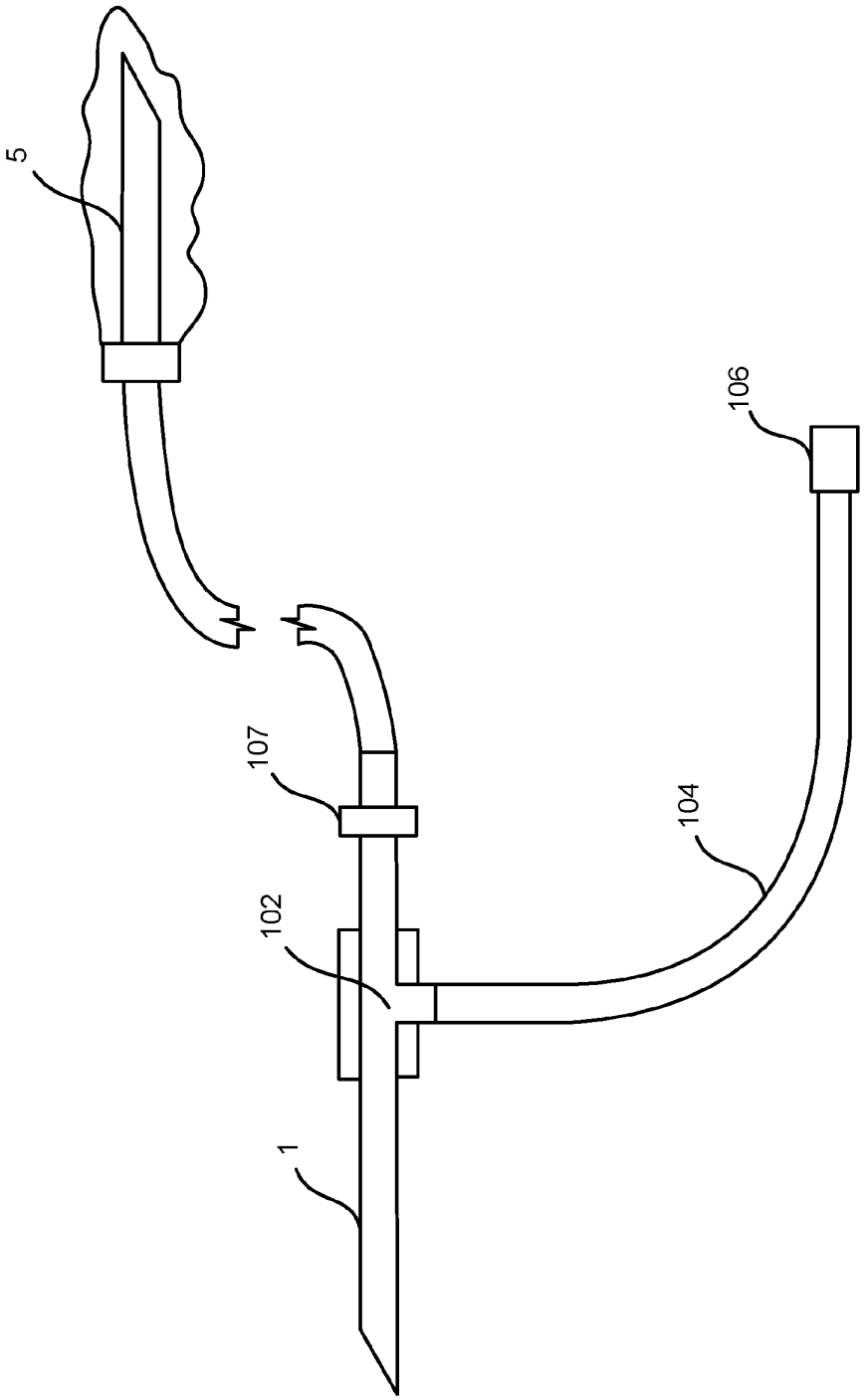


FIG. 4

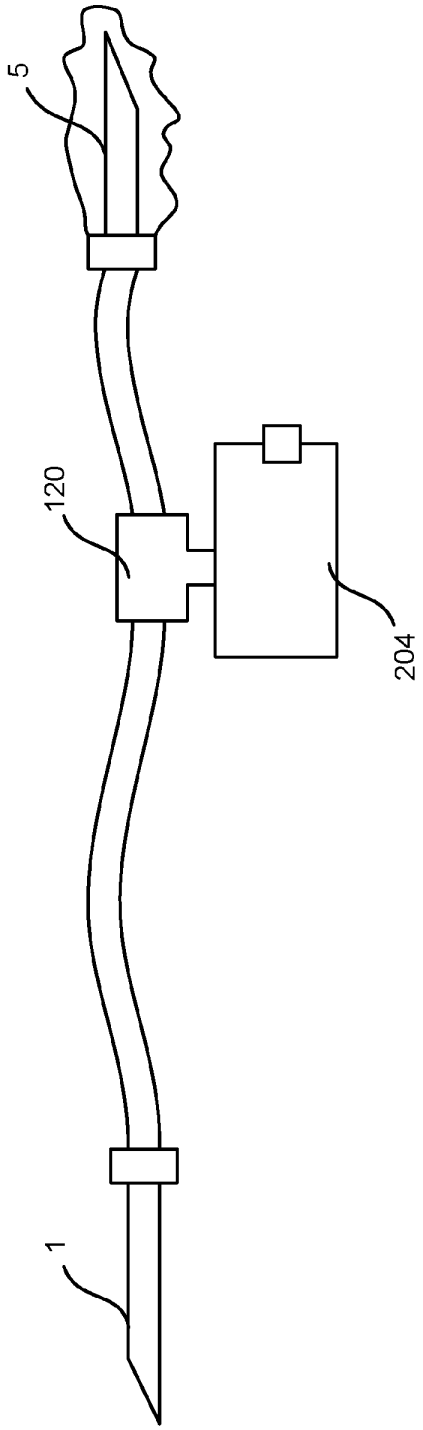


FIG. 5

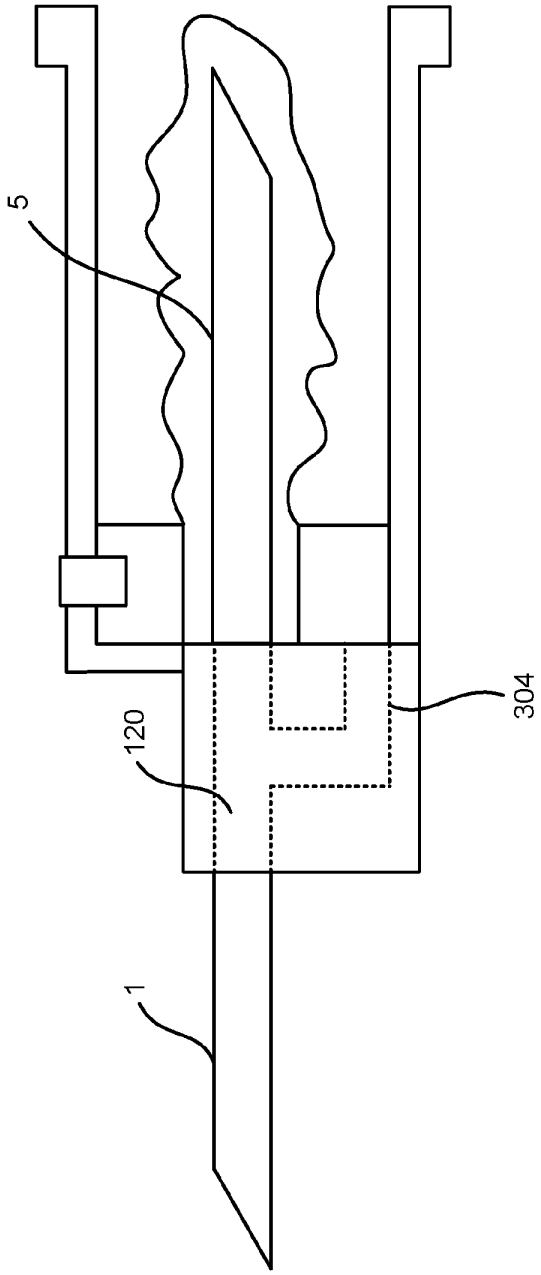


FIG. 6

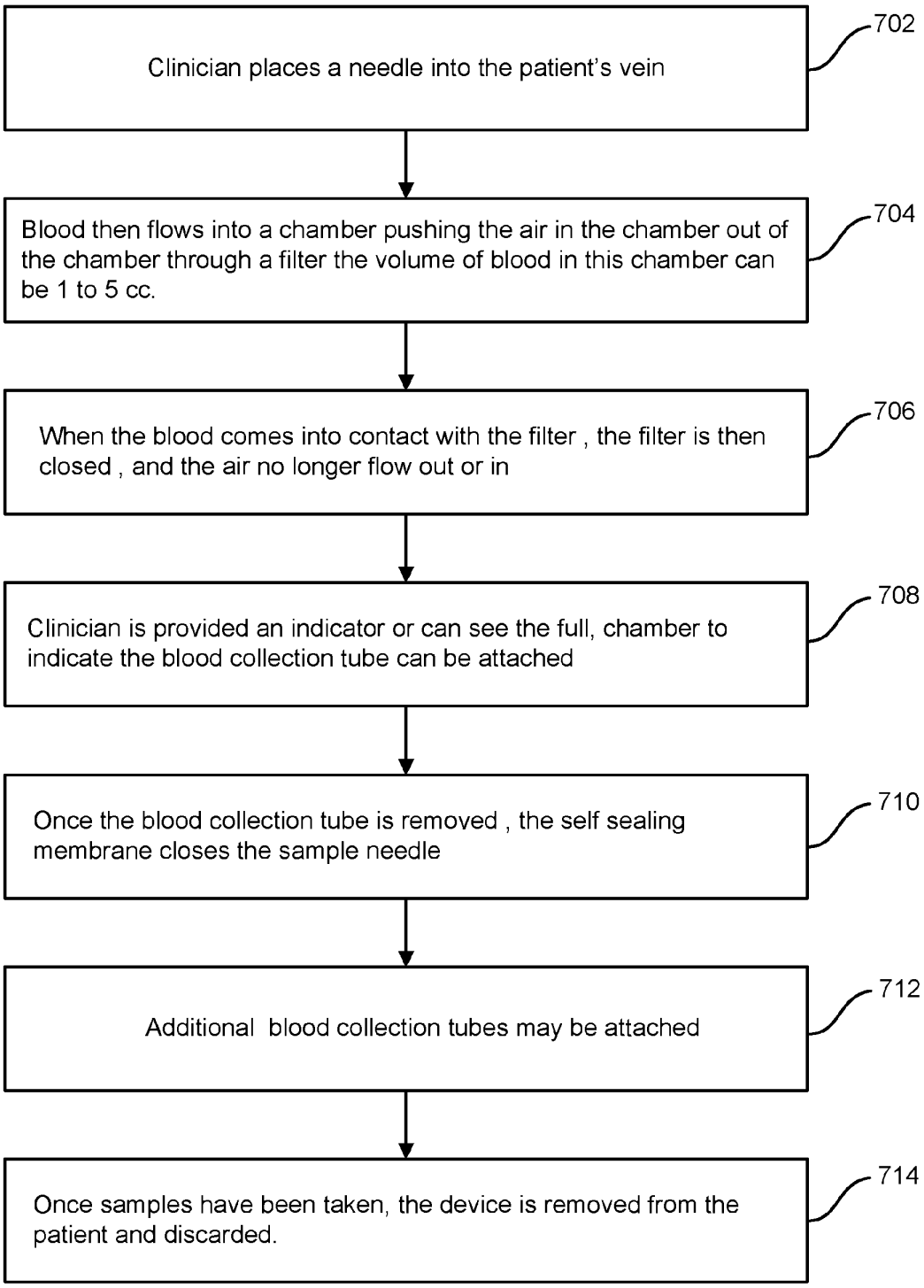

Clinician places a needle into the patient's vein
702
Blood then flows into a chamber pushing the air in the chamber out of the chamber through a filter the volume of blood in this chamber can be 1 to 5 cc.
704
When the blood comes into contact with the filter , the filter is then closed , and the air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

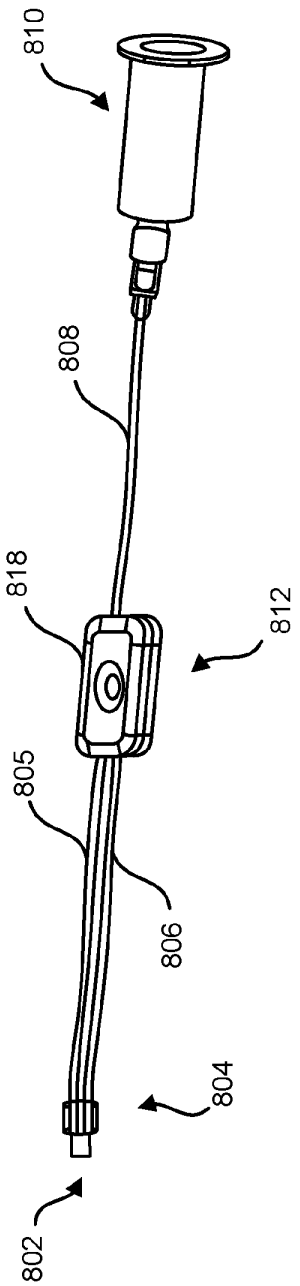


FIG. 8A

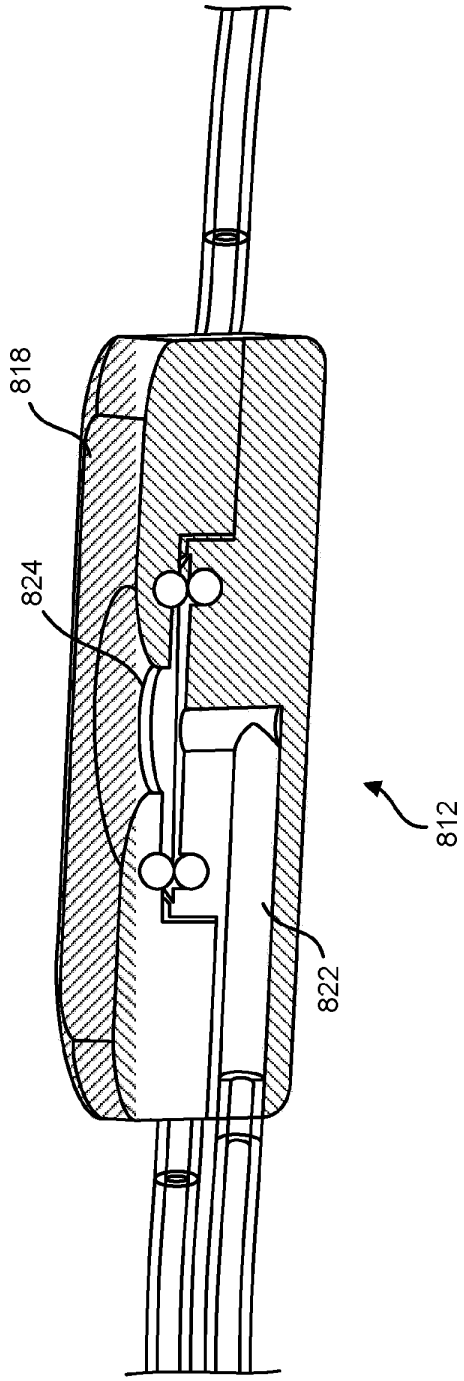


FIG. 8B

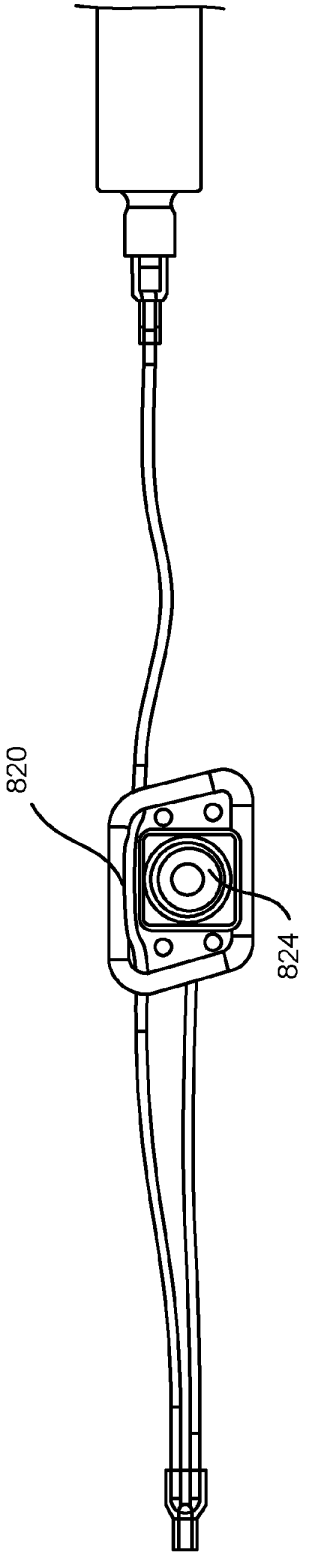


FIG. 8C

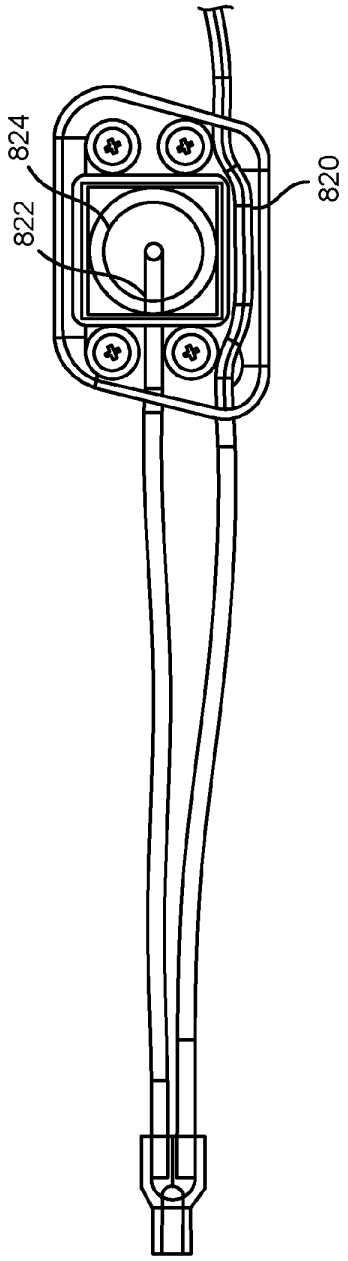


FIG. 8D

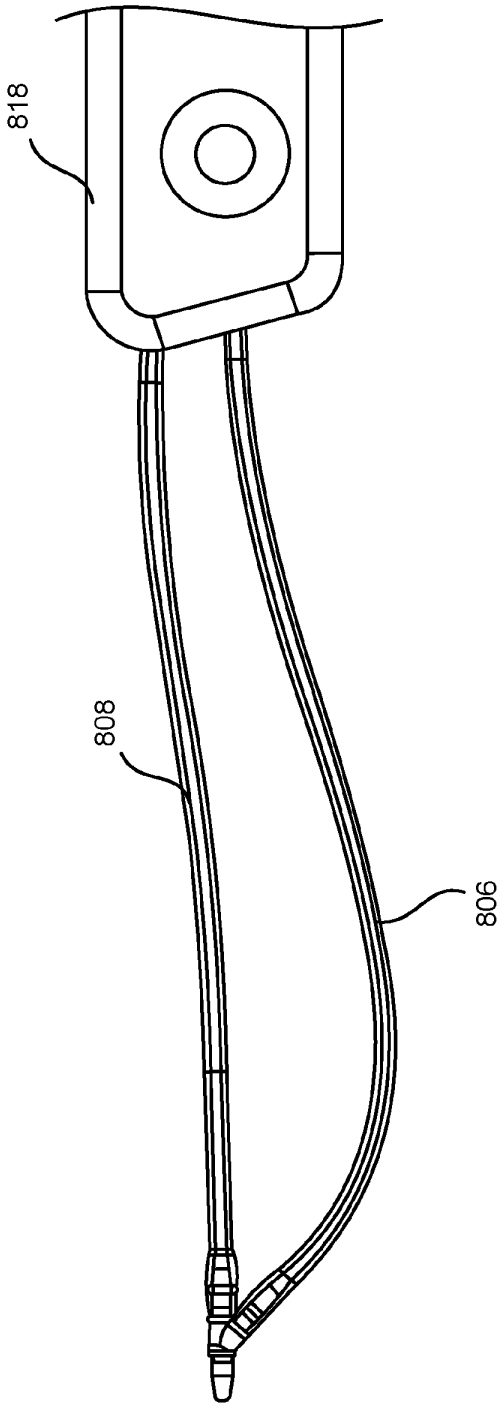


FIG. 8E

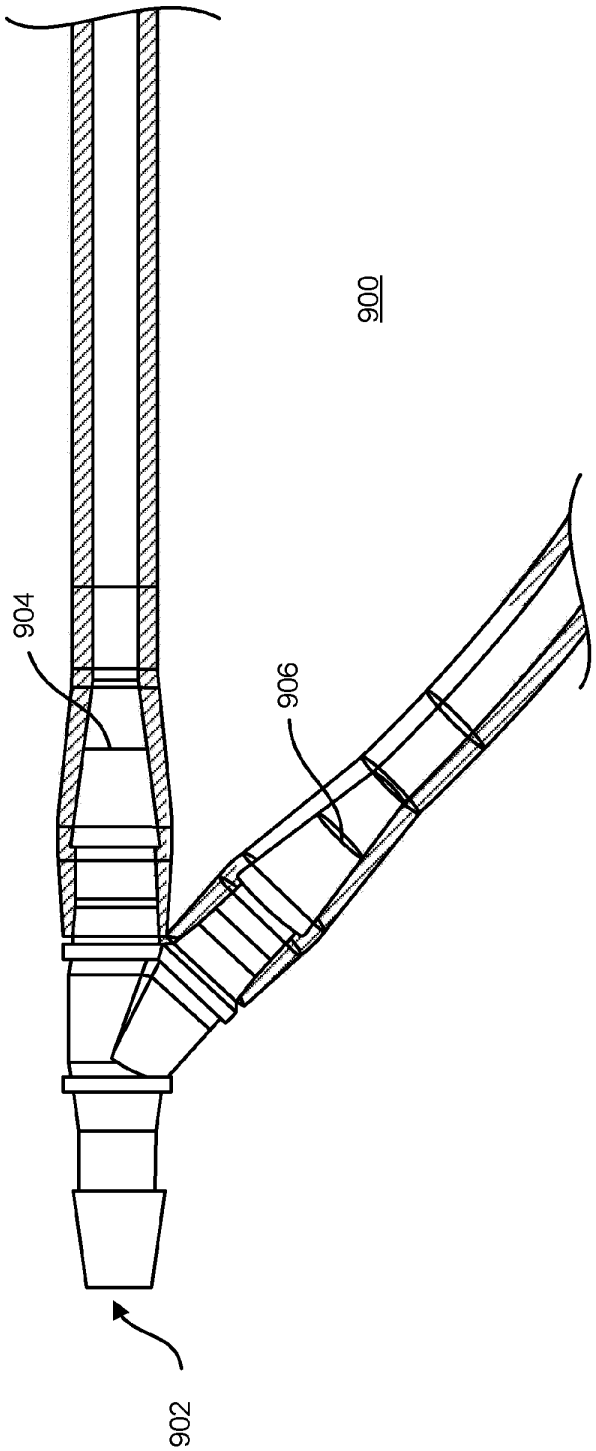


FIG. 9

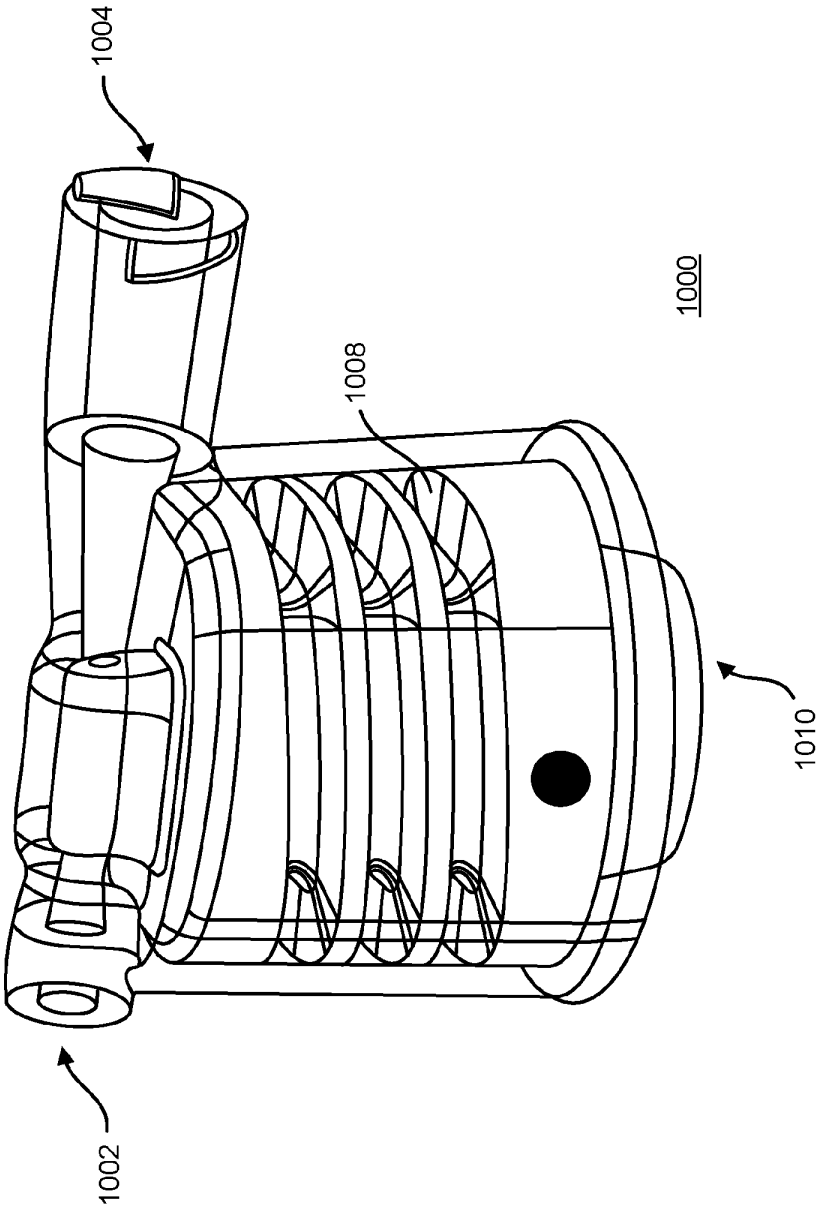


FIG. 10A

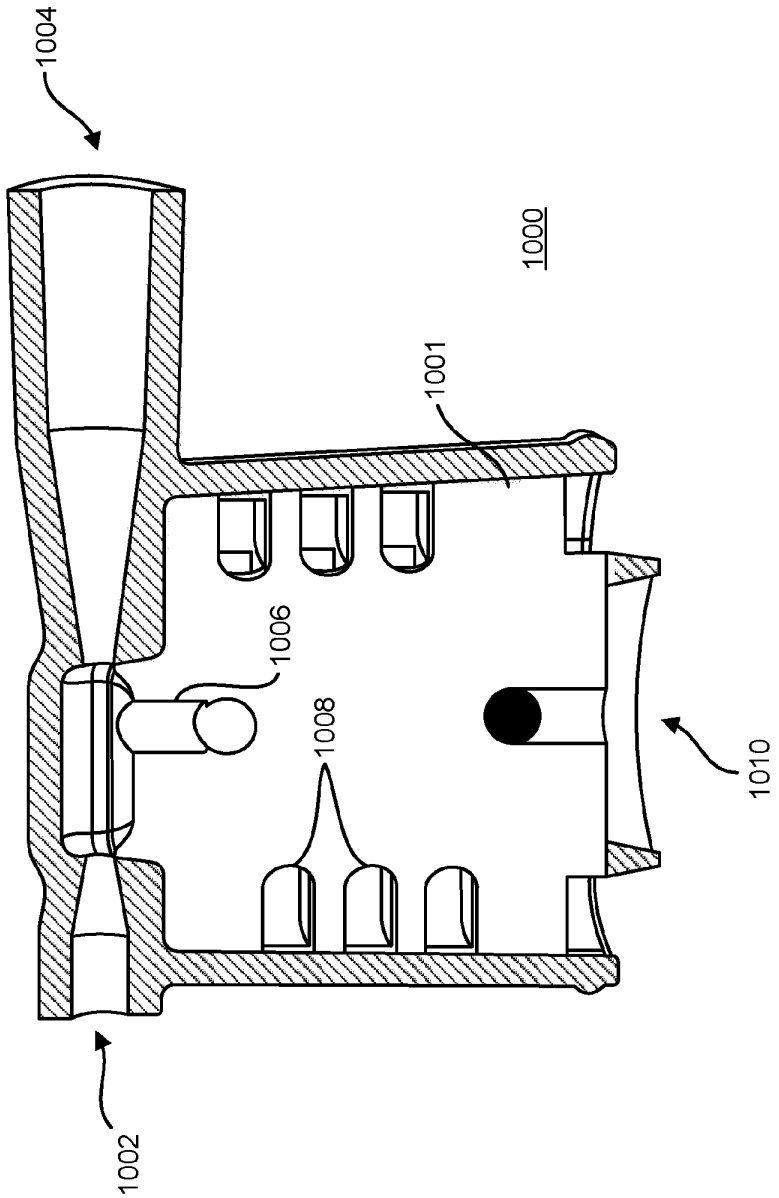


FIG. 10B

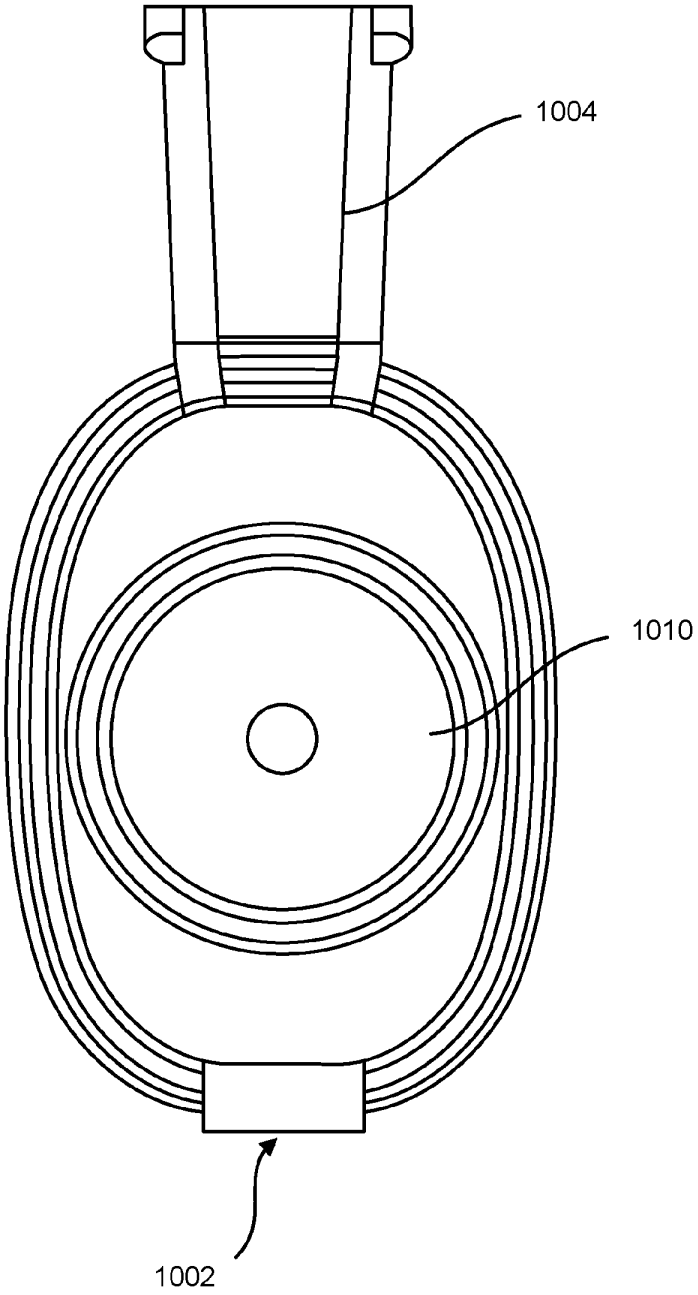


FIG. 10C

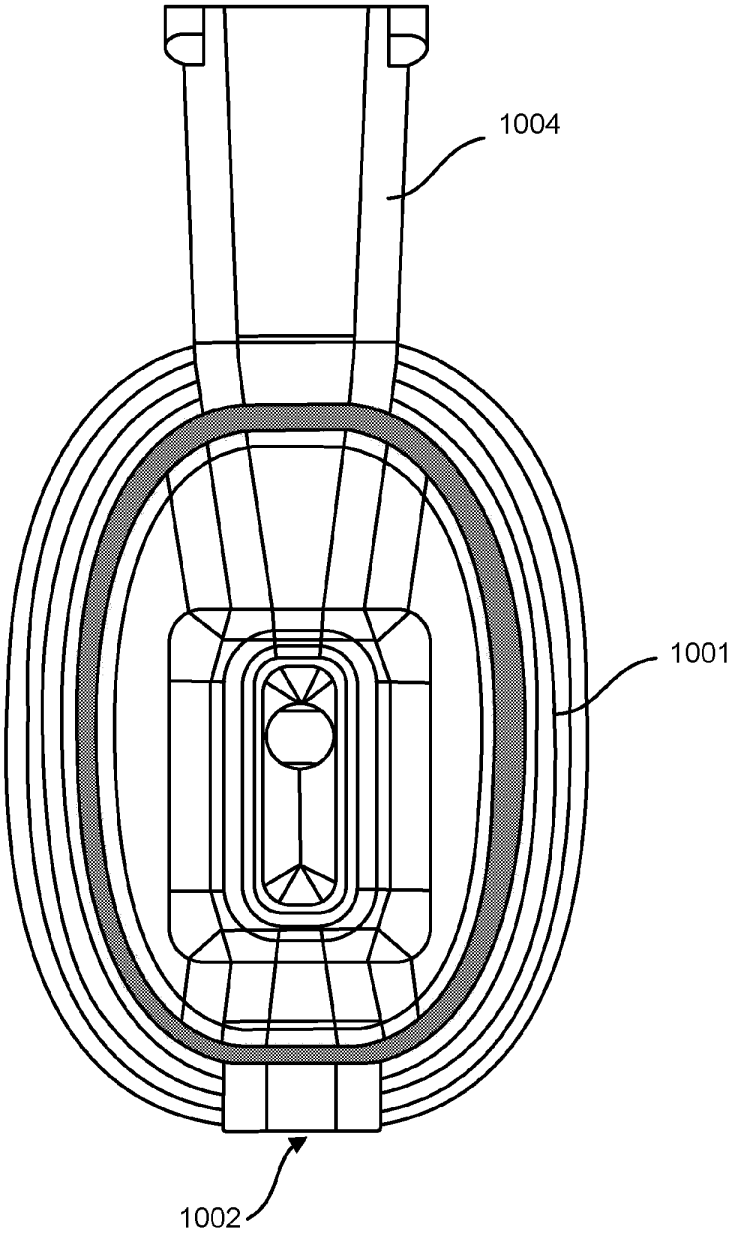


FIG. 10D

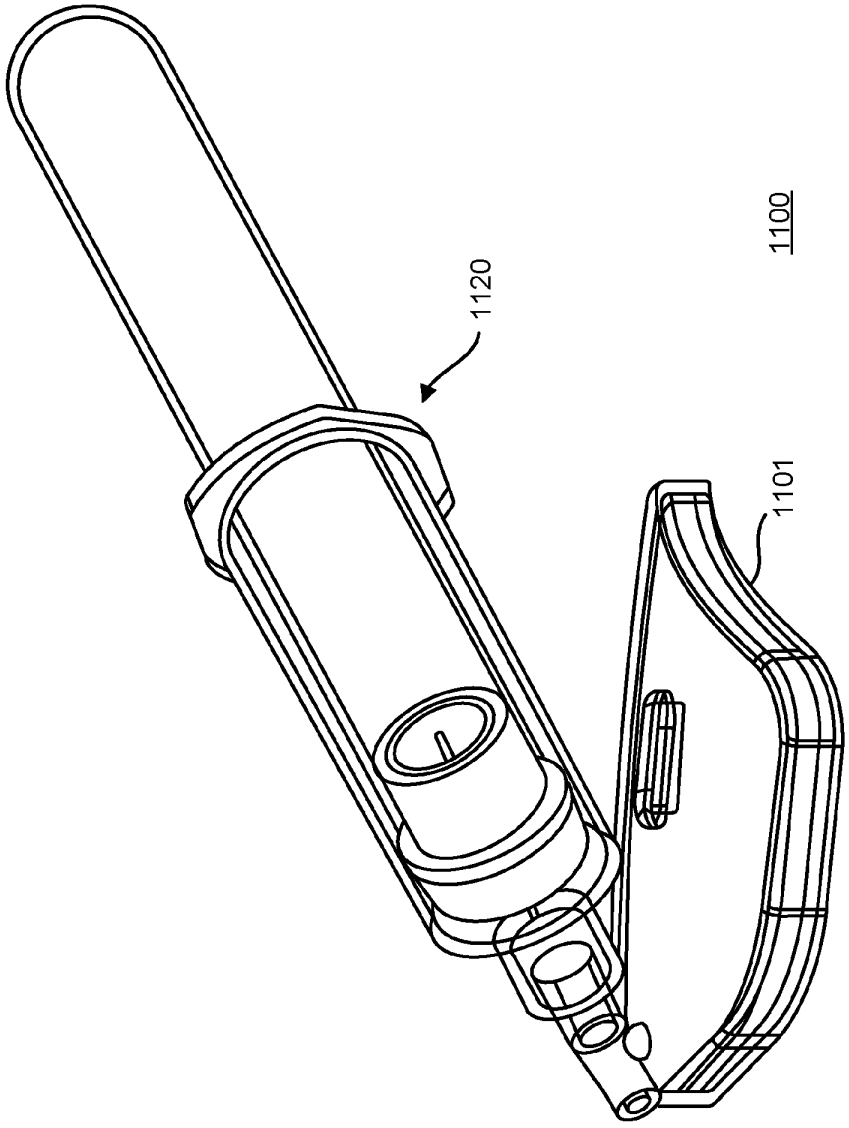


FIG. 11A

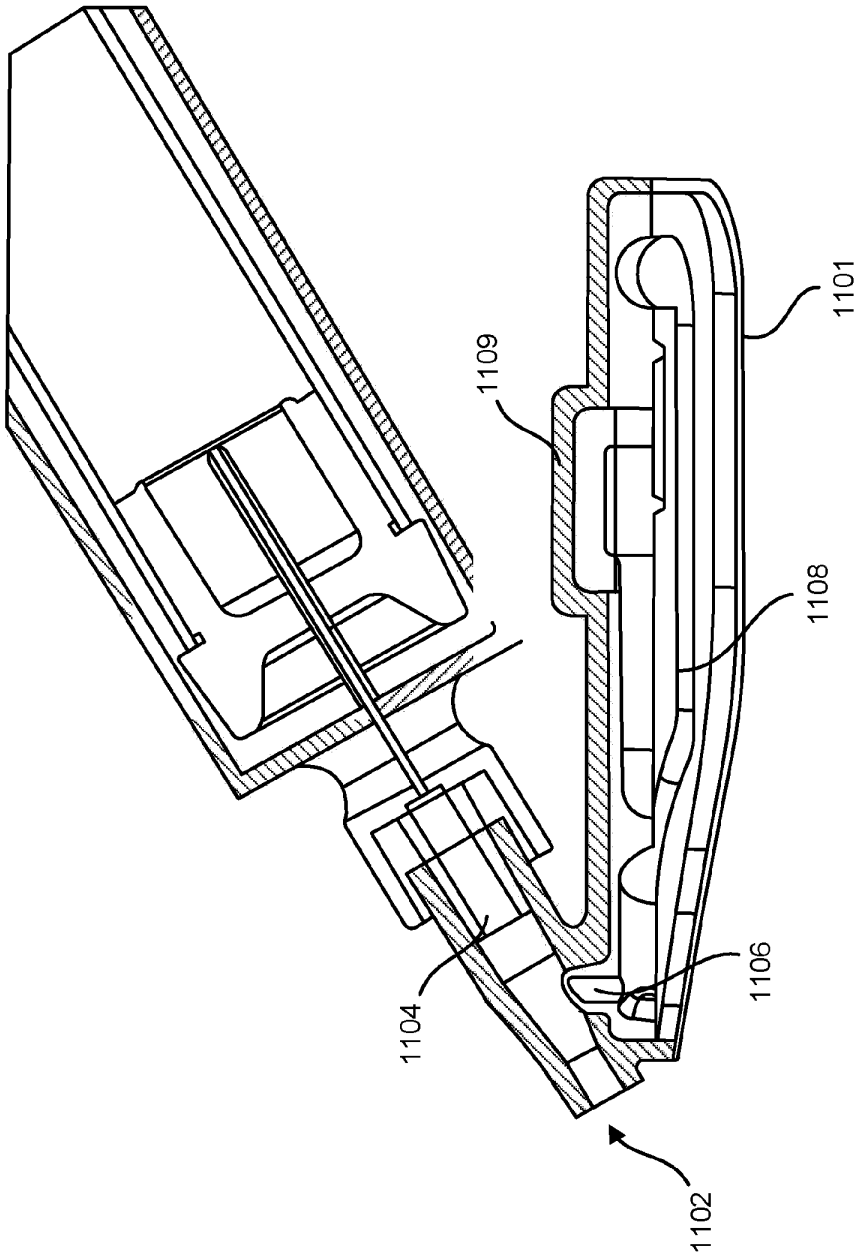


FIG. 11B

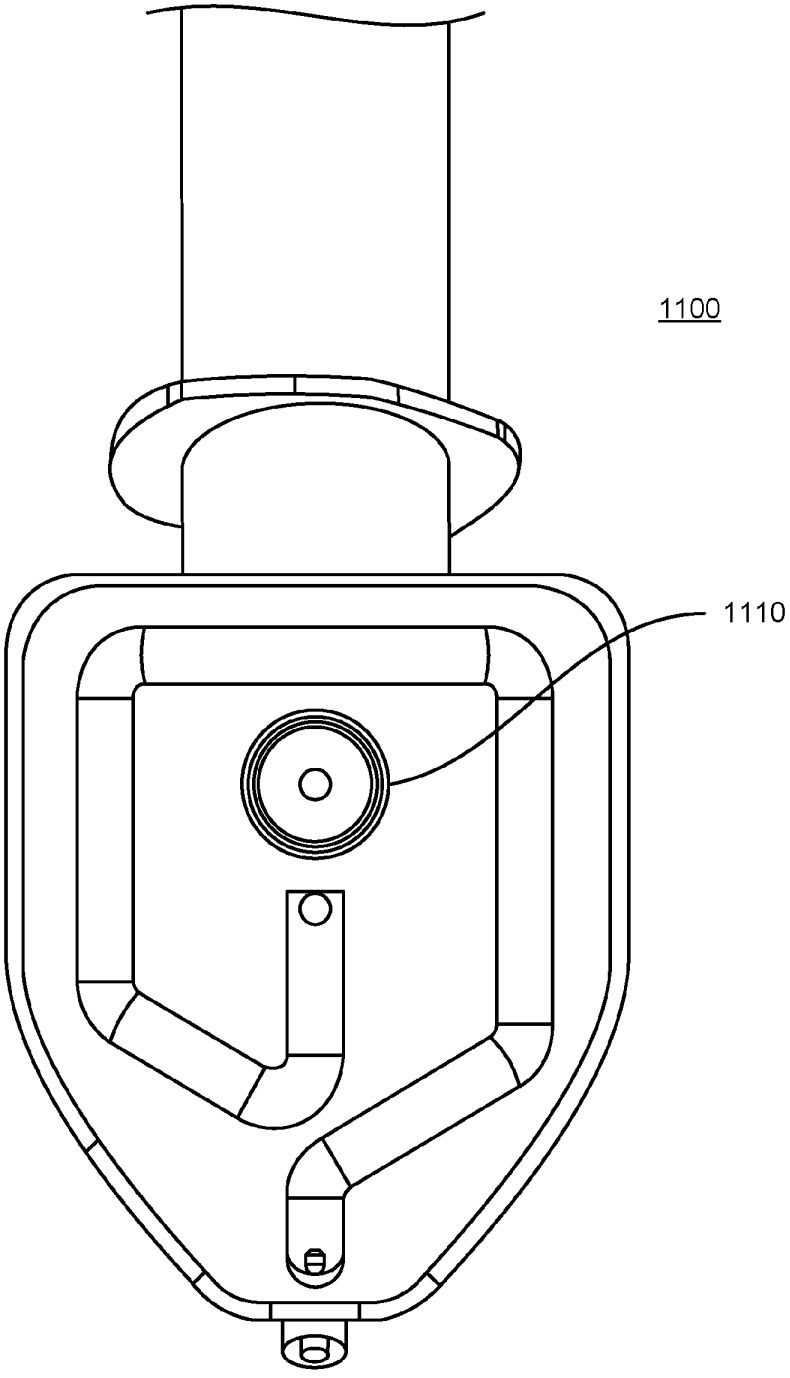


FIG. 11C

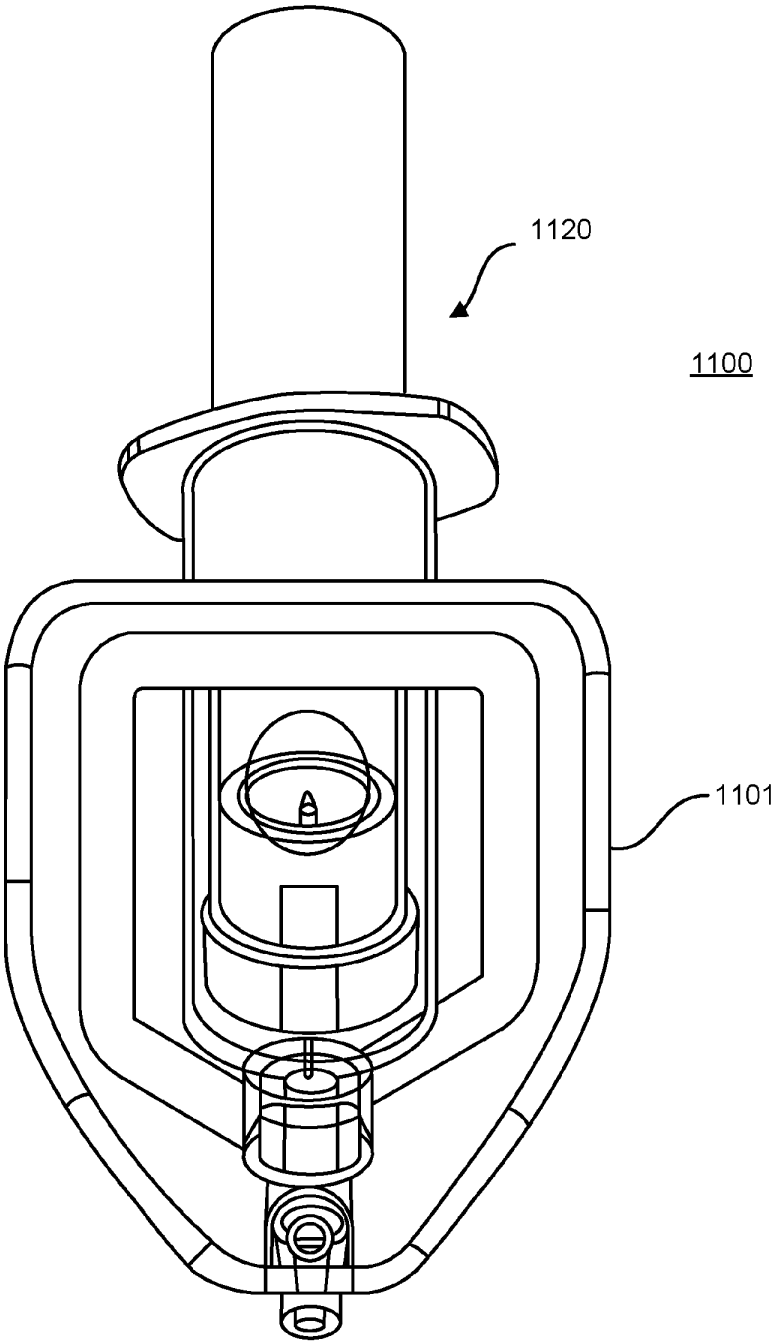


FIG. 11D

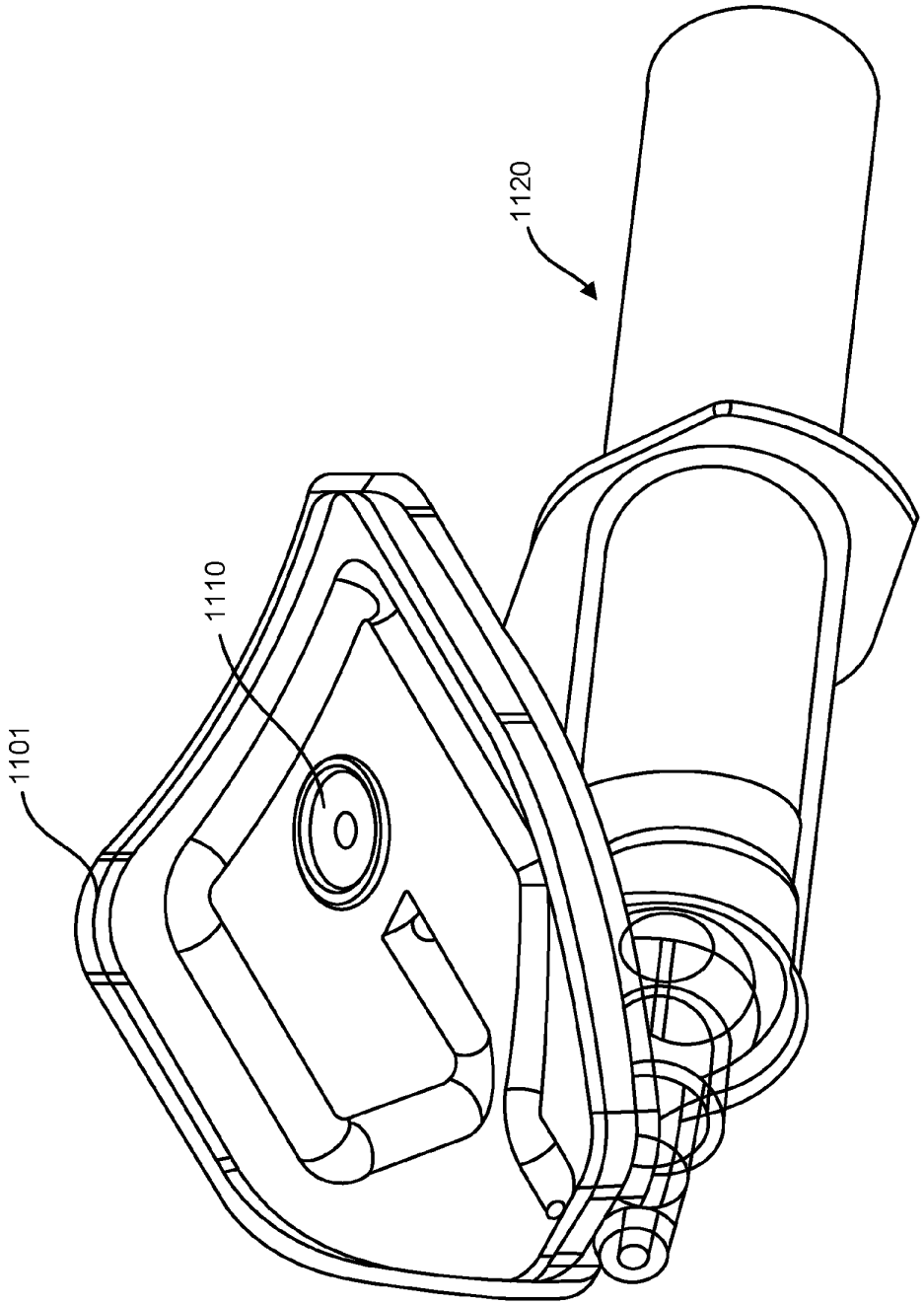


FIG. 11E

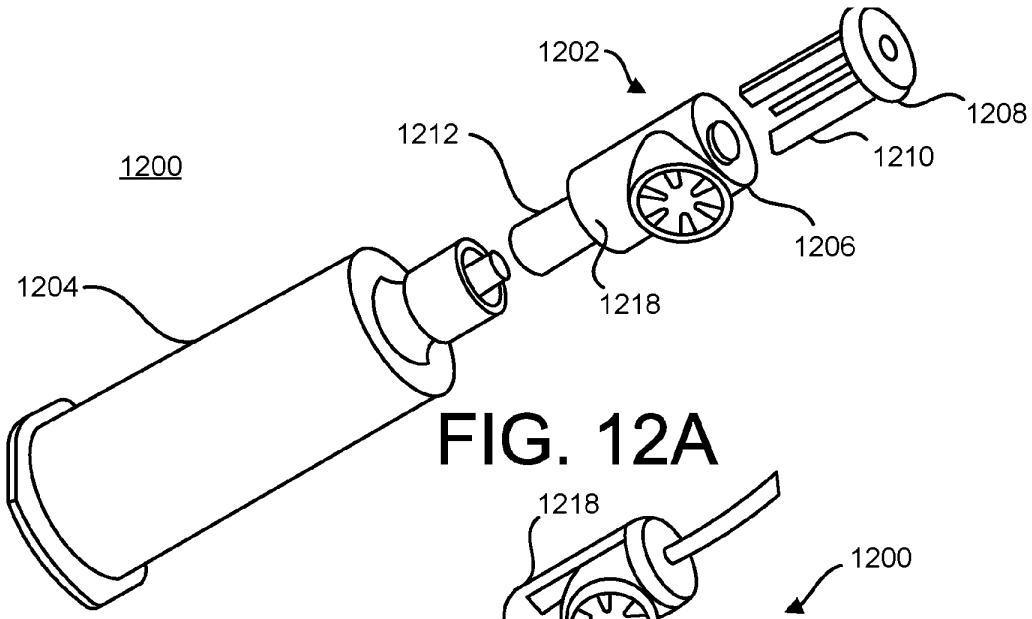


FIG. 12A

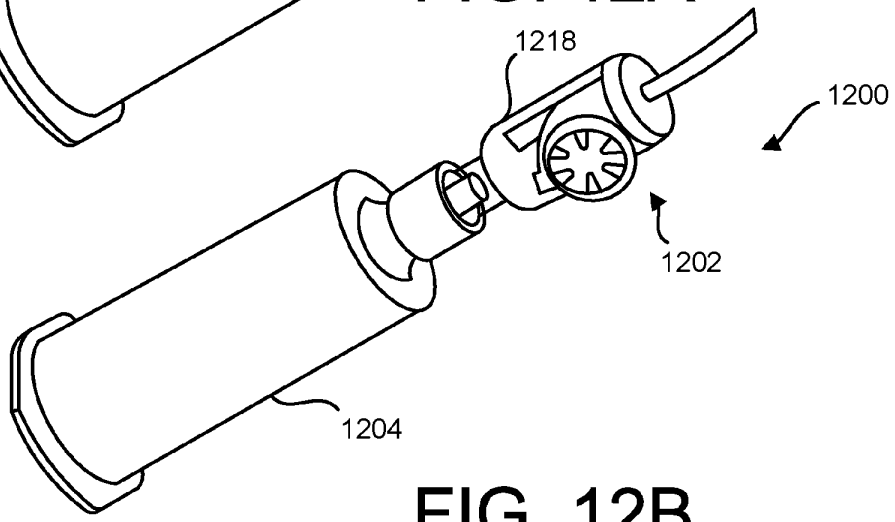


FIG. 12B

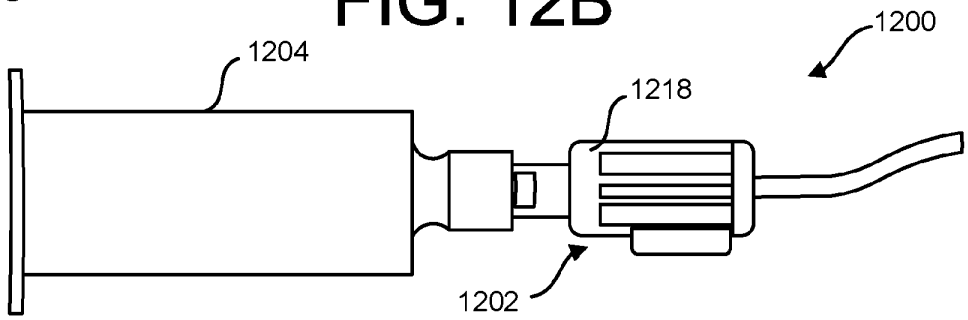


FIG. 12C

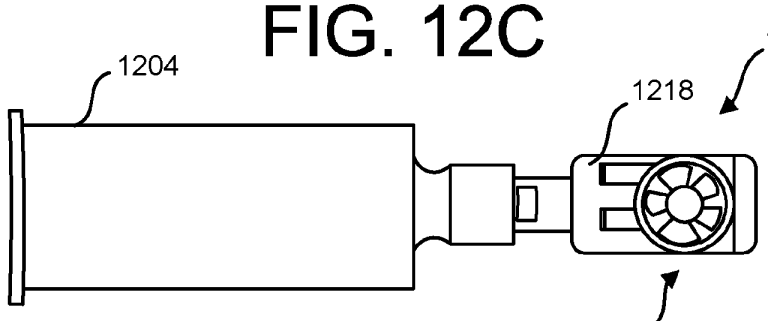


FIG. 12D

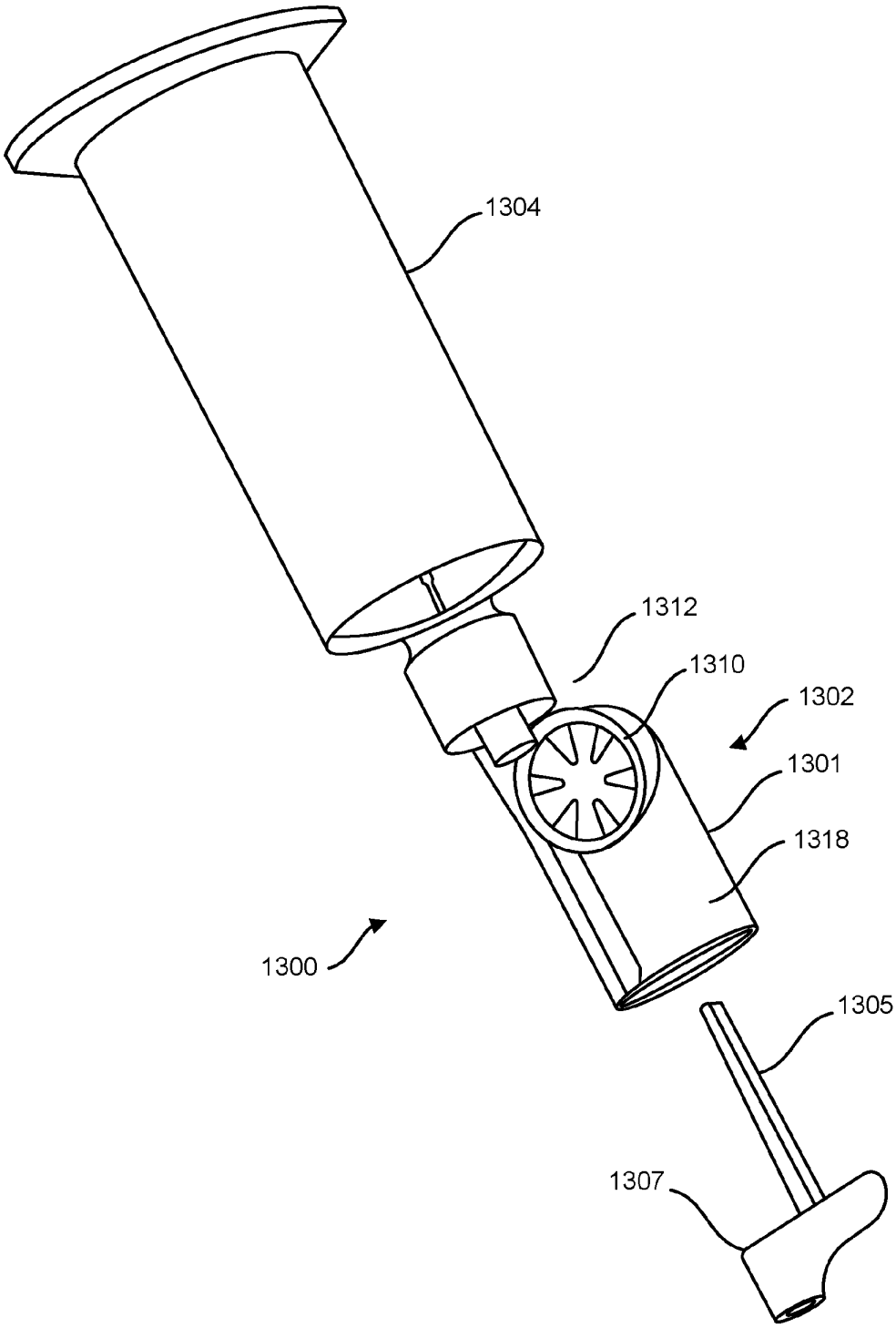


FIG. 13A

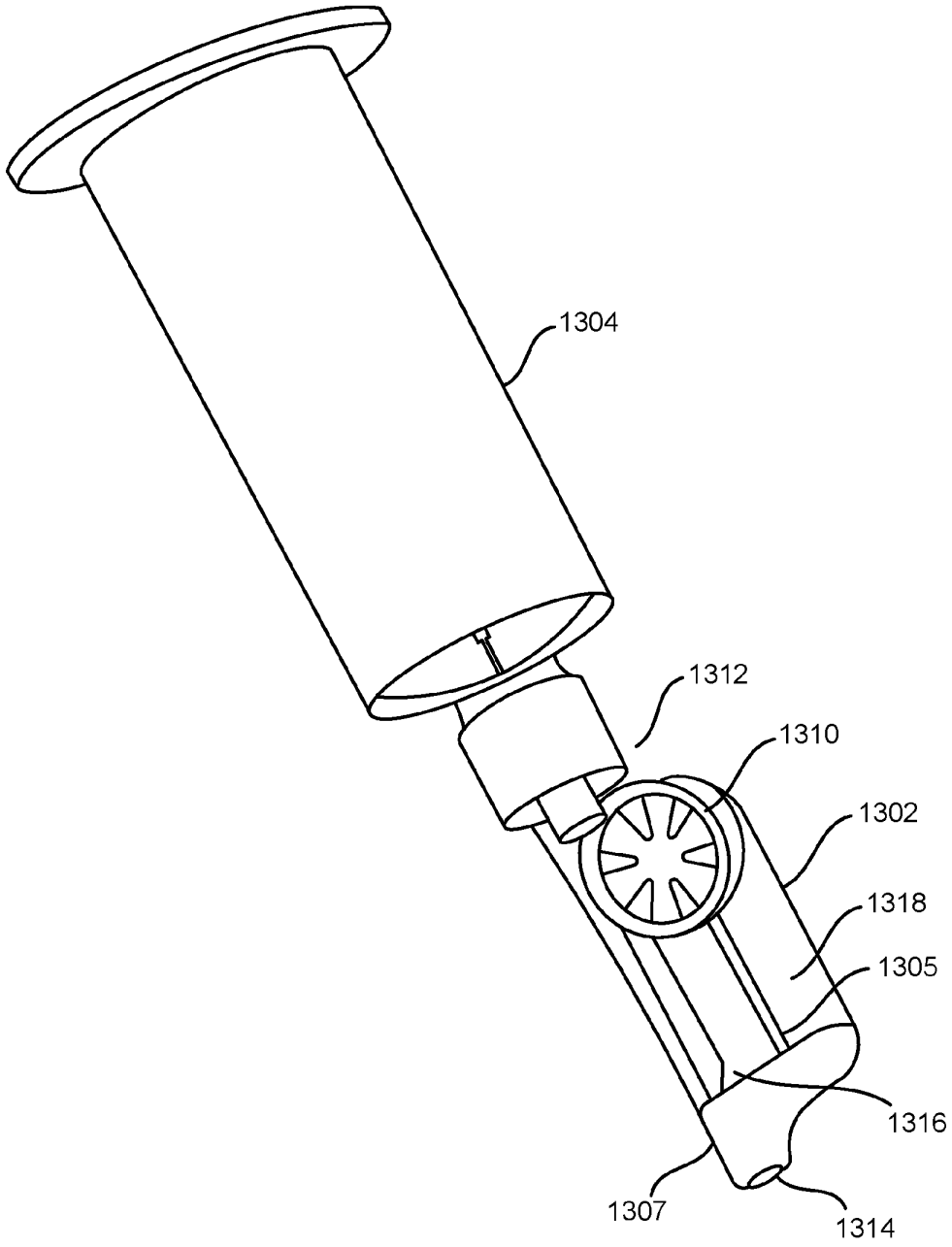


FIG. 13B

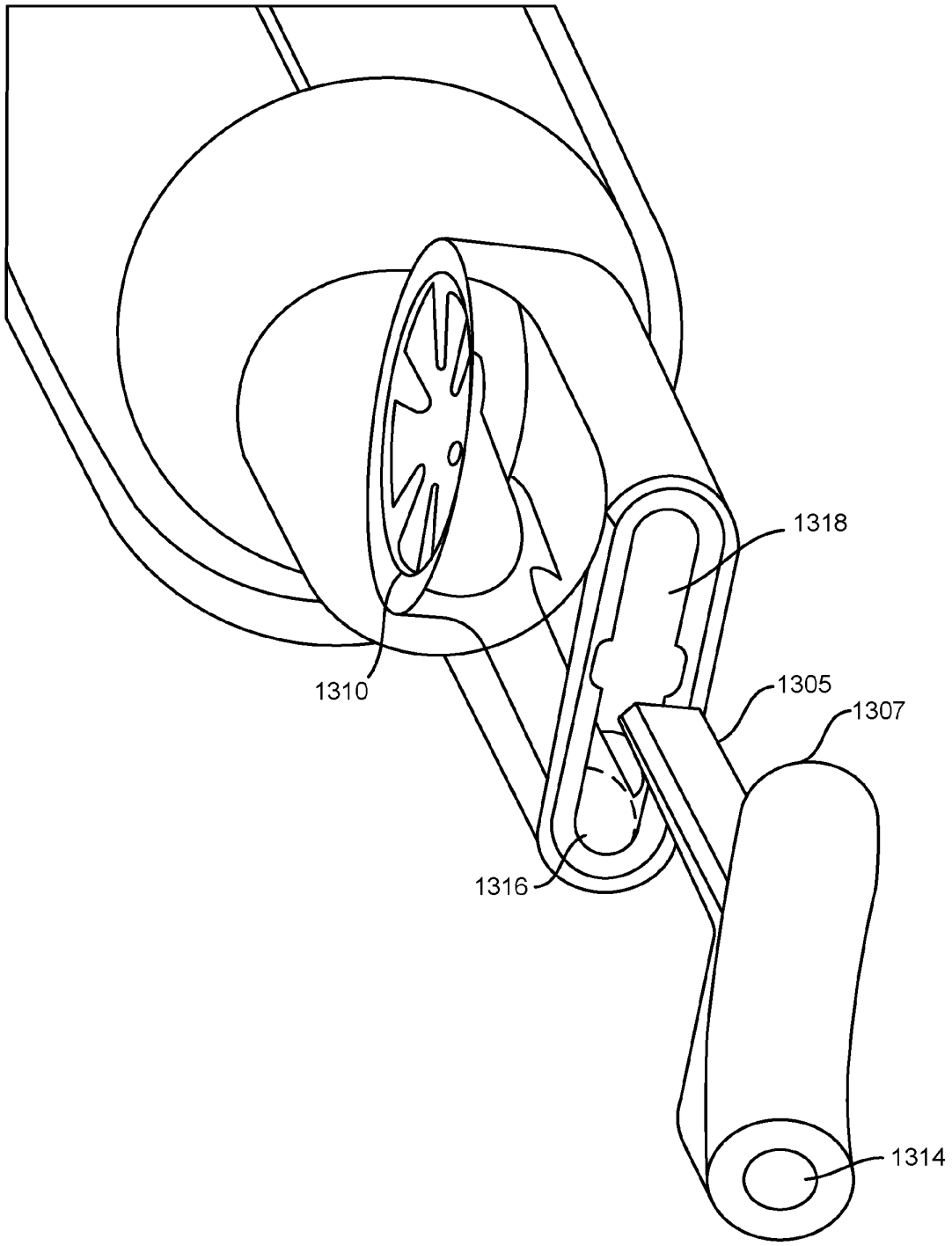


FIG. 13C

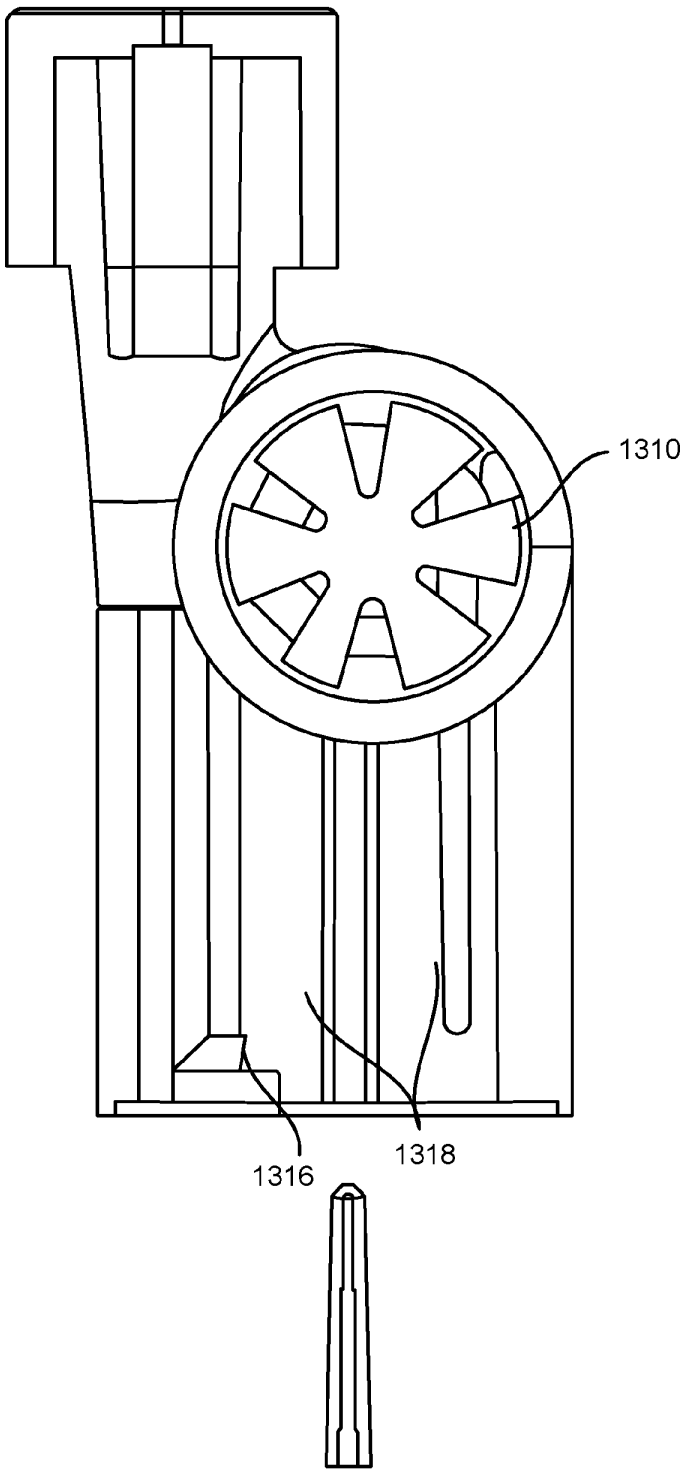


FIG. 13D

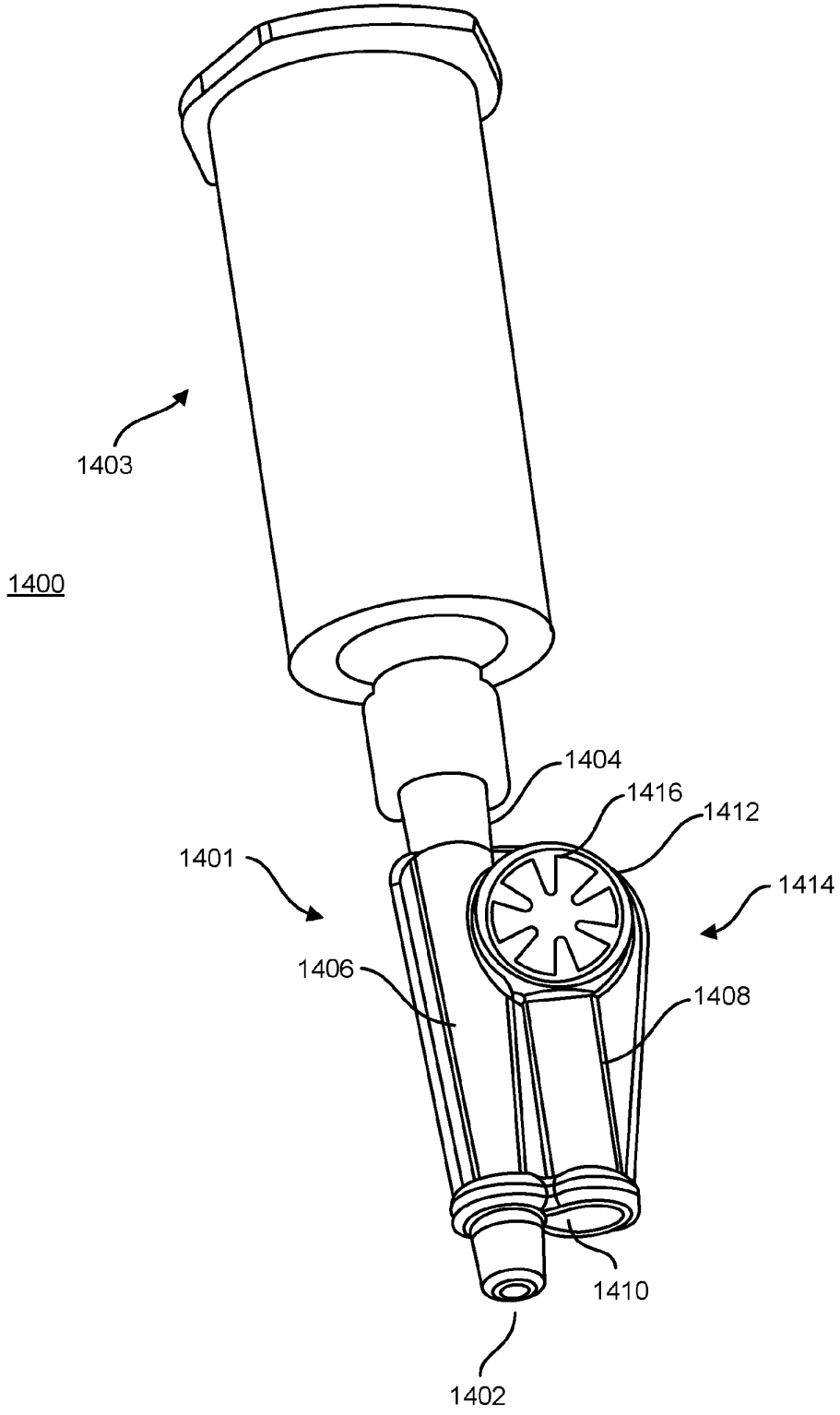


FIG. 14A

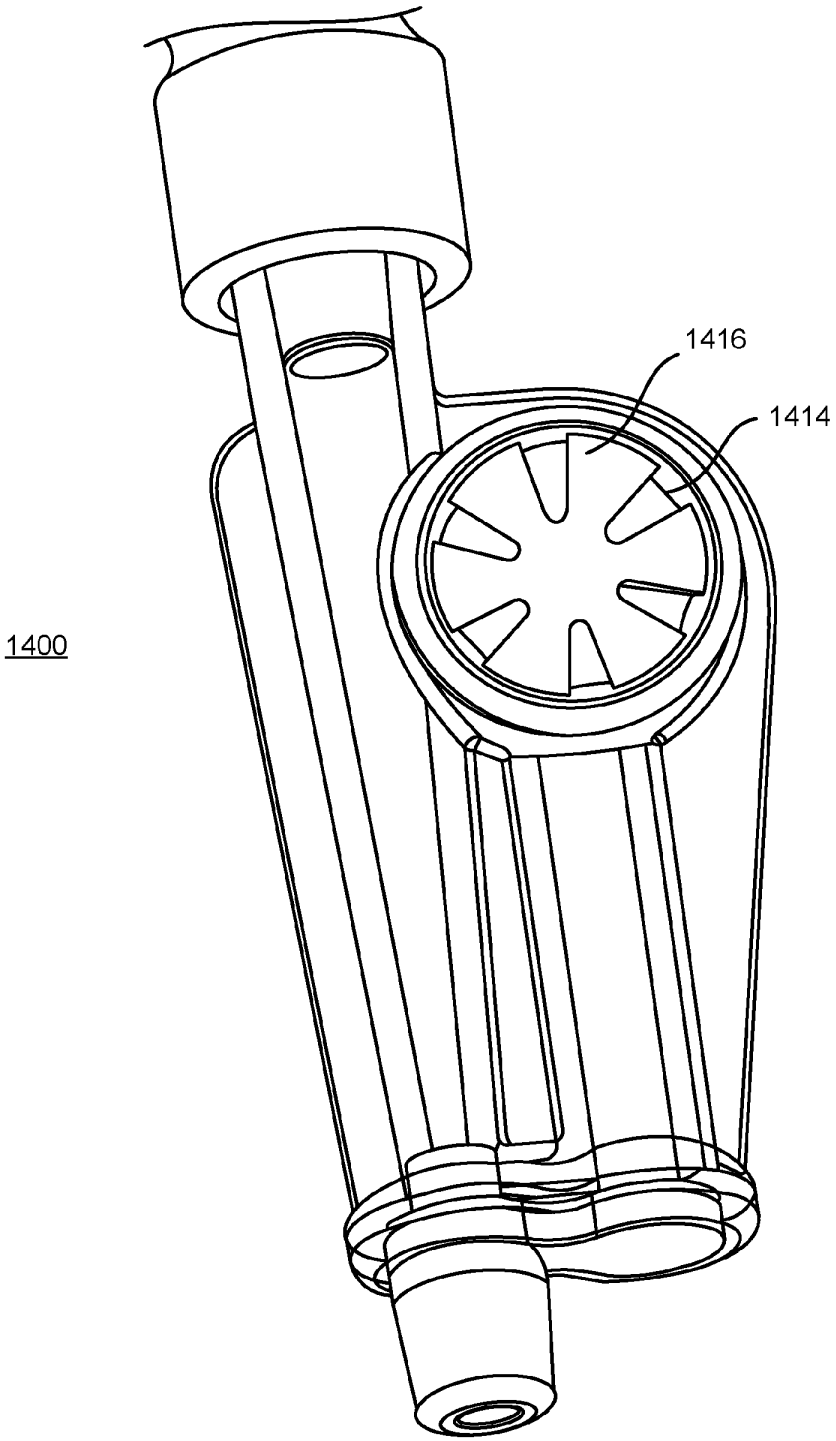


FIG. 14B

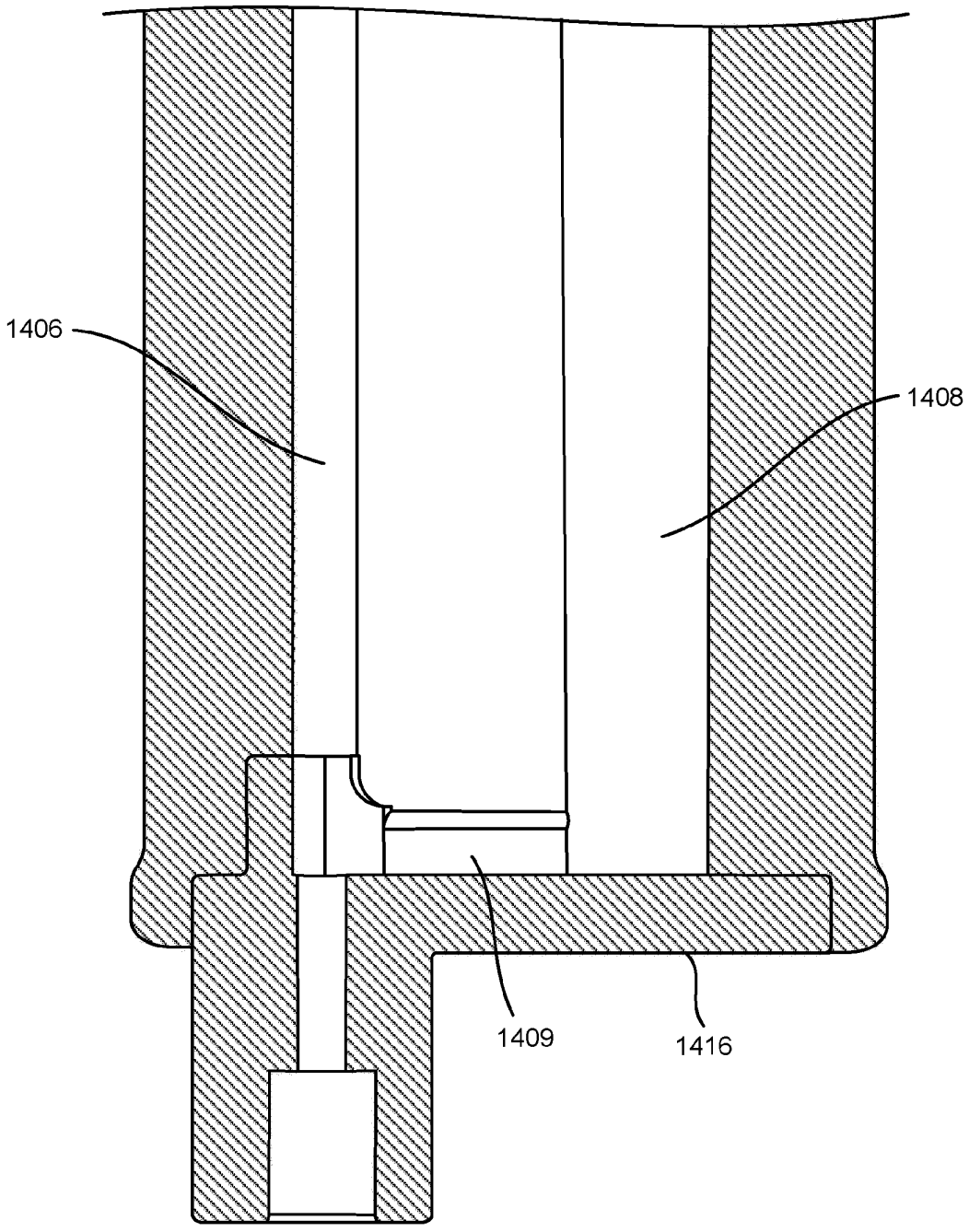


FIG. 14C

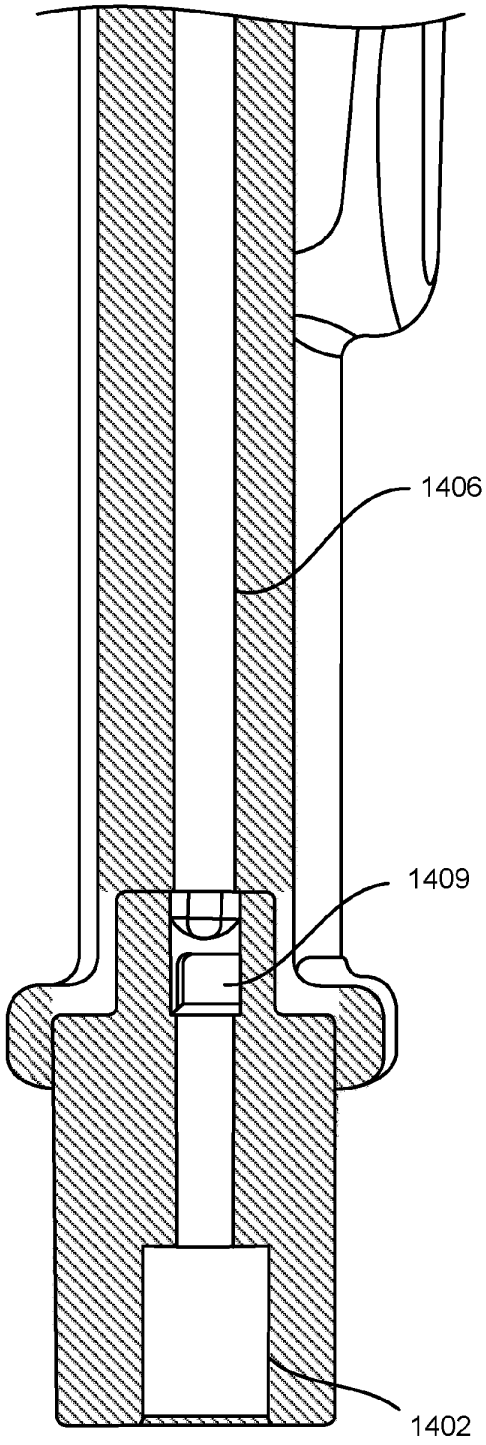


FIG. 14D

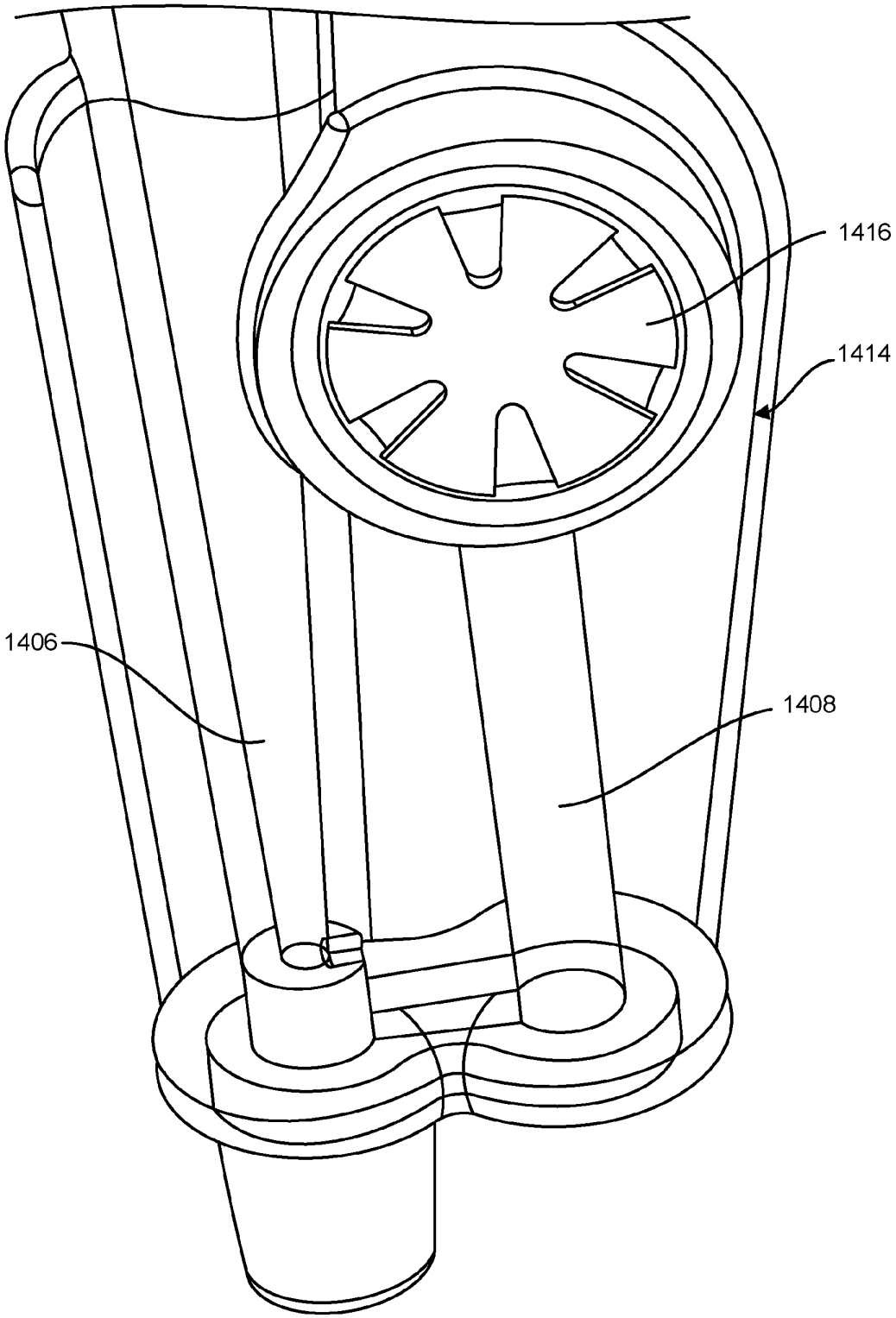


FIG. 14E

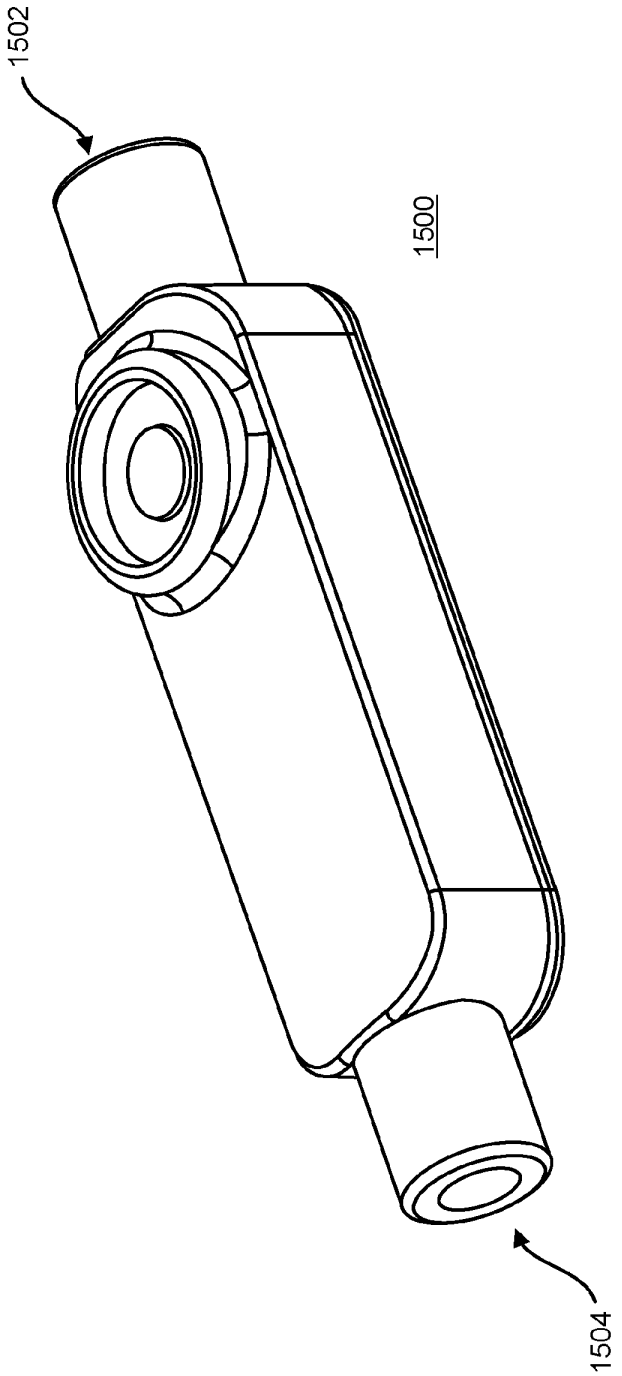


FIG. 15A

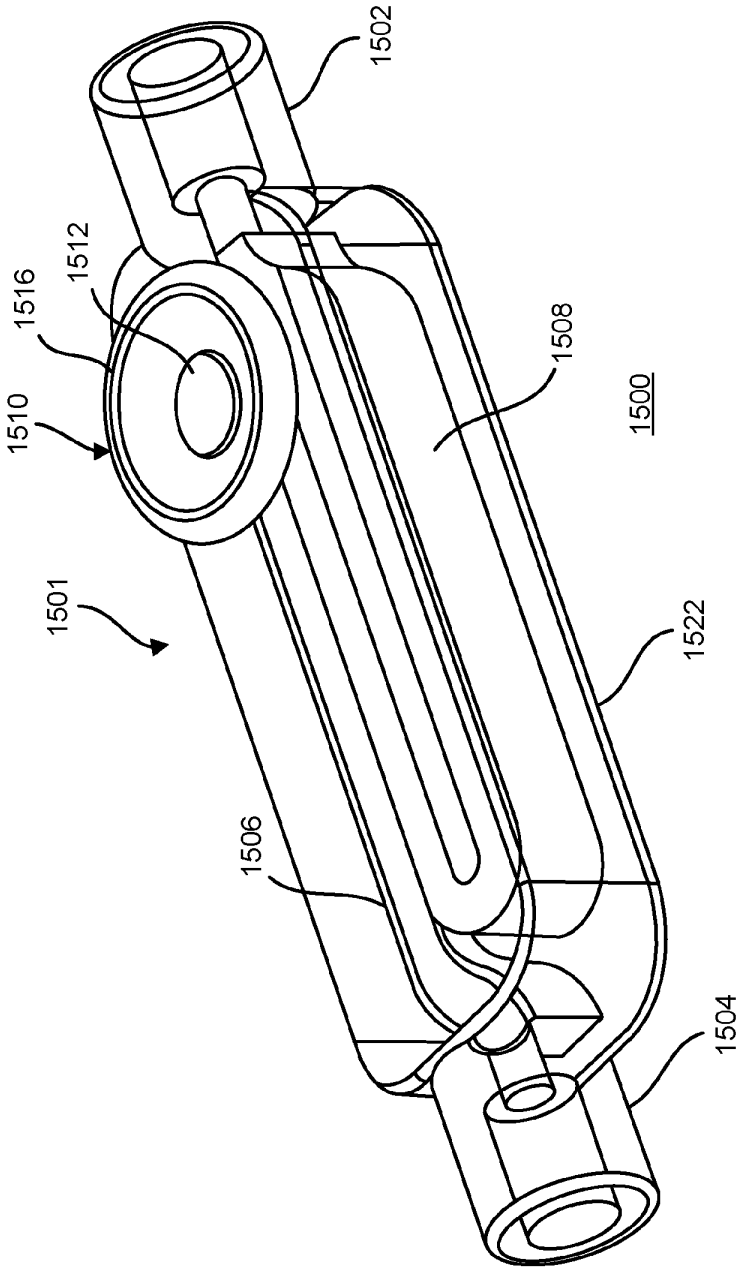


FIG. 15B

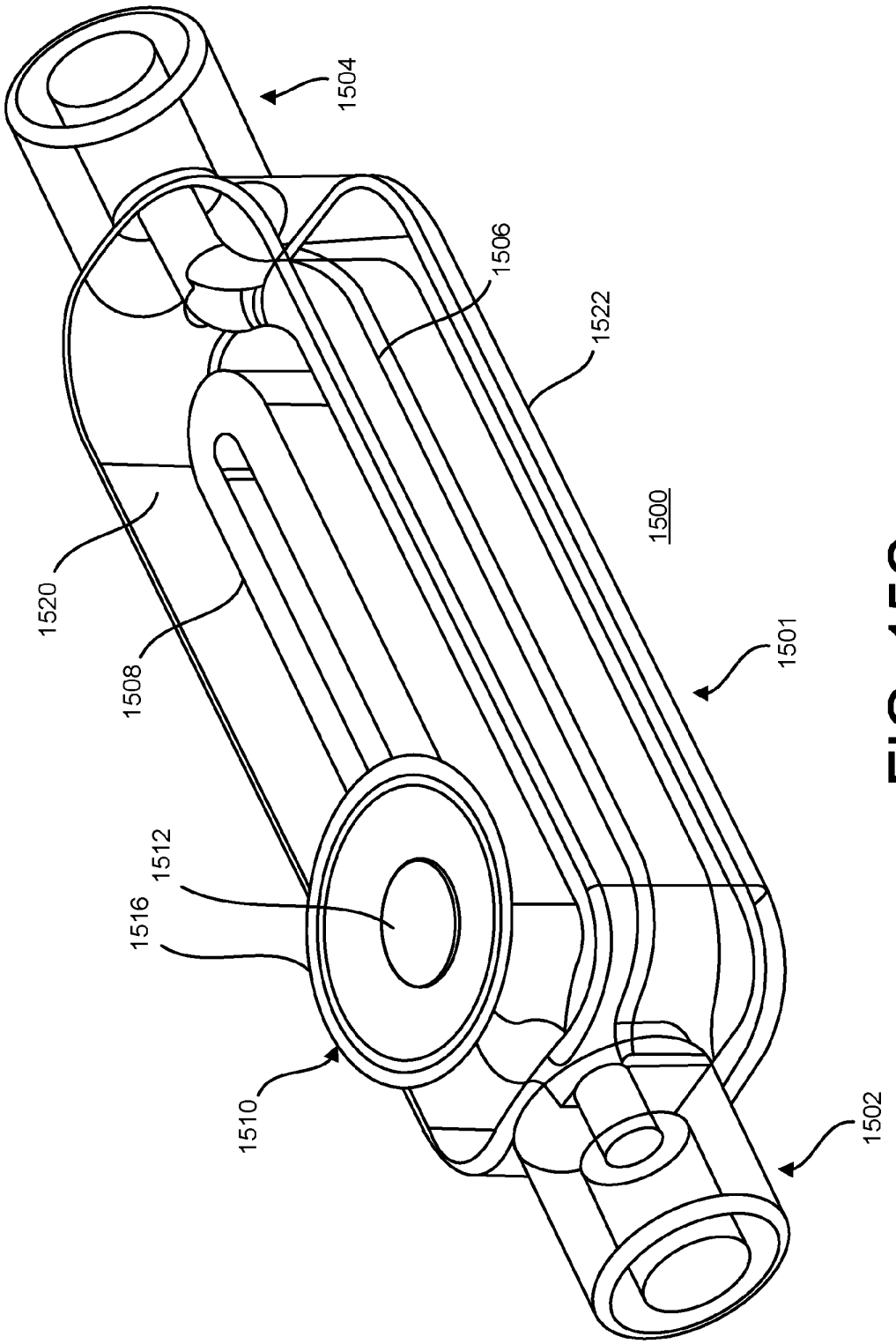


FIG. 15C

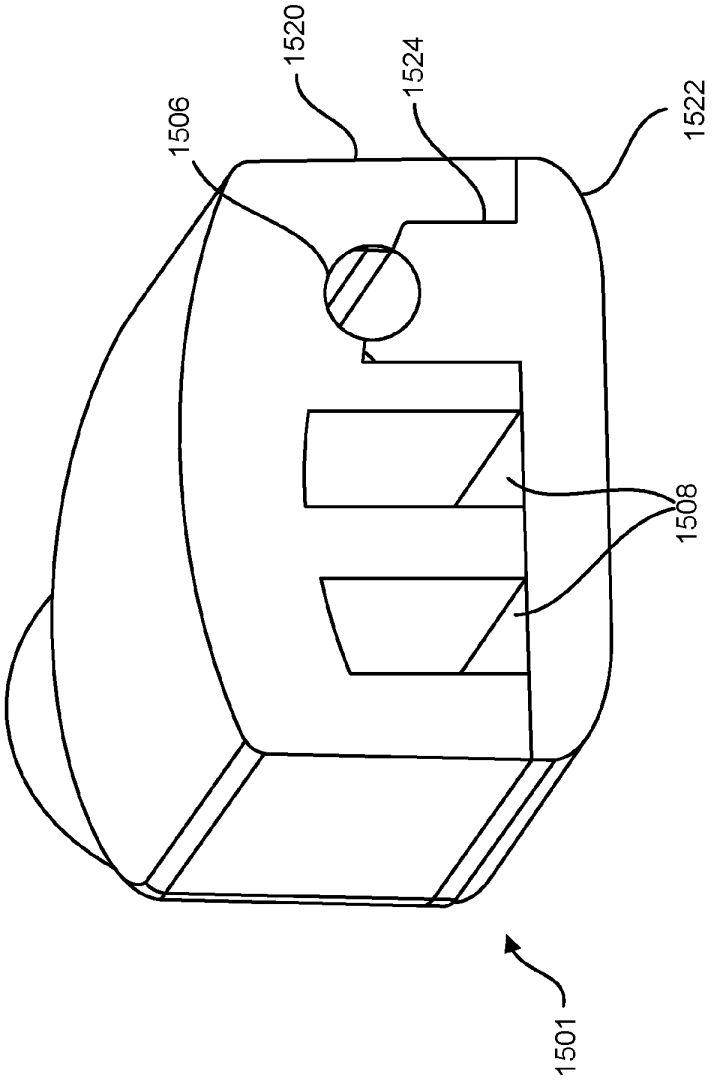


FIG. 15D

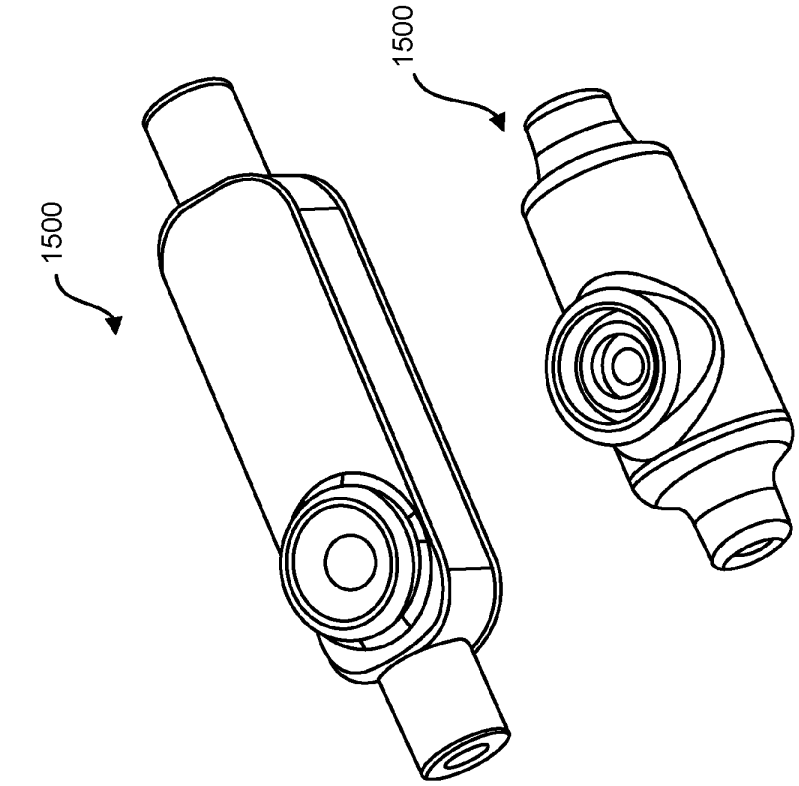


FIG. 15F

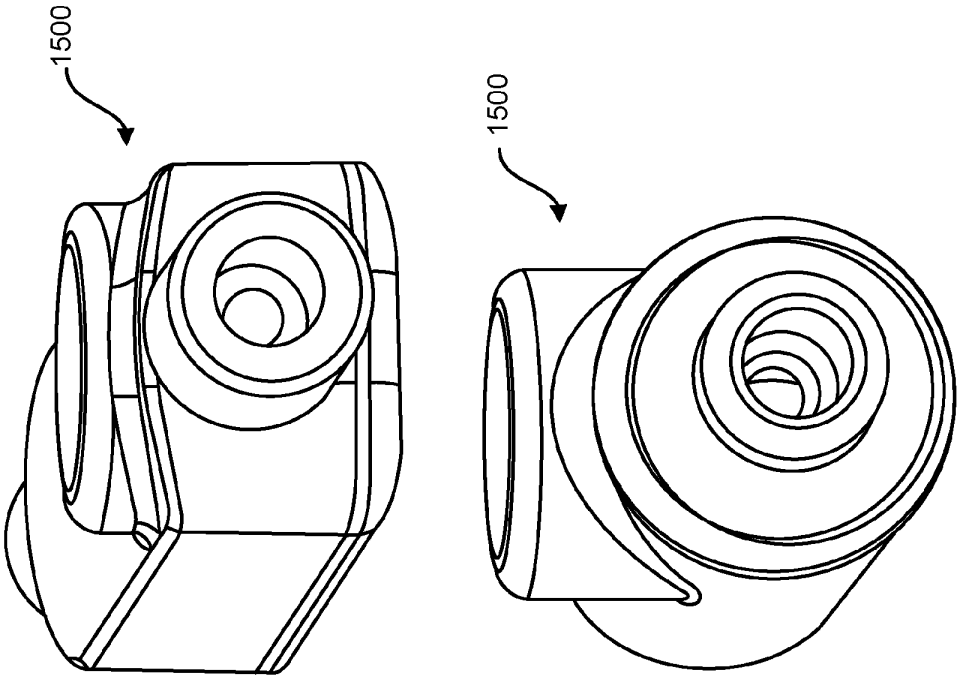


FIG. 15E

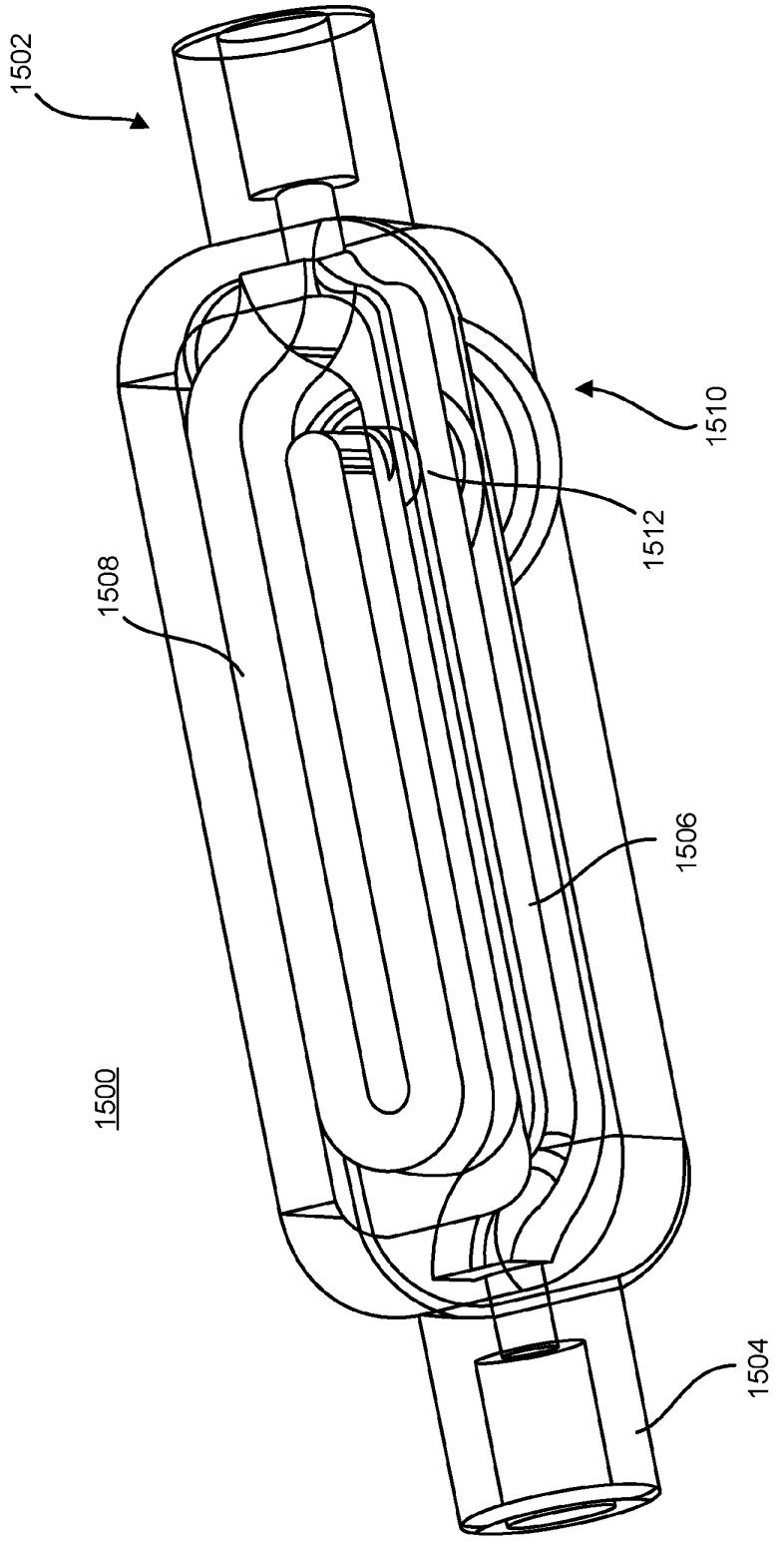


FIG. 15G

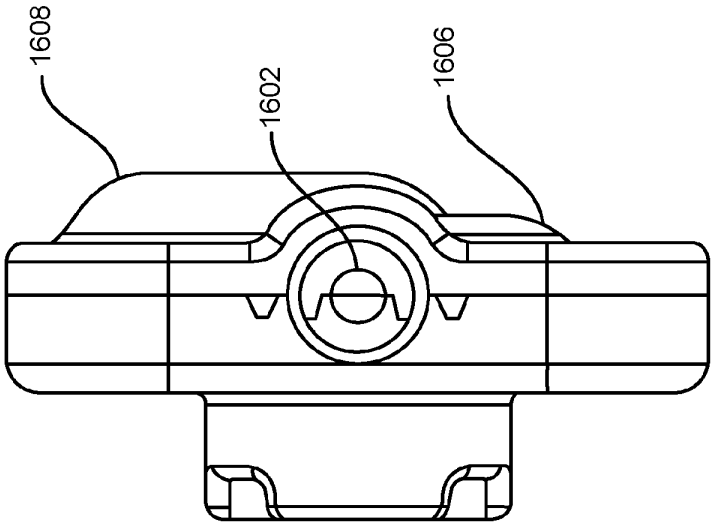


FIG. 16C

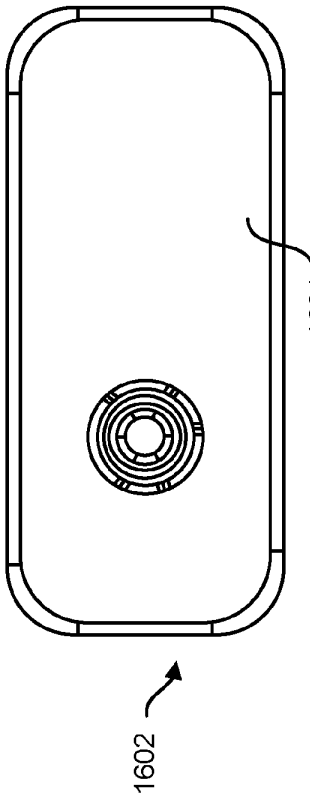


FIG. 16A

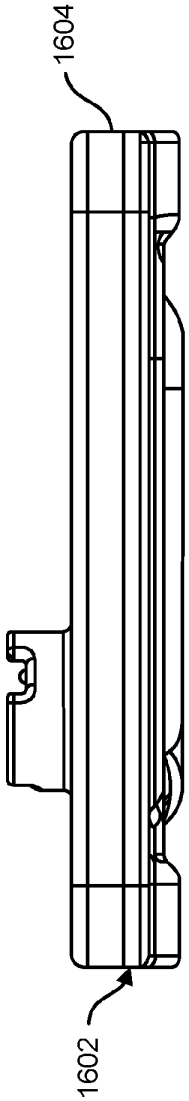


FIG. 16B

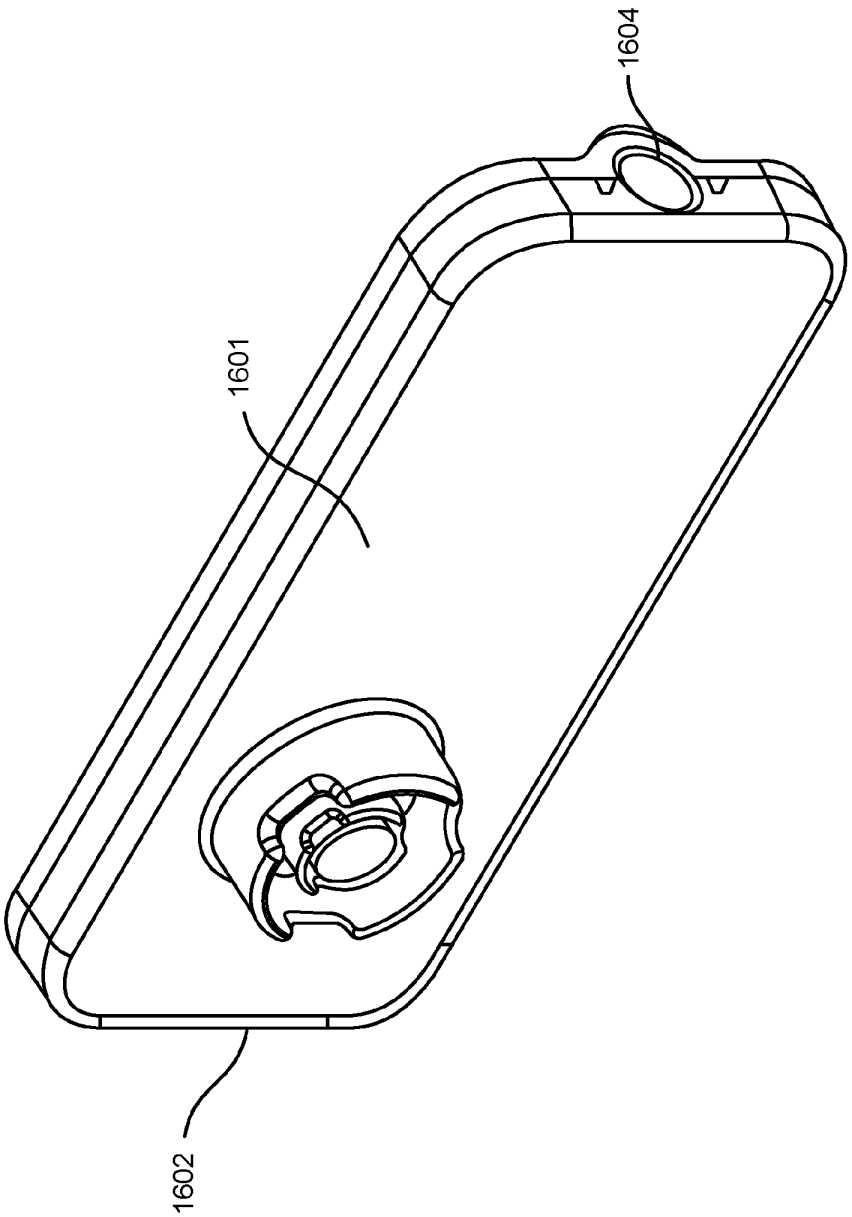


FIG. 16D

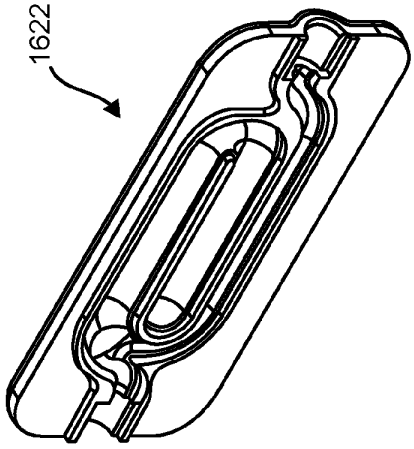


FIG. 17B



FIG. 17E

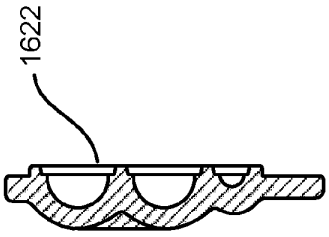


FIG. 17D

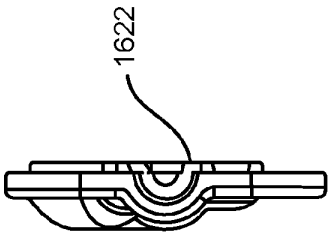


FIG. 17C

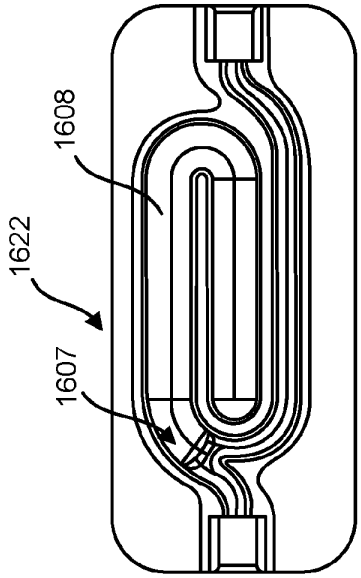


FIG. 17A

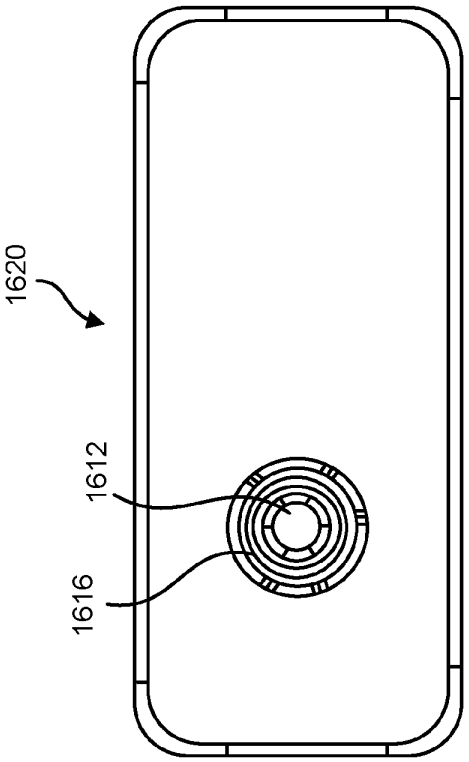


FIG. 18A

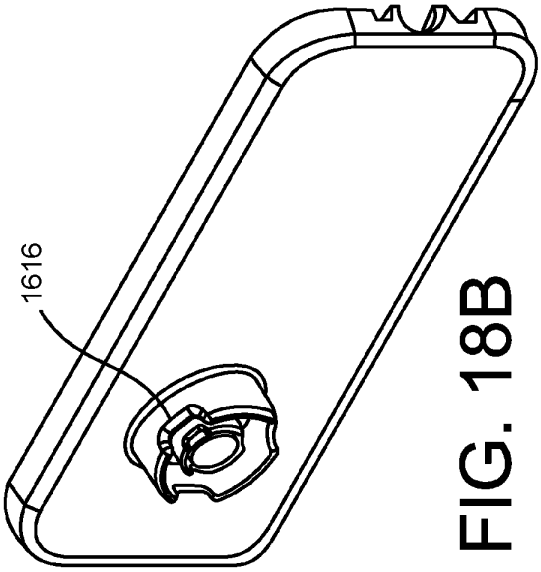


FIG. 18B



FIG. 18C

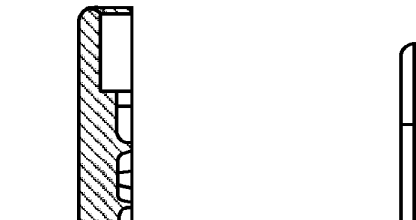


FIG. 18F

FIG. 18D

FIG. 18E

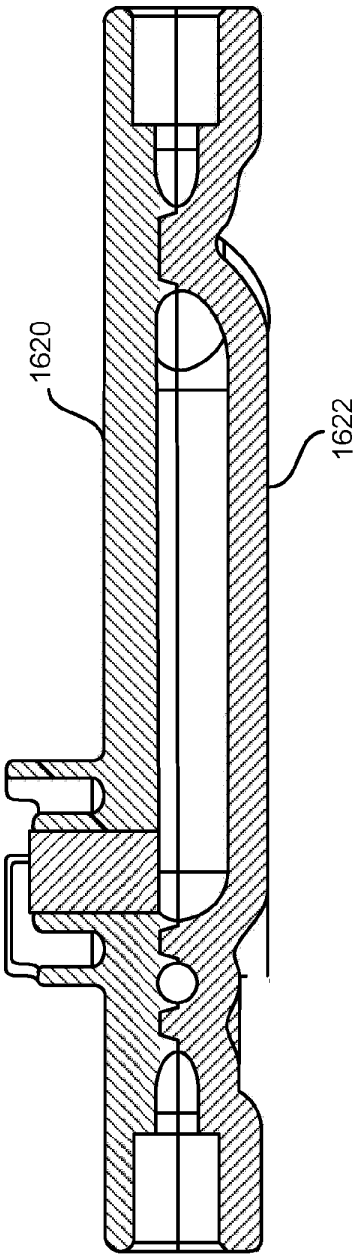


FIG. 19A

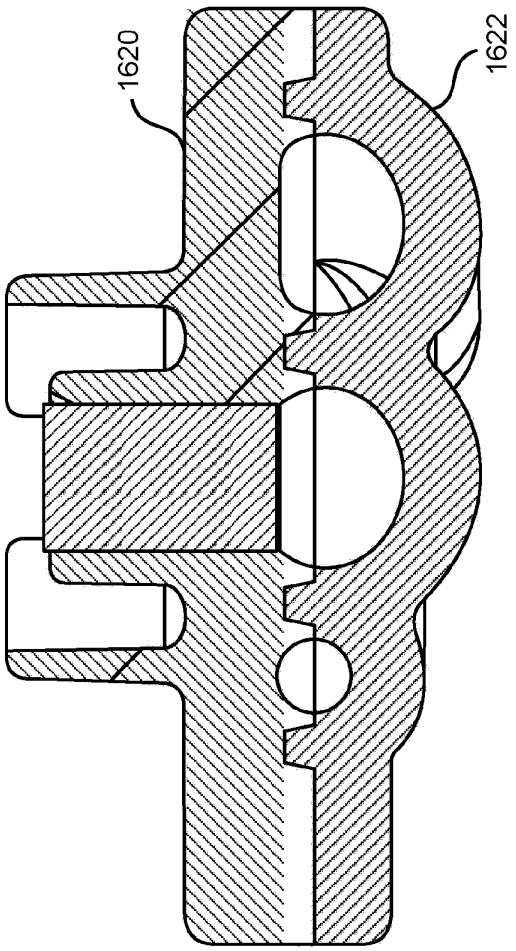


FIG. 19B

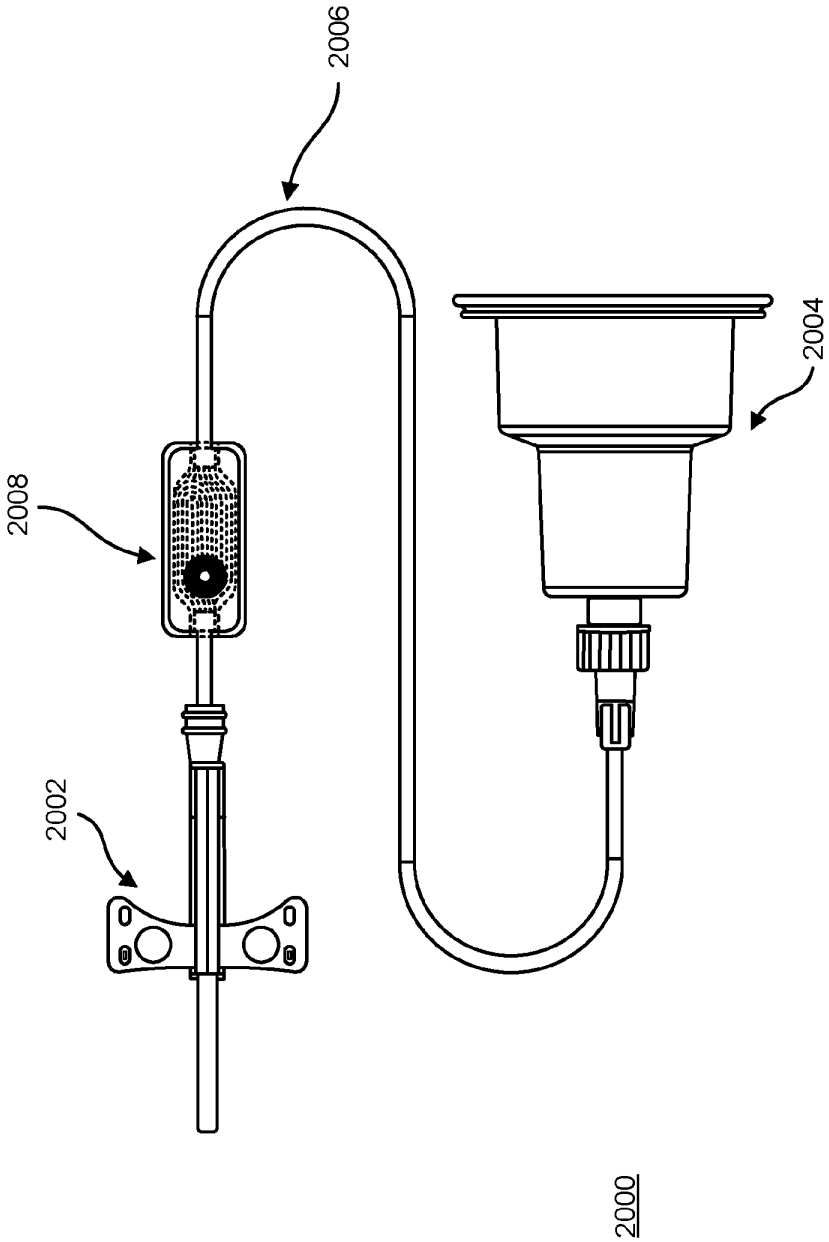


FIG. 20

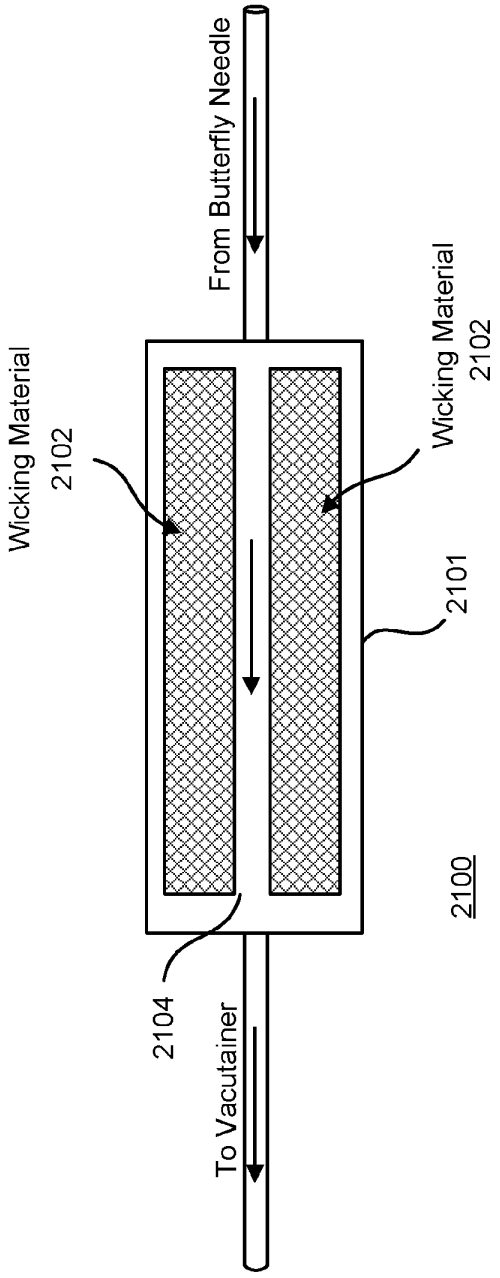

From Butterfly Needle
Wicking Material
2102
Wicking Material
2102
2101
2100
2104
To Vacutainer

FIG. 21

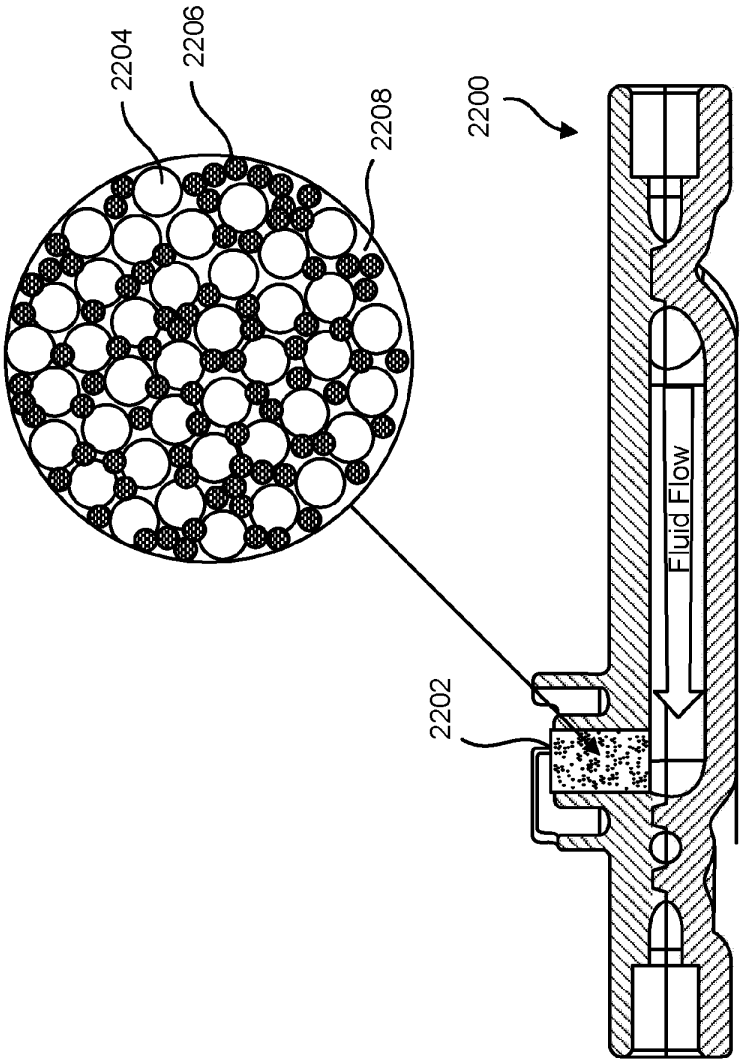


FIG. 22A

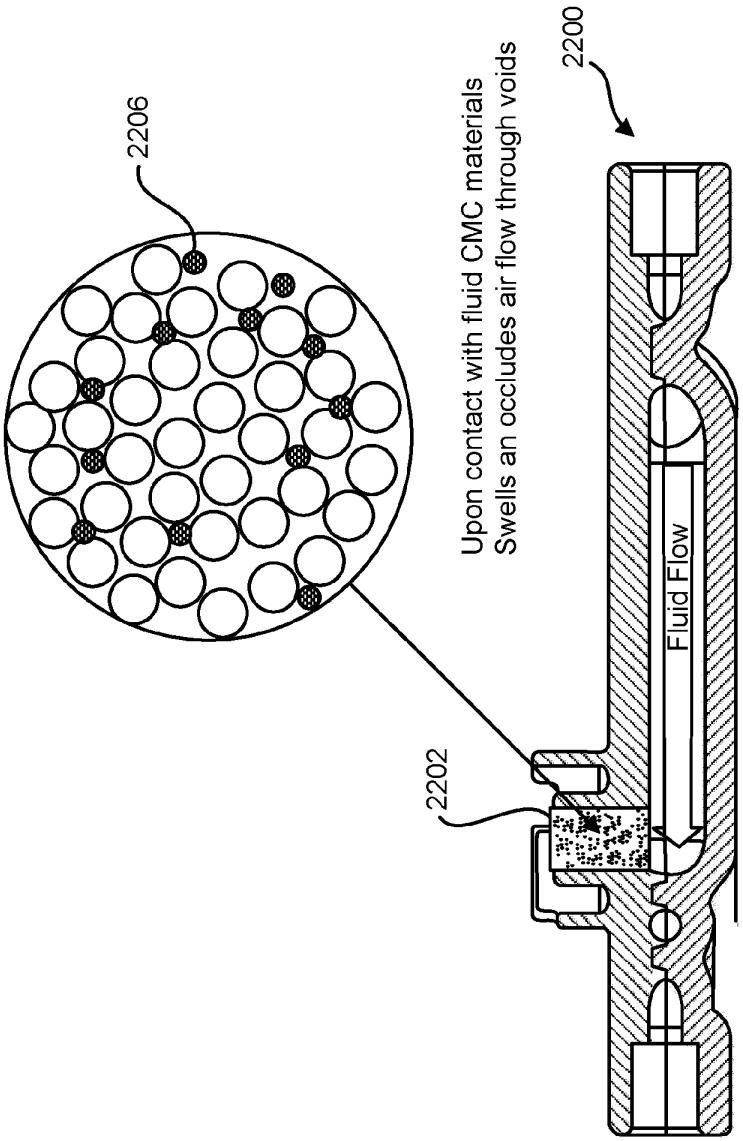

2206
2200
Upon contact with fluid CMC materials
Swells an occludes air flow through voids
Fluid Flow
2202

FIG. 22B

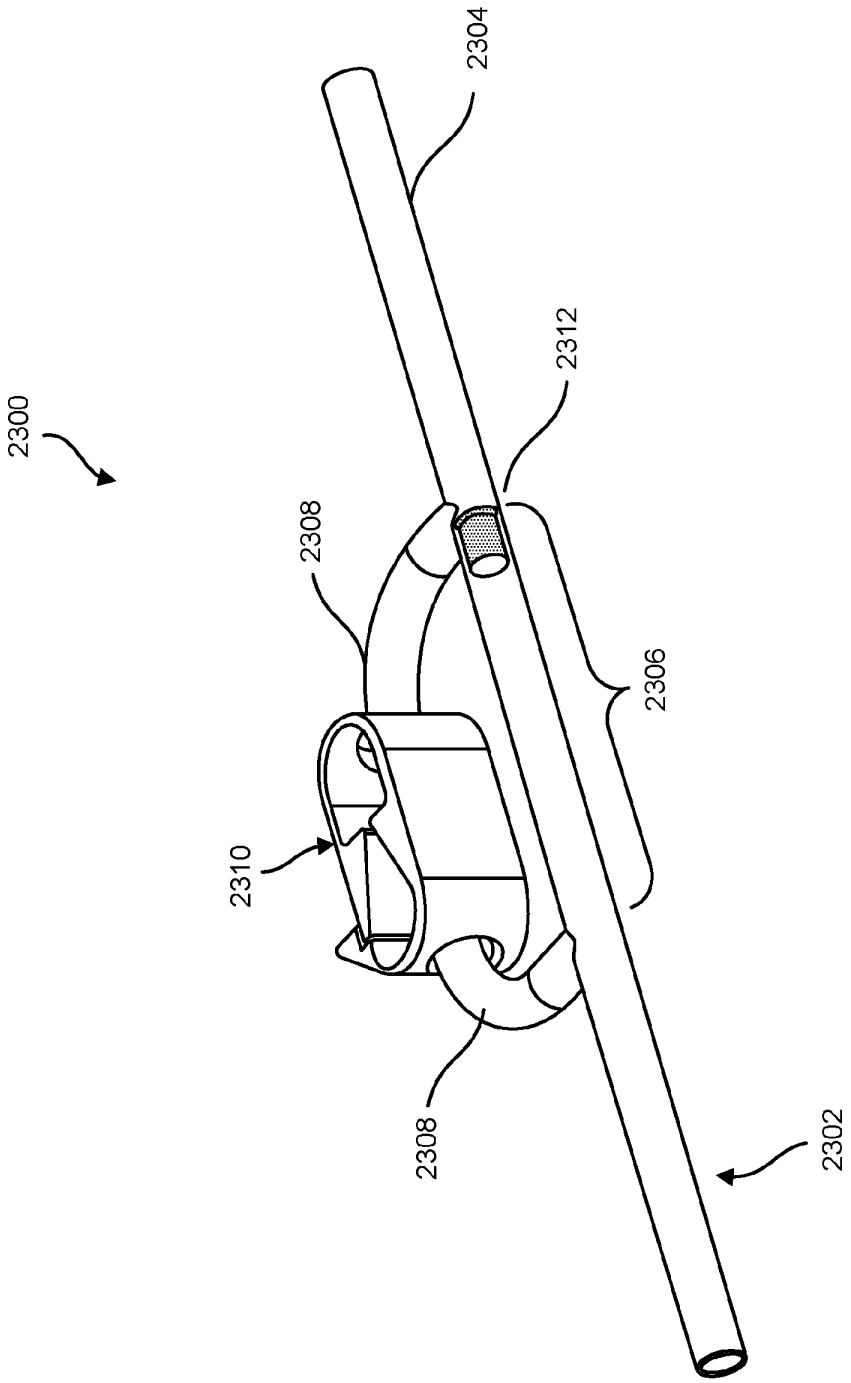


FIG. 23A

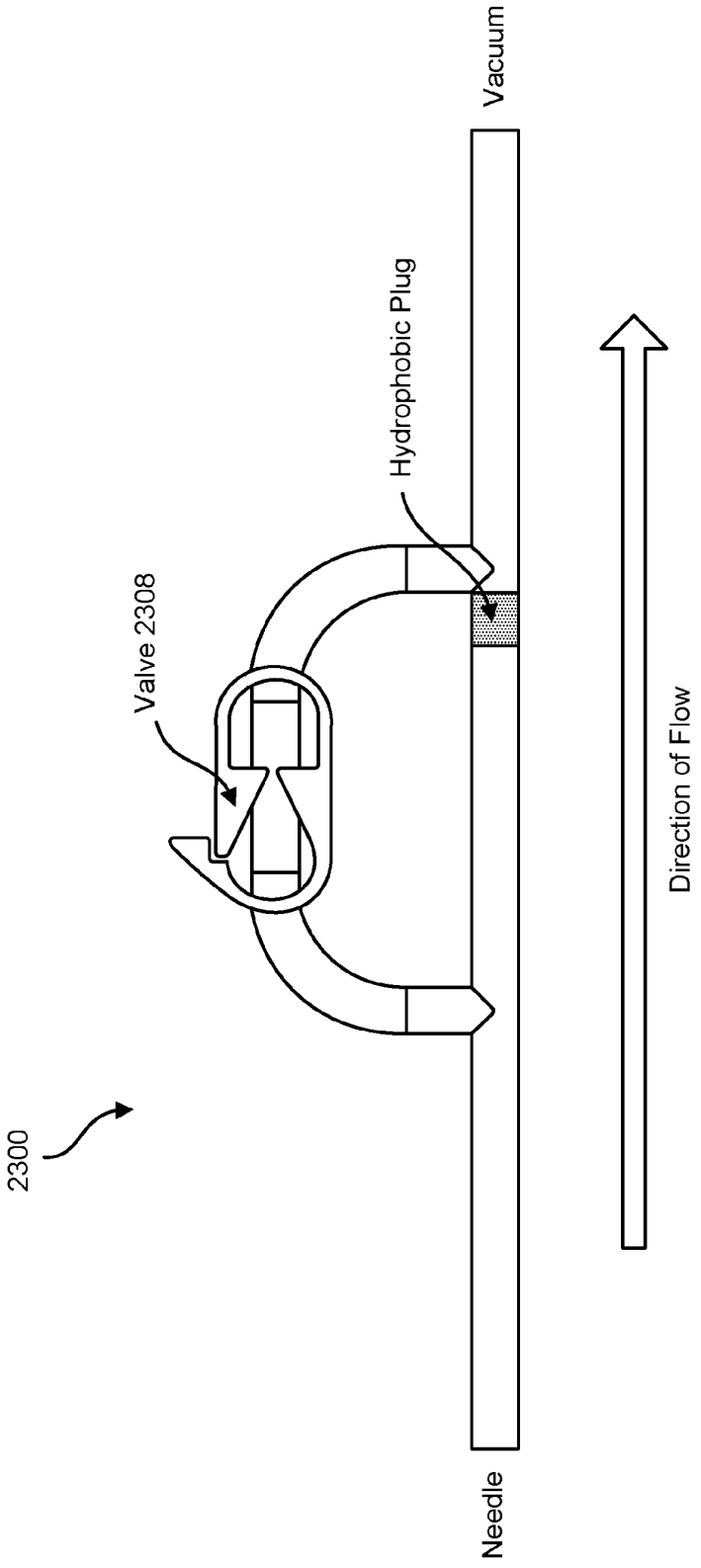

Vacuum
Hydrophobic Plug
Valve 2308
Direction of Flow
2300
Needle

FIG. 23B

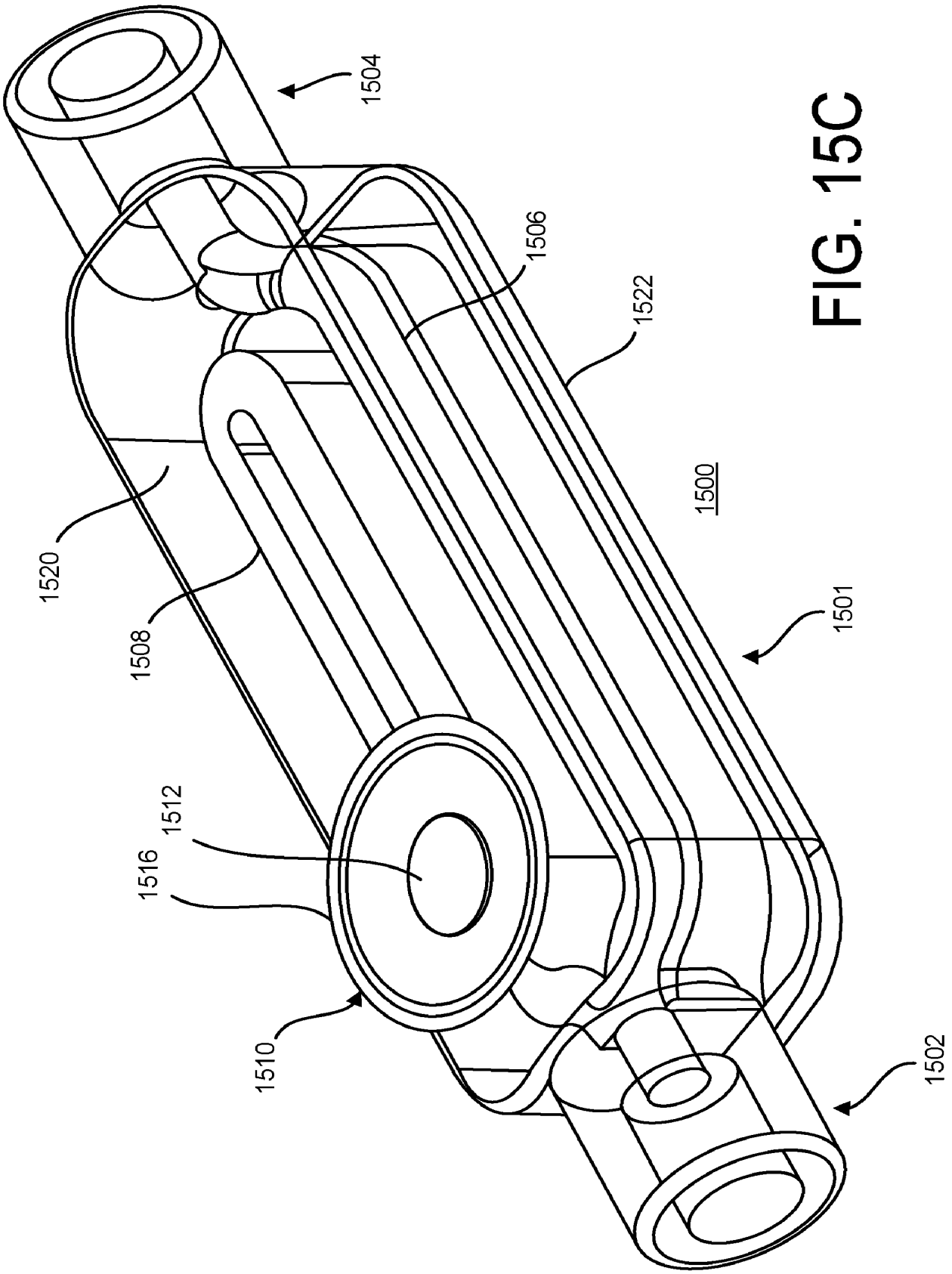


FIG. 15C

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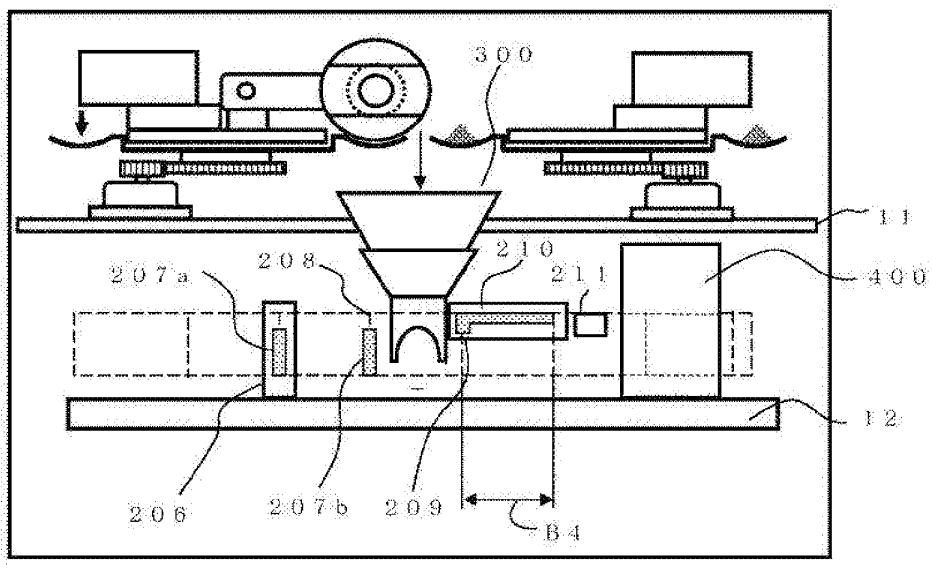
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(43) [Published date] January 9, 2020 (2020.1.9)
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(51) [International patent classification]
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B65B 61 /00 (2006.01)
B26F 1/18 (2006.01)
[FI]
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B65B 61/00
B26F 1/18
[Request for examination] Unclaimed
[Number of claims] 7
[Application form] OL
[Total number of pages]] 15

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(22) [Application date] June 26, 2018 (2018.6.26)
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[Identification number] 100107928
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[Name] Shigeyuki Yamamoto
(72) [Inventor]
[Name] Taku Yamamoto
(72) [Inventor]
[Name] Kunio Fukatsu
[Theme code (reference)]
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3E056
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4C047CC15
4C047JJ03
4C047JJ13
4C047JJ15
4C047JJ24
4C047JJ32
4C047JJ33
4C047JJ40

wrap up close

(57) [Summary]
[Problem] To provide a drug packaging device and a method for manufacturing a packaged dr ug that does not break at the perforated portion of the packaging paper during transportation. A packaging paper storage unit in which V-shaped packaging paper is wound, a transport path for pulling out and transporting the packaging paper from the packaging paper storage unit, a nd a transport path provided in the middle of the transportation path. a heat sealing unit that forms a heat seal for dividing the packaging paper into individual packages; and a drive roller for sandwiching and driving the packaging paper containing the medicine supplied by the med icine supply unit, and a driving roller provided downstream in the transportation direction of t he packaging paper from the driving roller, and the heat seal a perforation forming part for for ming perforations in the portion heat-sealed by the part.
[Selection drawing] Fig. 4



The scope of the claims open —

Claims:

1.

A packaging paper storage unit around which V-shaped packaging paper is wound, a transport path for pulling out and transporting the packaging paper from the packaging paper storage unit,

A heat seal portion provided in the middle of the transport path for forming a heat seal for dividing the packaging paper into individual packages

; A drug supply unit that supplies each package,

a drive roller that sandwiches and drives the packaging paper containing the drug supplied by the drug supply unit, and a downstream downstream of the drive roller in the transportation direction of the packaging paper

. and a perforation forming section provided in the heat-sealing section for forming perforations in the portion heat-sealed by the heat-sealing section

.

2.

The perforation 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

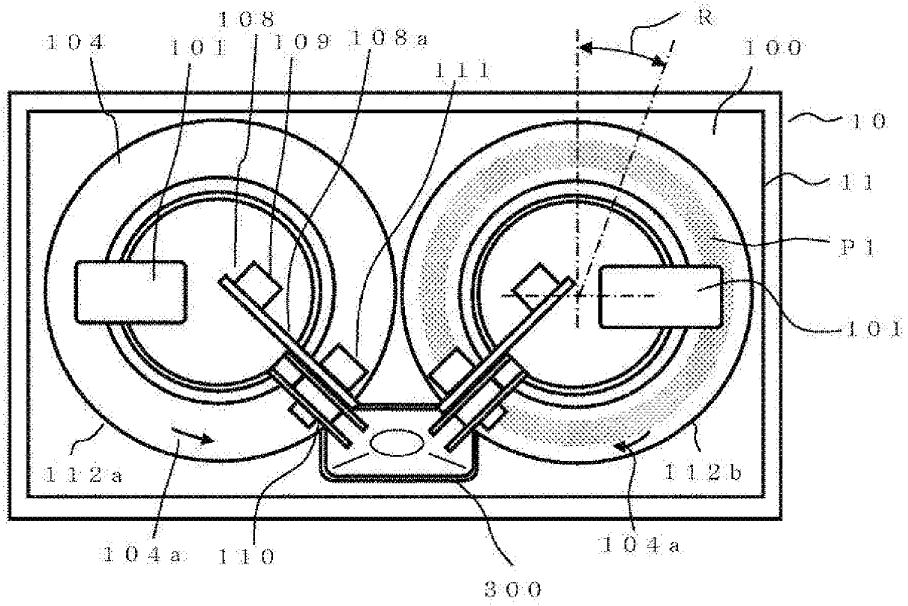
432c Perforating blade tip

B Packaging paper

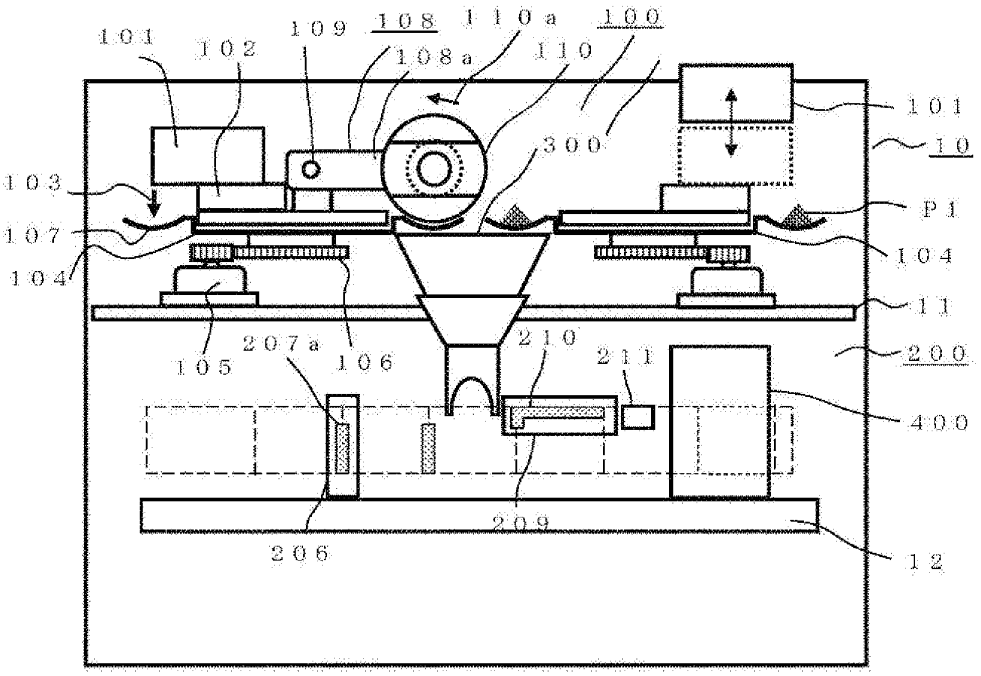
B2, B3 Conveyance path (conveyance path)

drawing open —

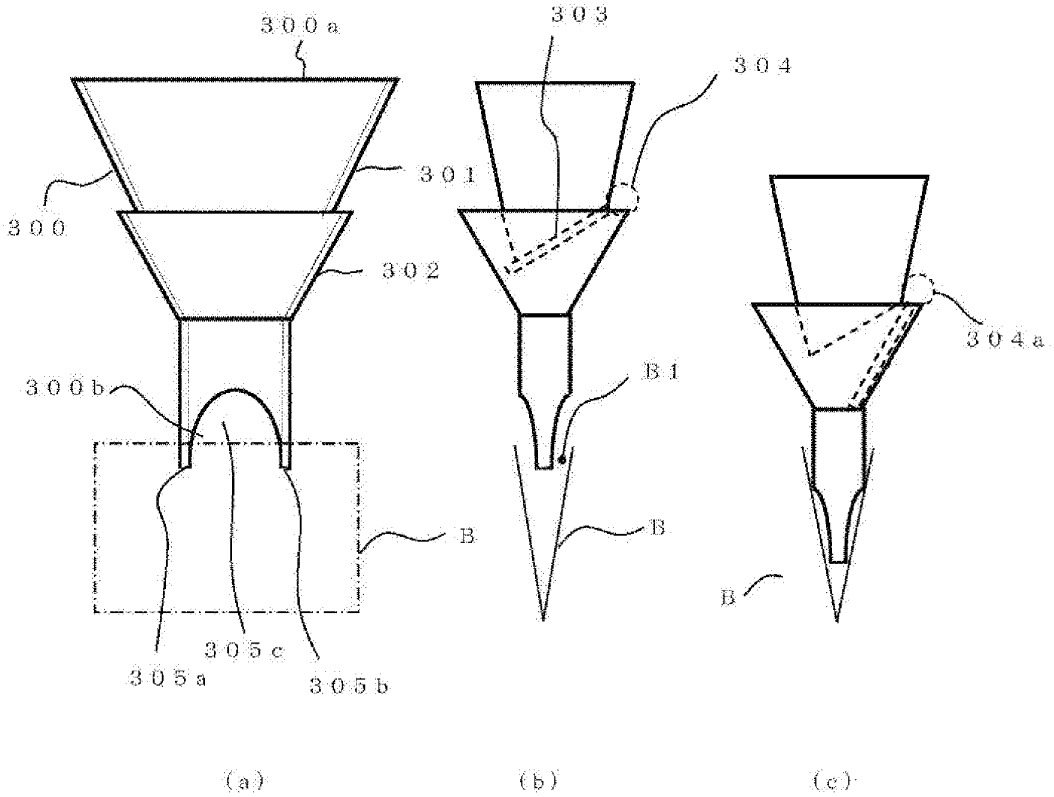
[Fig. 1]



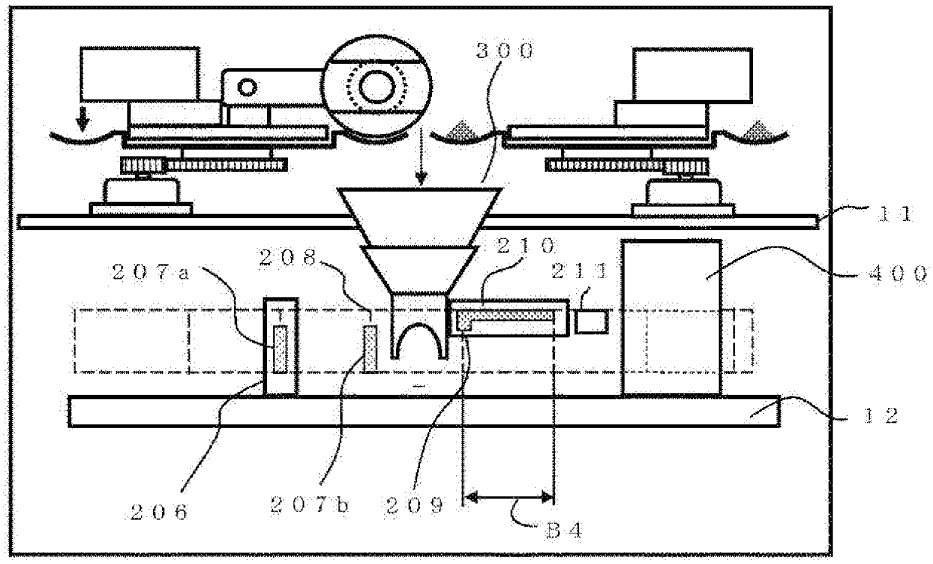
[Figure 2]



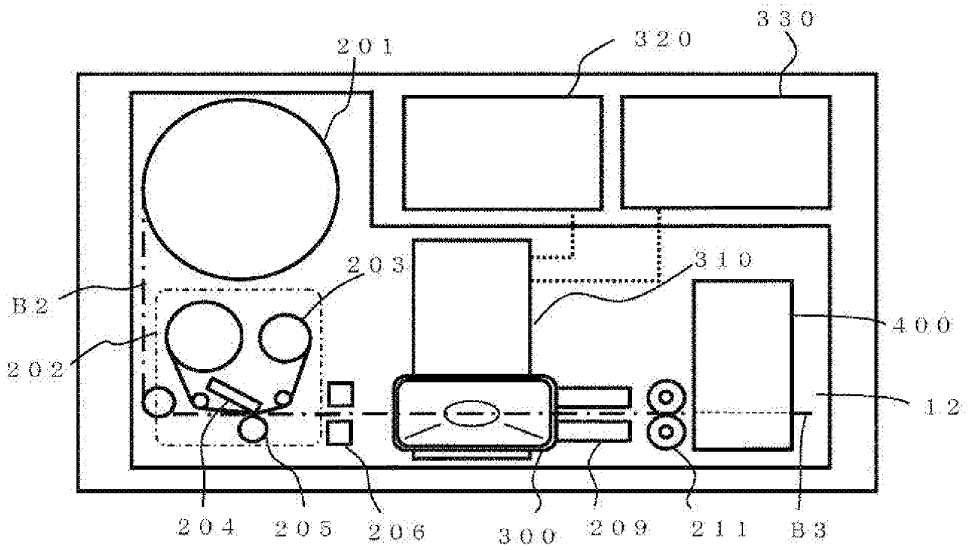
[Figure 3]



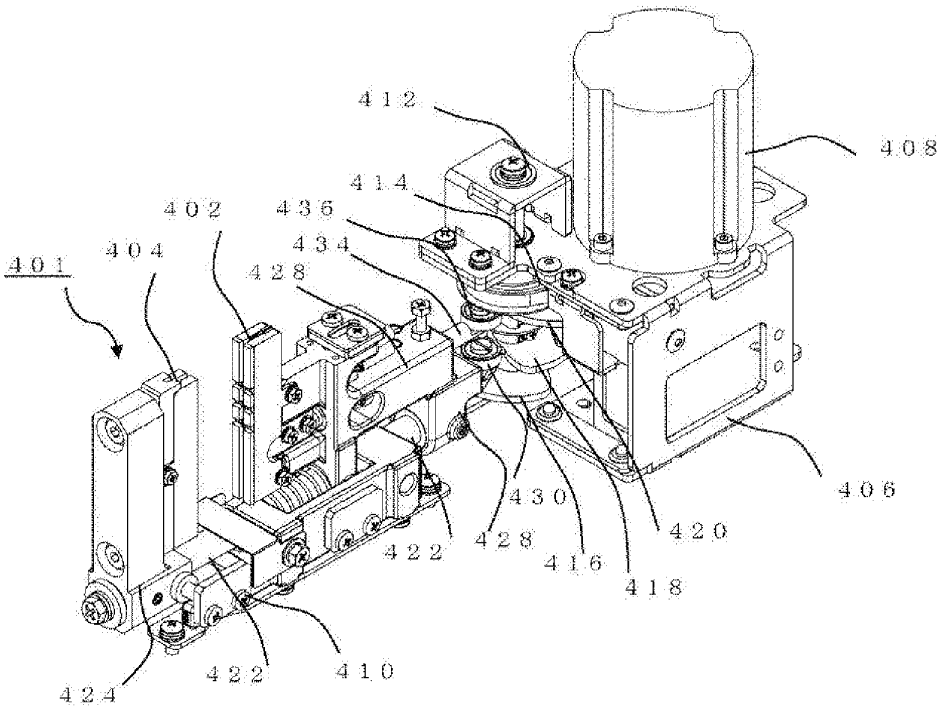
[Figure 4]



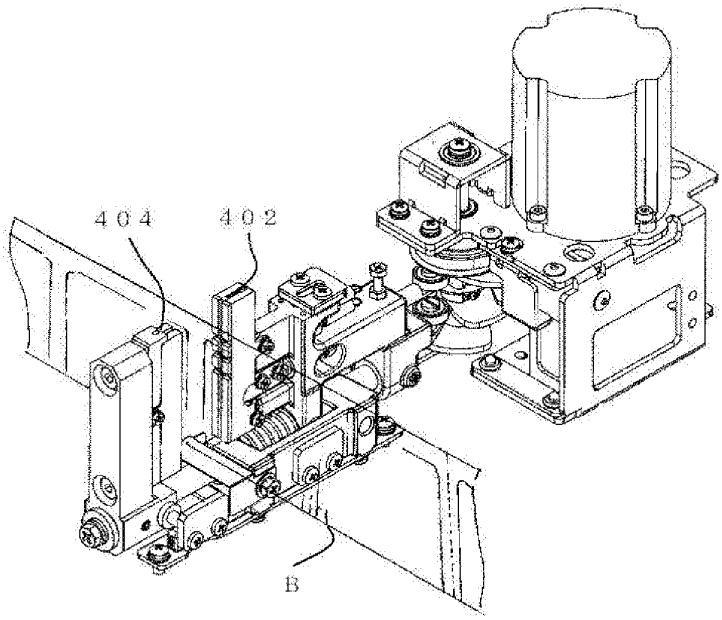
[Figure 5]



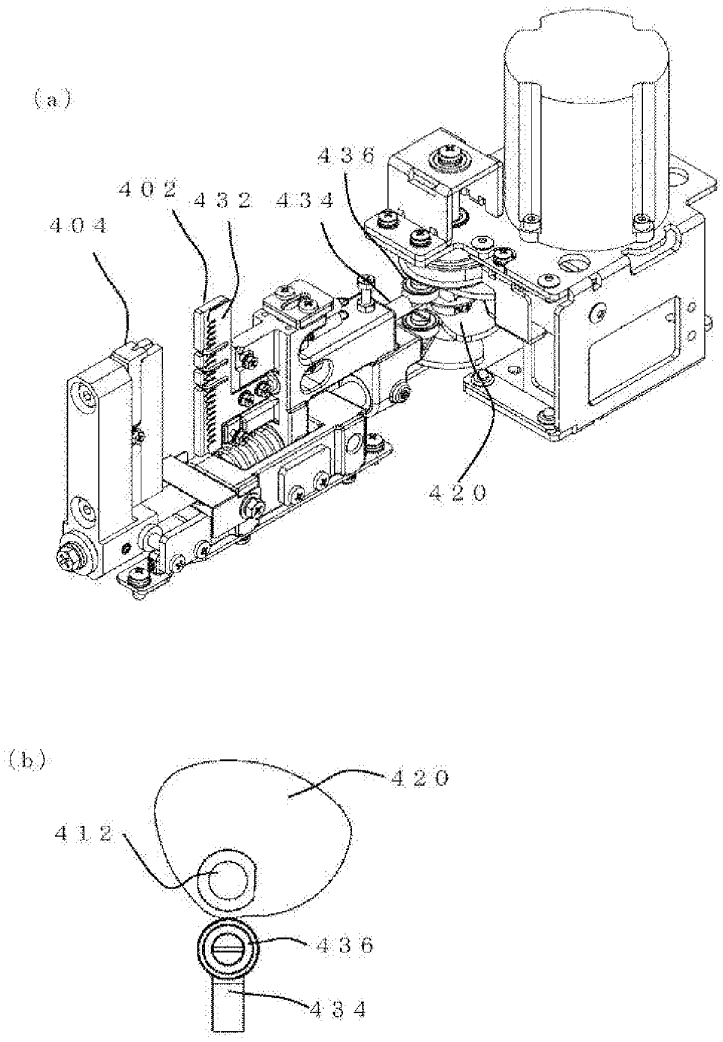
[Fig. 6]


412
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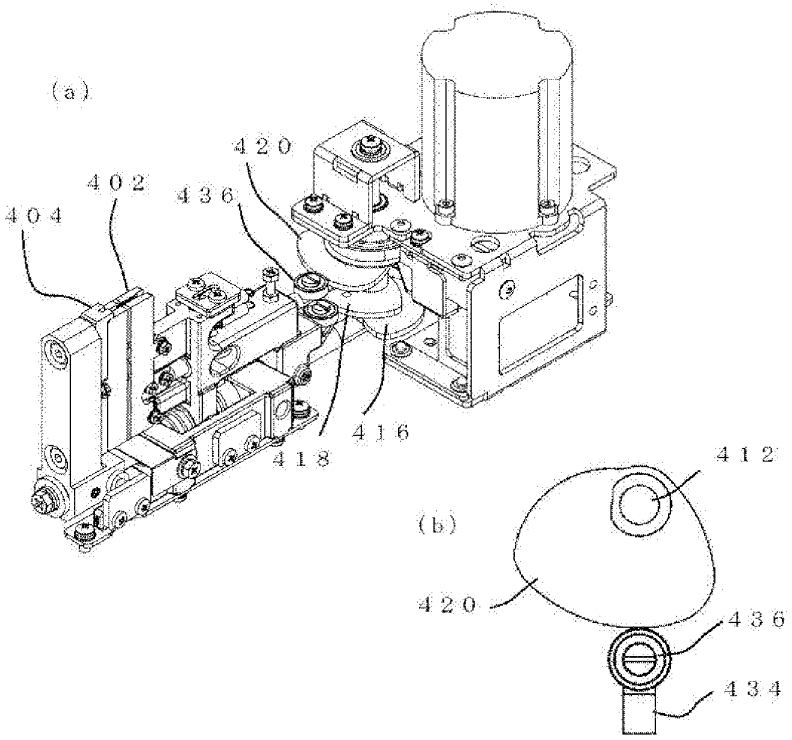
[Fig. 7]


404
402
B

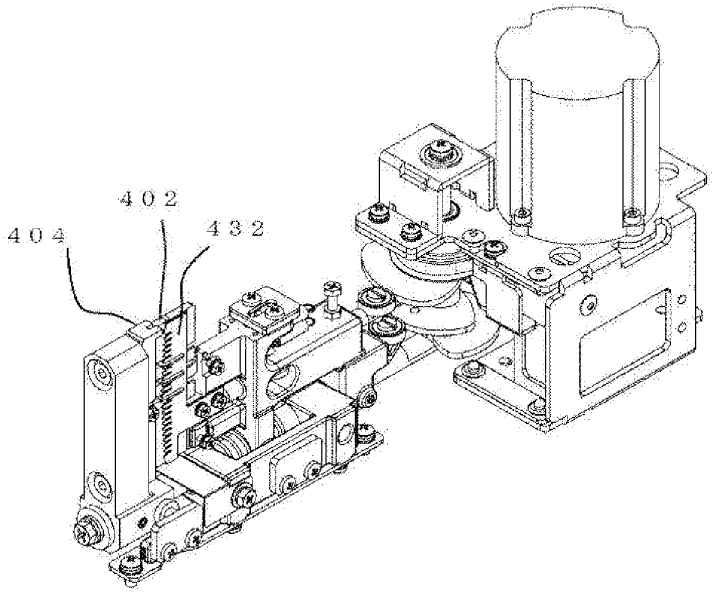
[Fig. 8]



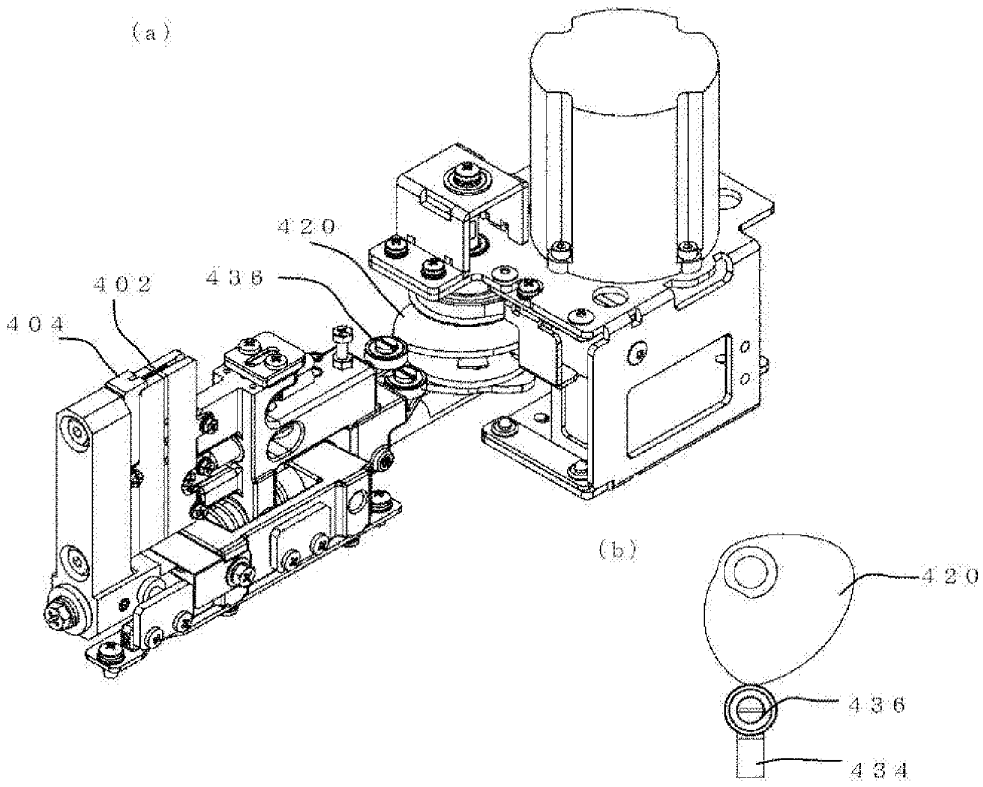
[Fig. 9]



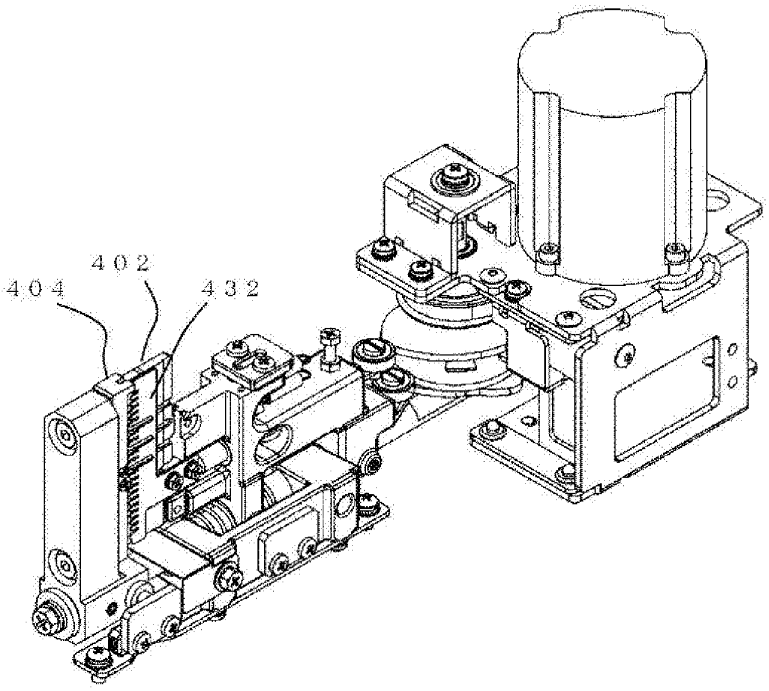
[Fig. 10]



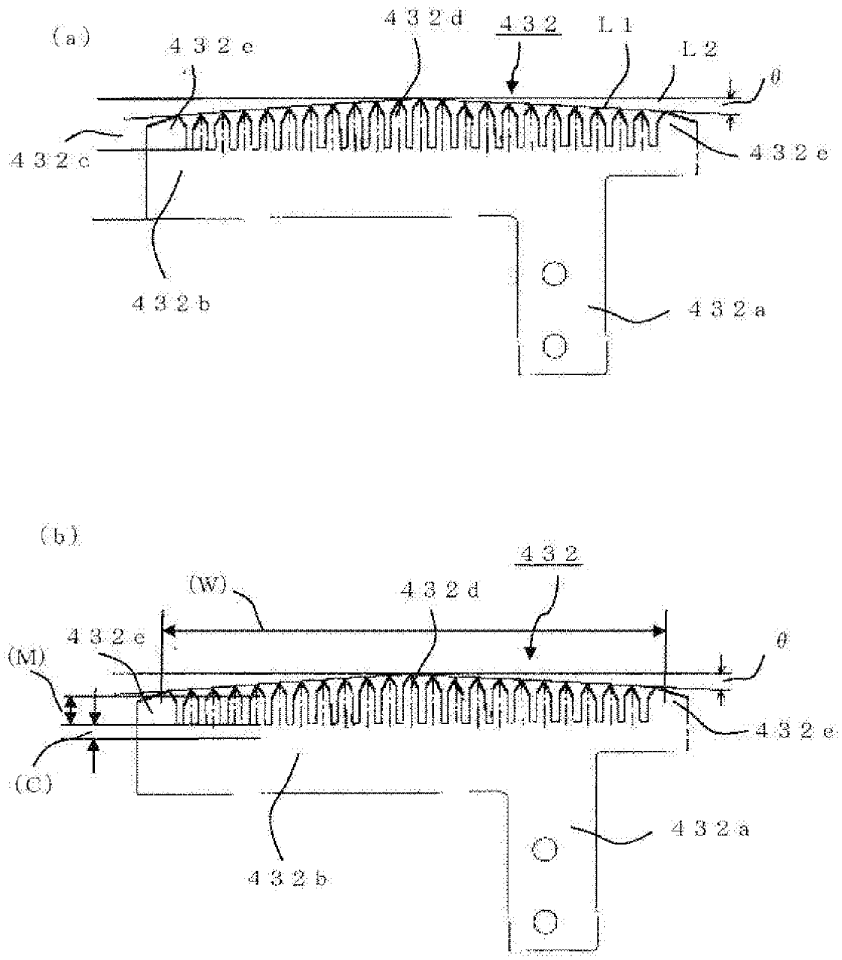
[Fig. 11]



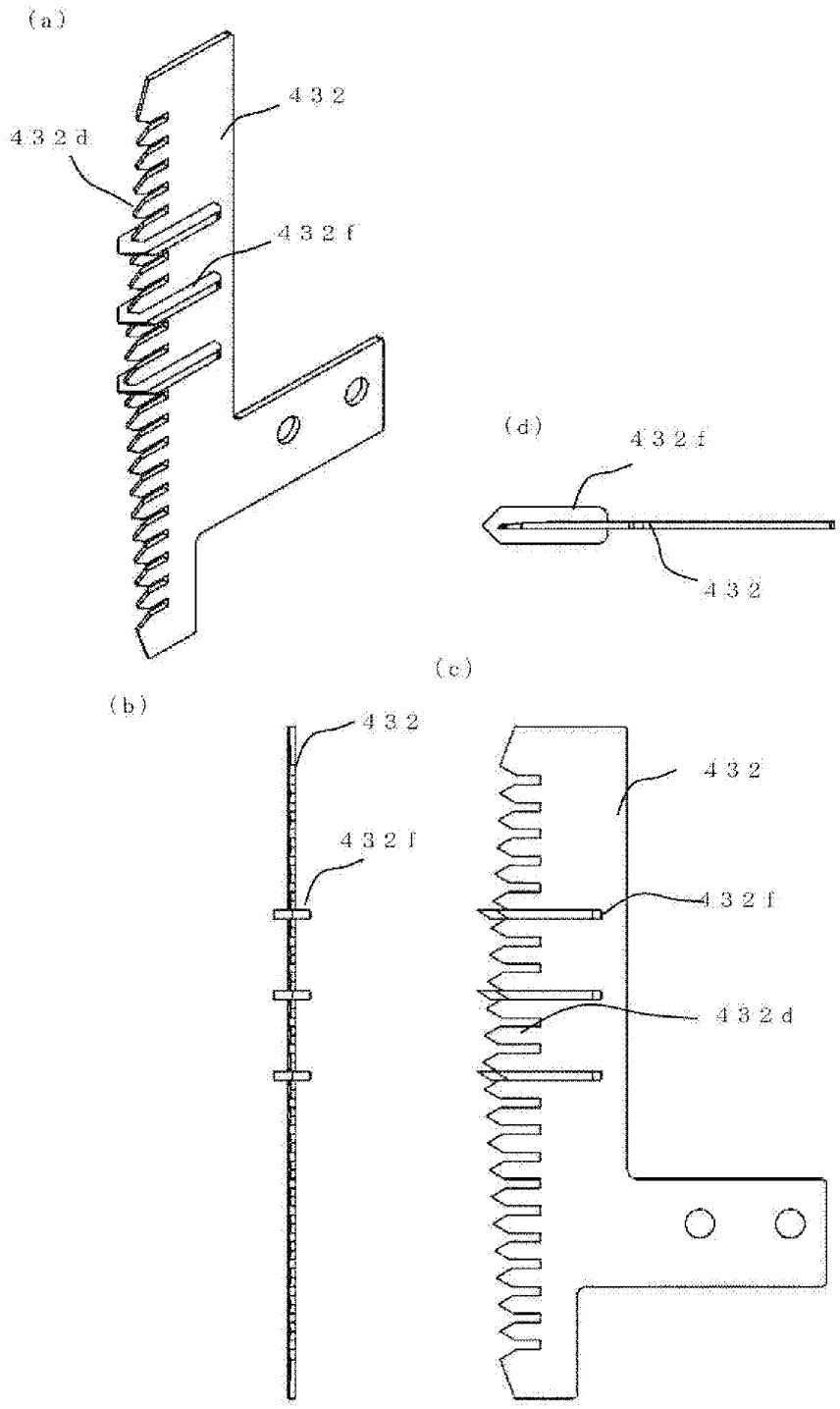
[Fig. 12]



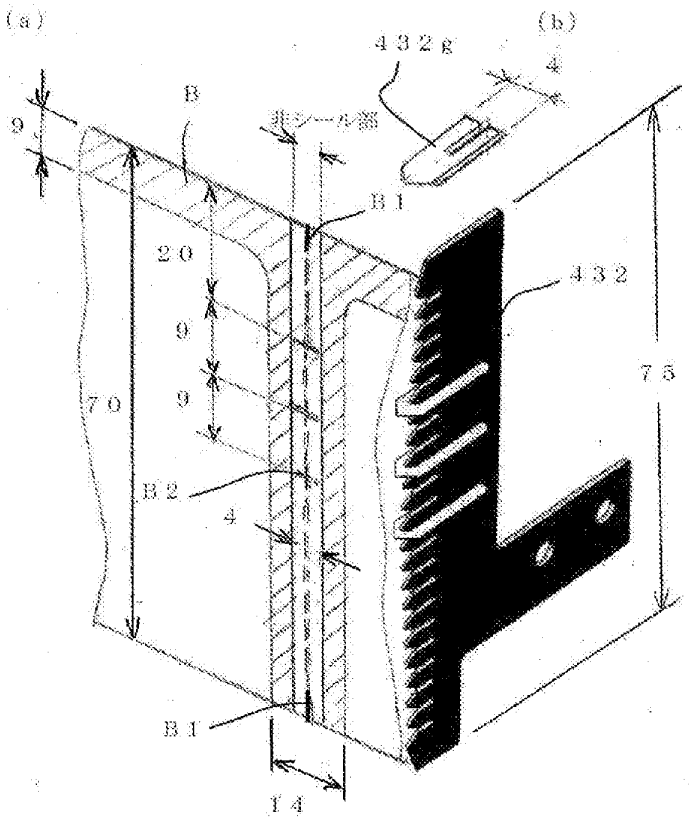
[Fig. 13]


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

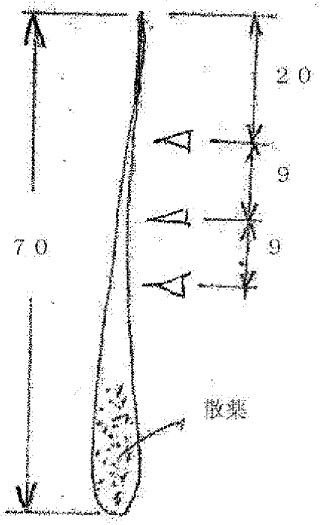
[Fig. 14]



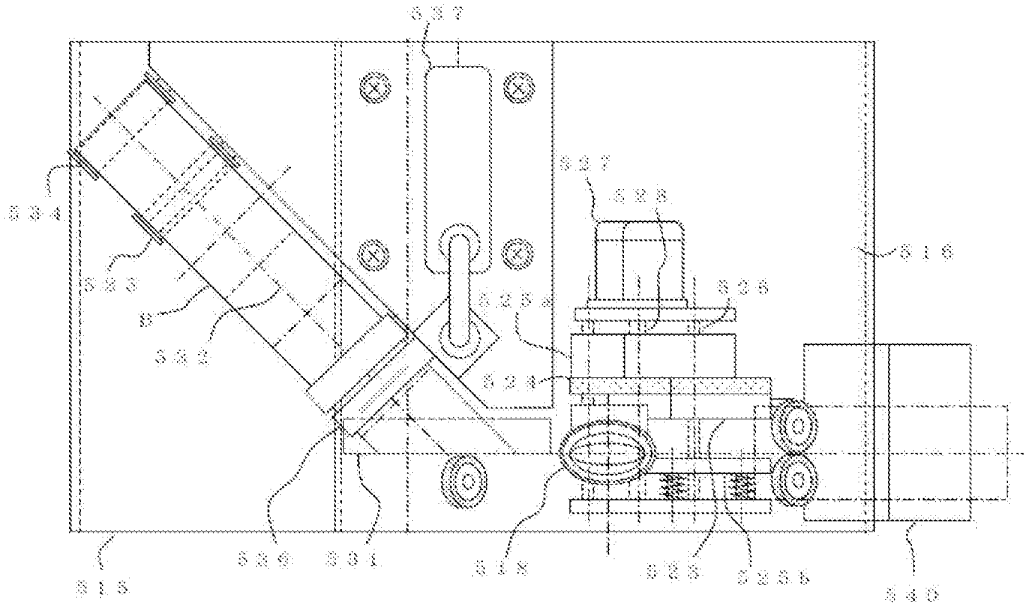
[Fig. 15]



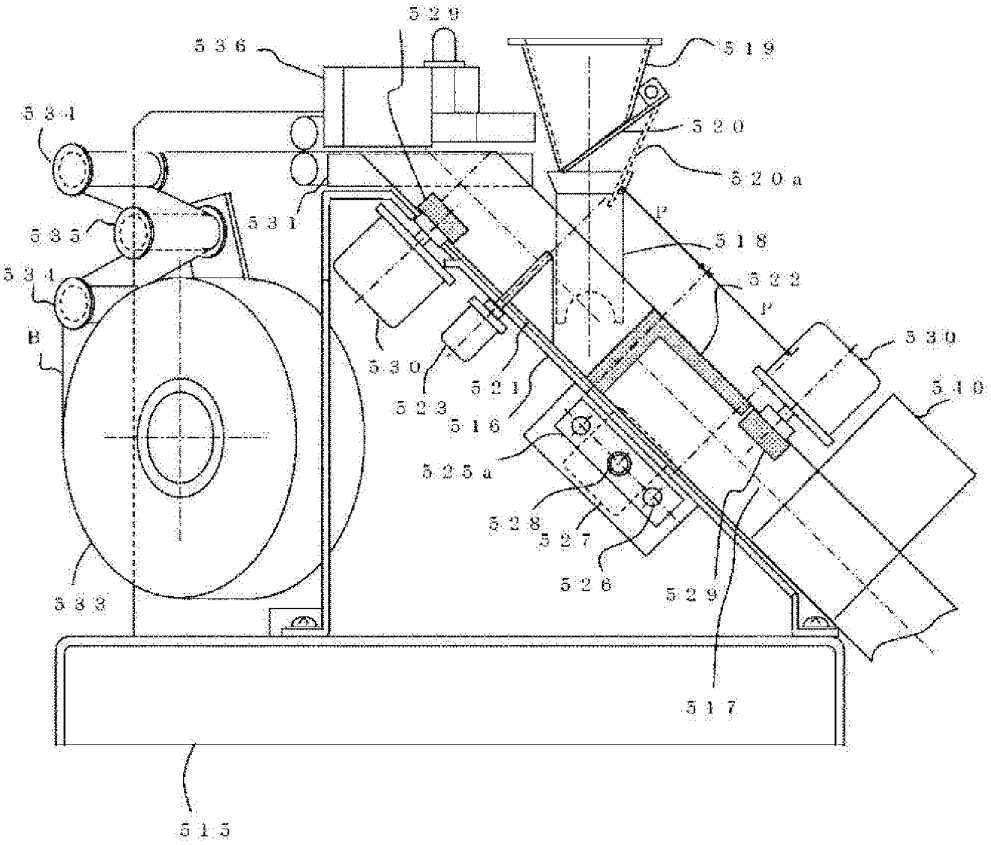
[Fig. 16]



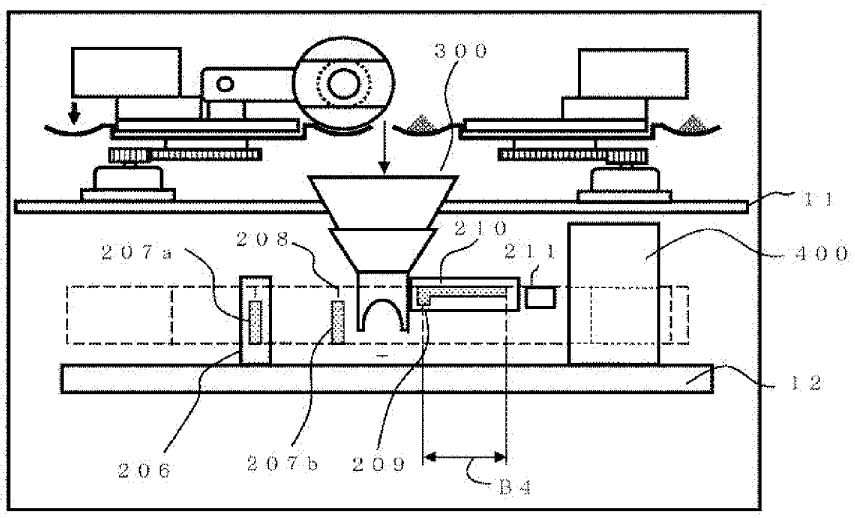
[Fig. 17]



[Fig. 18]



drawing	open	—



Representative drawing

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Espacenet

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

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

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Applicant(s): TOSHO INC ± (株式会社トーショー)

Classification: **- international:** ***A61J3/00; B65B61/00***
- cooperative:

Application number: JP20180120789 20180626 Global Dossier

Priority number(s): JP20180120789 20180626

Abstract of JP2020000340 (A)

To provide a medicine dispensing/packaging device that is never cut in a perforation portion of the dispensing/packaging paper during conveyance, and provide a production method of the dispensing/packaging medicine.SOLUTION: A medicine dispensing/packaging device has: a dispensing/packaging paper storage part where the V-folded dispensing/packaging paper is wound; a conveyance path for drawing the dispensing/packaging paper out of the dispensing/packaging paper storage part, and conveying it; a heat seal part provided in the middle of the conveyance path, and forming a heat seal to divide a dispensing/packaging paper into one package at a time; a medicine supplying part provided in the middle of the conveyance path, and supplying medicine by one package at a time between the dispensing/packaging papers; a drive roller for holding the dispensing/packaging paper where the medicine supplied by the medicine supplying part is stored, and performing conveyance drive; and a perforation making part provided at a conveyance direction down-stream of the dispensing/packaging paper from the drive roller, and forming the perforation in a portion heat-sealed by the heat seal part.SELECTED DRAWING: Figure 4

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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）

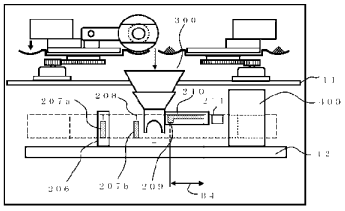
(21)出願番号　特願2018-120789 (P2018-120789)
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最終頁に続く

(54)【発明の名称】薬剤分包装置及び分包薬剤の製造方法

【要約】
【課題】搬送中に分包用紙のミシン目部分で切れることの無い薬剤分包装置及び分包薬剤の製造方法を提供する。
【解決手段】Ｖ字折りされた分包用紙が巻回された分包用紙収納部と、前記分包用紙収納部から分包用紙を引出して搬送する搬送路と、前記搬送路の途中に設けられ、前記分包用紙を１個包分ずつに区分するヒートシールを形成するヒートシール部と、前記搬送路の途中に設けられ、前記分包用紙間に薬剤を１包分ずつ供給する薬剤供給部と、前記薬剤供給部によって供給された薬剤が収納された分包用紙を挟持して搬送駆動する駆動ローラと、前記駆動ローラよりも前記分包用紙の搬送方向下流に設けられ、前記ヒートシール部によってヒートシールされた部分にミシン目を形成するミシン目作成部と、を有する。
【選択図】図４



【特許請求の範囲】
【請求項１】
Ｖ字折りされた分包用紙が巻回された分包用紙収納部と、
前記分包用紙収納部から分包用紙を引出して搬送する搬送路と、
前記搬送路の途中に設けられ、前記分包用紙を１個包分ずつに区分するヒートシールを形成するヒートシール部と、
前記搬送路の途中に設けられ、前記分包用紙間に薬剤を１包分ずつ供給する薬剤供給部と、
前記薬剤供給部によって供給された薬剤が収納された分包用紙を挟持して搬送駆動する駆動ローラと、
前記駆動ローラよりも前記分包用紙の搬送方向下流に設けられ、前記ヒートシール部によってヒートシールされた部分にミシン目を形成するミシン目作成部と、
を有する薬剤分包装置。
【請求項２】
前記ミシン目作成部は、
前記分包用紙の搬送路の一方の面側に設けられ、ミシン刃が突没自在に収納された刃収納部と、
前記分包用紙の搬送路の他方の面側に、前記刃収納部と対向して設けられ、前記刃収納部から突出した前記ミシン刃との間で前記分包用紙にミシン目を形成する刃受け部と、
前記刃収納部と前記刃受け部とをそれぞれ前記分包用紙側に移動させて分包用紙を挟持するように駆動する第１の駆動部と、
前記刃収納部と前記刃受け部とによって前記分包用紙を挟持した状態で、前記刃収納部のミシン刃を前記刃受け部側に突出するように駆動することにより前記分包用紙にミシン目を形成する第２の駆動部と、
を有する請求項１記載の薬剤分包装置。
【請求項３】
前記ミシン刃は、
基部と、
前記基部から突出して設けられ、先端に山形の刃先が形成された複数の刃片が、隣接する刃片との間に所定の間隔を設けて形成された刃先部と、を有し、
前記第２の駆動部は、
前記ミシン刃の刃片の途中まで前記刃受け部側に突出させることにより、前記分包用紙にミシン目を形成し、
前記ミシン刃の基部まで前記刃受け部側に突出させることにより、前記分包用紙を切断する、
ことを特徴とする請求項２記載の薬剤分包装置。
【請求項４】
前記ミシン刃は、
前記分包用紙の搬送方向と直交する方向の両端部の刃片の刃の幅が内側の刃片の刃の幅よりも大きく形成され、これら両端部の刃片により分包用紙の搬送方向と直交する方向の両端部に切断開始部を形成する、
ことを特徴とする請求項３記載の薬剤分包装置。
【請求項５】
前記ミシン刃は、
前記それぞれの刃片が、中央部の刃片の基部からの長さが最も長く、端部に行くにつれて長さが徐々に短くなるように形成された、
ことを特徴とする請求項３又は請求項４記載の薬剤分包装置。
【請求項６】
前記ミシン刃は、
前記複数の刃片と刃片との間に、前記刃片の厚さよりも刃幅の広い横刃片を挿入するこ

とにより、十字状の刃を複数形成し、この十字状の刃により分包用紙に形成されるミシン目に、ミシン目に沿って分離されたときの切断開始部を形成する、
ことを特徴とする請求項３乃至請求項５のいずれか１項記載の薬剤分包装置。
【請求項７】
予め収納されたＶ字折りされた分包用紙を搬送路に引出し、
前記引出された分包用紙に１個包分ずつに区分するヒートシール部を形成し、
前記ヒートシール部が形成された分包用紙間に薬剤を１個包分ずつ供給して収納し、
前記薬剤が収納された分包用紙を駆動ローラにより挟持して１個包分ずつ搬送駆動し、
前記駆動ローラよりも前記分包用紙の搬送方向の下流側で、前記分包用紙のヒートシールされた部分にミシン目を形成する、
分包薬剤の製造方法。
【発明の詳細な説明】
【技術分野】
【０００１】
本発明は、薬剤を１個包分ずつ供給して分包する薬剤分包装置及び分包薬剤の製造方法に関する。
【背景技術】
【０００２】
薬剤調剤業務の自動化のために薬剤分包装置が開発され実用に供している。このような薬剤分包装置の例として特許文献１記載のものがある。
【０００３】
すなわち、Ｖ字折りされた分包用紙が巻回されたロールから、分包用紙の端部が引出され、複数の支持軸を介して搬送方向に向かって下方に傾斜した搬送路に沿って搬送され、漏斗状の薬剤ホッパ部に供給される。薬剤ホッパよりも下流側には、熱圧接部が設けられており、この熱圧接部にはヒートシール及びミシン目形成部が設けられている。そして、ヒートシールによって１個包を分離するＴ字形状のヒートシールが成されるとともに、各個包に分離するためのミシン目が形成される。ヒートシールが成された後に１個包分の薬剤が薬剤ホッパから分包用紙間に供給される。
【０００４】
薬剤が供給されると、熱圧接部よりも下流側に設けられた駆動ローラによって分包用紙が挟持されて１個包分の長さだけ引き出されて、次の個包のためのヒートシールとミシン目の作成が行われる。このような個包化動作を繰返すことによって１処方分の分包薬剤が作成される。
【先行技術文献】
【特許文献】
【０００５】
【特許文献１】特開２０１２－１３１５５１号公報
【発明の概要】
【発明が解決しようとする課題】
【０００６】
特許文献１記載の装置では、分包用紙を搬送する駆動ローラがミシン目作成部よりも下流側に設けられている。このため、駆動ローラによって分包用紙を引出した際に、分包用紙に過大な負荷が掛かるとミシン目部分で分包用紙が切れてしまうという虞があった。また、分包用紙間の下部には薬剤が封入されているので駆動ローラは必然的に分包用紙の上方を挟持して搬送する必要がある。搬送中に分包用紙が切れないようにするためには、分包用紙の上端にはミシン目（カット）を入れることができない。その結果、老人や筋力の衰えた人は上端側からミシン目に沿って切り取ることが困難であるという問題もあった。
【０００７】
そこで従来の分包機では、用紙の下端にミシン目（カット）を入れて、下側から切り取るようにする場合もあったが、これでは都度分包用紙を逆さにする必要があり、そのとき

に印字の向きが逆になって視認性が悪く、さらに切り取った後、もう一度逆さに元の状態にして、手で横方向に切って開封する必要があり、その不便さが指摘されていた。
【０００８】
本発明が解決しようとする課題は、搬送中に分包用紙のミシン目（カット）部分で切れることの無いようにした薬剤分包装置及び分包薬剤の製造方法を提供することを目的とする。また、第２の課題は、服用者が１個包をミシン目に沿って切断するのが容易なように分包用紙の上端部側にミシン目（カット）が入れられることのできる服用者にとって利便性の高い薬剤分包装置及び分包薬剤の製造方法を提供することを目的とする。
【０００９】
さらに、副次的な効果としては、このように分包用紙の上下端にミシン目（カット）を設けることで、長い分包用紙を例えば１日３包（朝・昼・晩）ごとに折りたたんで保管するような場合に、その折り目がしっかり付けやすいので、全て折りたたんだときの外観がきちんとしているという点も上げておきたい。
【課題を解決するための手段】
【００１０】
本発明の薬剤分包装置は、Ｖ字折りされた分包用紙が巻回された分包用紙収納部と、前記分包用紙収納部から分包用紙を引出して搬送する搬送路と、前記搬送路の途中に設けられ、前記分包用紙を１個包分ずつに区分するヒートシールを形成するヒートシール部と、前記搬送路の途中に設けられ、前記分包用紙間に薬剤を１包分ずつ供給する薬剤供給部と、前記薬剤供給部によって供給された薬剤が収納された分包用紙を挟持して搬送駆動する駆動ローラと、前記駆動ローラよりも前記分包用紙の搬送方向下流に設けられ、前記ヒートシール部によってヒートシールされた部分にミシン目を形成するミシン目作成部と、を有する。
【００１１】
また、本発明の分包薬剤の製造方法は、予め収納されたＶ字折りされた分包用紙を搬送路に引出し、前記引出された分包用紙に１個包分ずつに区分するヒートシール部を形成し、前記ヒートシール部が形成された分包用紙間に薬剤を１個包分ずつ供給して収納し、前記薬剤が収納された分包用紙を駆動ローラにより挟持して１個包分ずつ搬送駆動し、前記駆動ローラよりも前記分包用紙の搬送方向の下流側で、前記分包用紙のヒートシールされた部分にミシン目を形成する。
【図面の簡単な説明】
【００１２】
【図１】実施形態の散薬自動分包機の円盤配分部の平面の断面図。
【図２】実施形態の散薬自動分包機の落下ホッパの上昇位置を示す正面の断面図。
【図３】落下ホッパの構造と動作概要を示す図。
【図４】実施形態の散薬自動分包機の落下ホッパの下降位置を示す正面の断面図。
【図５】実施形態の散薬自動分包機の印刷包装機部の平面の断面図。
【図６】実施形態のミシン目作成装置の斜視図で、刃収納部と刃受け部とが開いた状態を示す図。
【図７】実施形態のミシン目作成装置の斜視図で、刃収納部と刃受け部との間に分包用紙が搬送されている状態を示す図。
【図８】実施形態のミシン目作成装置の斜視図で、刃収納部と刃受け部とが開いた状態で刃収納部のカバーを外した図。
【図９】実施形態のミシン目作成装置の斜視図で、刃収納部と刃受け部とが閉じてミシン目を作成している状態を示す図。
【図１０】実施形態のミシン目作成装置の斜視図で、刃収納部と刃受け部とが閉じてミシン目を作成している状態の刃収納部のカバーを外した図。
【図１１】実施形態のミシン目作成装置の斜視図で、刃収納部と刃受け部とが閉じて分包用紙を切断している状態を示す図。
【図１２】実施形態のミシン目作成装置の斜視図で、刃収納部と刃受け部とが閉じて分包

用紙を切断している状態の刃収納部のカバーを外した図。
【図１３】実施形態のミシン目作成装置のミシン刃の形状と移動距離を説明するための図。
【図１４】実施形態のミシン目作成装置のミシン刃の形状を説明するための図。
【図１５】実施形態のミシン目作成装置のミシン刃の形状と分包用紙との関係を説明するための図。
【図１６】実施形態の散薬自動分包機で製造された分包薬剤の例を示す図。
【図１７】第２の実施形態の印刷包装機を説明するための平面図。
【図１８】第２の実施形態の印刷包装機を説明するための正面図。
【発明を実施するための形態】
【００１３】
以下、実施形態に係る散薬自動分包機を、図面を用いて説明する。
以下の説明では散薬自動分包機を例にとって説明するが、本発明は散薬自動分包機に限定されるものではなく、錠剤自動分包機にも適用可能である。また、特許第６２５５５２８号公報や特開２０００－２４０８７号公報に記載されたような複数の薬剤を１つの個包に分包する薬剤分包装置にも適用可能なことは勿論である。
【００１４】
図１は本実施形態の散薬自動分包機の平面図、図２は散薬自動分包機の正面図である。筐体１０の中間台１１の上部には薬剤供給部である円盤配分部１００、中間台１１の下部には、薬剤包装部である印刷包装機２００が配置されている。また３００は落下ホッパであって、円盤配分部１００から放出される散薬をこの落下ホッパ３００の内面側を通して、印刷包装機２００側に導入する働きをなすものである。
【００１５】
円盤配分部１００には２組の配分部が設けられている。円盤配分部１００において、１０１は着脱自在な散薬カセットで、事前に別の場所で、当該処方に必要な分量の散薬が装填され、係員の手動操作か、図示しないロボットアーム等の自動装置によって、別の棚から振動台１０２に載置される。振動台１０２は、図示しない電磁石などによって振動を発生させ、この振動力を散薬カセット１０１に伝達させることで、散薬カセット１０１内の散薬を振動輸送し、矢印１０３の方向に散薬を少量ずつ落下させるものである。
【００１６】
１０４は水平に配置された配分円盤で、大きな円輪がステッピング・モータ１０５によって、歯車１０６を介して矢印１０４ａ方向に回転させられるようになっている。さらに配分円盤１０４の外周方向の上面には円弧状凹面１０７を形成していている。ここで、ステッピング・モータ１０５を連続的に回転しながら、振動台１０２を駆動すると、散薬が配分円盤１０４の円弧状凹面１０７に少量ずつ落下して、ドーナツ状の散薬の山Ｐ１を形成することができる。この動作を「円周撒き動作」と呼ぶこととする。
【００１７】
また、１０８は掻き出しディスク部で、レバー１０８ａが軸１０９を中心にして上下に回動できる。このレバー１０８ａの先端には、その円周外周がシリコンゴム製のディスク１１０が取り付けられ、モータ１１１で矢印１１０ａ方向に回転可能である。このディスク１１０は２枚の円板の間に羽根が設けられた水車状の形状である。なお、このディスク１１０の円板の直径は、円弧状凹面１０７の凹面の直径と同一である。
【００１８】
先の「円周撒き動作」の場合は、このディスク１１０は上方に回動して待避していて、ドーナツ状の散薬の山Ｐ１の形成を妨げない。次に「１包分配分動作」時は、掻き出しディスク部１０８のディスク１１０が下方に回動して、ディスク１１０が、円弧状凹面１０７に隙間なく密着する。この状態で、モータ１１１を駆動するとディスク１１０の円板に設けられた羽根によって円弧状凹面１０７の上の散薬が落下ホッパ３００に掻き落とされる。そして、ステッピング・モータ１０５を所定角度Ｒだけ回転させると、その角度分の散薬の量が、落下ホッパ３００側に払出される。ここで、先の所定角度Ｒとは、別に処方

箋から指定される１個包に包装すべき用量分の角度である。
【００１９】
例えば、処方箋で、ある散薬を１個包あたり１ｇで３６個包作成する場合にあっては、事前に散薬カセット１０１に３６ｇの散薬を装填しておき、これを「円周撒き動作」で、全量をドーナツ状に均一に撒く。次に「１包分配分動作」で、ディスク１１０を回転させながら、ステッピング・モータ１０５を１０度回転させると、正しく１個包分の１ｇの散薬が落下ホッパ３００に払出させることができるものである。このような円盤配分部１００と落下ホッパ３００で薬剤供給部を構成する。
【００２０】
円盤配分部１００には、左右に対称形に、２組の円盤部１１２ａと１１２ｂが配置しているが、これは、一方の円盤部１１２ａで「円周撒き動作」しているときは、他方の円盤部１１２ｂが「１包分配分動作」を出来るようにして、複数の連続する処方において無駄時間がなく、連続的に分包できるようにするためのものである。
【００２１】
図３は落下ホッパ３００の形状と動作の概要を示すものである。落下ホッパ３００は上ホッパ３０１と下ホッパ３０２の二重構造となっており、上ホッパ３０１の下開放部３０３を開閉自在なシャッタ３０４で閉鎖している。上ホッパ３０１の上端は、円盤配分部１００からの散薬を受け入れる上開口部３００ａが形成されている。下ホッパ３０２の下端部は図３（ａ）（ｂ）に示すように楔状に形成され、両端に突部である爪部３０５ａ、３０５ｂが形成され、その間に散薬を払出す凹部（下開口部）３０５ｃが形成されている。この落下ホッパ３００は全体として上下移動できるようになっている。そして、「１包分配分動作」で、円盤配分部１００から散薬を払出すタイミングでは、図３（ａ）（ｂ）の上位置に位置する。この時、シャッタ３０４は図３（ｂ）の側面図に示すように閉鎖しているので、落下した散薬は一旦このシャッタ３０４上に保持される。
【００２２】
このとき落下ホッパ３００の下端の左右の爪部３０５ａと３０５ｂは、搬送される谷折り状に二つ折された分包用紙Ｂの開放端Ｂ１にその先端を入れ込んでいる。
【００２３】
散薬の放出時は図３（ｃ）のように、落下ホッパ３００全体を下方に移動するが、左右の爪部３０５ａ、３０５ｂｃ楔状の形状が、落下ホッパ３００が分包用紙Ｂ間に進入するときのガイドの働きをしている。この状態でシャッタを３０４ａのように開くと、散薬は分包用紙Ｂの内部に収納されるものである。その後、落下ホッパ３００は図３（ｂ）の位置まで上昇する。
【００２４】
次に、図４と図５を用いて印刷包装機２００の構成と動作を説明する。図４は散薬分包機の正面の断面図であって、区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。

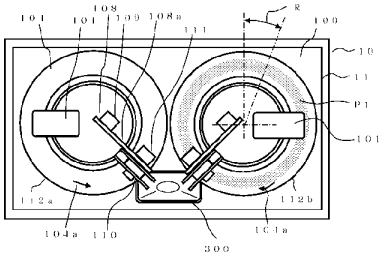
【符号の説明】

【００６１】

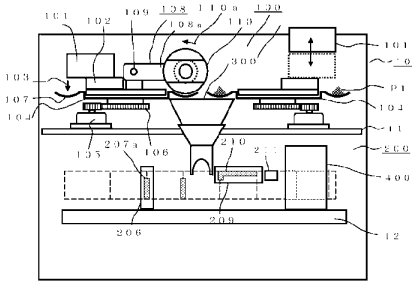
１００・・・円盤配分部（薬剤供給部）
２００・・・印刷包装機
２０１・・・分包用紙ロール（分包用紙収納部）
２０６・・・縦シール機構
２０９・・・横シール機構
２１１・・・駆動ローラ
３００・・・落下ホッパ（薬剤供給部）
４００・・・ミシン目作成装置
４０２・・・刃収納部
４０４・・・刃受け部
４１６，４１８・・・カム板
４２０・・・カム板

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）

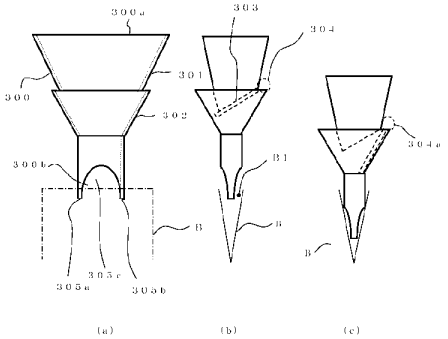
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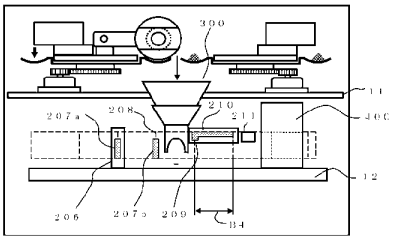
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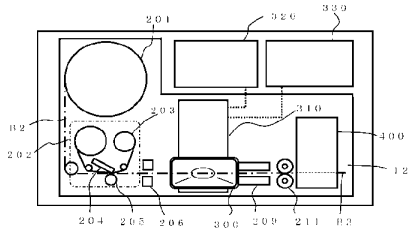
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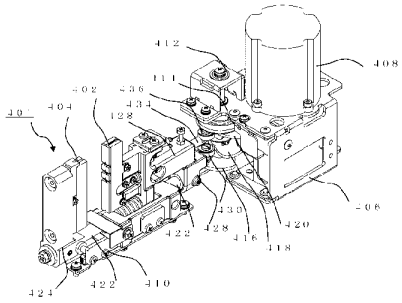
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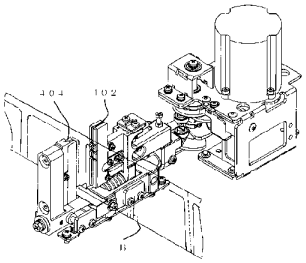
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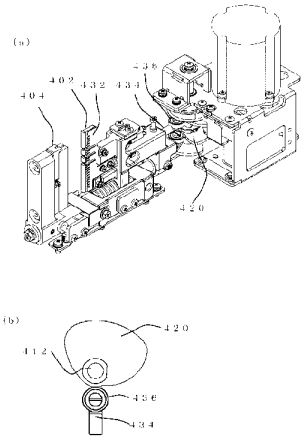
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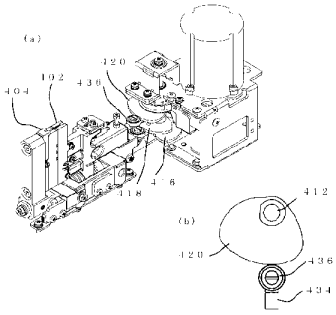
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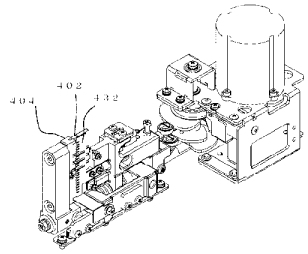
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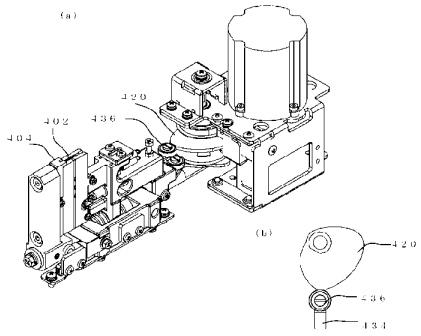
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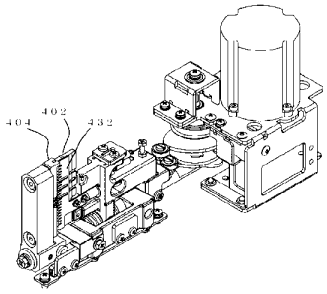
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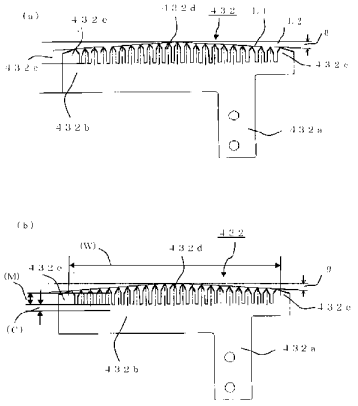
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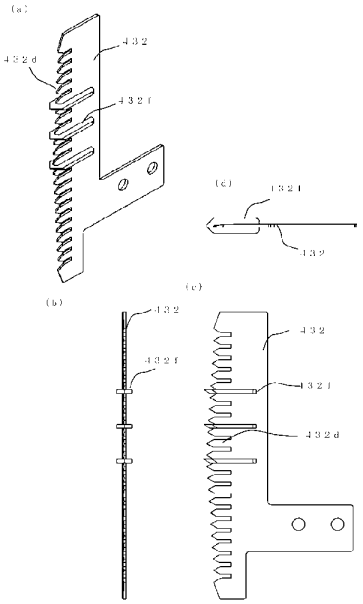
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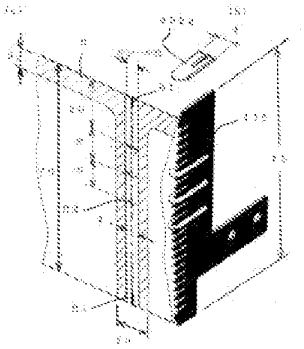
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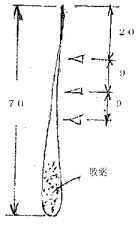
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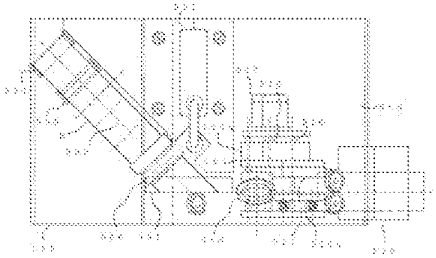
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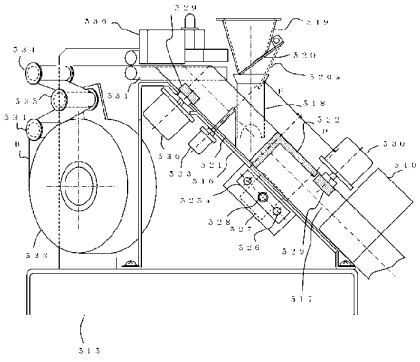
【図１６】



【図１７】



【図１８】



フロントページの続き

Fターム 参考

J-PlatPat 特許情報プラットフォーム English close

Literature display help

1 / 1 display

Japanese Patent Application Laid-Open No. 08-257018

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

Display format of the document display screen:
text display PDF display
primary literature | PAJ

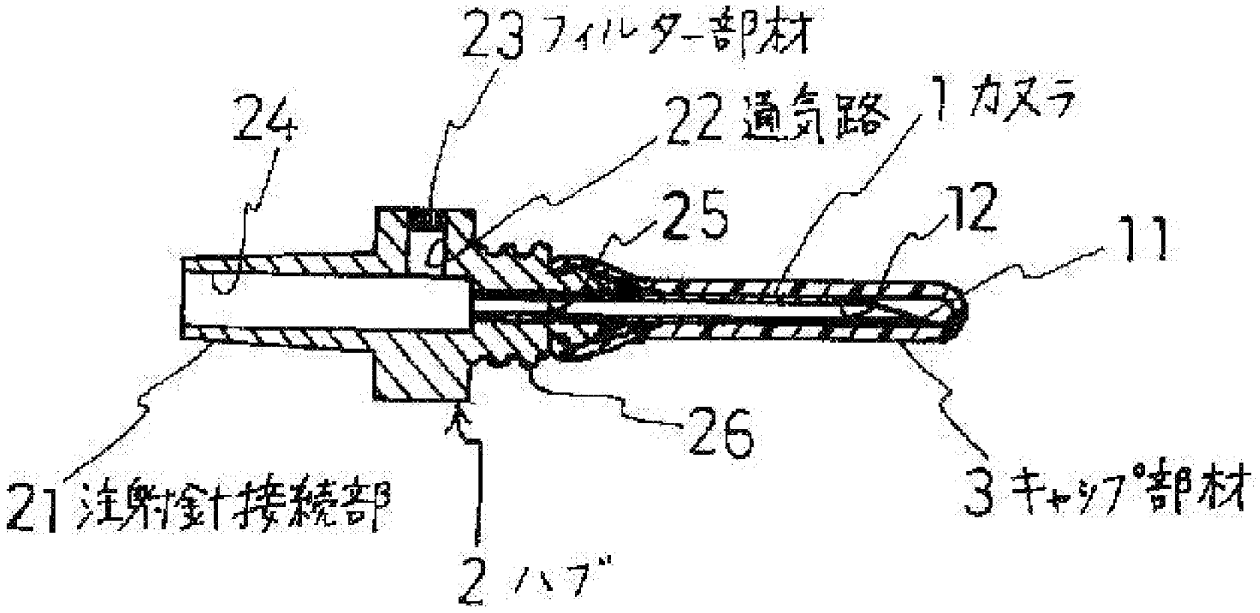
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A61M 5/32
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A61B 5/14 300 E 7638-2J
A61M 5/32
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(21) [Application number] Japanese Patent Application 7-62943
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(71) [Applicant]

[Identification number] 000135036
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[Name] Ikegami filial piety

wrap up close

(57) [Summary]
[Purpose] When the cutting edge of an injection needle connected to this needle is inserted in to a blood vessel, blood flows into the intermediate portion of the transparent hub, which caus es the cutting edge to be inserted into the blood vessel. To provide a blood collection adapter capable of confirming that
The blood collection adapter comprises a hollow cannula 1 having a cutting edge 11 at its tip, a transparent hollow hub 2 supporting and fixing the rear end of the cannula 1 at its tip, and a cannula 1 crowned. It consists of a cap member 3 made of a rubber elastic body. An injectio n needle connecting portion 21 is provided at the rear end portion of the hub 2, and an air pa ssage 22 is provided at the intermediate portion of the hub 2. The outlet of the air passage 22 is gas-permeable and liquid-impermeable. is closed with a filter member 23 of .



The scope of the claims open

[Scope of Claims]

[Claim 1] A hollow cannula having a cutting edge at its tip, a tip supporting and fixing a rear end of the cannula, and a liquid-tight hub of an injection needle at the rear end of the cannula. It consists of a transparent hollow hub equipped with an insertable injection needle connector, and a cap member made of a rubber elastic body covering the cannula, and a hollow between the tip of the hub and the injection needle connector. A blood collection adapter in which an air passage is provided in a portion to communicate the hollow portion with the outside air, and an outlet of the air passage is closed with a gas-permeable and liquid-impermeable filter member.

2. The blood collection adapter according to claim 1, wherein the injection needle connecting portion is formed on a luer tip that can be fitted to the hub of the injection needle.

3. The blood collection adapter according to claim 2, wherein the luer tip is concentrically and externally provided with female coupling means that can be coupled with the hub of the injection needle.

4. A blood collection needle comprising an injection needle connected to the blood collection adapter of claim 1.

detailed description open —

Description: BACKGROUND OF THE INVENTION

1.

Field of the Invention The present invention relates to blood collection adapters. More specifically, it is a blood-collecting adapter used for a vacuum blood-collecting tube for collecting blood from a blood vessel, which can be used as a blood-collecting needle by connecting an ordinary injection needle, and has a cutting edge inserted into the blood vessel. The present invention relates to a blood collection adapter capable of confirming that

2.

Description of the Related Art Conventionally, when collecting blood using a blood collection tube, a blood collection needle as shown in FIG. 4 is used to collect blood. . However, in such blood sampling, which relies on intuition and experience, it is not possible to check whether the cutting edge has been inserted into the blood vessel for beginners with little intuition or experience, or for patients with narrow blood vessels that are difficult to see or cannot be seen. As a result, it places a heavy burden on both the person collecting blood and the person receiving blood. Blood collection had to be repeated, which was uneconomical. Therefore, there has been proposed a blood collection needle that can confirm that the cutting edge has been inserted into a blood vessel (Japanese Unexamined Patent Publication No. 4-132541, etc.).

[0003] In the blood collection needle disclosed in JP-A-4-132541, the hub is provided with a v entilation hole for communication between the inner cavity of the elastic tip and the outside at mosphere, and an air-permeable filter is attached to the outer opening of the ventilation hole. By confirming the blood (so-called flashback) flowing into the blood collection needle, it is con firmed that the cutting edge has been inserted into the blood vessel. However, since the blood collection needle described above tries to guide the blood that has flowed into the elastic tip t o the ventilation hole of the transparent hub, it is necessary to confirm flashback.It takes a lo ng time, and there is a problem that the blood collected inside the elastic tip may leak. SUMM ARY OF THE INVENTION The present invention has been made in view of the above-mentione d circumstances

.

To provide a blood collecting adapter which enables confirmation of the insertion of a cutting e dge into a blood vessel by blood flowing into an intermediate part of the blood vessel. Another object of the present invention is to provide a blood collection needle comprising a combinatio n of this blood collection adapter and an injection needle.

[0005]

To solve the above problems, the present invention provides a hollow cannula having a cutting edge at its distal end, and a distal end of the hollow cannula supporting and fixing the rear en d of the cannula. and a transparent hollow hub equipped with an injection needle connecting portion to which the injection needle hub can be inserted in a liquid-tight manner at its rear e nd, and a cap member made of a rubber elastic body covering the cannula, An air passage is provided in the hollow portion between the distal end portion of the hub and the injection nee dle connection portion to communicate the hollow portion with the outside air, and the outlet of the air passage is closed with a gas-permeable and liquid-impermeable filter member. A re movable blood collection adapter is used. In addition, a configuration in which an injection ne edle is connected to this blood collection adapter is adopted. Here, the injection needle conne ction part may be formed in a luer tip that can be fitted with the hub of the injection needle c onnected thereto, and the luer tip is concentrically threaded with the hub of the injection need le. A female coupling means may be provided which may be mated or luer coupled.

[0006]

[Operation] According to the above configuration, when the blood collection adapter is attache d to the blood collection needle holder, the injection needle is connected to the injection needl e connecting portion, and the injection needle is inserted into the blood vessel, the hollow por tion of the injection needle and the blood collection are removed. Air existing in the hollow por tion of the adapter passes through the gas-permeable filter member through the gas-permea ble filter member by the inflowing blood, and is expelled to the outside. It flows into the hollo w portion of the adapter and then through the air passage to reach the filter member. Therefo re, by observing the air passage formed in the transparent hub, insertion of the injection need le into the blood vessel can be easily confirmed. Also, at this time, since the filter member is i

mpermeable to liquid, blood does not leak through the filter member to the outside.

[0007]

Next, an embodiment of the present invention will be described with reference to the drawing s. FIG. 1 is a vertical cross-sectional view of a blood sampling adapter according to one embo diment of the present invention, FIG. 2 is a diagram showing another embodiment, and FIG. 3 shows a state in which an injection needle is attached to the blood sampling adapter shown in FIG. FIG. 10 shows. As shown in FIG. 1, the blood collection adapter of the present invention comprises a hollow cannula 1 having a cutting edge 11 at its distal end, and a transparent holl ow hub 2 supporting and fixing the rear end of this cannula 1 at its distal end. , the rubber ela stic body crowned on the cannula 1It consists of a cap member 3 made of An injection needle connecting portion 21 is provided at the rear end portion of the hub 2, and an air passage 22 i s provided at the intermediate portion of the hub 2. The outlet of the air passage 22 is gas-pe rmeable and liquid-impermeable. is closed with a filter member 23 of .

The hub 2 is a hollow member made of transparent synthetic resin such as polyethylene, poly propylene, polyester, or polystyrene, and consists of a front end, an intermediate portion, and a rear end. The rear end of the cannula 1 generally made of stainless steel is inserted into the hollow portion 25 at the tip of the hub 2 and fixed with an adhesive. It is covered with a cap member 3 made of isoprene rubber, butadiene rubber, nitrile rubber or the like. A male coupli ng means such as a male screw 26 is formed on the outer wall of the tip of the hub 2 so that i t can be screwed into a blood collection needle holder (not shown).

[0009] The rear end of the hub 2 is an injection needle connecting portion 21 having a hollow portion 24 communicating with a hollow portion 25 at the distal end of the hub 2, and is gene rally external so that a hub 41 of the injection needle 4 can be fitted. It is formed into a so-cal led luer tip whose diameter is reduced in a tapered shape. For example, as shown in FIG. A h ood-shaped female coupling means 27 extending concentrically from the intermediate portion of the hub 2 toward the injection needle connection portion 21 is provided, and a male couplin g means (not shown) is provided on the outer wall of the end portion of the hub 41 of the inje ction needle 4 . (not connected) may be threaded or luer connected. As the injection needle c onnecting portion 21, a male coupling member that is inserted into the hub 41 of the injection needle 4 is usually employed. coupling members can also be employed.

The intermediate portion of the hub 2 is a wide brim-like projecting portion, and is provided w ith an air passage 22 that communicates a hollow portion 24 with the outside air. ing. This filt er member 23 is a gas-permeable and liquid-impermeable filter (hydrophobic filter), and as su ch a filter, a layered filter made of a polymer sintered body such as polypropylene or polyethyl ene is usually preferably employed. However, a film-like so-called membrane filter made of a hydrophobic resin such as polypropylene or polyethylene may also be used.

Next, use of the blood collection adapter of the present inventionwill be described with referen ce to FIG. First, the blood collection adapter A is attached to a blood collection needle holder (not shown), and the injection needle 4 is connected to the injection needle connecting portio

n 21 of the blood collection adapter A. As shown in FIG. Next, when the cutting edge 43 of th e injection needle 4 is pierced into the blood vessel, the air existing in the hollow portion 44 of the injection needle 4 and the hollow portions 24 and 25 of the blood collection adapter A is p ushed into the air passage of the blood collection adapter A by the inflowing blood. 22, it per meates the gas-permeable filter member 23 and is expelled to the outside. Then, the blood p asses through the hollow portion 44 of the injection needle 4 and flows into the hollow portion 24 of the blood collection adapter A, passes through the air passage 22 and reaches the filter member 23 . Therefore, by observing the injection needle connecting portion 21 and the air p assage 22 provided on the transparent hub 2, it is possible to easily confirm that the cutting e dge 43 of the injection needle 4 has been inserted into the blood vessel. At this time, since th e filter member 23 is impermeable to liquid, the blood will not pass through the filter member 23 and leak to the outside.

INDUSTRIAL APPLICABILITY

As is clear from the above description, the following effects can be obtained by adopting the b lood sampling adapter of the present invention.

①It is economical because it can be used as a blood collection needle by connecting a normal injection needle.

②Since it can be easily confirmed that the cutting edge of the injection needle connected to t his has been pierced into the blood vessel, it is possible to eliminate the burden on the subjec t of blood collection due to re-insertion of the injection needle.

③No need to redo blood collection.

Brief description of the drawing

open —

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 is a vertical cross-sectional view of a blood sampling adapter according to one embodi ment of the present invention;

FIG. 2 is a diagram showing another embodiment of the present invention;

3 is a view showing a state where an injection needle is attached to the blood collection adapt er shown in FIG. 1; FIG.

FIG. 4 is a diagram showing a conventional blood collection needle;

[Description of Reference Symbols]

1 Cannula

2 Hub

21 Injection needle connecting portion

22 Air passage

23 Filter member

27 Female coupling means

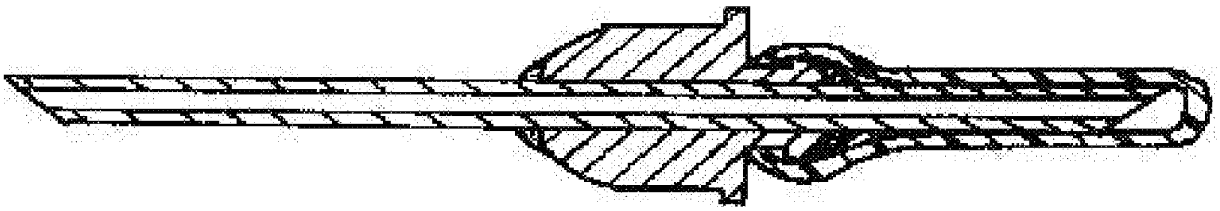
3 Cap member

4 Injection needle

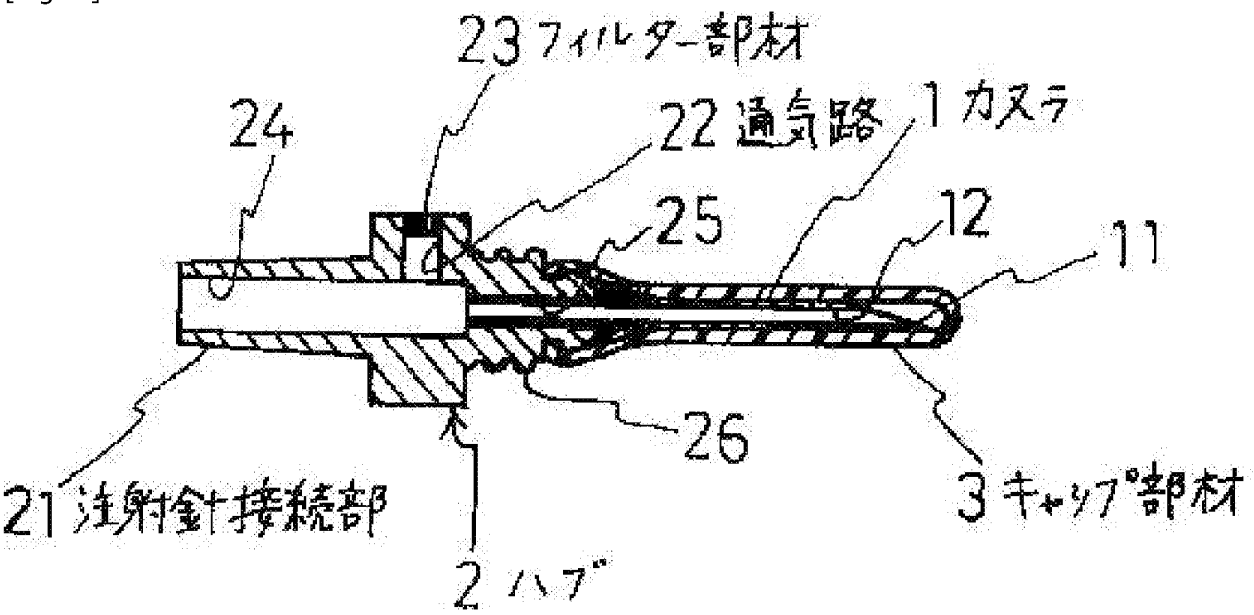
A Blood sampling adapter

drawing open —

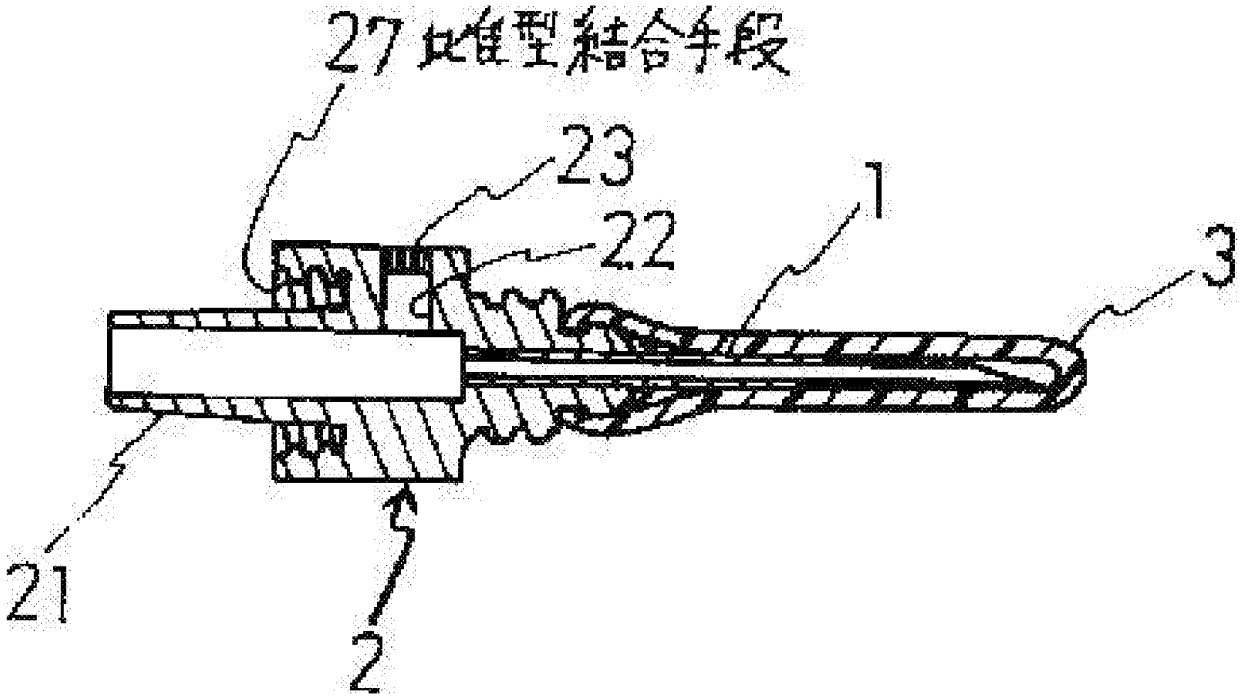
[Figure 4]



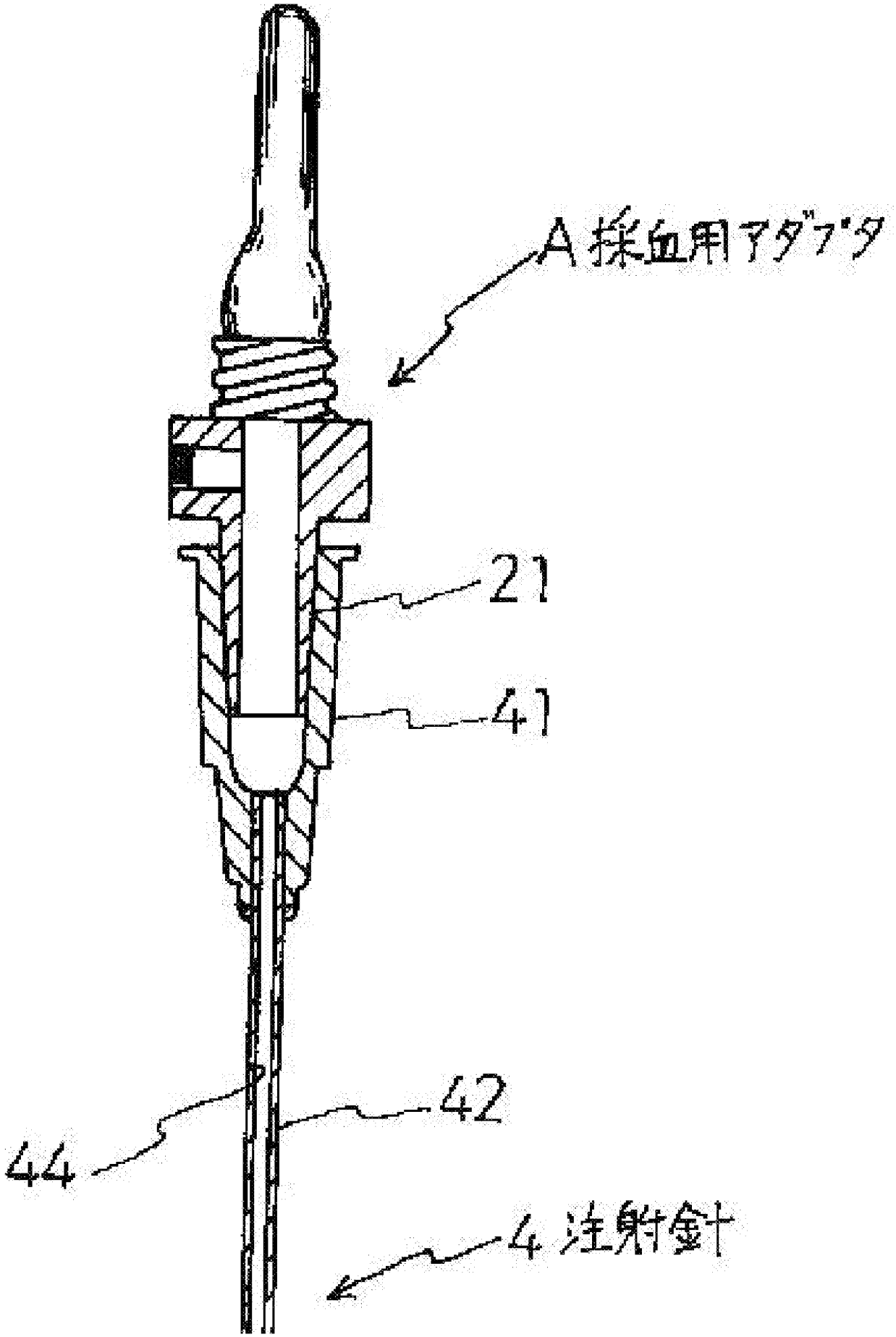
[Fig. 1]



[Figure 2]



[Figure 3]


A 採血用アダプタ
21
41
42
44
4 注射針

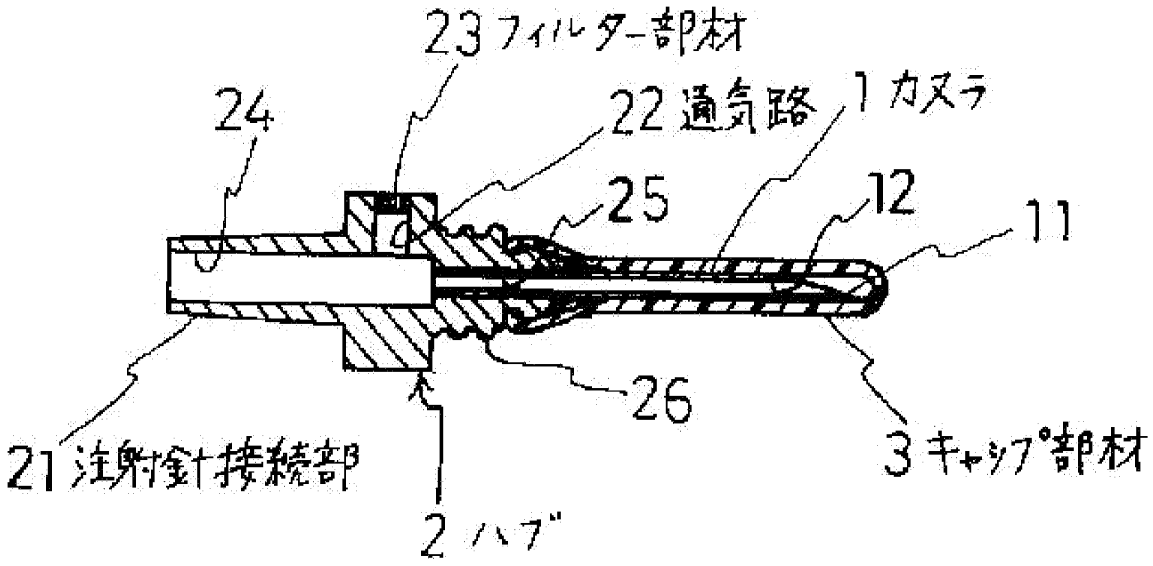


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Representative drawing | 1 | 2 | 3 | Four

Magnify and Rotate



Representative drawing

1 / 1 display

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Bibliographic data: JPH08257018 (A) — 1996-10-08

BLOOD-GATHERING ADAPTER

Inventor(s): HIGAKI YOSHIO; IKEGAMI TAKASHI ± (HIGAKI YOSHIO, ; IKEGAMI TAKASHI)

Applicant(s): NISSHO KK ± (NISSHO CORP)

Classification: **- international:** ***A61B5/15; A61B5/154; A61M5/32;*** (IPC1-7): A61B5/14; A61M5/32

- cooperative: **A61B5/15003 (EP)**; **A61B5/150213 (EP)**; **A61B5/150389 (EP)**; **A61B5/150473 (EP)**; **A61B5/150503 (EP)**; **A61B5/150732 (EP)**; **A61B5/1535 (EP)**; A61B5/150572 (EP); A61B5/1545 (EP)

Application number: JP19950062943 19950322

Priority number(s): JP19950062943 19950322

Abstract of JPH08257018 (A)

PURPOSE: To provide a blood-gathering adapter by which the fact that the edge tip is stuck into a blood vessel can be confirmed since blood flows in an intermediate part of its transparent hub when the edge tip of an injection needle connected to this is stuck into a blood vessel. CONSTITUTION: A blood gathering adapter is composed of a hollow cannula 1 having the edge tip 11 on the tip, a transparent hollow hub 2 to support and fix a rear end part of this cannula 1 by its tip part and a cap member 3 which is put on the cannula 1 and is made of a rubber elastic body. An injection needle connecting part 21 is arranged in a rear end part of the hub 2, and a ventilating passage 22 is arranged in an intermediate part of the hub 2, and an outlet of this ventilating passage 22 is blocked up by a gas permeable and liquid impermeable filter member 23.

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特開平8－257018

(43)公開日　平成８年(1996)10月８日

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Ａ６１Ｍ	5/32			Ａ６１Ｍ	5/32	

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(22)出願日　平成７年(1995)３月22日

(71)出願人　000135036
株式会社ニッショー
大阪府大阪市北区本庄西３丁目９番３号

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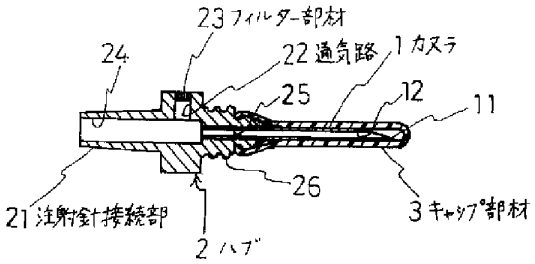
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大阪市北区豊崎３丁目３番13号　株式会社ニプロ内

(54)【発明の名称】　採血用アダプタ

(57)【要約】

【目的】　これに接続される注射針の刃先が血管に刺入されたときに、その透明なハブの中間部分に血液が流れ込み、これによって刃先が血管内に刺入されたことを確認できる採血用アダプタを提供する。

【構成】　採血用アダプタは、先端に刃先１１を有する中空のカヌラ１と、その先端部でこのカヌラ１の後端部を支持し固定する透明な中空のハブ２と、カヌラ１に被冠されたゴム弾性体製のキャップ部材３からなっている。そして、ハブ２の後端部には注射針接続部２１が設けられており、ハブ２の中間部には通気路２２が設けられ、この通気路２２の出口はガス透過性かつ液体不透過性のフィルター部材２３で塞がれている。



【特許請求の範囲】
【請求項１】　先端に刃先を有する中空のカヌラと、その先端部で該カヌラの後端部を支持し固定するとともに、その後端部に注射針のハブを液密に挿着可能な注射針接続部を備えた透明な中空のハブと、前記カヌラに被冠されたゴム弾性体製のキャップ部材とからなり、前記ハブの先端部と注射針接続部の間の中空部分に、該中空部分を外気と連通する通気路が設けられ、該通気路の出口がガス透過性かつ液体不透過性のフィルター部材で塞がれてなる採血用アダプタ。
【請求項２】　注射針接続部が注射針のハブと嵌合可能なルアーチップに形成されている請求項１に記載の採血用アダプタ。
【請求項３】　ルアーチップと同心状かつその外側に注射針のハブと結合可能な雌型結合手段を設けた請求項２に記載の採血用アダプタ。
【請求項４】　請求項１の採血用アダプタに注射針を接続してなる採血針。
【発明の詳細な説明】
【０００１】
【産業上の利用分野】本発明は採血用アダプタに関する。より詳しくは、血管より血液を採取するための真空採血管に用いる採血用アダプタであって、これに通常の注射針を接続することにより採血針として使用できるとともに、刃先が血管に刺入されたことを確認することができる採血用アダプタに関する。
【０００２】
【従来の技術】従来より、採血管による採血に際して、図４に示すような採血針を用いて採血しており、勘と経験によって刃先が血管内に入ったことを確認していた。しかしながら、このような勘と経験に頼る採血では、勘や経験の乏しい初心者や、血管が細くて見にくいまたは見えない患者の場合、血管内への刃先の刺入を確認できないため、何回も刺し直したりすることがあり、そのため、採血者にとっても被採血者にとっても大きな負担を強いられることになり、また、場合によっては、新たに真空採血管、採血針、その他の採血器具を用意して採血のし直しをしなければならず、不経済であった。そこで、刃先が血管に刺入されたことを確認することができる採血針が提案されている（特開平４－１３２５４１号公報など）。
【０００３】上記特開平４－１３２５４１号公報の採血針は、ハブに弾性チップの内腔部と外部雰囲気とを連通させる通気孔を設け、この通気孔の外部口部に通気性フィルタを取り付けたことを特徴とするもので、採血針に流入する血液（いわゆるフラッシュバック）を確認することにより、刃先が血管に刺入されたことを確認するようにしたものである。しかしながら、上記の採血針は弾性チップ内に流入した血液を透明なハブの通気孔に導こうとするものなので、フラッシュバックの確認に要する時間が長く、また、弾性チップの内部に溜まった血液が漏れる虞があり問題である。
【０００４】
【発明が解決しようとする課題】本発明は、上記の事情に鑑みてなされたもので、これに接続される注射針の刃先が血管に刺入されたときに、その透明なハブの中間部分に血液が流れ込み、これによって刃先が血管内に刺入されたことを確認できる採血用アダプタを提供することを目的とする。また、この採血用アダプタと注射針の組合せからなる採血針を提供することを目的とする。
【０００５】
【課題を解決するための手段】本発明は、上記の課題を解決するために、先端に刃先を有する中空のカヌラと、その先端部で該カヌラの後端部を支持し固定するとともに、その後端部に注射針のハブを液密に挿着可能な注射針接続部を備えた透明な中空のハブと、前記カヌラに被冠されたゴム弾性体製のキャップ部材とからなり、前記ハブの先端部と注射針接続部の間の中空部分に、該中空部分を外気と連通する通気路が設けられ、該通気路の出口がガス透過性かつ液体不透過性のフィルター部材で塞がれてなる採血用アダプタを採用している。また、この採血用アダプタに注射針を接続した構成を採用している。ここで、注射針接続部はこれに接続される注射針のハブと嵌合可能なルアーチップに形成してもよく、また、ルアーチップの外側にはこれと同心状に注射針のハブと螺合あるいはルアー結合可能な雌型結合手段を設けてもよい。
【０００６】
【作用】上記構成によれば、採血用アダプタを採血針ホルダーに取り付け、その注射針接続部に注射針を接続して、この注射針を血管に刺入すると、注射針の中空部分および採血用アダプタの中空部分に存在する空気が、流入する血液により採血用アダプタの通気路を通りガス透過性のフィルター部材を透過して外部に追い出されるので、血液は注射針の中空部分を通って採血用アダプタの中空部分に流入し、さらに通気路を通ってフィルター部材に達する。従って、透明なハブに形成された通気路を観察すれば、容易に注射針の血管内への刺入を確認することができる。また、この時、フィルター部材が液体不透過性なので、血液がフィルター部材を透過して外部に漏れることはない。
【０００７】
【実施例】次に本発明の実施例について図面に基づいて説明する。図１は本発明の一実施例に係る採血用アダプタの縦断面図であり、図２は他の実施例を示す図、図３は図１に示す採血用アダプタに注射針を取り付けた状態を示す図である。図１に示すように、本発明の採血用アダプタは、先端に刃先１１を有する中空のカヌラ１と、その先端部でこのカヌラ１の後端部を支持し固定する透明な中空のハブ２と、カヌラ１に被冠されたゴム弾性体

製のキャップ部材３からなっている。そして、ハブ２の後端部には注射針接続部２１が設けられており、ハブ２の中間部には通気路２２が設けられ、この通気路２２の出口はガス透過性かつ液体不透過性のフィルター部材２３で塞がれている。

【０００８】ハブ２は例えばポリエチレンやポリプロピレン、ポリエステル、ポリスチレンなどの透明な合成樹脂で中空に形成された部材であり、先端部と中間部および後端部からなる。ハブ２の先端部の中空部分２５には一般にステンレス鋼で形成されたカヌラ１の後端部が挿入され、接着剤で固定されており、このカヌラ１にはゴム弾性体の例えば天然ゴムや、イソプレンゴム、ブタジエンゴム、ニトリルゴムなどで形成されたキャップ部材３が被せられている。また、ハブ２の先端部の外壁には雄型結合手段の例えば雄ネジ２６が形成されており、採血針ホルダー（図示していない）に螺合できるようになっている。

【０００９】ハブ２の後端部はハブ２の先端部の中空部分２５と連通する中空部分２４を有する注射針接続部２１になっており、注射針４のハブ４１を嵌合できるよう一般に外径がテーパ状に縮径された所謂ルアーチップに形成されている。ルアーチップに形成された注射針接続部２１の外側には、採血操作の途中で注射針４のハブ４１が注射針接続部２１から脱落することがないように、例えば図２に示すように、ハブ２の中間部から注射針接続部２１方向にこれと同心状に延びるフード状の雌型結合手段２７を設け、注射針４のハブ４１の端部外壁に設けた雄型結合手段（図示していない）と螺合またはルアー結合するようにしてもよい。尚、注射針接続部２１としては通常、注射針４のハブ４１に挿着される雄型の結合部材が採用されるが、注射針のハブを雄型の結合端に形成することにより雌型の結合部材を採用することもできる。

【００１０】ハブ２の中間部は幅広の鍔状に突出した部分であり、中空部分２４を外気と連通する通気路２２が設けられており、通気路２２の出口はフィルター部材２３で塞がれている。このフィルター部材２３はガス透過性かつ液体不透過性のフィルター（疎水性フィルター）であり、このようなフィルターとしては、通常ポリプロピレンやポリエチレンなどのポリマー焼結体からなる層状のフィルターが好適に採用されるが、ポリプロピレンやポリエチレンなどの疎水性樹脂からなる膜状のいわゆるメンブレンフィルターであっても構わない。

【００１１】次に、本発明の採血用アダプタの使用について図３を用いて説明する。先ず、採血用アダプタＡを採血針ホルダー（図示していない）に取り付け、採血用アダプタＡの注射針接続部２１に注射針４を接続する。次に注射針４の刃先４３を血管に刺入すると、注射針４の中空部分４４および採血用アダプタＡの中空部分２４、２５に存在する空気が、流入する血液により採血用アダプタＡの通気路２２を通りガス透過性のフィルター部材２３を透過して外部に追い出される。すると、血液は注射針４の中空部分４４を通って採血用アダプタＡの中空部分２４に流入し、さらに通気路２２を通ってフィルター部材２３に達する。従って、透明なハブ２に設けられた注射針接続部２１や通気路２２を観察すれば、容易に注射針４の刃先４３の血管内への刺入を確認することができる。また、この時、フィルター部材２３が液体不透過性なので、血液がフィルター部材２３を透過して外部に漏れることはない。

【００１２】

【発明の効果】以上説明してきたことから明らかなように、本発明の採血用アダプタを採用することにより、次のような効果を奏することができる。

通常の注射針を接続することにより採血針として使用することができるので、経済的である。

これに接続された注射針の刃先が血管に刺入されたことを容易に確認できるので、注射針の刺し直しによる被採血者の負担を無くすることができる。

採血のし直しをしなくて済む。

【図面の簡単な説明】

【図１】本発明の一実施例に係る採血用アダプタの縦断面図である。

【図２】本発明の他の実施例を示す図である。

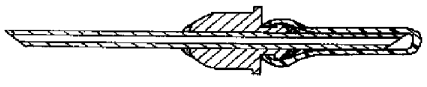
【図３】図１に示す採血用アダプタに注射針を取り付けた状態を示す図である。

【図４】従来の採血針を示す図である。

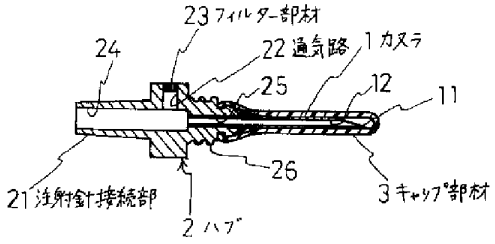
【符号の説明】

１　カヌラ
２　ハブ
２１　注射針接続部
２２　通気路
２３　フィルター部材
２７　雌型結合手段
３　キャップ部材
４　注射針
Ａ　採血用アダプタ

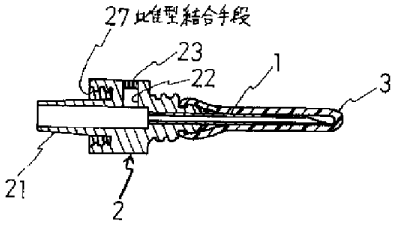
【図４】



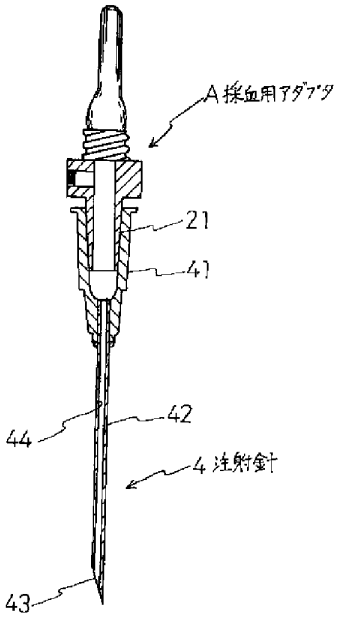
【図１】


23 フィルター部材
24
22 通気路
1 カヌラ
25
12
11
21 注射針接続部
26
2 ハブ
3 キャップ部材

【図２】


27 血液型結合手段
23
22
1
3
21
2

【図３】


A 採血用アダプタ
21
41
42
44
4 注射針
43

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B60R 16/02 630J
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Karasawa [Examiner] Nobuhide Kato

(56) [Reference]
[Reference] Japanese Unexamined Patent Publication No. 2000-228126 (JP, A) [Reference] Japanese Unexamined Patent Publication No. 2007-076491 (JP, A) [Reference] Japanese Utility Model Laid-Open No. 61-161852 (JP, U) [Reference] JP-A-06-156114 (JP, A) (58) [Field investigated] (Int.Cl., DB name) B60R 16/02 B60R 16/027

The scope of the claims open ---

(57) [Scope of Claims]

[Claim 1] A sensor

having a plurality of detection areas and is mounted in a predetermined range of a grip portion of a steering wheel of a vehicle so as to cover the grip portion gripped by the driver. a sensor data generation unit that generates sensor data including position data indicating which detection area is being touched based on a contact detection signal obtained from the touch sensor

; a detection unit that detects whether or not the grip is gripped and an input operation to the touch sensor; the detection unit

detects that the driver is gripping the grip, and the touch sensor detects a control unit that controls an operation target device to be operated by the touch sensor in response to the specific input operation when it is detected that a specific input operation has been performed on the control device

; A control device for an operation target device in

a vehicle, characterized in that , when a direction indicator is operated , the vehicle is in a specific state , and the section disables control of the operation target device. 2. A contact detection signal obtained from a touch sensor which has a plurality of detection areas and is mounted in a predetermined range of a grip portion of a steering wheel of a vehicle so as to cover the grip portion gripped by the driver. a sensor data generator that generates sensor data including position data indicating which detection area is being touched, based on

a detection unit that detects whether or not the driver is gripping the grip based on the sensor data and an input operation to the touch sensor

; and when it is detected that a specific input operation has been performed on the touch sensor, the operation target device to be operated by the touch sensor in response to the specific input operation. and a control unit for controlling the operation target device,

wherein

the control unit invalidates the control of the operation target device by determining that the vehicle is in a specific state when the shift position of the shift lever is reversed. A control device for an operation target device in a vehicle. 3. The touch sensor includes a part of the plurality of detection areas and includes a grip detection area for detecting contact of a driver's palm and another part of the plurality of detection areas, and includes a grip detection area for detecting contact with the driver's palm. and an operation detection area for detecting the specific input operation caused by the contact of the grip detection area, and the detection unit detects when the driver grips the grip based on sensor data based on the contact detection signal obtained from the grip detection area. 3. The specific input operation is detected by sensor data based on a contact detection signal obtained from the operation detection area . Con

trol device. [Claim 4]

Based on a contact detection signal obtained from a touch sensor that has a plurality of dete ction areas and is attached to a predetermined range of a grip portion gripped by a driver on a steering wheel of a vehicle so as to cover the grip portion. a sensor data generation unit tha t generates sensor data including position data indicating whether a detection area is being to uched; and based on the sensor data, whether or not the driver is gripping the grip and the to uch

sensor a detection unit that detects an input operation to the touch sensor, and the

detection unit detects that the driver is gripping the grip, and detects that a specific input op eration has been performed on the touch sensor and a control unit

that controls an operation target device to be operated by the touch sensor in response to th e specific input operation, wherein the touch sensor includes a part of the plurality of detectio n areas

. , a grip detection area for detecting the contact of the driver's palm, and an operation dete ction area for detecting the specific input operation by finger contact, including other parts of the plurality of detection areas, are set,

The detection unit detects whether or not the driver is gripping the grip by sensor data base d on the contact detection signal obtained from the grip detection area, and the sensor based on the contact detection signal obtained from the operation detection area. A control device fo r an operation target device in a vehicle, wherein the specific input operation is detected by d ata, and the

control unit disables control of the operation target device when the vehicle is in a specific st ate.

5.

The controller controls, as the specific input operation, two points spaced apart in the circum ferential direction in a cross section of the steering wheel when the grip is cut in the radial dir ection with respect to the operation detection area. is operated with two fingers to control the operation target device5. The control device for an operation target device in a vehicle accordi ng to claim 3 or 4, characterized in that :

6.

The controller determines that the vehicle is in a specific state when the rotation angle of th e steering wheel exceeds a predetermined angle, and invalidates the control of the device to b e operated . A control device for an operation target device in a vehicle according to any one of claims 1 to 4 .

7.

The touch sensor comprises a first touch sensor mounted in a predetermined range of the gr ip portion gripped with the left hand of the driver and a second touch sensor mounted in a pre determined range of the grip portion gripped with the right hand of the driver. a touch sensor;

The control unit controls, as the specific input operation, the operation target device accordi ng to a pattern of a combination of a first input operation on the first touch sensor and a seco nd input operation on the second touch sensor. The control

device for an operation target device in a vehicle according to any one of claims 1 to 6, char acterized in that it controls the

8.

A driver grips a touch sensor which has a plurality of detection areas and is mounted within a predetermined range of a grip of a steering wheel of a vehicle so as to cover said grip. detec ting whether or not

a specific input operation has been performed on the touch sensor; detecting whether or not a direction indicator has been operated; When it is detected that the driver is not in a specifi c state, it is detected that the driver is gripping the touch sensor, and it is detected that the s pecific input operation is performed, the touch sensor detects An operation target device to be operated is controlled , and control of the operation target device is disabled when it is detec ted that the vehicle is in a specific state in which a direction indicator is operated. A control m ethod for an operation target device in a vehicle. 9. A driver grips a touch sensor which has a plurality of detection areas and is mounted within a predetermined range of a grip portion of a steering wheel of a vehicle so as to cover said grip portion to be gripped by the driver. It is detected whether or not a specific input operation has been performed on the touch sensor, and the shift position of the shift lever is reversed.

It is detected that

the vehicle is not in a specific state in which the shift position of the shift lever is in reverse , it is detected that the driver is gripping the touch sensor, and the specific When it is detected that the input operation is performed, the touch sensor controls the operation target device to be operated, and the vehicle is in a specific state in which the shift position of the shift lever is in reverse.

A control method for an operation target device in a vehicle, comprising: invalidating control of the operation target device when the operation target device is detected .

10.

The touch sensor includes a part of the plurality of detection areas, a grip detection area for

detecting a contact of the driver's palm, and another part of the plurality of detection areas, w herein and an operation detection area for detecting the specific operation due to contact with the

grip detection area, and detecting that the driver is gripping the touch sensor by contact of t he palm with the

grip detection area. 10. The method of controlling an operation target device in a vehicle acc ording to

claim 8, wherein the execution of the specific input operation is detected by finger contact . 11.

A driver grips a touch sensor which has a plurality of detection areas and is mounted within a predetermined range of a grip portion of a steering wheel of a vehicle so as to cover said gri p portion. detecting whether or not there is,

detecting whether or not a specific input operation has been performed on the touch sensor,

detecting whether the vehicle is in a specific state,

detecting that the vehicle is not in a specific state, detecting that the driver is gripping the to uch sensor, and performing the specific input operation When the operation is detected, the o peration target device to be operated is controlled by the touch sensor, and the touch sensor

includes a part of the plurality of detection areas and detects the contact of the driver's pal m. A grip detection area for detection and an operation detection area for detecting the specifi c operation by finger contact, which includes another part of the plurality of detection areas, a re set,

A palm contact with the grip detection area detects that the driver is gripping the touch sens or, and a finger contact with the operation detection area detects

that the specific input operation has been performed.

A control method for an operation target device in a vehicle characterized by:

12.

As said specific input operation, two points spaced apart in a circumferential direction in a cr oss section of said steering wheel when said grip is cut in said operation detection area by two fingers. 12. The method of controlling an operation target device in a vehicle according to clai m 10, wherein the operation target device is controlled according to an operation pattern . 13. When the rotation angle of the steering wheel exceeds a predetermined angle, it is deter mined that the vehicle is in a specific state, and the

control of the device to be operated is invalidated. The method for controlling an operation t arget device in a vehicle according to any one of Claims 1 to 1 .

14.

The touch sensor comprises a first touch sensor mounted in a predetermined range of the gr ip held by the driver's left hand and a second touch sensor mounted in a predetermined range of the grip held by the driver's right hand. and a touch sensor, and

according to a pattern of a combination of a first input operation on the first touch sensor an

d a second input operation on the second touch sensor as the specific input operation, the ope ration target.

14. The method for controlling an operation target device in a vehicle according to any one o f claims 8 to 13, characterized in that the device is controlled .

detailed description open —

Description: BACKGROUND OF THE INVENTION 1.

Field of the Invention The present invention relates to a vehicle operation control system for controlling the operation of a vehicle, such as an on-vehicle device such as a navigation syste m installed in a vehicle, or a transmission, a direction indicator, or the like. The present invent ion relates to a control device and a control method for controlling an operation target device, which is an operation target device. 2. Description of the Related Art Vehicles in which opera tion switches for operating vehicle-mounted equipment such as a navigation system are arran ged on a steering wheel have become widespread (see Patent Document 1). By arranging the operation switch on the steering wheel, the driver does not have to reach for the in-vehicle eq uipment when operating the in-vehicle equipment, thereby improving operability. As described in Japanese Patent Application Laid-Open No. 2002-200015, the operation switch is actually n ot the annular portion of the steering wheel, which is the grip portion that the driver grips, bu t the central portion where the airbag is accommodated and the circular portion. It is usually arranged in the connecting part connecting between the annular parts. Therefore, in order to operate the operation switch, the driver needs to release his/her hand from the gripped annul ar portion or move the hand largely. Patent Literature 2 describes that operation switches are arranged on the back surface and the inner side surface of the annular portion. [Prior Art Doc uments] [Patent Documents] [Patent Document 1] Japanese Patent Laid- Open Publication N o. 2007-106353 [Patent Document 2] Japanese Patent Laid-Open Publication No. 2005-34812 3 [Patent Document 3] Japanese Patent Laid- Open Publication No. 2008-195220 [Invention] Overview] [Problems to be solved by the invention]

According to the invention disclosed in Patent Document 2, since the operation switches are arranged on the annular portion, the operation switches can be operated without releasing the hand from the annular portion or moving the hand largely . child
can be However, the operation switch described in Patent Literature 2 is a push-button key or a key with projections and depressions, and such keys may interfere with the driver's operation of the steering wheel. It is not preferable to provide large irregularities in the annular portion gripped by the driver. In addition, when an operation unit such as an operation switch is arranged in the annular portion, the driver does not have the intention to operate the operation target device, unlike the case where the driver grips the annular portion for normal driving. In such cases, it is required to prevent the operation target device from being operated carelessly. Furthermore, depending on the state of the vehicle, erroneous operations may be caused, and it is required to reduce erroneous operations as much as possible.
[0005]

In order to meet such a demand, the present invention enables a device to be operated to be operated without removing the hand from the grip or moving the hand largely, and the driver can operate the steering wheel. It is an object of the present invention to provide a control device and a control method for an operation target device in a vehicle, which can greatly reduce the possibility of hindrance during operation. Another object of the present invention is to provide a control device and a control method for an operation target device in a vehicle that can significantly reduce erroneous operations.
SUMMARY OF THE INVENTION In order to solve the above-described problems of the prior art, the present invention has a plurality of detection areas and a grip portion of a steering wheel
a driver . A sensor that generates sensor data including position data indicating which detection area is being touched, based on a contact detection signal obtained from a touch sensor attached to cover the grip in a predetermined range of data generator and
a detection unit for detecting whether or not a driver is gripping the grip based on the sensor data and an input operation to the touch sensor; an operation target to be operated by the touch sensor in response to the specific input operation when it is detected that a specific input operation is performed on the touch sensor. a controller for controlling a device , wherein the controller determines that the vehicle is in a specific state when the direction indicator is operated , and invalidates the control of the device to be operated. A controller for a target device is provided. [0007] In order to solve the above-described problems of the prior art, the prese

nt invention has a plurality of detection areas, and a steering wheel of a vehicle is provided with a grip portion within a predetermined range of the grip portion to be gripped by the driver. A sensor data generation unit that generates sensor data including position data indicating which detection area is being touched based on a contact detection signal obtained from a touch sensor that is mounted so as to cover it; and based on the sensor data, a detection unit that detects whether or not a driver is gripping the grip portion and an input operation to the touch sensor; the detection unit detects that the driver is gripping the grip portion; and a control unit that controls an operation target device to be operated by the touch sensor in response to the specific input operation when it is detected that a specific input operation has been performed on the touch sensor. A control device for an operation target device in a vehicle, wherein the control unit invalidates control of the operation target device by determining that the vehicle is in a specific state when the shift position of the shift lever is in reverse. I will provide a.

[0008]

In the above-described control device for an operation target device in a vehicle, the touch sensor includes a grip detection area ; An operation detection area set, and the detection unit is based on a contact detection signal obtained from the grip detection area. Preferably, sensor data is used to detect whether or not a driver is gripping the grip portion, and sensor data based on a contact detection signal obtained from the operation detection area is used to detect the specific input operation.

[0009]

In order to solve the above-described problems of the prior art, the present invention has a plurality of detection areas,

A position indicating which detection area is being touched based on a contact detection signal obtained from a touch sensor attached to a predetermined range of a grip portion of a steering wheel gripped by a driver so as to cover the grip portion. a sensor data generation unit that generates sensor data including data; a detection unit that detects whether or not a driver is gripping the grip based on the sensor data and an input operation to the touch sensor; When the detection unit detects that the driver is gripping the grip and also detects that a specific input operation has been performed on the touch sensor, the specific input operation is performed. Accordingly, a control unit for controlling an operation target device to be operated by the touch sensor, wherein the touch sensor includes part of the plurality of detection areas and detects contact of the driver's palm. A detection area and an operation detection area that includes other parts of the plurality of detection areas and detects the specific input operation by finger contact are set, and the detection unit obtains information from the grip detection area. Detecting whether or not the driver is gripping the grip by sensor data based on the contact detection signal obtained from the operation detection area, detecting the specific input operati

on by sensor data based on the contact detection signal obtained from the operation detection area, The control unit disables control of the operation target device when the vehicle is in a specific state.

[0010]

In the above-described control device for an operation target device in a vehicle, the control unit is configured to, as the specific input operation, cut the grip portion in the radial direction of the steering wheel with respect to the operation detection area. It is preferable that the operation target device is controlled in accordance with a pattern in which two locations spaced apart in the circumferential direction on the cross section of are operated with two fingers.

In the above control device for an operation target device in a vehicle, the control unit further disables control of the operation target device by determining that the vehicle is in a specific state when the rotation angle of the steering wheel exceeds a predetermined angle. It is preferable to

In the above-described control device for an operation target device in a vehicle, the touch sensors include a first touch sensor of a grip portion gripped by a driver's right hand. and a second touch sensor attached to the controller, and the control unit performs a first input operation on the first touch sensor and a second input operation on the second touch sensor as the specific input operation. It is preferable that the operation target device is controlled according to a combination pattern of and.

[0011] In order to solve the above-described problems of the prior art, the present invention has a plurality of detection areas, and a grip portion of a steering wheel

gripped by a driver , has a grip portion within a predetermined range. It detects whether or not the driver is gripping a touch sensor mounted so as to cover the part , detects whether or not a specific input operation has been performed on the touch sensor, and detects whether or not the direction indicator has been operated. detects whether the vehicle is not in a specific state in which the direction indicator is operated, detects that the driver is gripping the touch sensor, and detects whether the specific input operation is detected to be performed, control the operation target device to be operated by the touch sensorand, when it is detected that the vehicle is in a specific state in which the direction indicator is operated, the control of the operation target device is invalidated . offer.

[0012]

In order to solve the above-described problems of the prior art, the present invention has a plurality of detection areas, and a steering wheel of a vehicle is provided with a grip portion within a predetermined range of the grip portion to be gripped by the driver. It detects whether or not the driver is gripping a touch sensor mounted so as to cover it, detects whether or not a specific input operation has been performed on the touch sensor, and shifts the shift position of the shift lever to reverse. It is detected that the vehicle is not in a specific state in which the shift position of the shift lever is in reverse, it is detected that the driver is gripping the touch sensor, and the specific When it is detected that the input operation is performed, the tou

ch sensor controls the operation target device to be operated, and the vehicle is in a specific state in which the shift position of the shift lever is in reverse. If it is detected, the control of the operation target device is invalidated.

A control method for an operation target device in a vehicle is provided.

[0013]

In the above-described control method for a device to be operated in a vehicle, the touch sensor includes a grip detection area ; An operation detection area set, and the driver grips the touch sensor by contact of the palm with the grip detection area. It is preferable to detect that the specific input operation has been performed by a finger touching the operation detection area.

[0014]

In order to solve the above-described problems of the prior art, the present invention has a plurality of detection areas, and a steering wheel of a vehicle is provided with a grip portion in a predetermined range so as to cover the grip portion to be gripped by the driver. Detects whether the driver is gripping the attached touch sensor, detects whether a specific input operation has been performed on the touch sensor, and detects whether the vehicle is in a specific state. and when it is detected that the vehicle is not in a specific state, it is detected that the driver is gripping the touch sensor, and it is detected that the specific input operation is performed, A touch sensor controls an operation target device to be operated, and the touch sensor includes a grip detection area that includes a part of the plurality of detection areas and detects contact with the driver's palm, and the plurality of detection areas. and an operation detection area for detecting the specific operation by finger contact is set, and the driver is gripping the touch sensor by palm contact with the grip detection area and detecting that the specific input operation has been performed by touching the operation detection area with a finger.

[0015]

In the method for controlling an operation target device in a vehicle described above, the specific input operation is a circumferential direction in a cross section of the steering wheel when the grip portion is cut in the radial direction of the steering wheel with respect to the operation detection area. It is preferable that the device to be operated is controlled according to a pattern in which two locations spaced apart from each other are operated with two fingers.

In the above method for controlling an operation target device in a vehicle, it is preferable that control of the operation target device is invalidated on the assumption that the vehicle is in a specific state when the rotation angle of the steering wheel exceeds a predetermined angle. .

In the control method for the operation target device in the vehicle,The touch sensor includes a first touch sensor and a second touch sensor and controlling the operation target device according to a pattern of a combination of a first input operation on the first touch sensor and a second input operation on the second touch sensor as the specific input operation. is preferred.

EFFECTS OF THE INVENTION According to the control device and control method for the devi ce to be operated in the vehicle of the present invention, the device to be operated can be op erated without releasing the hand from the grip portion or moving the hand largely

.

Therefore, it is possible to greatly reduce the possibility of hindrance when the driver operates the steering wheel. In addition, erroneous operations can be greatly reduced.

BRIEF DESCRIPTION OF THE DRAWINGS

[0017]

FIG. 1 is a block diagram showing an embodiment of a control device for an operation target device in a vehicle according to the present invention;

FIG. 2 is a partial plan view showing an example of a vehicle provided with a control device fo r an operation-targeted device according to one embodiment;

FIG. 3 is a diagram showing an example of positions and ranges where touch sensors are mou nted on a steering wheel according to one embodiment;

4A and 4B are diagrams showing other examples of the positions and ranges where the touch sensor is mounted on the steering wheel according to the embodiment; FIG.

FIG. 5 is a diagram showing an example of attaching a touch sensor to a modified steering wh eel;

FIG. 6 is a partial perspective view showing an example of a portion of the steering wheel fro m which sensor data can be obtained while the touch sensor portion is being gripped;

FIG. 7 is a cross-sectional view showing coordinates in the circumferential direction of the cro ss-section of the touch sensor;

8 is a plan view showing a state in which the touch sensor shown in FIG. 6 is unfolded; FIG.

9 is a schematic diagram showing a state in which each area shown in FIG. 8 is converted into uniform sizes; FIG.

FIG. 10 is a diagram showing an example of requirements for determining that the touch sens or portion of the steering wheel is being gripped;

FIG. 11 is a schematic diagram showing an example of a specific input operation on the touch sensor;

FIG. 12 is a schematic diagram showing another example of a specific input operation on the t ouch sensor;

13A and 13B are schematic diagrams showing still another example of a specific input operati on on the touch sensor; FIG.

FIG. 14 is a flowchart for explaining the operation of one embodiment;

FIG. 15 is a diagram for explaining the rotation angle of the steering wheel;

16 is a flow chart showing a specific example of processing in step S4 of FIG. 14; FIG.

FIG. 17 is a schematic perspective view showing a configuration example for changing colors when a touch sensor is operated;

FIG. 18 is a schematic perspective view showing a configuration example for changing the tac

tile sensation when the touch sensor is operated;

19 is a plan view showing a configuration example of a steering wheel; FIG.

BEST MODE FOR CARRYING OUT THE INVENTION An embodiment of a control device and con trol method

for

an operation target device in a vehicle according to the present invention will be described b elow with reference to the accompanying drawings. 1 and 2, the in-vehicle device 100 is mou nted inside the dashboard of the vehicle. In the example shown in FIG. 1, the in-vehicle devic e 100 includes a control unit 10, a navigation processing unit 11, an audio reproduction unit 1 2, a television (TV) tuner 13, a video signal processing unit 14, a video display unit 15, an au dio signal processing unit 16. , a display element 17 and a storage unit 18 . The control unit 1 0 includes a detection unit 10a. The navigation processing unit 11 has a storage unit for hold ing map data, a GPS antenna, etc. The control unit 10 and the navigation processing unit 11 work together to provide route guidance

.

The audio reproducing unit 12 reproduces an audio signal recorded on an optical disk such as a compact disk or a semiconductor memory under the control of the control unit 10 . The TV t uner 13 receives TV broadcast wave signals from a predetermined broadcasting station under the control of the control unit 10 . A video signal output from the navigation processing unit 1 1 or the TV tuner 13 is input to the video signal processing unit 14 via the control unit 10, pro cessed, and displayed on a video display unit 15 such as a liquid crystal panel.

[0020]

Audio signals output from the navigation processing unit 11 , the audio reproduction unit 12 , and the TV tuner 13 are input to the audio signal processing unit 16 via the control unit 10 , processed, and produced by the external speaker 20 . The audio signal processor 16 includes an amplifier. The speaker 20 is installed inside the door of the vehicle or the like. The display element 17 is, for example, a light-emitting diode (LED), and is turned on or off according to t he contact state of the touch sensor 21 described later under the control of the control unit 10 . The display element 17 is arranged, for example, on the housing of the in-vehicle device 100 so that it can be visually recognized by the driver. The display element 17 may be separated f rom the in-vehicle device 100 and arranged near the steering wheel 200 of the vehicle. The st orage unit 18 is a non-volatile memory. As shown in FIG. 2, the touch sensor 21, which is an operation unit, is attached to an annular portion 200r of the steering wheel 200. As shown in FIG

.

The annular portion 200r is a grip portion that is gripped by the driver during driving. In the e xample shown in FIG. 2, the touch sensor 21 is located at the annular portion 200r.

It is mounted in a predetermined angle range on each of the left and right sides. The touch se nsor 21 is a so-called multi-point detection (multi-touch) touch sensor capable of detecting co

ntact at multiple points. The touch sensor 21 is preferably mounted on the circumference of t he cross section in the radial direction of the annular portion 200r within a range of 360°. Eve n if the range is less than 360°, it is sufficient that it covers substantially the entire circumfere nce of the cross section of the annular portion 200r.

The driver grips the portion of the annular portion 200r on which the touch sensor 21 is mounted. In FIG. 1 , the output of the touch sensor 21 is input to the sensor data generator 22 . When the touch sensor 21 is touched with a hand, a contact detection signal is input to t he sensor data generator 22 . Based on the input contact detection signal, the sensor data ge neration unit 22 generates sensor data including position data indicating from which position o n the touch sensor 21 the contact detection signal was obtained, and supplies the sensor data to the control unit 10 . The touch sensor 21 and the sensor data generator 22 may be integrat ed, or the sensor data generator 22 may be provided within the controller 10 .

As the touch sensor 21, for example, a projective capacitance (mutual capacitance) type touch sensor can be use d. As the touch sensor 21 attached to the annular portion 200r, for example, a flexible touch p anel developed by Micro Technology Laboratory can be adopted. This flexible touch panel has a structure in which an ultra-thin glass plate having a thickness of 0.02 to 0.05 mm is used as a sensor portion, and an ultra-thin glass plate and a PET (polyethylene terephthalate) film are bonded together. Even if the touch sensor 21 is attached to the annular portion 200r, the touc h sensor 21 does not have unevenness that can be sensed by the hand or fingers, so that it h ardly interferes with the operation of the steering wheel 200 by the driver. do not have.

[0024]

As shown by the dashed line in FIG. 2, it is preferable to wire the electric wire connecting th e touch sensor 21 and the in-vehicle device 100 through the inside of the steering wheel 200 and the dashboard. 1 and 2, a steering angle sensor 31 detects the rotation angle of a steeri ng wheel 200. As shown in FIG .

The direction indicator sensor 32 detects operation of the direction indicator 320 . The shift le ver sensor 33 detects where the shift position by the shift lever 330 is. Detection signals from the steering angle sensor 31 , direction indicator sensor 32 , and shift lever sensor 33 are sup plied to the control section 10 via the in-vehicle communication section 34 . An example of t he position and range of mounting the touch sensor 21 on the annular portion 200r of the ste ering wheel 200 will be described with reference to FIG .

Note that up, down, right, and left refer to up, down, right, and left when the steering wheel 2 00 is viewed from the driver's position when the steering wheel 200 is not rotated (the vehicle is traveling straight ahead). Suppose that FIG. 3A shows an example in which the touch senso r 21 is attached to the entire circumference of the annular portion 200r. FIG. 3B is the same a s FIG. 2, and shows an example in which the touch sensors 21 are mounted separately from e

ach other within predetermined angular ranges on the left and right above the annular portion 200r. FIG. 3C shows an example in which the touch sensor 21 is mounted in a predetermined angular range only on the upper right side of the annular portion 200r.

FIG.

3(D) shows an example in which the touch sensors 21 are spaced apart from each other wit hin predetermined angular ranges on the left and right sides below the annular portion 200r. F IG. 3(E) is an example in which the touch sensor 21 is mounted over a relatively wide angular range above the top of the annular portion 200r. FIG. 3(E) corresponds to connecting the left and right touch sensors 21 in FIG. 3(B).

FIG.

4 shows an example in which the left and right touch sensors 21 in FIG. 3B are divided into an upper touch sensor 21a and a lower touch sensor 21b. In the example of FIG. 4, the upper touch sensor 21a detects contact with the index finger and thumb of the hand, and the lower touch sensor 21b mainly detects contact with the palm, middle finger, and ring finger. Figure 5 shows a modified steering wheel that is not circular.

This is an example in which a touch sensor 21 is attached to a rule 201. FIG. The touch senso r 21 is attached to the left and right straight portions 201 s of the modified steering wheel 20 1 . The driver grips the linear portion 201s, which is the grip portion, while driving, and the to uch sensor 21 detects contact with the palm or fingers. Here, as shown in FIG. 2, the touch sensors 21 are mounted on the left and right sides above the annular portion 200r

.

Describe how palm and finger contact is detected. FIG. 6 shows an example of a range in whic h the palm and fingers are in contact when the driver grips the touch sensor 21 on the right si de of FIG. The manner in which the driver grips the annular portion 200r and the size of the h and are not uniform, and FIG. 6 is merely an example. In the example shown in FIG. 6, a pl urality of detection areas R indicated by hatched Tp are portions where the contact of the pal m is detected, and a plurality of detection areas R indicated by hatched Tt are those of the th umb

.

This is the part that detects contact. Hereinafter, they are referred to as a palm contact detect ion section Tp and a thumb contact detection section Tt. The back side of the touch sensor 2 1, which is not visible in FIG. 6, is in contact with the forefinger.

As shown in FIG .

6, the touch sensor 21 has a plurality of detection regions R as detection portions for detecti ng contact of palms and fingers. Coordinates are set in each detection area R of the touch sen sor 21 . As shown in FIG. 6, in the circumferential direction of the annular portion 200r, the de tection region R located at the lower end of the touch sensor 21 is set to 0, and the detection region R located at the upper end is 1, 2, 1, 2, 2, . . . , 30, 31 and the coordinates in the circu mferential direction are set. Let the circumferential coordinate of the annular portion 200r in t

he touch sensor 21 be the Y coordinate.

[0032]

FIG. 7 is a cross-sectional view of the annular portion 200r cut in the radial direction of the a nnular portion 200r at the portion where the touch sensor 21 is mounted. As shown in FIG. 7, in the cross-section of the annular portion 200r, a detection region R positioned, for example, on the inner diameter side of the annular portion 200r is assumed to be coordinate 0. As sho wn in FIG. 7 from the inner diameter side to the front side, from the front side to the outer di ameter side, from the outer diameter side to the back side, and from the back side to the inne r diameter side in the counterclockwise direction of FIG. are set to 1, 2, . . . , 21, 22. Let the c oordinate in the circumferential direction of the cross section of the touch sensor 21 be the X coordinate. The sensor data generator 22 can obtain position data indicating where on the tou ch sensor 21 the driver is touching from the X and Y coordinates of the detection area R from which the contact detection signal is obtained.

FIG.

8 shows the development of the touch sensor 21 shown in FIG. FIG. 9 schematically shows a state in which each area of the touch sensor 21 shown in FIG. 8 is converted into uniform size s. 8 and 9, in addition to the palm contact detection portion Tp and the thumb contact detecti on portion Tt, the index finger contact detection portion Ti, which is a plurality of detection re gions R in contact with the index finger, is also shown. If the touch sensor 21 is touched by th e middle finger, the ring finger, or the little finger, the touch sensor 21 also detects the contact of those fingers. In this embodiment, the driver uses the thumb or forefinger suitable for perf orming a specific input operation on the touch sensor 21 as a finger for operation.

[0034]

The details of the input operation with the thumb or index finger will be described later. Base d on the sensor data output from the sensor data generator 22, the detector 10a of the contro ller 10 detects that an input operation has been performed on the touch sensor 21 with the th umb or forefinger. Based on the sensor data output from the sensor data generation unit 22, t he detection unit 10a also detects that the annular portion 200r (touch sensor 21) is gripped. The control unit 10 controls the operation target device according to a specific input operation performed on the touch sensor 21 .

[0035]

An example of the device to be operated is the vehicle-mounted device 100 . Specifically, th e control unit 10

In accordance with the input operation, the navigation processing unit 11 can perform control related to route guidance, the audio reproduction unit 12 can reproduce or stop audio signals, and the track (music) to be reproduced can be advanced or reversed. In addition, the control unit 10 can switch the receiving channel in the TV tuner 13 or control the amplification unit of the audio signal processing unit 16 to decrease or increase the sound volume according to a s pecific input operation.

Another

example of the device to be operated is a vehicle motion control device for controlling the m otion of a vehicle. Specifically, the control unit 10 may control the transmission, the direction i ndicator, the on/off of the air conditioner, the set temperature of the air conditioner, and the li ke, through the in-vehicle communication unit 34 . When the operation target device is a vehi cle motion control device, it is preferable to input the sensor data output from the sensor data generator 22 to a control portion of the vehicle to control the vehicle motion control device. T he control unit that controls the operation target device may be the control unit 10 in the vehi cle-mounted device 100 or may be a control unit outside the vehicle-mounted device 100 pro vided in the vehicle. According to this embodiment, the extremely thin touch sensor 21 is att ached to the annular portion 200r gripped by the driver, and the device to be operated is oper ated by operating the touch sensor 21

.

The device to be operated can be operated without releasing the hand or moving the hand lar gely. In addition, since the touch sensor 21 has no irregularities on the surface of the annular portion 200r, there is almost no possibility that it will interfere with the operation of the steeri ng wheel 200 by the driver.

[0038]

By the way, when the driver does not intend to operate the operation target device, such as when the driver grips the annular portion 200r for normal driving, the operation target device should be prevented from being inadvertently operated. is required. Therefore, in this embodi ment, the following measures are taken to avoid erroneous operations not intended by the dri ver. As shown in FIGS. 8 and 9, a plurality of detection areas R on the touch sensor 21 are p rovided with a grip detection area Arg for detecting contact of the palm and an operation inpu t by the thumb or forefinger

.

An operation detection area Arv for detecting an input and an operation invalid area Ariv whic h is an intermediate area between the grip detection area Arg and the operation detection are a Arv and invalidates an operation input are set. The palm contact detection portion Tp is loca ted within the grip detection area Arg, and the thumb contact detection portion Tt and the for efinger contact detection portion Ti are located within the operation detection area Arv. Like the grip detection area Arg and the operation detection area Arv, the operation invalid area Ar iv has a detection area R for detecting the contact of the palm or fingers

.

22 can be made an operation invalid area by processing to invalidate the input operation from the operation invalid area Ariv. Further, by configuring the touch sensor 21 so that the detecti on area R is not provided in the range of the operation invalid area Ariv, the operation invalid area may be set. This case is substantially equivalent to the example shown in FIG.

[0041]

When the driver grips the annular portion 200r for normal driving, the palm contact detectio n portion Tp, the thumb contact detection portion Tt, and the index finger contact detection p ortion Ti are relatively close to each other. Therefore, in order to accurately distinguish betwee n the case where the driver simply grips the annular portion 200r and the case where the driv er touches the touch sensor 21 to operate the operation target device, the operation invalid ar ea Ariv is provided. When the driver intends to operate the device to be operated, the driver i ntentionally extends his or her thumb or forefinger to touch the touch sensor 21 to perform a specific input operation, which will be described later. The control unit 10 controls the operatio n target device according to the input operation when a specific input operation, which will be described later, is performed within the operation detection area Arv.

[0042]

It is also necessary to avoid erroneous operation of the operation target device when the dri ver carelessly touches the operation detection area Arv without gripping the annular portion 2 00r for driving. Therefore, in the present embodiment, the detection unit 10a determines that the annular portion 200r is gripped when a palm contact detection portion Tp having a predet ermined area or more is obtained in the grip detection area Arg. The control unit 10 is configu red to control the operation target device when the annular portion 200r is gripped and a spec ific operation is performed within the operation detection area Arv. The area of the palm conta ct detection portion Tp for determining that the annular portion 200r is being gripped may be appropriately set by statistically examining the area when a plurality of drivers grip the steeri ng wheel 200 in a normal gripping manner. Just do it.

The area of the palm contact detection portion Tp in the grip detection area Arg is an example of requirements for determining that the driver is gripping the annular portion 200r ,

and the requirements for determination are limited to this. isn't it. FIG. 10 shows a cross sec tion of the annular portion 200r cut at the portion of the grip detection area Arg of the touch s ensor 21. As shown in FIG. The detection unit 10a can determine that the annular portion 200 r is being gripped when the angle θ in the circumferential direction of the cross-section of the palm contact detection portion Tp is equal to or greater than a predetermined angle. The pred etermined angle is, for example, 180°.

[0044]

As described above, in the present embodiment, it is determined whether or not the driver is gripping the annular portion 200r (touch sensor 21), and operation input to the touch sensor 21 is performed only when the driver is gripping the annular portion 200r. is accepted, it is po ssible to avoid an erroneous operation when the operation detection area Arv is carelessly tou ched. In this embodiment, as a preferred configuration, the operation detection area Arv is pr ovided at a position separated from the grip detection area Arg by a predetermined distance, so that the driver intentionally performs a specific input operation on the touch sensor 21. You can detect exactly what you are doing. Therefore, erroneous operations can be greatly reduce d. In this embodiment, the area of the palm contact detection portion Tp in the grip detectio

n area Arg and the angle θ in the circumferential direction of the cross section are used as req uirements for determining whether or not the driver is gripping the annular portion 200r

.

Therefore, it can be accurately determined whether or not the user is gripping the annular por tion 200r. Therefore, it is possible to avoid an erroneous operation when the driver carelessly t ouches the operation detection area Arv without gripping the annular portion 200r. When the detection unit 10a detects that the driver is gripping the annular portion 200r (touch sensor 2 1) based on the sensor data based on the contact detection signal from the grip detection are a Arg, the control unit

10

The display element 17 is turned on in order to inform the driver that the operation input by t he operation detection area Arv is possible. The driver can determine whether or not the oper ation target device can be operated by the touch sensor 21 by turning on/off the display elem ent 17 . It is preferable to arrange the display element 17 near the steering wheel 200 .

[0047]

By the way, when the touch sensor 21 is attached to the entire circumference of the annular portion 200r as shown in FIG. , the position where the driver grips the touch sensor 21 is not fixed. Therefore, the positions of the grip detection area Arg and the operation detection area Arv described with reference to FIGS. 8 and 9 and the operation invalid area Ariv provided as necessary are dynamically changed according to the position at which the driver grips the tou ch sensor 21. Must be set.

Therefore ,

when the touch sensor 21 is gripped while the grip detection area Arg and the like are not se t, the control section 10 sets the area including the palm contact detection portion Tp as the g rip detection area Arg. A predetermined range of Y coordinates including the palm contact det ection part Tp is defined as a grip detection area A

rg. As described above, since the palm contact detection portion Tp has a predetermined area or more, a portion of the plurality of detection regions R on the touch sensor 21 that is detect ed to be touched with a predetermined area or more is the palm contact detection portion Tp. becomes. Alternatively, as described with reference to FIG. 10, in the circumferential direction of the cross section obtained by cutting the annular portion 200r at the portion of the touch s ensor 21, the portion detected to be touched at a predetermined angle or more becomes the palm contact detection portion Tp. . After setting the grip detection area Arg, the control unit 10 sets a predetermined range of Y coordinates above the grip detection area Arg as the oper ation detection area Arv

.

In this case, if necessary, a predetermined range of Y coordinates adjacent to the grip detecti on area Arg is set as the operation invalid area Ariv, and the grip detection area Arg is positio ned away from the grip detection area Arg. 11 to 13, examples of specific input operations p

erformed by the driver on the touch sensor 21 using his thumb or forefinger will now be descr ibed

.

11A to 11E schematically show half of the touch sensor 21, which is the front side or the back side facing the driver, in a plane view. The operations shown in FIGS. 11A to 11E are perform ed with the thumb on the front side and with the index finger on the back side. In FIG. 11A, D R is a rightward drag by sliding the thumb or forefinger on the touch sensor 21 (operation detection area Arv), and DL is a leftward dragging by sliding the thumb or forefinger to the right. It is a directional drag. D U is an upward drag that slides the thumb or forefinger upward; is a downward drag that slides in t he direction the thumb or index finger is pointing.

In FIG . 11(A), instead of the

rightward drag D R , leftward drag D L , upward drag D U , and downward drag D D , the tou ch sensor 21 is flicked with the thumb or forefinger in the respective directions. It may be a fli ck.

FIG.

11(B) shows a tap T of tapping the touch sensor 21 with the thumb or index finger. FIG. 11 (C) shows an arc drag DC in which the thumb or forefinger is dragged on the touch sensor 21 so as to draw an arc. F IG. 11(D) shows a zigzag drag DZ in which the thumb or forefinger is dragged on the touch sensor 21 in a zigzag p attern. FIG. 11(E) shows a symbol input drag DS that is dragged as if writing a symbol with the thumb or forefinger . FIG. 11E shows a state in which the number 3 is drawn as a symbol. As symbols, it is preferable to use numbers and alphabets that are relatively easy to recognize.

[0053]

FIGS. 12A to 12D show a schematic plan view of a front portion 21f, which is the front half o f the touch sensor 21, and a rear portion 21r, which is the rear half of the touch sensor 21, wh en the touch sensor 21 is opened. . The front portion 21f is the portion of X coordinates 0 to 1 1 shown in FIGS. 8 and 9, and the rear portion 21r is the portion of X coordinates 12 to 22. A s shown in FIG. Strictly speaking, in the examples shown in FIGS. 8 and 9, the front portion 2 1f and the back portion 21r do not have the same area, but in FIGS. Shown in area. 12A to 1 2D, for ease of understanding, the rear surface portion 21r is not viewed from the rear surfac e side of the annular portion 200r, but is seen through the rear surface portion 21r from the fr ont surface portion 21f. state. As shown in FIGS. 12A to 12D, a combination of an input oper ation with the thumb on the front portion 21f and an input operation with the index finger on t he back portion 21r can be used as a specific input operation on the touch sensor 21

.

good. FIG. 12A shows an example of performing both a rightward drag DTR in which the thum b slides rightward on the front portion 21f and a rightward drag DIR in which the index finger slides righ tward on the back portion 21r. FIG. 12A is realized by dragging both the thumb and index finger from the inner circumference side to the outer circumference side of the annular portion 200r. A pat tern in which both the thumb and the forefinger are dragged in the direction opposite to that i

n FIG. 12A may be employed.

FIG. 12B shows an example of performing both a leftward drag DTL

in which the thumb slides leftward on the front portion 21f and a rightward drag DIR in which the index finger slides rightward on the back portion 21r. is. FIG. 12B is realized by dragging t he thumb from the outer peripheral side to the inner peripheral side of the annular portion 20 0r and dragging the index finger from the inner peripheral side to the outer peripheral side of the annular portion 200r. FIG. 12C shows an example of performing both a rightward drag DTR in which the thumb slides rightward on the front portion 21f and a leftward drag DIL in which the i ndex finger slides leftward on the back portion 21r. FIG. 12C is realized by dragging the thumb from the in ner circumference side to the outer circumference side of the annular portion 200r and draggi ng the index finger from the outer circumference side to the inner circumference side of the a nnular portion 200r. FIG . 12(D) shows an example of performing both an upward drag D TU

in which the thumb slides upward on the front portion 21f and a downward drag D ID in whic h the index finger slides downward on the back portion 21r. is. A pattern in which the thumb i s dragged downward and the index finger is dragged upward may be adopted, or a pattern in which both the thumb and the index finger are dragged upward or downward may be adopte d. Here, various patterns are shown in which the input operation with the thumb on the front portion 21f and the input operation with the index finger on the back portion 21r are combine d. [0057]

As shown in FIGS. 12A to 12D, if a pattern combining an input operation with the thumb and an input operation with the index finger is used as a specific input operation for controlling the device to be operated, erroneous operations are greatly reduced. can be reduced. Furthermo re, as shown in FIGS. 3(A), (B), (D), (E) and FIGS. 4 and 5, when the touch sensors 21 (21a, 21b) can be operated with the left and right hands

,

, a combination of left and right hand operations can be used as a specific input operation for controlling the operation target device. FIGS. 13A to 13D show operations by the left and righ t hands when the left touch sensor 21 in FIG. 3B is the left touch sensor 21L and the right tou ch sensor 21 is the right touch sensor 21R. Examples of combined patterns are shown. Here, a plane corresponding to the front portion 21f of FIG. 12 operated by the thumb is shown as a schematic plane.

FIG. 13A shows a leftward drag DTL

for sliding the thumb leftward on the left touch sensor 21L and a rightward drag DTR for slidi ng the thumb rightward on the right touch sensor 21R. This pattern is a combination of FIG. 1 3B shows a combination of a rightward drag DTR in which the thumb slides rightward on the le ft touch sensor 21L and a leftward drag DTL in which the thumb slides leftward on the right to

uch sensor 21R . pattern. FIG. 13C shows an upward drag D in which the thumb is slid upwa rd on both the left touch sensor 21L and the right touch sensor 21R.

This pattern is a combination of TUs . FIG. 13(D) shows a pattern in which a downward drag DTD of sliding th e thumb downward is combined for both the left touch sensor 21L and the right touch sensor 21R. If a combination of input operations with left and right hands is used as a specific input operation for controlling the device to be operated, the driver grasps the annular portion 200r with both hands, which contributes to safe driving

.

It is possible to contribute. In particular, the example of FIG. 3B is most preferable in that it c ontributes to safe driving because the touch sensor 21 is mounted at the most appropriate po sition for gripping the annular portion 200r with both hands. An input operation may be accep ted when the left and right touch sensors 21 are gripped with both hands. A state may be ado pted in which input operations are not accepted when one hand is removed from the touch se nsor 21 . When one hand leaves the touch sensor 21, the state of accepting the input operatio n may be continued. Even when a specific input operation with only one hand is used, if the in put operation is accepted when the left and right touch sensors 21 are gripped with both hand s, it contributes to safe driving.

. When the driver grips the annular portion 200r for normal driving and does not intend to o perate the device to be operated, he accidentally combines the input operation with the thum b and the input operation with the index finger

.

It is considered that the possibility of becoming a specific pattern combining input operations with left and right hands is relatively low. Therefore, when using only a specific pattern in whi ch an input operation with the thumb and an input operation with the index finger are combin ed, or a specific pattern in which an input operation with the left and right hands is combined, one of the devices for avoiding the above-described erroneous operation. Some or all of them may be omitted. Of course, even when only a specific pattern combining input operations with the left and right hands is used, it is preferable to employ a device for avoiding the above-des cribed erroneous operation. The storage unit 18 stores a table that associates the above-des cribed specific input operations or patterns of combinations of specific input operations with ty pes of control for the device to be operated

.

The control unit 10 controls the operation target device according to the operation input to th e touch sensor 21 according to the table stored in the storage unit 18 . The storage unit 18 m ay be provided within the control unit 10 .

[0064]

The processing executed by the control unit 10 in this embodiment will be described again u sing the flowchart of FIG. 14 . In FIG. 13, the control unit 10 acquires sensor data output fro

m the sensor data generation unit 22 in step S1. In step S2, the control unit 10 determines w hether or not the annular portion 200r is being gripped based on the detection output from th e detection unit 10a. If it is determined that the annular portion 200r is gripped (YES), the co ntrol unit 10 shifts the process to step S3, and if it is not determined that the annular portion 200r is gripped (NO), the control unit 10 returns the process to step S1. At step S3, the cont rol section 10 determines whether or not there is an input operation based on the detection o utput from the detection section 10a

.

If it is determined that an input operation has been performed (YES), the control unit 10 mov es the process to step S4, and if it is not determined that an operation input has been perfor med (NO), the control unit 10 returns the process to step S1. In step S4, the control unit 10 d etermines whether or not to permit the operation of the operation target device by the input o peration in step S3. If it is determined that the operation is permitted (YES), the control secti on 10 moves the process to step S5, and if it is not determined that the operation is permitte d (NO), the control section 10 returns the process to step S1. As described above, the contr ol unit 10 permits the operation of the operation target device when a specific input operation is performed within the operation detection area Arv, and permits the operation of the operati on target device when a specific input operation is performed within the operation invalid area Ariv

.

, the operation to the operation target device is not permitted. Further, even if some input ope ration is performed within the operation detection area Arv, the control unit 10 does not permi t the operation to the operation target device unless the above-described specific input operat ion is performed, and only when the specific input operation is performed. Permission to opera te the operation target device.

[0067]

The control unit 10 confirms an operation based on the input operation in step S5, executes control according to the confirmed operation on the operation target device in step S6, and re turns the process to step S1. .

[0068]

Further, in step S4, when the vehicle is in a specific state, it is preferable to disallow (that is, disable) the control of the device to be operated. The rotation angle of the steering wheel 200 is set in the control unit 10 for determining whether or not to permit control of the device to b e operated. As shown in FIG. 15, a state in which the steering wheel 200 is not rotated is ass umed to be a rotation angle of 0°. Touch sensor 21 within a range of 30°

input operation to the touch sensor 21 is enabled and permitted, and if the rotation angle exc eeds ±30°, the input operation to the touch sensor 21 is disabled and not permitted.

When the turning angle exceeds ±30°, the vehicle is in a specific state

such as turning right or left, or cornering. If an attempt is made to control the device to be o

perated in such a specific state, there is a high possibility that an erroneous operation will occ ur. In other words, there is a high possibility that an operation input in such a specific state is an operation input unintended by the user. Moreover, it is not preferable in terms of safety. Th erefore, in this embodiment, when the vehicle is in a specific state, control of the operation ta rget device is disabled. As described above, the rotation angle of the steering wheel 200 det ected by the steering angle sensor 31 is input to the controller 10

.

The control unit 10 switches between enabling and disabling the input operation to the touch sensor 21 according to the rotation angle of the steering wheel 200 detected by the steering a ngle sensor 31 . A detection signal from the direction indicator sensor 32 is also input to the c ontrol unit 10 . Therefore, the control unit 10 may invalidate the input operation to the touch sensor 21 when the direction indicator 320 is operated by the detection signal from the directi on indicator sensor 32 . When the direction indicator 320 is operated, it can be considered to be in a specific state in which the steering wheel 200 is rotated over a predetermined rotation angle. In some cases, the direction indicator 320 is also used for operations other than signali ng a right turn or left turn, but the operation of the direction indicator 320 here is an operatio n for signaling a right turn or a left turn.

[0071]

Furthermore, it is not preferable to perform a specific input operation on the touch sensor 21 to control the operation target device while the vehicle is being reversed. There is a high possi bility that an erroneous operation will occur, and this is not preferable in terms of safety. Ther efore, it is preferable that the control unit 10 invalidates the input operation to the touch sens or 21 even when the shift position of the shift lever 330 is reversed by the detection signal fro m the shift lever sensor 33 . When the rotation angle of the steering wheel 200 exceeds a pre determined angle of ±30°, for example, or when the direction indicator 320 is operated, and when the shift position of the shift lever 330 is reversed, the operation target device Although it is preferable to disable the control for , only one of them may be disabled. It should be not ed that disabling the control of the operation target device means disabling the control of the operation target device by disabling the specific input operation even if the above-described s pecific input operation is performed

.

Even if some sensor data is input from the sensor data generation unit 22 to the control unit 1 0, the control unit 10 may invalidate the sensor data. As a result, it is sufficient to invalidate t he control on the operation target device.

[0073]

A specific example of the processing of step S4 in FIG. 14 will be described with reference to the flowchart in FIG. In FIG. 16, in step S41, the control unit 10 determines whether or not th e shift position of the shift lever 330 is reverse. If the shift position is reverse (YES), in step S 45, the control unit 10 disallows the input operation in step S3, and proceeds to step S1 in FI

G. If the shift position is not reverse (NO), control unit 10 determines in step S42 whether dir ection indicator 320 has been operated. If the direction indicator 320 is operated (YES), the c ontroller 10 disallows the input operation in step S3 in step S45, and proceeds to step S1 in F IG. If the direction indicator 320 has not been operated (NO), the controller 10 determines i n step S43 whether or not the rotation angle of the steering wheel 200 has exceeded a predet ermined angle

.

If the rotation angle of the steering wheel 200 exceeds the predetermined angle (YES), in ste p S45, the control unit 10 disallows the input operation in step S3, and proceeds to step S1 in FIG.

Let If the rotation angle of steering wheel 200 does not exceed the predetermined angle (N O), control unit 10 determines in step S44 whether or not a specific input operation has been performed within operation detection area Arv. If a specific input operation has not been perfo rmed (NO), in step S45, the control unit 10 disallows the input operation in step S3, and proc eeds to step S1 in FIG. If the input operation is disallowed in step S45, control of the operatio n target device is invalidated. If a specific input operation is performed (YES), the control unit 10 permits the input operation in step S3 in step S46, and proceeds to step S5 in FIG. Altho ugh all steps S41, S42 and S43 are provided in the example shown in FIG. 16, only one or tw o of these steps may be provided

.

Moreover, when providing all of steps S41, S42, and S43 or two of these steps, the order is ar bitrary. Although referred to as a shift lever 330 here, the shape of the operating portion for s witching between straight forward and backward movement of the vehicle and for changing th e gear ratio of the transmission is arbitrary, and may be any of floor shift, column shift, paddl e shift, and the like. All of these are included in the shift lever.

As described

above, when the vehicle is in a specific state such as right turn, left turn, cornering, or rever se, if the control of the device to be operated is disabled, the driver can No input operation is performed on the touch sensor 21 . Therefore, it contributes to the improvement of safety.

[0077]

The operation according to this embodiment is summarized as follows. The detection unit 10 a (first detection unit) detects a first area of the touch sensor 21 attached to the grip portion (annular portion 200r or straight portion 201s) of the steering wheels 200 and 201 held by th e driver. Detects that the An example of the first area is the grip detection area Arg. The dete ction unit 10a (second detection unit) performs a specific input operation on a second area of the touch sensor 21 located above the first area while the first area is being touched. Detect what has been done. An example of the second area is the operation detection area Arv. Since the thumb or forefinger is positioned higher than the palm during driving, the upper side of th e first area may be the second area. When the first area is touched and a specific input operat

ion is performed, the touch sensor 21 controls the operation target device to be operated acco rding to the specific input operation. The upper area is an area above the first area when the steering wheel 200 is not rotated and the driver grips the grip

.

It is preferable to determine that the first area is being touched when it is detected that the fir st area is being touched over a predetermined area.

[0079]

Moreover, from another viewpoint, it is as follows. The detection unit 10a (first detection uni t) is mounted in a predetermined range of the grip portion (annular portion 200r or linear port ion 201s) of the steering wheels 200 and 201 that the driver grips so as to cover the grip port ion. The touch sensor 21 touches the first area on the touch sensor 21 at a predetermined an gle or more in the circumferential direction of the cross section of the steering wheels 200 and 201 when the grip portion is cut in the radial direction. to detect The detection unit 10a (seco nd detection unit) detects that a specific input operation is performed on a second area of the touch sensor 21 that is different from the first area while the first area is being touched at a p redetermined angle or more. Detect what has been done. When the first area is touched at th e predetermined angle or more and a specific input operation is performed, the operation targ et device to be operated by the touch sensor 21 is controlled according to the specific input op eration.

The second

area is preferably an area located above the first area. The area located above is an area loc ated above the first area when the driver grips the grip portion while the steering wheel 200 i s not rotated.

FIGS.

17 and 18 show examples of construction for effectively informing the driver that the touch s ensor 21 has been operated. 17 and 18 are schematic diagrams in which the touch sensor 21 is expanded and converted into a rectangular shape, similar to FIG. FIG. 17 shows an exampl e in which a color changing sheet 41 containing a coloring substance is provided on the lower surface side of the touch sensor 21 . By using a transparent conductive film for the touch sens or 21 , the driver can see the color of the color change sheet 41 arranged on the lower surfac e of the touch sensor 21 through the touch sensor 21 . The driver can recognize that the touc h sensor 21 has been operated by changing the color of the color change sheet 41 at the porti on where the touch sensor 21 is touched under the control of the control unit 10 .

FIG.

18 shows an example in which a tactile feedback sheet 42 for changing the tactile sense (ha nd feeling) is provided on the upper surface side of the touch sensor 21 . As the tactile feedba ck sheet 42, for example, a sheet called "E-Sense" developed by Senseg of Finland can be ad opted. This sheet provides tactile feedback by charging the film. Even if the tactile feedback s heet 42 is provided on the upper surface side of the touch sensor 21, the touch sensor 21 can

detect the contact of a finger or the like. When the touch sensor 21 is operated via the tactile feedback sheet 42 , the driver can recognize that the touch sensor 21 has been operated by c hanging the tactile sensation of the tactile feedback sheet 42 under the control of the control unit 10 . can.

[0083]

Next, a configuration example of the steering wheel will be described with reference to FIG. 19 . A steering wheel 210 shown in FIG. 19 is configured to output a control signal to an oper ation target device from the steering wheel 210 . In FIG. 19, the same parts as those in FIGS. 1 and 2 are denoted by the same reference numerals, and the description thereof will be omit ted as appropriate. As shown in FIG. 19, the steering wheel 210 includes, for example, a sens or data generation unit 23 similar to the sensor data generation unit 22 in FIG. I have it. The controller 24 has a detector 24a similar to the detector 10a and a control signal generator 24 b. When the steering wheel 210 is mounted on the vehicle, the control signal generator 24b generates a control signal for controlling the device to be operated in accordance with a specif ic input operation to the touch sensor 21. FIG

.

The control signal output from the control signal generator 24b is output to the output termin al 26 via the cable 25. FIG. By connecting the output terminal 26 to the device to be operate d, the device to be operated can be controlled by the control signal. Examples of specific input operations are similar to FIGS. 11-13. The requirements for the control signal generator 24b t o generate the control signal are the same as those described above. The present invention i s not limited to the embodiments described above, and various modifications can be made wit hout departing from the gist of the present invention

.

The touch sensor 21 may be detachably attached to the annular portion 200r using a hook-an d-loop fastener. Although the annular portion 200r is used as the grip portion, the grip portion does not necessarily have to be annular.

[0086]

The touch sensor 21 need not be composed of one sheet, and may be composed of a pluralit y of touch sensor pieces. If the touch sensor 21 is composed of a plurality of touch sensor pie ces, the shape of each touch sensor piece can be simplified, which is advantageous in manufa cturing touch sensors. Note that when the touch sensor 21 is composed of a plurality of touch sensor pieces, the touch sensor pieces do not necessarily have to be arranged without gaps. T he touch panel 21 of the present embodiment is mounted so as to cover the grip portion. It al so includes that the sensor 21 is mounted over the grip portion with a gap between the pieces of the touch sensor.

[0087]

Furthermore, the range in which the touch sensor 21 is provided is not limited to the grip po rtion (annular portion 200r or the straight portion 201s) that the driver grips during driving. Y

ou may extend to the surface of the connection part which connects between. In FIG. 2, the c onnection part is the part located between the left and right hands in the state shown in FIG. 2, and in FIG. In this way, the touch sensor 21 may be extended to the surface of the connect ing portion, and the operation detection area Arv may be set at a position near the grip portio n of the connecting portion. If the position is close to the grip portion, the driver can operate t he operation target device without releasing the hand from the grip portion or moving the han d largely during driving. Therefore, even if the touch sensor 21 is extended to the surface of t he connecting portion, there is almost no possibility that the driver's operation of the steering wheels 200, 201, 210 will be hindered.

10 , 24 control units 10a

, 24a detection unit 11 navigation processing unit 12 audio reproduction unit 13 televisio n tuner 14 video signal processing unit 15 video display unit 16 audio signal processing u nit 17 display element 18 storage unit 20 speaker 21 touch sensors 22, 23 sensor data generator 24b control signal generator 25 cable

26 output terminal

31 steering angle sensor

32 direction indicator sensor

33 shift lever sensor

34 in-vehicle communication section

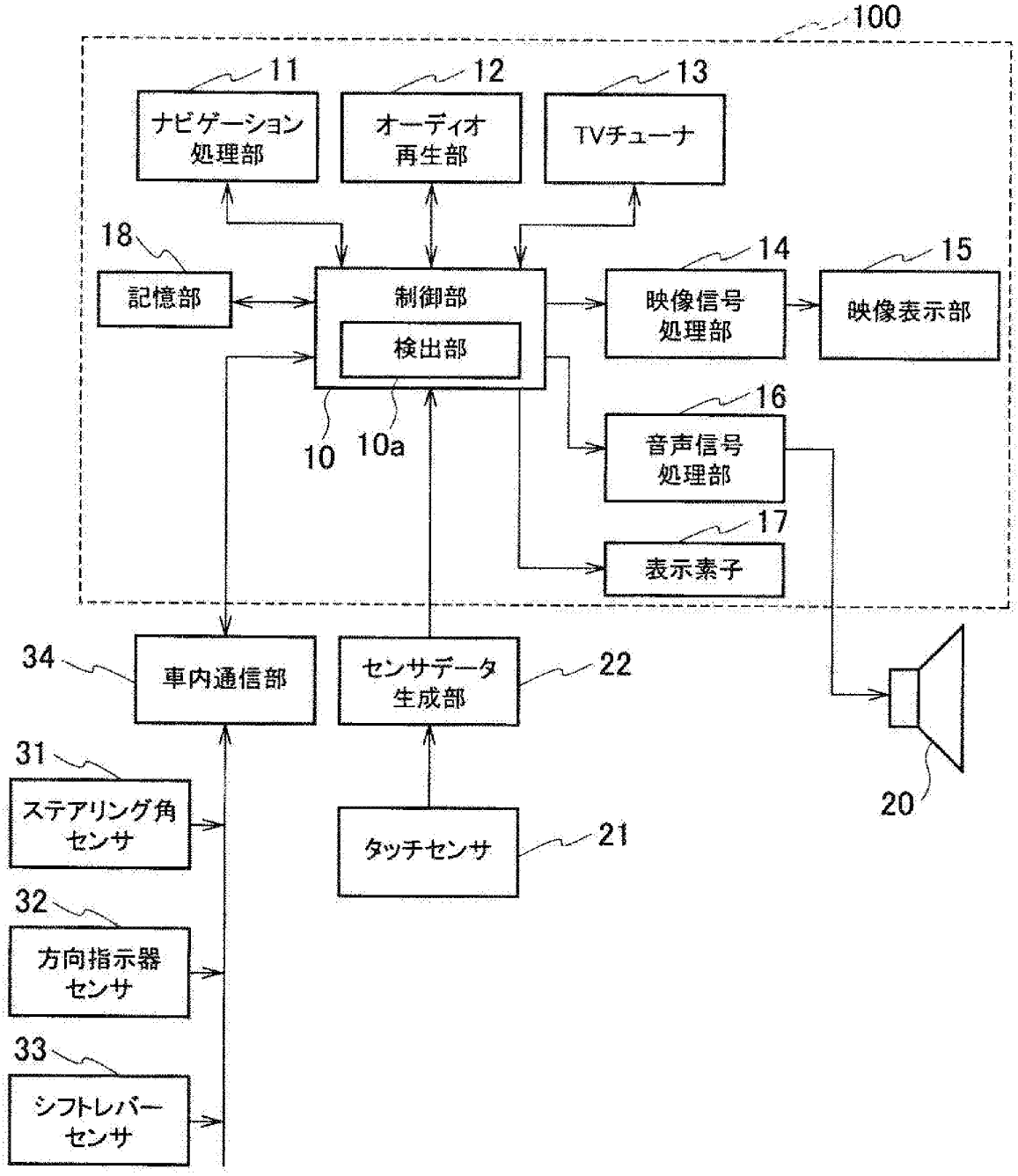
200, 201, 210 steering wheel

200r annular section (grip section)

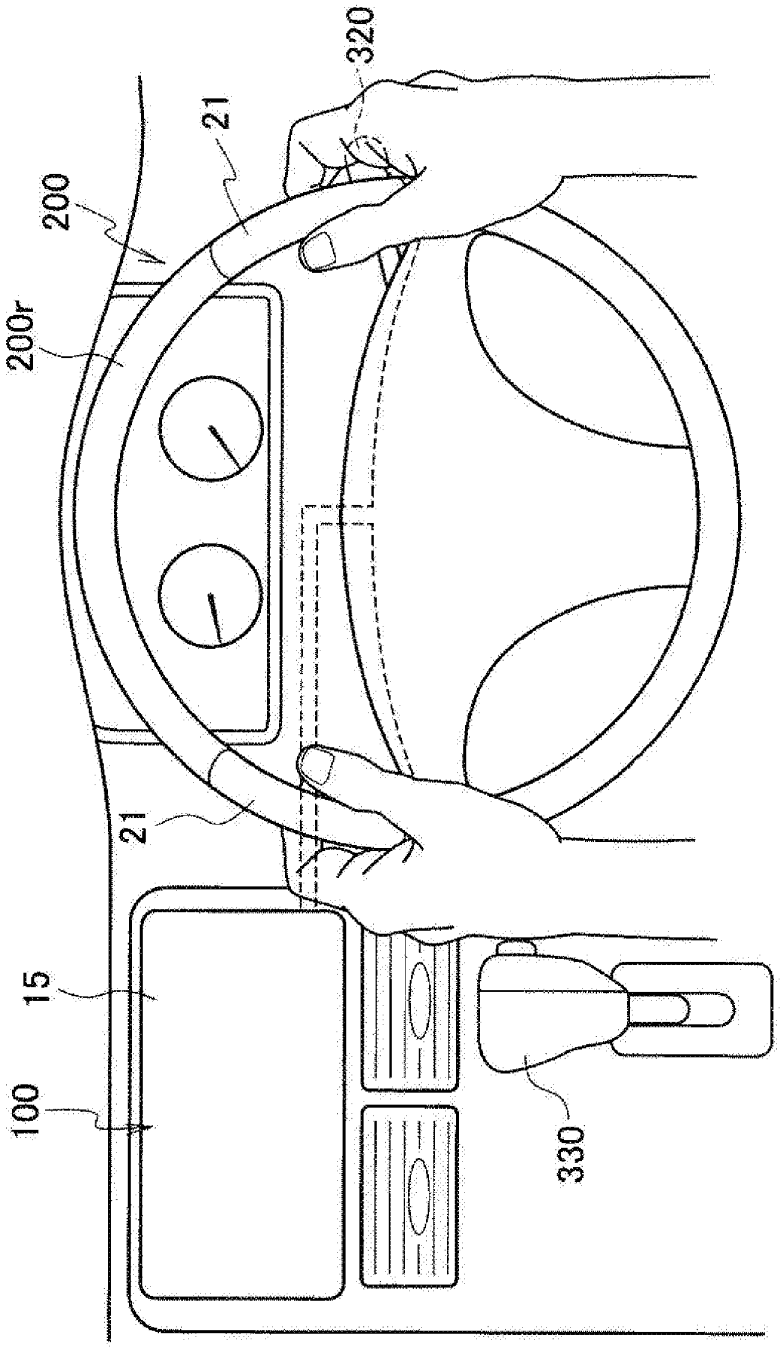
201s linear section (grip section)

drawing	open —

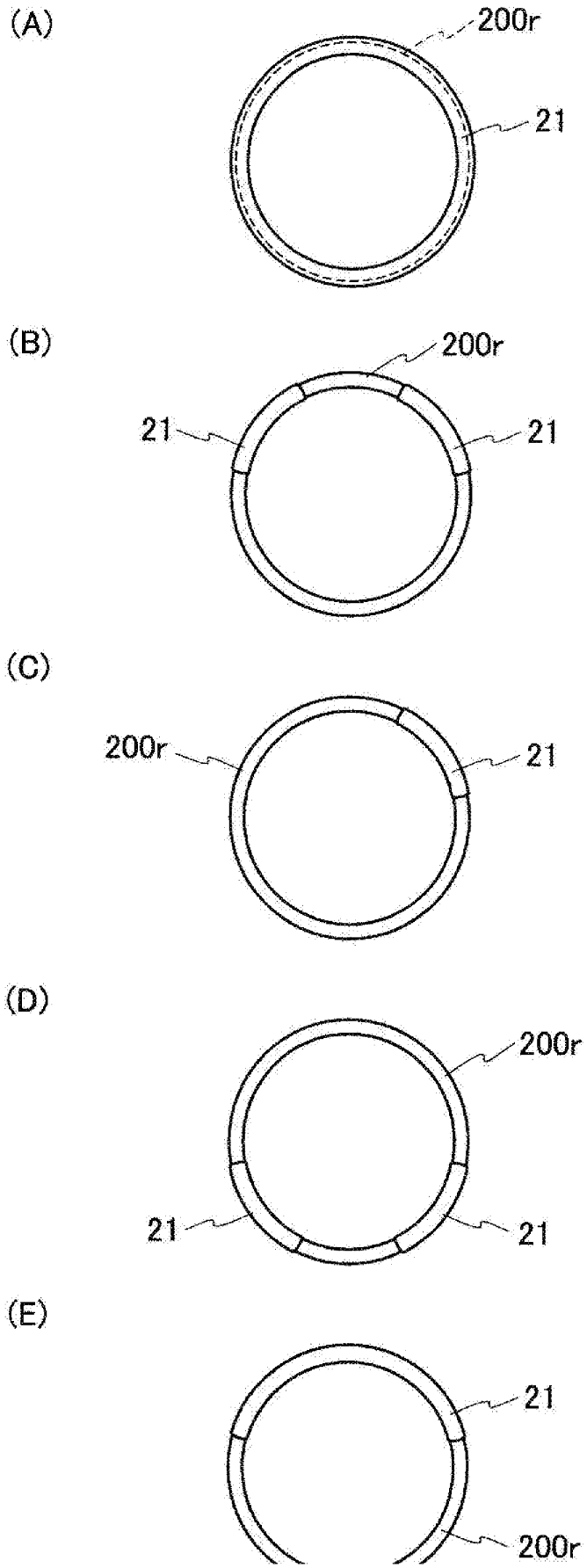
[Fig. 1]


100
11
ナビゲーション処理部
12
オーディオ再生部
13
TVチューナ
18
記憶部
制御部
検出部
14
映像信号処理部
15
映像表示部
10
10a
16
音声信号処理部
17
表示素子
34
車内通信部
センサデータ生成部
22
20
31
ステアリング角センサ
タッチセンサ
21
32
方向指示器センサ
33
シフトレバーセンサ

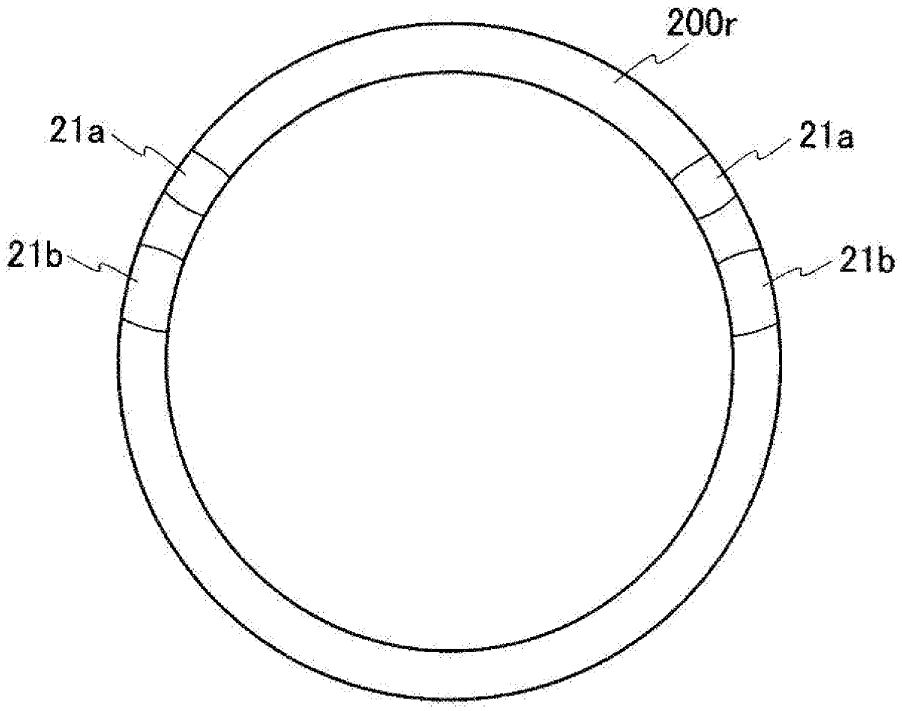
[Figure 2]


320
21
200
200r
21
15
100
330

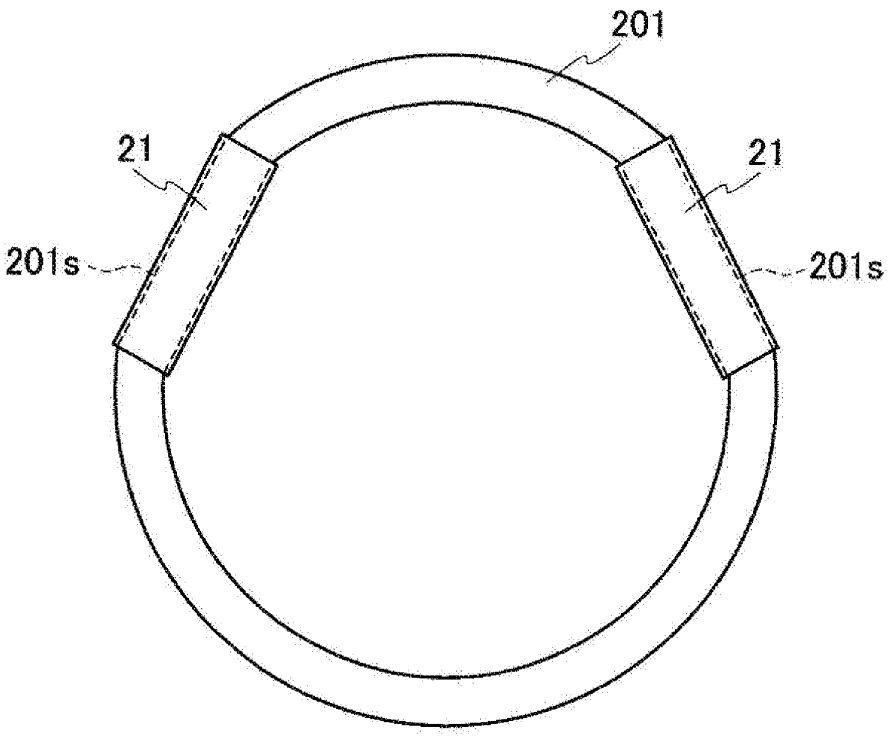
[Figure 3]


(A)
200r
21
(B)
200r
21
21
(C)
200r
21
(D)
200r
21
21
(E)
21
200r

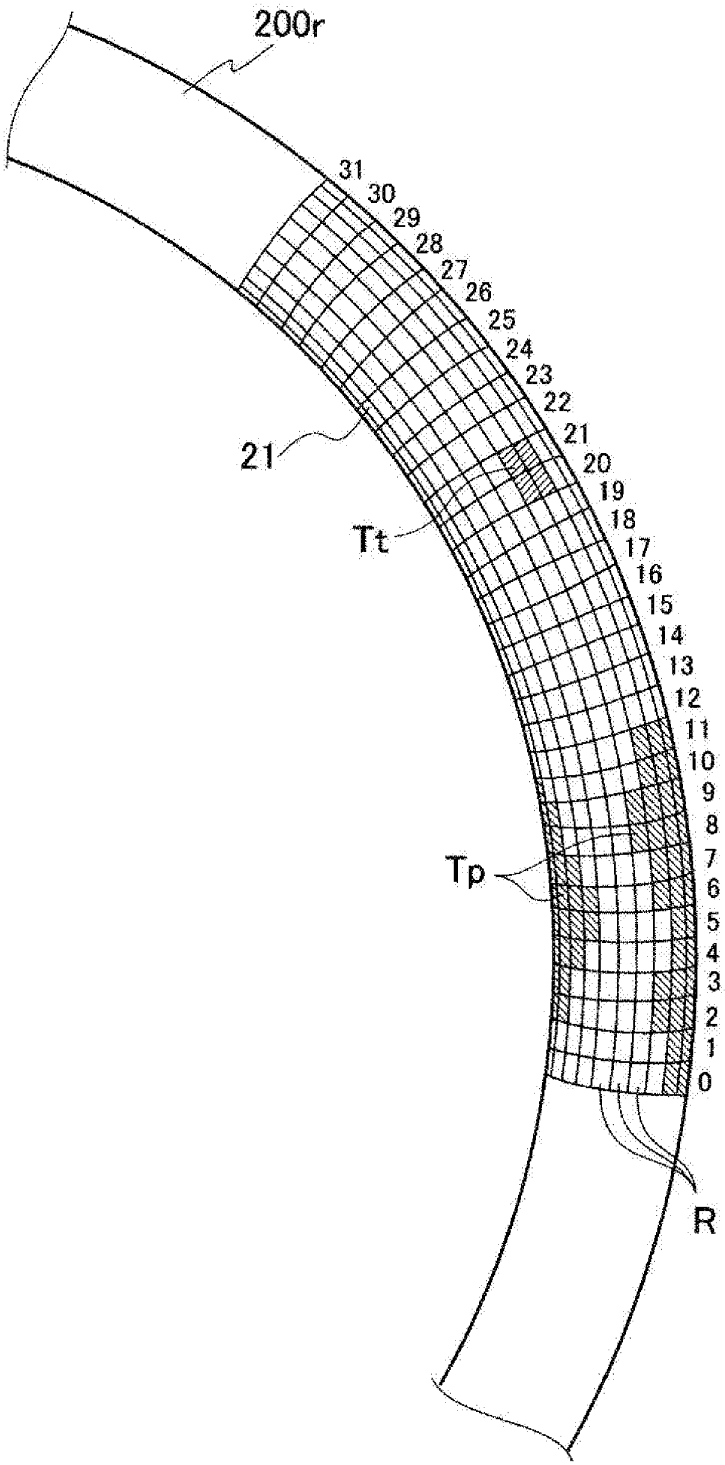
[Figure 4]



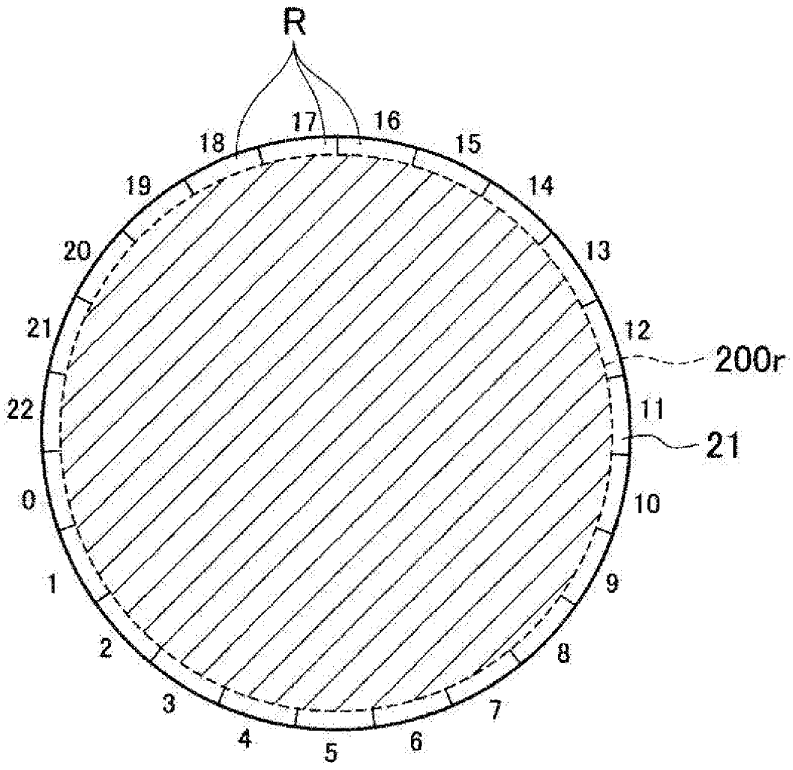
[Figure 5]



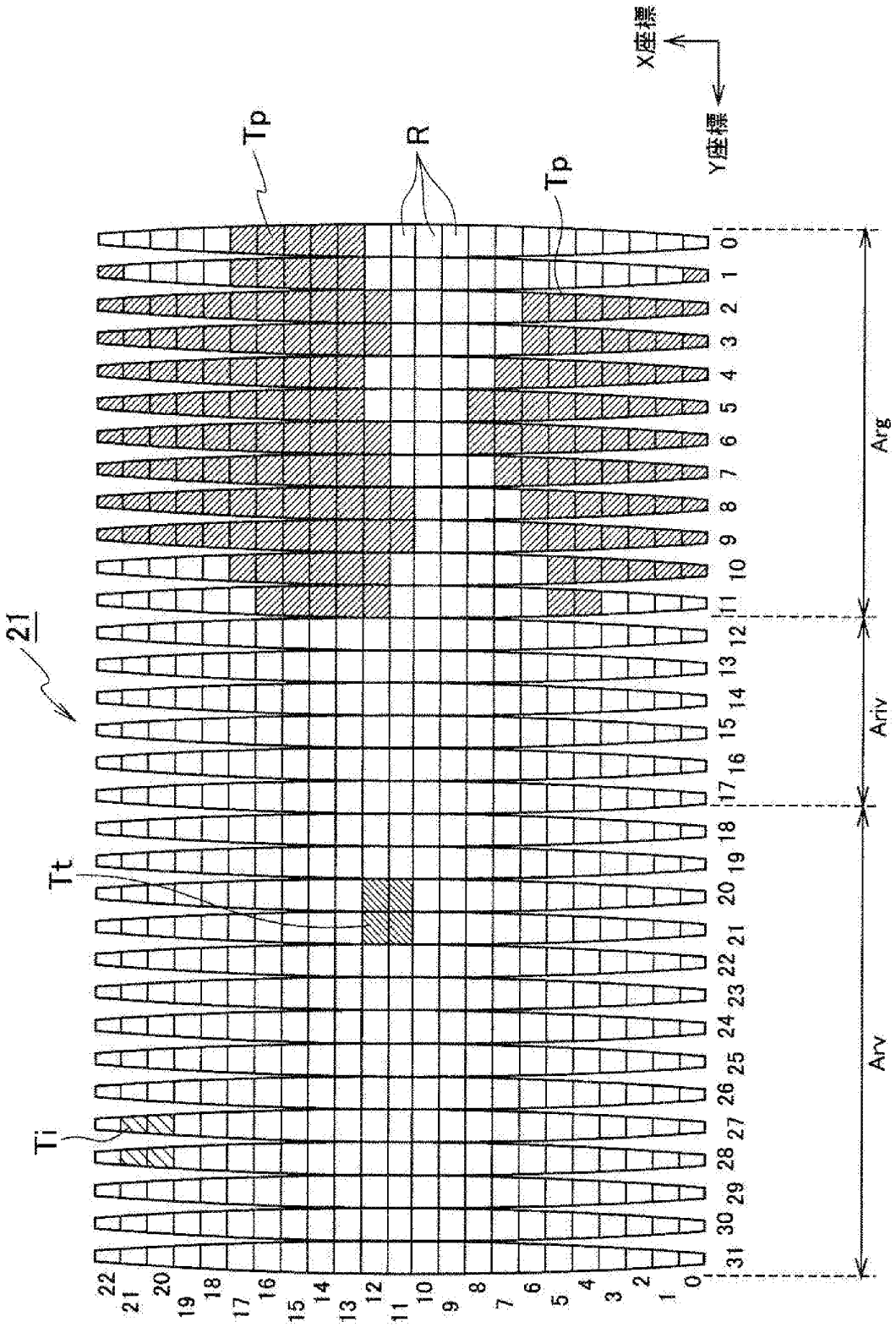
[Fig. 6]


200r
31
30
29
28
27
26
25
24
23
22
21
20
19
18
17
16
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
21
Tt
Tp
R

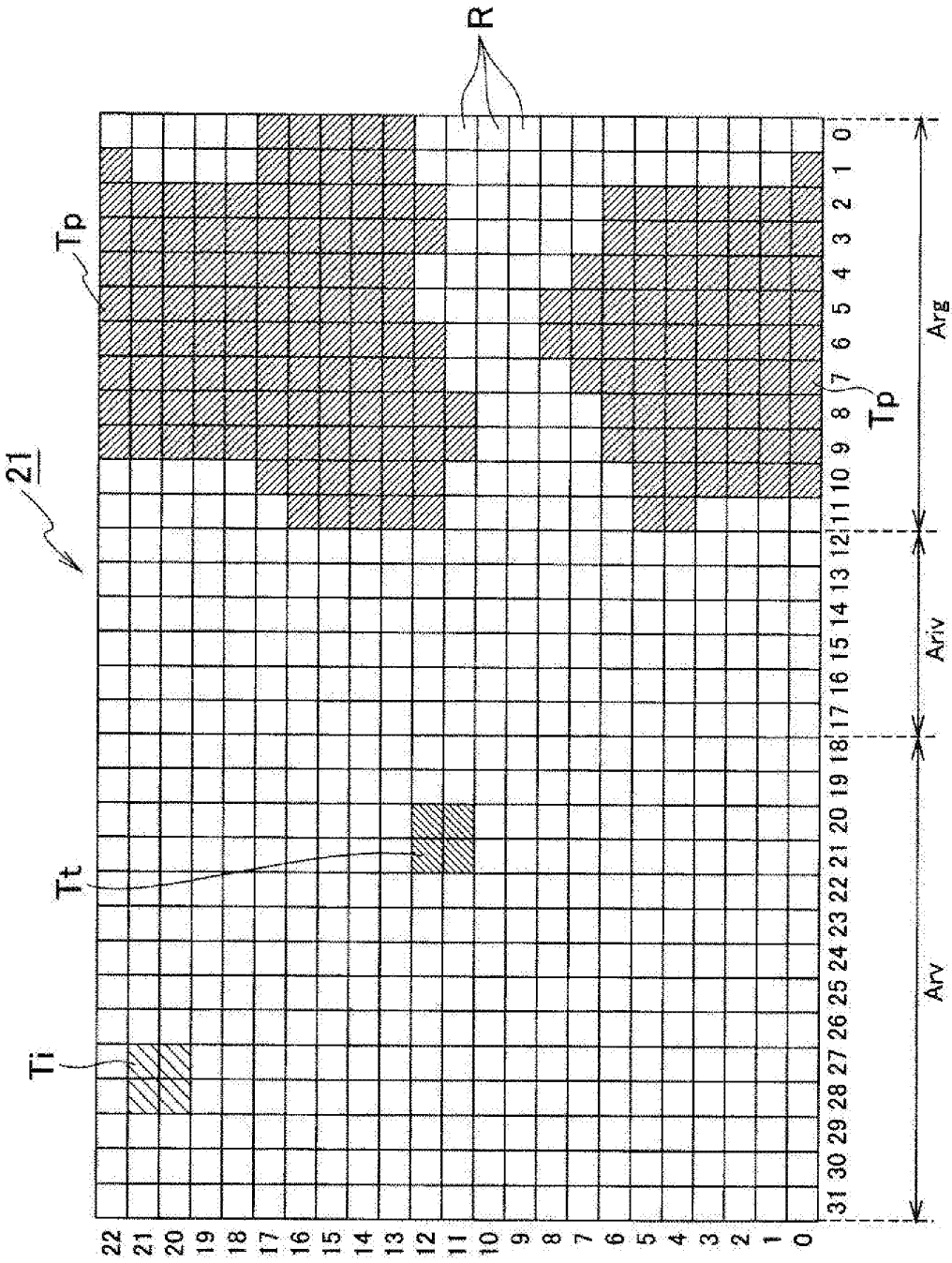
[Fig. 7]


R
17
16
18
15
19
14
20
13
21
12
200r
22
11
21
0
10
1
9
2
8
3
7
4
6
5

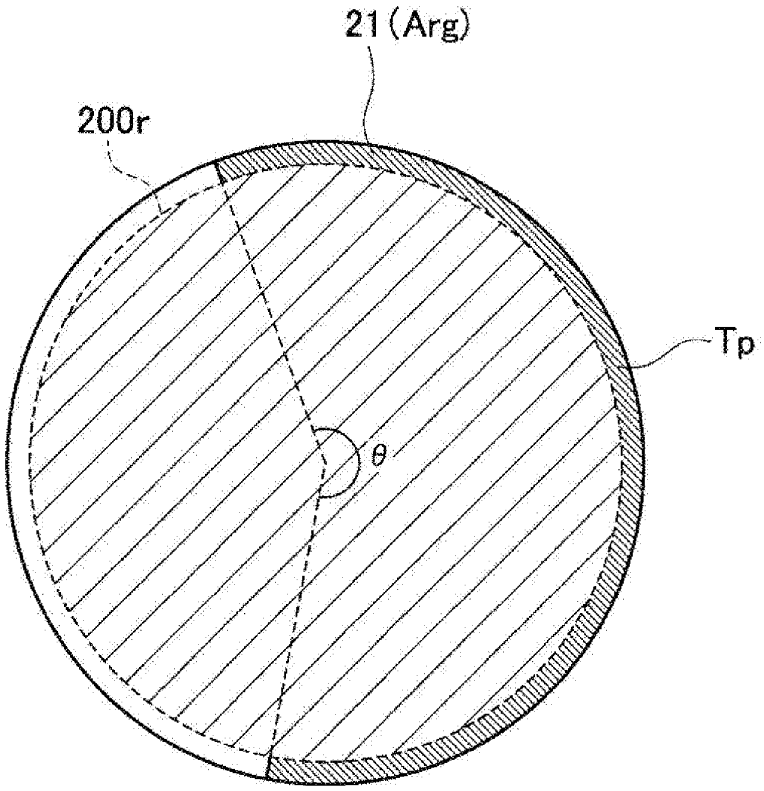
[Fig. 8]


X座標
Y座標
Tp
R
Tp
21
Tt
Ti
Arg
Ariv
Arv

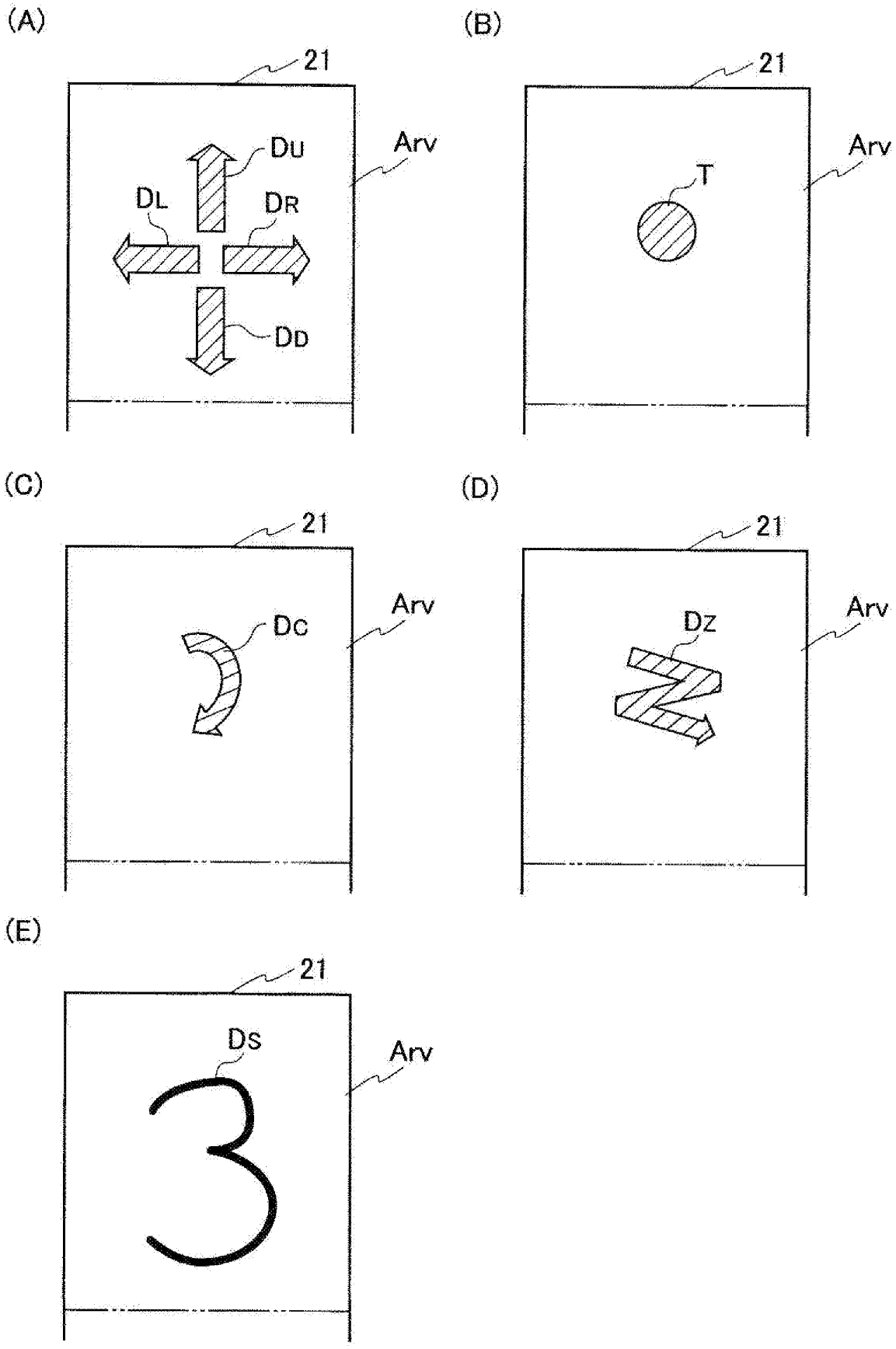
[Fig. 9]


R
Tp
21
Tt
Ti
Tp
Arg
Ariv
Arv
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31
22 21 20 19 18 17 16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0

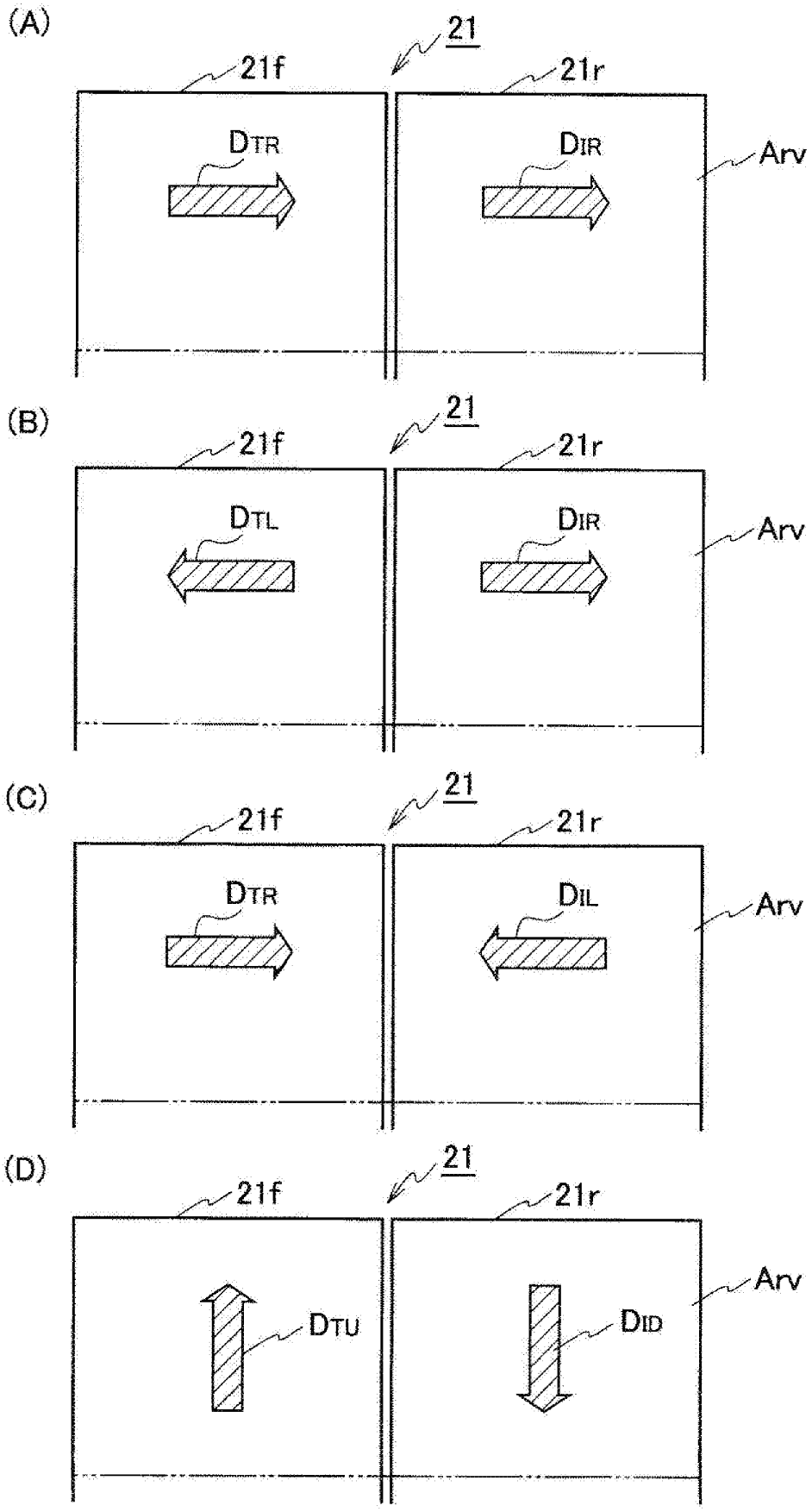
[Fig. 10]


21 (Arg)
200r
Tp
θ

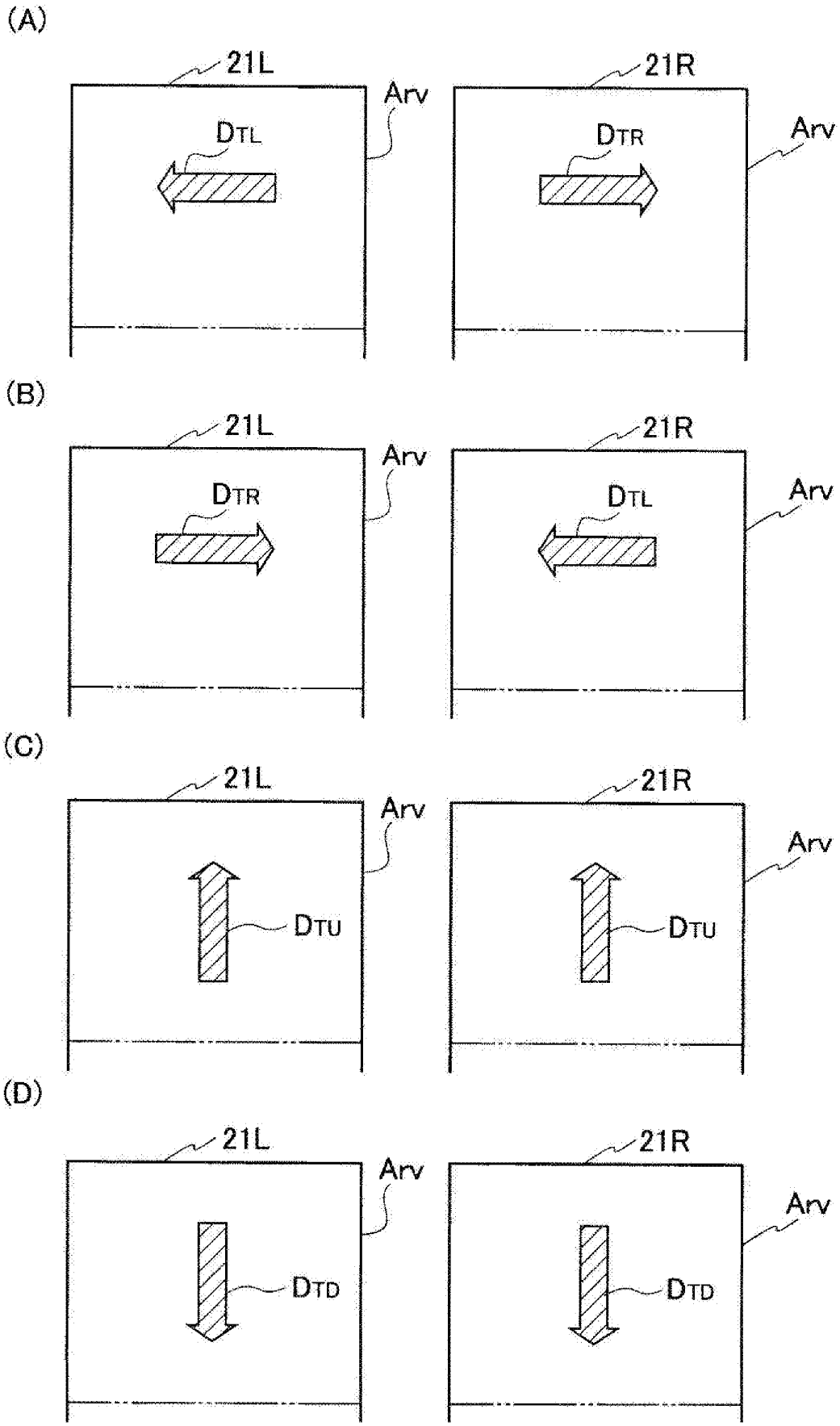
[Fig. 11]


(A)
21
Arv
DU
DL
DR
DD
(B)
21
Arv
T
(C)
21
Arv
DC
(D)
21
Arv
DZ
(E)
21
Arv
DS
3

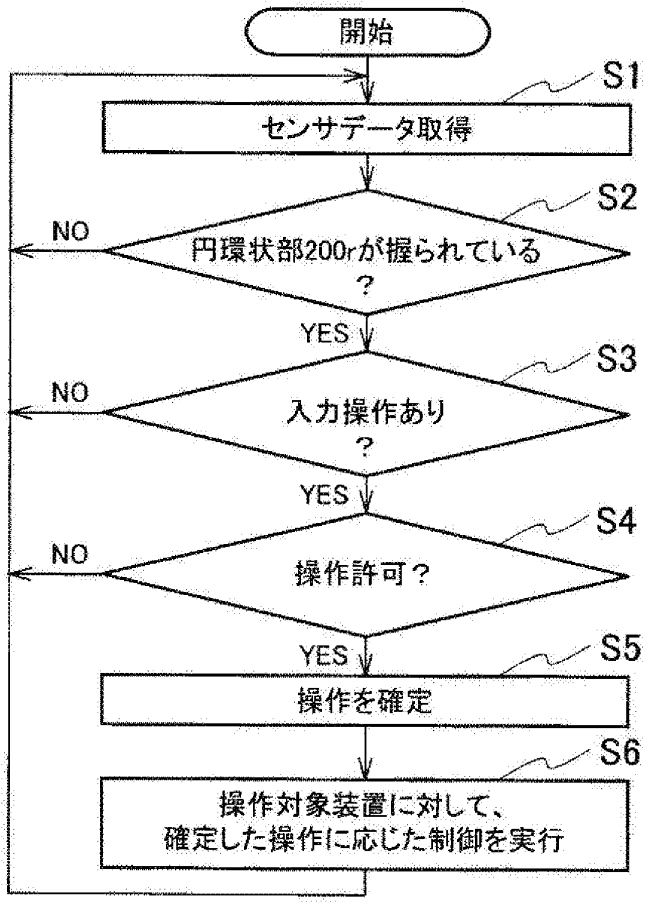
[Fig. 12]


(A)
21
21f
21r
DTR
DIR
Arv
(B)
21
21f
21r
DTL
DIR
Arv
(C)
21
21f
21r
DTR
DIL
Arv
(D)
21
21f
21r
DTU
DID
Arv

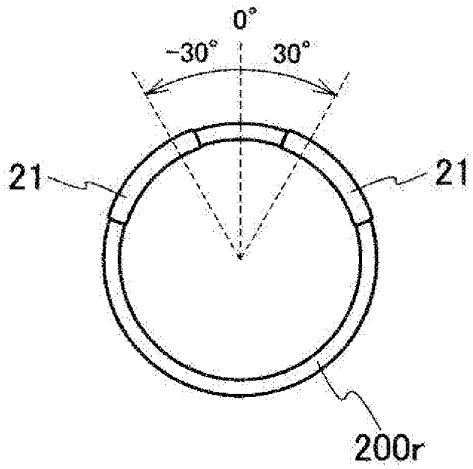
[Fig. 13]


(A)
21L
Arv
DTL
21R
Arv
DTR
(B)
21L
Arv
DTR
21R
Arv
DTL
(C)
21L
Arv
DTU
21R
Arv
DTU
(D)
21L
Arv
DTD
21R
Arv
DTD

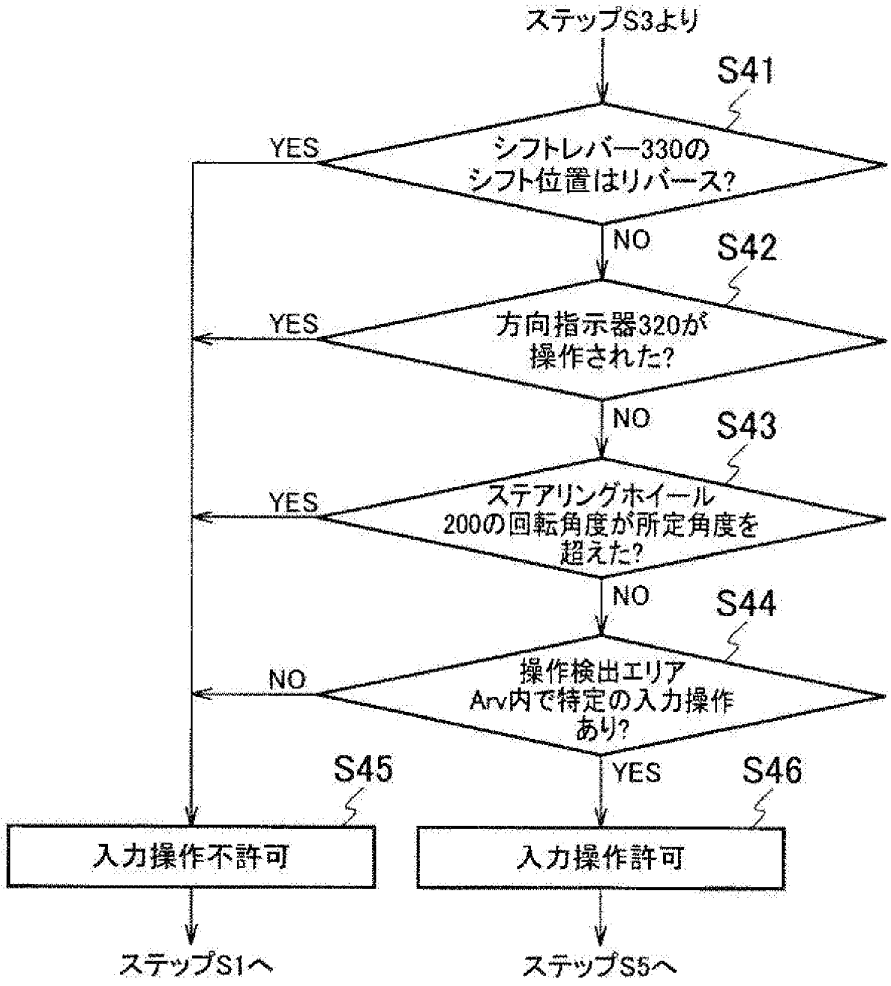
[Fig. 14]


開始
S1
センサデータ取得
S2
NO
円環状部200rが握られている
？
YES
S3
NO
入力操作あり
？
YES
S4
NO
操作許可？
YES
S5
操作を確定
S6
操作対象装置に対して、
確定した操作に応じた制御を実行

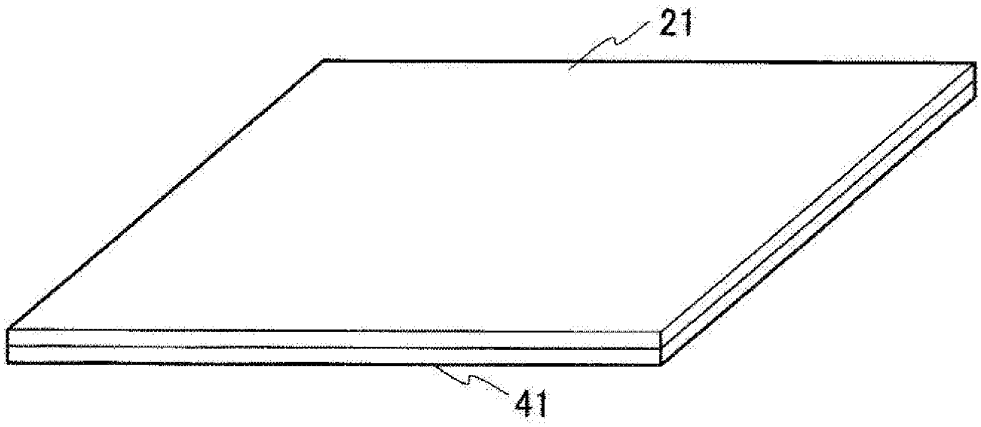
[Fig. 15]



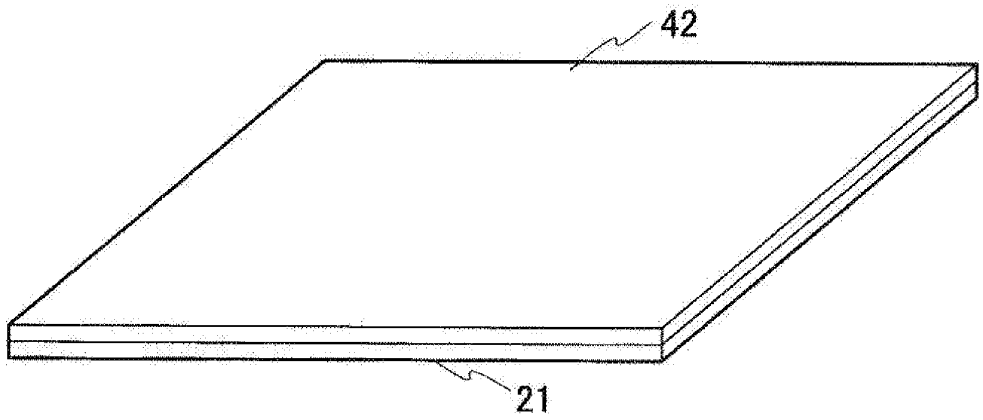
[Fig. 16]


ステップS3より
S41
シフトレバー330の
シフト位置はリバース?
YES
NO
S42
方向指示器320が
操作された?
YES
NO
S43
ステアリングホイール
200の回転角度が所定角度を
超えた?
YES
NO
S44
操作検出エリア
Arv内で特定の入力操作
あり?
NO
YES
S45
S46
入力操作不許可
入力操作許可
ステップS1へ
ステップS5へ

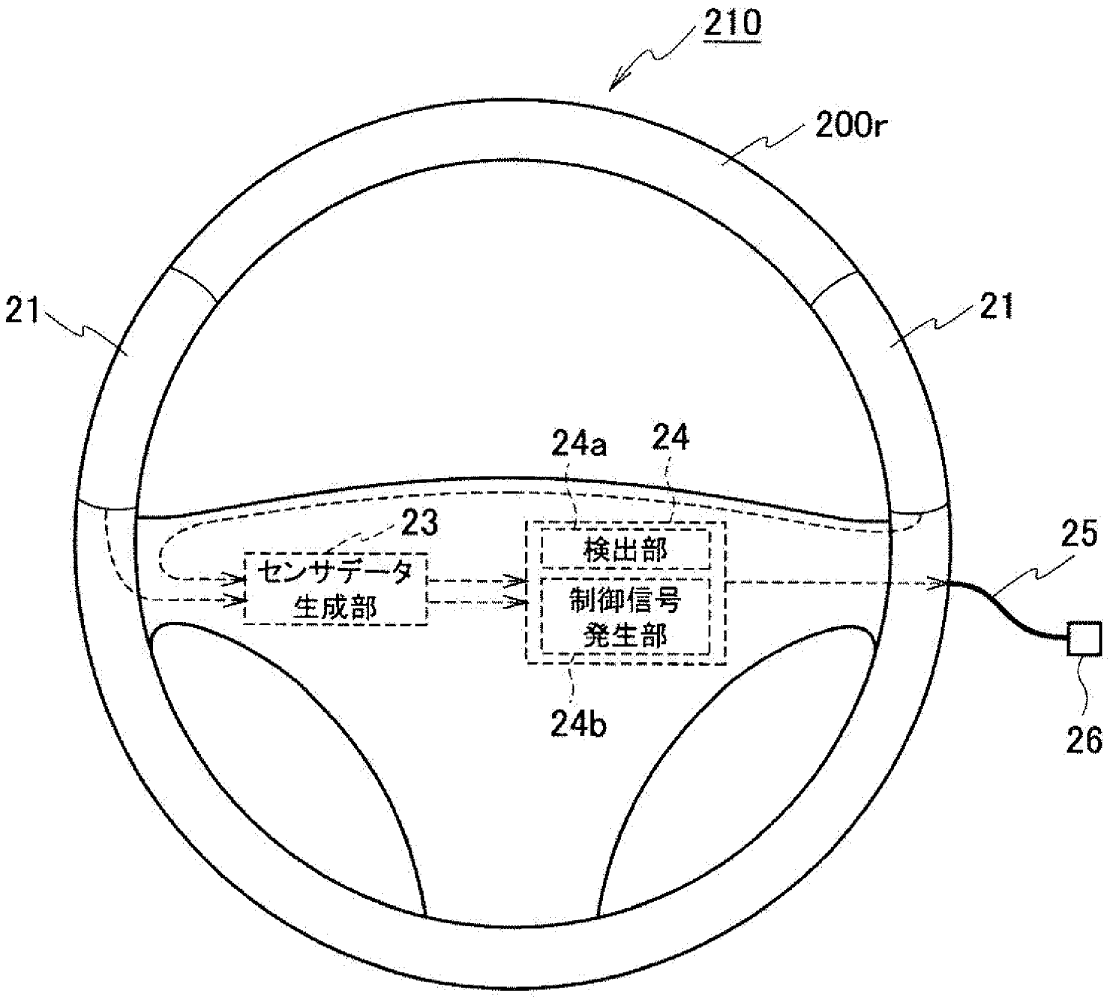
[Fig. 17]


21
41

[Fig. 18]



[Fig. 19]



drawing open —

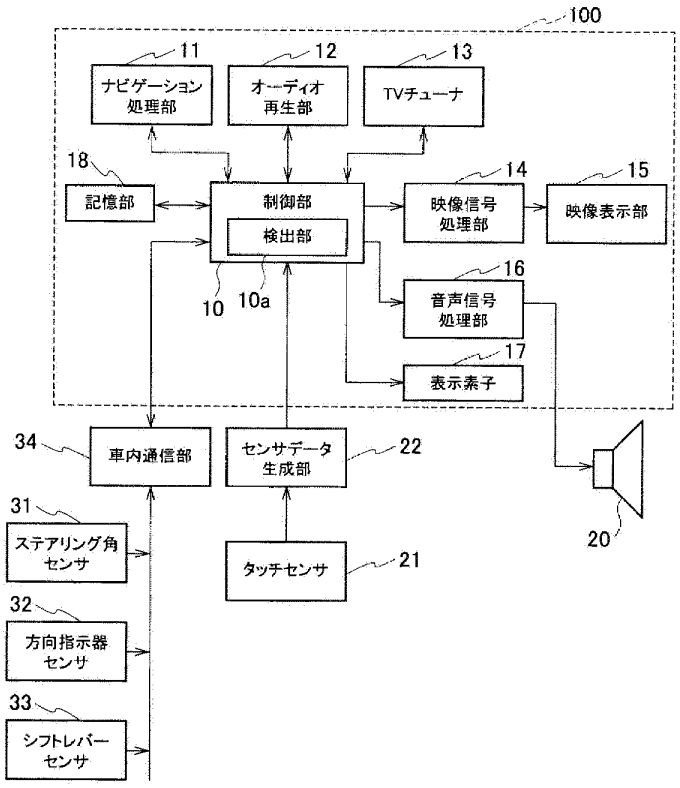


Figure 1

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DEVICE AND METHOD FOR CONTROLLING OPERATION TARGET DEVICE IN VEHICLE

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Applicant(s): JVC KENWOOD CORP, ; 株式会社ＪＶＣケンウッド

Classification: **- international:** ***B60R16/02; B60R16/027***
- cooperative:

Application number: JP20120043554 20120229 Global Dossier

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Abstract of JP2013075652 (A)

PROBLEM TO BE SOLVED: To provide a control device for controlling an operation target device in a vehicle, which can operate the operation target device without detaching or largely shifting a hand from a gripping part.SOLUTION: A sensor data generation part 22 generates sensor data based on a contact detection signal obtained from a touch sensor 21 mounted to cover the gripping part of a steering wheel. A detection part 10a detects whether the driver grips the gripping part or not and an input operation to the touch sensor 21. When it is detected by the detection part 10a that the driver grips the holding part and it is detected that a specific input operation has been performed to the touch sensor 21, a control part 10 controls the operation target device according to the specific input operation. The control part 10 invalidates the control of the operation target device when the vehicle is in a specific condition.

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最終頁に続く

(54)【発明の名称】車両における操作対象装置の制御装置及び制御方法

(57)【特許請求の範囲】
【請求項１】
複数の検出領域を有し、車両のステアリングホイールにおける運転者が握る握持部の所定の範囲に、前記握持部を覆うように装着されたタッチセンサから得られる接触検出信号に基づいて、どの検出領域が触られているかを示す位置データを含むセンサデータを生成するセンサデータ生成部と、
前記センサデータに基づいて、運転者が前記握持部を握っているか否か、及び、前記タッチセンサに対する入力操作を検出する検出部と、
前記検出部によって運転者が前記握持部を握っていることが検出され、かつ、前記タッチセンサに対して特定の入力操作が行われたことが検出された場合に、前記特定の入力操作に応じて、前記タッチセンサによって操作する対象の操作対象装置を制御する制御部と、
を備え、
前記制御部は、方向指示器が操作されたとき車両が特定の状態にあるとして、前記操作対象装置の制御を無効とすることを特徴とする車両における操作対象装置の制御装置。
【請求項２】
複数の検出領域を有し、車両のステアリングホイールにおける運転者が握る握持部の所定の範囲に、前記握持部を覆うように装着されたタッチセンサから得られる接触検出信号に基づいて、どの検出領域が触られているかを示す位置データを含むセンサデータを生成するセンサデータ生成部と、

前記センサデータに基づいて、運転者が前記握持部を握っているか否か、及び、前記タッチセンサに対する入力操作を検出する検出部と、
前記検出部によって運転者が前記握持部を握っていることが検出され、かつ、前記タッチセンサに対して特定の入力操作が行われたことが検出された場合に、前記特定の入力操作に応じて、前記タッチセンサによって操作する対象の操作対象装置を制御する制御部と、
を備え、
前記制御部は、シフトレバーのシフト位置がリバースとなったとき車両が特定の状態にあるとして、前記操作対象装置の制御を無効とすることを特徴とする車両における操作対象装置の制御装置。
【請求項３】
前記タッチセンサには、前記複数の検出領域の一部を含み、運転者の手のひらの接触を検出するグリップ検出エリアと、前記複数の検出領域の他の一部を含み、指の接触による前記特定の入力操作を検出する操作検出エリアとが設定されており、
前記検出部は、前記グリップ検出エリアから得られる接触検出信号に基づくセンサデータによって運転者が前記握持部を握っているか否かを検出し、前記操作検出エリアから得られる接触検出信号に基づくセンサデータによって前記特定の入力操作を検出する
ことを特徴とする請求項１または２に記載の車両における操作対象装置の制御装置。
【請求項４】
複数の検出領域を有し、車両のステアリングホイールにおける運転者が握る握持部の所定の範囲に、前記握持部を覆うように装着されたタッチセンサから得られる接触検出信号に基づいて、どの検出領域が触られているかを示す位置データを含むセンサデータを生成するセンサデータ生成部と、
前記センサデータに基づいて、運転者が前記握持部を握っているか否か、及び、前記タッチセンサに対する入力操作を検出する検出部と、
前記検出部によって運転者が前記握持部を握っていることが検出され、かつ、前記タッチセンサに対して特定の入力操作が行われたことが検出された場合に、前記特定の入力操作に応じて、前記タッチセンサによって操作する対象の操作対象装置を制御する制御部と、
を備え、
前記タッチセンサには、前記複数の検出領域の一部を含み、運転者の手のひらの接触を検出するグリップ検出エリアと、前記複数の検出領域の他の一部を含み、指の接触による前記特定の入力操作を検出する操作検出エリアとが設定されており、
前記検出部は、前記グリップ検出エリアから得られる接触検出信号に基づくセンサデータによって運転者が前記握持部を握っているか否かを検出し、前記操作検出エリアから得られる接触検出信号に基づくセンサデータによって前記特定の入力操作を検出し、
前記制御部は、車両が特定の状態にあるときに、前記操作対象装置の制御を無効とすることを特徴とする車両における操作対象装置の制御装置。
【請求項５】
前記制御部は、前記特定の入力操作として、前記操作検出エリアに対して、前記握持部を前記ステアリングホイールの径方向に切断したときの断面における周方向に離間した２箇所を２つの指によって操作したパターンに応じて、前記操作対象装置を制御することを特徴とする請求項３または４に記載の車両における操作対象装置の制御装置。
【請求項６】
前記制御部は、さらに、前記ステアリングホイールの回転角度が所定の角度を超えたとき車両が特定の状態にあるとして、前記操作対象装置の制御を無効とすることを特徴とする請求項１～４のいずれか１項に記載の車両における操作対象装置の制御装置。
【請求項７】
前記タッチセンサは、運転者が左手で握る握持部の所定の範囲に装着された第１のタッチセンサと右手で握る握持部の所定の範囲に装着された第２のタッチセンサとを含み、

前記制御部は、前記特定の入力操作として、前記第１のタッチセンサに対する第１の入力操作と前記第２のタッチセンサに対する第２の入力操作との組み合わせによるパターンに応じて、前記操作対象装置を制御する

ことを特徴とする請求項１～６のいずれか１項に記載の車両における操作対象装置の制御装置。

【請求項８】

複数の検出領域を有し、車両のステアリングホイールにおける運転者が握る握持部の所定の範囲に、前記握持部を覆うように装着されたタッチセンサを運転者が握っているか否かを検出し、

前記タッチセンサに対して特定の入力操作が行われたか否かを検出し、

方向指示器が操作されたか否かを検出し、

車両が、方向指示器が操作された特定の状態にはないことが検出され、運転者が前記タッチセンサを握っていることが検出され、かつ、前記特定の入力操作が行われたことが検出された場合に、前記タッチセンサによって操作する対象の操作対象装置を制御し、車両が、方向指示器が操作された特定の状態にあることが検出された場合には、前記操作対象装置を制御を無効とする

ことを特徴とする車両における操作対象装置の制御方法。

【請求項９】

複数の検出領域を有し、車両のステアリングホイールにおける運転者が握る握持部の所定の範囲に、前記握持部を覆うように装着されたタッチセンサを運転者が握っているか否かを検出し、

前記タッチセンサに対して特定の入力操作が行われたか否かを検出し、

シフトレバーのシフト位置がリバースとなったか否かを検出し、

車両が、シフトレバーのシフト位置がリバースとなった特定の状態にはないことが検出され、運転者が前記タッチセンサを握っていることが検出され、かつ、前記特定の入力操作が行われたことが検出された場合に、前記タッチセンサによって操作する対象の操作対象装置を制御し、車両が、シフトレバーのシフト位置がリバースとなった特定の状態にあることが検出された場合には、前記操作対象装置を制御を無効とする

ことを特徴とする車両における操作対象装置の制御方法。

【請求項１０】

前記タッチセンサには、前記複数の検出領域の一部を含み、運転者の手のひらの接触を検出するグリップ検出エリアと、前記複数の検出領域の他の一部を含み、指の接触による前記特定の操作を検出する操作検出エリアとが設定されており、

前記グリップ検出エリアに対する手のひらの接触によって、運転者が前記タッチセンサを握っていることを検出し、

前記操作検出エリアに対する指の接触によって、前記特定の入力操作が行われたことを検出する

ことを特徴とする請求項８または９に記載の車両における操作対象装置の制御方法。

【請求項１１】

複数の検出領域を有し、車両のステアリングホイールにおける運転者が握る握持部の所定の範囲に、前記握持部を覆うように装着されたタッチセンサを運転者が握っているか否かを検出し、

前記タッチセンサに対して特定の入力操作が行われたか否かを検出し、

車両が特定の状態にあるか否かを検出し、

車両が特定の状態にはないことが検出され、運転者が前記タッチセンサを握っていることが検出され、かつ、前記特定の入力操作が行われたことが検出された場合に、前記タッチセンサによって操作する対象の操作対象装置を制御し、

前記タッチセンサには、前記複数の検出領域の一部を含み、運転者の手のひらの接触を検出するグリップ検出エリアと、前記複数の検出領域の他の一部を含み、指の接触による前記特定の操作を検出する操作検出エリアとが設定されており、

前記グリップ検出エリアに対する手のひらの接触によって、運転者が前記タッチセンサを握っていることを検出し、
前記操作検出エリアに対する指の接触によって、前記特定の入力操作が行われたことを検出する
ことを特徴とする車両における操作対象装置の制御方法。
【請求項１２】
前記特定の入力操作として、前記操作検出エリアに対して、前記握持部を前記ステアリングホイールの径方向に切断したときの断面における周方向に離間した２箇所を２つの指によって操作したパターンに応じて、前記操作対象装置を制御することを特徴とする請求項１０または１１に記載の車両における操作対象装置の制御方法。
【請求項１３】
前記ステアリングホイールの回転角度が所定の角度を超えたとき車両が特定の状態にあるにあるとして、前記操作対象装置の制御を無効とすることを特徴とする請求項８～１１のいずれか１項に記載の車両における操作対象装置の制御方法。
【請求項１４】
前記タッチセンサは、運転者が左手で握る握持部の所定の範囲に装着された第１のタッチセンサと右手で握る握持部の所定の範囲に装着された第２のタッチセンサとを含み、
前記特定の入力操作として、前記第１のタッチセンサに対する第１の入力操作と前記第２のタッチセンサに対する第２の入力操作との組み合わせによるパターンに応じて、前記操作対象装置を制御する
ことを特徴とする請求項８～１３のいずれか１項に記載の車両における操作対象装置の制御方法。
【発明の詳細な説明】
【技術分野】
【０００１】
本発明は、車両に搭載されているナビゲーション装置等の車載機器、または、変速機や方向指示器等の車両の動作を制御する車両動作制御装置を操作対象装置とし、操作対象装置を制御する制御装置及び制御方法に関する。
【背景技術】
【０００２】
車両に搭載されているナビゲーション装置等の車載機器を操作するための操作スイッチをステアリングホイールに配置した車両が普及している（特許文献１参照）。操作スイッチをステアリングホイールに配置すれば、運転者は車載機器を操作する際に車載機器まで手を伸ばす必要がないので、操作性が向上する。特許文献１に記載されているように、操作スイッチは、実際には、運転者が手で握る握持部であるステアリングホイールの円環状部ではなく、エアバッグが収納されているセンター部と円環状部との間を連結する連結部に配置されるのが通常である。従って、運転者は、操作スイッチを操作するために、握っている円環状部から手を離したり、手を大きくずらしたりする必要がある。特許文献２には、円環状部の背面や内側側面に操作スイッチを配置することが記載されている。
【先行技術文献】
【特許文献】
【０００３】
【特許文献１】特開２００７－１０６３５３号公報
【特許文献２】特開２００５－３４８１２３号公報
【特許文献３】特開２００８－１９５２２０号公報
【発明の概要】
【発明が解決しようとする課題】
【０００４】
特許文献２に記載の発明によれば、円環状部に操作スイッチを配置しているので、円環状部から手を離したり、手を大きくずらしたりすることなく、操作スイッチを操作するこ

とができる。しかしながら、特許文献２に記載されている操作スイッチは押しボタンによるキーや凹凸を設けたキーであり、この種のキーは運転者がステアリングホイールを操作する際の支障となる可能性がある。運転者が握る円環状部に大きな凹凸を設けることは好ましくない。また、円環状部に操作スイッチのような操作部を配置した場合、運転者が通常の運転のために円環状部を握っている場合のように、操作対象装置を操作しようとする意思がない場合に、不用意に操作対象装置が操作されないようにすることが求められる。さらに、車両の状態によっては誤操作を招く場合があり、誤操作を極力少なくすることが求められる。

【０００５】

本発明はこのような要望に対応するため、握持部から手を離したり、手を大きくずらしたりすることなく操作対象装置を操作することができ、運転者がステアリングホイールを操作する際に支障となる可能性を大幅に低減させることができる車両における操作対象装置の制御装置及び制御方法を提供することを目的とする。また、誤操作を大幅に低減させることができる車両における操作対象装置の制御装置及び制御方法を提供することを目的とする。

【課題を解決するための手段】

【０００６】

本発明は、上述した従来の技術の課題を解決するため、複数の検出領域を有し、車両のステアリングホイールにおける運転者が握る握持部の所定の範囲に、前記握持部を覆うように装着されたタッチセンサから得られる接触検出信号に基づいて、どの検出領域が触られているかを示す位置データを含むセンサデータを生成するセンサデータ生成部と、前記センサデータに基づいて、運転者が前記握持部を握っているか否か、及び、前記タッチセンサに対する入力操作を検出する検出部と、前記検出部によって運転者が前記握持部を握っていることが検出され、かつ、前記タッチセンサに対して特定の入力操作が行われたことが検出された場合に、前記特定の入力操作に応じて、前記タッチセンサによって操作する対象の操作対象装置を制御する制御部とを備え、前記制御部は、方向指示器が操作されたとき車両が特定の状態にあるとして、前記操作対象装置の制御を無効とすることを特徴とする車両における操作対象装置の制御装置を提供する。

【０００７】

本発明は、上述した従来の技術の課題を解決するため、複数の検出領域を有し、車両のステアリングホイールにおける運転者が握る握持部の所定の範囲に、前記握持部を覆うように装着されたタッチセンサから得られる接触検出信号に基づいて、どの検出領域が触られているかを示す位置データを含むセンサデータを生成するセンサデータ生成部と、前記センサデータに基づいて、運転者が前記握持部を握っているか否か、及び、前記タッチセンサに対する入力操作を検出する検出部と、前記検出部によって運転者が前記握持部を握っていることが検出され、かつ、前記タッチセンサに対して特定の入力操作が行われたことが検出された場合に、前記特定の入力操作に応じて、前記タッチセンサによって操作する対象の操作対象装置を制御する制御部とを備え、前記制御部は、シフトレバーのシフト位置がリバースとなったとき車両が特定の状態にあるとして、前記操作対象装置の制御を無効とすることを特徴とする車両における操作対象装置の制御装置を提供する。

【０００８】

上記の車両における操作対象装置の制御装置において、前記タッチセンサには、前記複数の検出領域の一部を含み、運転者の手のひらの接触を検出するグリップ検出エリアと、前記複数の検出領域の他の一部を含み、指の接触による前記特定の入力操作を検出する操作検出エリアとが設定されており、前記検出部は、前記グリップ検出エリアから得られる接触検出信号に基づくセンサデータによって運転者が前記握持部を握っているか否かを検出し、前記操作検出エリアから得られる接触検出信号に基づくセンサデータによって前記特定の入力操作を検出することが好ましい。

【０００９】

本発明は、上述した従来の技術の課題を解決するため、複数の検出領域を有し、車両の

ステアリングホイールにおける運転者が握る握持部の所定の範囲に、前記握持部を覆うように装着されたタッチセンサから得られる接触検出信号に基づいて、どの検出領域が触られているかを示す位置データを含むセンサデータを生成するセンサデータ生成部と、前記センサデータに基づいて、運転者が前記握持部を握っているか否か、及び、前記タッチセンサに対する入力操作を検出する検出部と、前記検出部によって運転者が前記握持部を握っていることが検出され、かつ、前記タッチセンサに対して特定の入力操作が行われたことが検出された場合に、前記特定の入力操作に応じて、前記タッチセンサによって操作する対象の操作対象装置を制御する制御部とを備え、前記タッチセンサには、前記複数の検出領域の一部を含み、運転者の手のひらの接触を検出するグリップ検出エリアと、前記複数の検出領域の他の一部を含み、指の接触による前記特定の入力操作を検出する操作検出エリアとが設定されており、前記検出部は、前記グリップ検出エリアから得られる接触検出信号に基づくセンサデータによって運転者が前記握持部を握っているか否かを検出し、前記操作検出エリアから得られる接触検出信号に基づくセンサデータによって前記特定の入力操作を検出し、前記制御部は、車両が特定の状態にあるときに、前記操作対象装置の制御を無効とすることを特徴とする車両における操作対象装置の制御装置を提供する。

【００１０】

上記の車両における操作対象装置の制御装置において、前記制御部は、前記特定の入力操作として、前記操作検出エリアに対して、前記握持部を前記ステアリングホイールの径方向に切断したときの断面における周方向に離間した２箇所を２つの指によって操作したパターンに応じて、前記操作対象装置を制御することが好ましい。

上記の車両における操作対象装置の制御装置において、前記制御部は、さらに、前記ステアリングホイールの回転角度が所定の角度を超えたとき車両が特定の状態にあるとして、前記操作対象装置の制御を無効とすることが好ましい。

上記の車両における操作対象装置の制御装置において、前記タッチセンサは、運転者が左手で握る握持部の所定の範囲に装着された第１のタッチセンサと右手で握る握持部の所定の範囲に装着された第２のタッチセンサとを含み、前記制御部は、前記特定の入力操作として、前記第１のタッチセンサに対する第１の入力操作と前記第２のタッチセンサに対する第２の入力操作との組み合わせによるパターンに応じて、前記操作対象装置を制御することが好ましい。

【００１１】

本発明は、上述した従来の技術の課題を解決するため、複数の検出領域を有し、車両のステアリングホイールにおける運転者が握る握持部の所定の範囲に、前記握持部を覆うように装着されたタッチセンサを運転者が握っているか否かを検出し、前記タッチセンサに対して特定の入力操作が行われたか否かを検出し、方向指示器が操作されたか否かを検出し、車両が、方向指示器が操作された特定の状態にはないことが検出され、運転者が前記タッチセンサを握っていることが検出され、かつ、前記特定の入力操作が行われたことが検出された場合に、前記タッチセンサによって操作する対象の操作対象装置を制御し、車両が、方向指示器が操作された特定の状態にあることが検出された場合には、前記操作対象装置を制御を無効とすることを特徴とする車両における操作対象装置の制御方法を提供する。

【００１２】

本発明は、上述した従来の技術の課題を解決するため、複数の検出領域を有し、車両のステアリングホイールにおける運転者が握る握持部の所定の範囲に、前記握持部を覆うように装着されたタッチセンサを運転者が握っているか否かを検出し、前記タッチセンサに対して特定の入力操作が行われたか否かを検出し、シフトレバーのシフト位置がリバースとなったか否かを検出し、車両が、シフトレバーのシフト位置がリバースとなった特定の状態にはないことが検出され、運転者が前記タッチセンサを握っていることが検出され、かつ、前記特定の入力操作が行われたことが検出された場合に、前記タッチセンサによって操作する対象の操作対象装置を制御し、車両が、シフトレバーのシフト位置がリバースとなった特定の状態にあることが検出された場合には、前記操作対象装置を制御を無効と

することを特徴とする車両における操作対象装置の制御方法を提供する。

【００１３】

上記の車両における操作対象装置の制御方法において、前記タッチセンサには、前記複数の検出領域の一部を含み、運転者の手のひらの接触を検出するグリップ検出エリアと、前記複数の検出領域の他の一部を含み、指の接触による前記特定の操作を検出する操作検出エリアとが設定されており、前記グリップ検出エリアに対する手のひらの接触によって、運転者が前記タッチセンサを握っていることを検出し、前記操作検出エリアに対する指の接触によって、前記特定の入力操作が行われたことを検出することが好ましい。

【００１４】

本発明は、上述した従来の技術の課題を解決するため、複数の検出領域を有し、車両のステアリングホイールにおける運転者が握る握持部の所定の範囲に、前記握持部を覆うように装着されたタッチセンサを運転者が握っているか否かを検出し、前記タッチセンサに対して特定の入力操作が行われたか否かを検出し、車両が特定の状態にあるか否かを検出し、車両が特定の状態にはないことが検出され、運転者が前記タッチセンサを握っていることが検出され、かつ、前記特定の入力操作が行われたことが検出された場合に、前記タッチセンサによって操作する対象の操作対象装置を制御し、前記タッチセンサには、前記複数の検出領域の一部を含み、運転者の手のひらの接触を検出するグリップ検出エリアと、前記複数の検出領域の他の一部を含み、指の接触による前記特定の操作を検出する操作検出エリアとが設定されており、前記グリップ検出エリアに対する手のひらの接触によって、運転者が前記タッチセンサを握っていることを検出し、前記操作検出エリアに対する指の接触によって、前記特定の入力操作が行われたことを検出することを特徴とする車両における操作対象装置の制御方法を提供する。

【００１５】

上記の車両における操作対象装置の制御方法において、前記特定の入力操作として、前記操作検出エリアに対して、前記握持部を前記ステアリングホイールの径方向に切断したときの断面における周方向に離間した２箇所を２つの指によって操作したパターンに応じて、前記操作対象装置を制御することが好ましい。

上記の車両における操作対象装置の制御方法において、前記ステアリングホイールの回転角度が所定の角度を超えたとき車両が特定の状態にあるにあるとして、前記操作対象装置の制御を無効とすることが好ましい。

上記の車両における操作対象装置の制御方法において、前記タッチセンサは、運転者が左手で握る握持部の所定の範囲に装着された第１のタッチセンサと右手で握る握持部の所定の範囲に装着された第２のタッチセンサとを含み、前記特定の入力操作として、前記第１のタッチセンサに対する第１の入力操作と前記第２のタッチセンサに対する第２の入力操作との組み合わせによるパターンに応じて、前記操作対象装置を制御することが好ましい。

【発明の効果】

【００１６】

本発明の車両における操作対象装置の制御装置及び制御方法によれば、握持部から手を離したり、手を大きくずらしたりすることなく操作対象装置を操作することができ、運転者がステアリングホイールを操作する際に支障となる可能性を大幅に低減させることができる。また、誤操作を大幅に低減させることができる。

【図面の簡単な説明】

【００１７】

【図１】本発明の車両における操作対象装置の制御装置の一実施形態を示すブロック図である。

【図２】一実施形態の操作対象装置の制御装置を備える車両の例を示す部分平面図である。

【図３】一実施形態におけるタッチセンサをステアリングホイールに装着する位置及び範囲の例を示す図である。

【図４】一実施形態におけるタッチセンサをステアリングホイールに装着する位置及び範囲の他の例を示す図である。
【図５】タッチセンサを変形ステアリングホイールに装着する例を示す図である。
【図６】ステアリングホイールにおけるタッチセンサの部分を握っている状態でセンサデータが得られる部分の例を示す部分斜視図である。
【図７】タッチセンサにおける断面周方向の座標を示す断面図である。
【図８】図６に示すタッチセンサを展開した状態を示す平面図である。
【図９】図８に示す各領域を均等の大きさに変換した状態を示す模式図である。
【図１０】ステアリングホイールにおけるタッチセンサの部分を握っていると判定するための要件の例を示す図である。
【図１１】タッチセンサに対する特定の入力操作の例を示す模式図である。
【図１２】タッチセンサに対する特定の入力操作の他の例を示す模式図である。
【図１３】タッチセンサに対する特定の入力操作のさらに他の例を示す模式図である。
【図１４】一実施形態の動作を説明するためのフローチャートである。
【図１５】ステアリングホイールの回転角度を説明するための図である。
【図１６】図１４のステップＳ４の具体的な処理の例を示すフローチャートである。
【図１７】タッチセンサを操作した際に色を変化させるための構成例を示す模式的な斜視図である。
【図１８】タッチセンサを操作した際に触覚を変化させるための構成例を示す模式的な斜視図である。
【図１９】ステアリングホイールの構成例を示す平面図である。
【発明を実施するための形態】
【００１８】
以下、本発明の車両における操作対象装置の制御装置及び制御方法の一実施形態について、添付図面を参照して説明する。図１，図２において、車載機器１００は、車両のダッシュボード内に装着されている。図１に示す例では、車載機器１００は、制御部１０，ナビゲーション処理部１１，オーディオ再生部１２，テレビジョン（ＴＶ）チューナ１３，映像信号処理部１４，映像表示部１５，音声信号処理部１６，表示素子１７，記憶部１８を備えている。制御部１０は検出部１０ａを含む。
【００１９】
ナビゲーション処理部１１は地図データを保持する記憶部とＧＰＳアンテナ等を有しており、制御部１０とナビゲーション処理部１１とが協同して経路案内を行う。オーディオ再生部１２は、制御部１０による制御に従って、例えばコンパクトディスク等の光ディスクや半導体メモリに記録されているオーディオ信号を再生する。ＴＶチューナ１３は、制御部１０による制御に従って、所定の放送局のＴＶ放送波信号を受信する。ナビゲーション処理部１１またはＴＶチューナ１３より出力された映像信号は、制御部１０を介して映像信号処理部１４に入力されて処理され、液晶パネル等の映像表示部１５に表示される。
【００２０】
ナビゲーション処理部１１，オーディオ再生部１２，ＴＶチューナ１３より出力された音声信号は、制御部１０を介して音声信号処理部１６に入力されて処理され、外部のスピーカ２０にて発音される。音声信号処理部１６は増幅部を含む。スピーカ２０は、車両のドアの内部等に設置されている。表示素子１７は例えば発光ダイオード（ＬＥＤ）であり、制御部１０による制御に従って、後述するタッチセンサ２１の接触状態に応じて点灯または消灯する。表示素子１７は、運転者から視認できるように、例えば車載機器１００の筐体に配置する。表示素子１７を車載機器１００から離して、車両のステアリングホイール２００の近傍に配置してもよい。記憶部１８は不揮発性のメモリである。
【００２１】
図２に示すように、操作部であるタッチセンサ２１は、ステアリングホイール２００の円環状部２００ｒに装着されている。円環状部２００ｒは、運転者が運転の際に握る部分である握持部である。図２に示す例では、タッチセンサ２１は、円環状部２００ｒにおけ

る左右それぞれの所定の角度範囲に装着されている。タッチセンサ２１は、複数箇所の接触を検出することができる、いわゆる多点検出（マルチタッチ）のタッチセンサである。タッチセンサ２１は、円環状部２００ｒの径方向の断面の周上に、３６０°の範囲で装着することが好ましい。３６０°未満の範囲であっても、実質的に円環状部２００ｒの断面の周のほぼ全体を覆っていればよい。

【００２２】

運転者は、円環状部２００ｒのタッチセンサ２１が装着された部分を握っている。図１において、タッチセンサ２１の出力はセンサデータ生成部２２に入力される。タッチセンサ２１を手で触ると、接触検出信号がセンサデータ生成部２２へと入力される。センサデータ生成部２２は、入力された接触検出信号に基づいて、タッチセンサ２１のどの位置から接触検出信号が得られたかを示す位置データを含むセンサデータを生成して制御部１０に供給する。タッチセンサ２１とセンサデータ生成部２２とを一体化してもよいし、センサデータ生成部２２を制御部１０内に設けてもよい。

【００２３】

タッチセンサ２１としては、例えば投影式静電容量（相互キャパシタンス）方式のタッチセンサを用いることができる。円環状部２００ｒに装着するタッチセンサ２１としては、一例として、ミクロ技術研究所が開発した可撓性を有するタッチパネルを採用することができる。この可撓性を有するタッチパネルは、センサ部を０．０２～０．０５ｍｍの板厚を有する超薄板ガラスとし、超薄板ガラスとＰＥＴ（ポリエチレンテレフタレート）フィルムとを貼り合わせた構造になっている。円環状部２００ｒにタッチセンサ２１を装着しても、タッチセンサ２１は手や指で知覚できるほどの凹凸を有さないので、運転者がステアリングホイール２００を操作する際に支障となることはほとんどない。

【００２４】

図２に破線にて示すように、タッチセンサ２１と車載機器１００とを結ぶ電線を、ステアリングホイール２００及びダッシュボードの内部を通して配線することが好ましい。

【００２５】

図１，図２において、ステアリング角センサ３１は、ステアリングホイール２００の回転角度を検出する。方向指示器センサ３２は、方向指示器３２０の操作を検出する。シフトレバーセンサ３３は、シフトレバー３３０によるシフト位置がどこにあるかを検出する。ステアリング角センサ３１，方向指示器センサ３２，シフトレバーセンサ３３の各検出信号は、車内通信部３４を介して制御部１０へと供給される。

【００２６】

図３を用いて、タッチセンサ２１をステアリングホイール２００の円環状部２００ｒに装着する位置及び範囲の例について説明する。なお、上、下、右、左とは、ステアリングホイール２００を回転させていない状態（車両が直進する状態）において、運転者の位置からステアリングホイール２００を見たときの上、下、右、左であるとする。図３（Ａ）は、円環状部２００ｒの全周にタッチセンサ２１を装着した例である。図３（Ｂ）は、図２と同様であり、円環状部２００ｒにおける上方で左右それぞれの所定の角度範囲にタッチセンサ２１を互いに離間させて装着した例である。図３（Ｃ）は、円環状部２００ｒにおける上方で右側のみの所定の角度範囲にタッチセンサ２１を装着した例である。

【００２７】

図３（Ｄ）は、円環状部２００ｒにおける下方で左右それぞれの所定の角度範囲にタッチセンサ２１を互いに離間させて装着した例である。図３（Ｅ）は、円環状部２００ｒにおける頂部を含む上方の比較的広い角度範囲にタッチセンサ２１を装着した例である。図３（Ｅ）は図３（Ｂ）における左右のタッチセンサ２１を連結したものに相当する。

【００２８】

図４は、図３（Ｂ）における左右のタッチセンサ２１を、上側のタッチセンサ２１ａと下側のタッチセンサ２１ｂとに分割した例である。図４の例では、上側のタッチセンサ２１ａは手の人差し指と親指による接触を検出し、下側のタッチセンサ２１ｂは主として手のひら，中指，薬指による接触を検出する。図５は、円形ではない変形ステアリングホイ

ール２０１にタッチセンサ２１を装着した例である。タッチセンサ２１は、変形ステアリングホイール２０１の左右の直線部２０１ｓに装着されている。運転者は握持部である直線部２０１ｓを握って運転し、タッチセンサ２１が手のひらや指による接触を検出する。

【００２９】

ここで、図２に示すように、タッチセンサ２１が円環状部２００ｒにおける上方で左右に装着されており、運転者がタッチセンサ２１の部分を握っている場合に、タッチセンサ２１によって手のひらや指の接触がどのように検出されるかについて説明する。図６は、図２の右側のタッチセンサ２１を運転者が握った場合に、手のひらと指が接触している範囲の例を示している。運転者が円環状部２００ｒを手で握る握り方、手の大きさは一様ではなく、図６は単なる例である。

【００３０】

図６に示す例では、ハッチングを付したＴｐで示す複数の検出領域Ｒが手のひらの接触を検出している部分であり、ハッチングを付したＴｔで示す複数の検出領域Ｒが親指の接触を検出している部分である。以下、手のひら接触検出部Ｔｐ、親指接触検出部Ｔｔと称することとする。図６では見えていない車両の進行方向側であるタッチセンサ２１の裏面側には、人差し指が接触する。

【００３１】

図６に示すように、タッチセンサ２１は手のひらや指の接触を検出する検出部分として複数の検出領域Ｒを有している。タッチセンサ２１の各検出領域Ｒには座標が設定されている。図６に示すように、円環状部２００ｒの周方向において、タッチセンサ２１の下端部に位置している検出領域Ｒを座標０とし、上端部に位置している検出領域Ｒまで１，２，…，３０，３１と周方向の座標を設定している。タッチセンサ２１における円環状部２００ｒの周方向の座標をＹ座標とする。

【００３２】

図７は、タッチセンサ２１を装着している部分で円環状部２００ｒの径方向に円環状部２００ｒを切断した断面図である。図７に示すように、円環状部２００ｒの断面において、例えば円環状部２００ｒの内径側に位置している検出領域Ｒを座標０とする。断面における周方向のそれぞれの検出領域Ｒに、円環状部２００ｒの内径側から正面側、正面側から外径側、外径側から裏面側、裏面側から内径側へと図７の反時計方向に１，２，…，２１，２２と座標を設定している。タッチセンサ２１における断面の周方向の座標をＸ座標とする。センサデータ生成部２２は、接触検出信号が得られた検出領域ＲのＸ座標，Ｙ座標によって運転者がタッチセンサ２１のどこを触っているかを示す位置データを得ることができる。

【００３３】

図６に示すタッチセンサ２１を展開すると、図８のようになる。図８に示すタッチセンサ２１の各領域を均等の大きさに変換した状態を模式的に示すと、図９のようになる。図８，図９においては、手のひら接触検出部Ｔｐと親指接触検出部Ｔｔに加えて、人差し指が接触している複数の検出領域Ｒである人差し指接触検出部Ｔｉも示している。なお、タッチセンサ２１に中指や薬指または小指が接触すれば、タッチセンサ２１はそれらの指の接触も検出する。本実施形態においては、運転者が、タッチセンサ２１上で特定の入力操作を行うのに好適な親指または人差し指を操作のための指として用いることとする。

【００３４】

親指または人差し指による入力操作の詳細については後に詳述することとする。制御部１０の検出部１０ａは、センサデータ生成部２２から出力されるセンサデータに基づいて、親指または人差し指によってタッチセンサ２１上で入力操作が行われたことを検出する。検出部１０ａは、センサデータ生成部２２から出力されるセンサデータに基づいて、円環状部２００ｒ（タッチセンサ２１）を握っていることも検出する。制御部１０は、タッチセンサ２１に対して行った特定の入力操作に応じて操作対象装置を制御する。

【００３５】

操作対象装置は一例として車載機器１００である。具体的には、制御部１０は、特定の

入力操作に応じて、ナビゲーション処理部１１における経路案内に関する制御を実行させたり、オーディオ再生部１２におけるオーディオ信号を再生または停止させたり、再生するトラック（楽曲）を進めたり戻したりすることができる。また、制御部１０は、特定の入力操作に応じて、ＴＶチューナ１３における受信チャンネルを切り換えたり、音声信号処理部１６の増幅部を制御して音量を減少または増加させたりすることができる。

【００３６】

操作対象装置の他の例は、車両の動作を制御する車両動作制御装置である。具体的には、制御部１０は、車内通信部３４を介して、変速機、方向指示器、エアーコンディショナのオン・オフ、エアーコンディショナの設定温度等を制御してもよい。なお、操作対象装置を車両動作制御装置とする場合には、センサデータ生成部２２から出力されるセンサデータを車両が有する制御部に入力して、車両動作制御装置を制御することが好ましい。操作対象装置を制御する制御部は、車載機器１００内の制御部１０であってもよいし、車両に備えられている車載機器１００外部の制御部であってもよい。

【００３７】

本実施形態によれば、運転者が握る円環状部２００ｒに極めて薄いタッチセンサ２１を装着して、タッチセンサ２１を操作することによって操作対象装置を操作するので、円環状部２００ｒから手を離したり、手を大きくずらしたりすることなく操作対象装置を操作することができる。また、タッチセンサ２１は円環状部２００ｒの表面上で凹凸がないため、運転者がステアリングホイール２００を操作する際に支障となる可能性はほとんどない。

【００３８】

ところで、運転者が通常の運転のために円環状部２００ｒを握っている場合のように、操作対象装置を操作しようとする意思がない場合に、不用意に操作対象装置が操作されないようにすることが必要となる。そこで、本実施形態においては、運転者が意図しない誤操作を回避するために、次のようにしている。

【００３９】

図８，図９に示すように、タッチセンサ２１上の複数の検出領域Ｒに、手のひらの接触を検出するためのグリップ検出エリアＡｒｇと、親指または人差し指による操作入力を有効として、操作入力を検出するための操作検出エリアＡｒｖと、グリップ検出エリアＡｒｇと操作検出エリアＡｒｖとの間の中間領域であり、操作入力を無効とする操作無効エリアＡｒivとを設定している。手のひら接触検出部Ｔｐはグリップ検出エリアＡｒｇ内に位置し、親指接触検出部Ｔｔ及び人差し指接触検出部Ｔｉは操作検出エリアＡｒｖ内に位置する。

【００４０】

操作無効エリアＡｒivは、グリップ検出エリアＡｒｇと操作検出エリアＡｒｖと同様に、手のひらまたは指の接触を検出する検出領域Ｒを有するものの、制御部１０（検出部１０ａ）またはセンサデータ生成部２２が操作無効エリアＡｒivからの入力操作を無効とするように処理することによって、操作無効エリアとすることができる。また、操作無効エリアＡｒivの範囲に検出領域Ｒを設けないようにタッチセンサ２１を構成することにより、操作無効エリアとしてもよい。この場合、図４に示す例と実質的に等価である。

【００４１】

運転者が通常の運転のために円環状部２００ｒを握っている場合には、手のひら接触検出部Ｔｐと親指接触検出部Ｔｔ及び人差し指接触検出部Ｔｉとは比較的近い位置となる。そこで、運転者が単に円環状部２００ｒを握っている場合と、操作対象装置を操作しようとしてタッチセンサ２１を触った場合とを的確に区別するために、本実施形態においては、操作無効エリアＡｒivを設けている。運転者は、操作対象装置を操作しようとする場合には、親指や人差し指を意図的に伸ばしてタッチセンサ２１を触って、後述する特定の入力操作を行うようにする。制御部１０は、操作検出エリアＡｒｖ内で後述する特定の入力操作が行われた場合に、入力操作に応じて操作対象装置を制御する。

【００４２】

運転者が運転のために円環状部２００ｒを握っていない状態で、操作検出エリアＡｒｖに不用意に触った場合に、操作対象装置が誤操作されることを回避することも必要である。そこで、本実施形態においては、検出部１０ａは、グリップ検出エリアＡｒｇで所定の面積以上の手のひら接触検出部Ｔｐが得られた場合に、円環状部２００ｒを握っていると判断する。制御部１０は、円環状部２００ｒを握っており、かつ、操作検出エリアＡｒｖ内で特定の操作が行われた場合に操作対象装置を制御するように構成している。円環状部２００ｒを握っていると判断する手のひら接触検出部Ｔｐの面積は、複数の運転者がステアリングホイール２００を通常の握り方で握った場合の面積を統計的に調べて、適宜に設定すればよい。

【００４３】

グリップ検出エリアＡｒｇにおける手のひら接触検出部Ｔｐの面積は、運転者が円環状部２００ｒを握っていると判定するための要件の一例であり、判定するための要件これに限定されるものではない。図１０は、タッチセンサ２１のグリップ検出エリアＡｒｇの部分で円環状部２００ｒを切断した断面を示している。検出部１０ａは、手のひら接触検出部Ｔｐの断面周方向の角度θが所定の角度以上のときに円環状部２００ｒを握っていると判断することができる。所定の角度は例えば１８０°である。

【００４４】

以上のように、本実施形態においては、運転者が円環状部２００ｒ（タッチセンサ２１）を握っているか否かを判定して、円環状部２００ｒを握っている場合のみタッチセンサ２１に対する操作入力を受け付けるようにしているので、操作検出エリアＡｒｖに不用意に触った場合の誤操作を回避することができる。本実施形態においては、好ましい構成として、操作検出エリアＡｒｖをグリップ検出エリアＡｒｇから所定の距離離間させた位置に設けているので、運転者が意図的にタッチセンサ２１に対して特定の入力操作を行っていることを的確に検出することができる。従って、誤操作を大幅に低減させることができる。

【００４５】

また、本実施形態においては、グリップ検出エリアＡｒｇにおける手のひら接触検出部Ｔｐの面積や断面周方向の角度θを、運転者が円環状部２００ｒを握っているか否かを判定する要件としているので、円環状部２００ｒを握っているか否かを的確に判定することができる。従って、運転者が円環状部２００ｒを握っていない状態で、操作検出エリアＡｒｖに不用意に触った場合の誤操作も回避することができる。

【００４６】

制御部１０は、検出部１０ａが、グリップ検出エリアＡｒｇからの接触検出信号に基づくセンサデータによって運転者が円環状部２００ｒ（タッチセンサ２１）を握っていることを検出した場合に、運転者に、操作検出エリアＡｒｖによる操作入力が可能であることを知らせるために、表示素子１７を点灯させる。運転者は、表示素子１７の点灯・消灯によって、タッチセンサ２１によって操作対象装置を操作することができるか否かを判断することができる。表示素子１７をステアリングホイール２００の近傍に配置する方が好ましい。

【００４７】

ところで、図３（Ａ）のように円環状部２００ｒの全周にタッチセンサ２１を装着したり、図３（Ｅ）のように比較的広い範囲にタッチセンサ２１を装着したりした場合には、運転者がタッチセンサ２１を握る位置は固定されない。そこで、図８及び図９で説明したグリップ検出エリアＡｒｇと操作検出エリアＡｒｖや、必要に応じて設ける操作無効エリアＡｒivの位置は、運転者がタッチセンサ２１を握った位置に応じて動的に設定する必要がある。

【００４８】

そこで、制御部１０は、グリップ検出エリアＡｒｇ等が未設定の状態でタッチセンサ２１が握られた場合には、手のひら接触検出部Ｔｐを含む領域をグリップ検出エリアＡｒｇに設定する。手のひら接触検出部Ｔｐを含むＹ座標の所定の範囲をグリップ検出エリアＡ

ｒｇとすればよい。前述のように、手のひら接触検出部Ｔｐは所定の面積以上となるので、タッチセンサ２１上の複数の検出領域Ｒにおいて所定の面積以上触られていることが検出された部分が手のひら接触検出部Ｔｐとなる。または、図１０で説明したように、タッチセンサ２１の部分で円環状部２００ｒを切断した断面周方向で、所定の角度以上触られていることが検出された部分が手のひら接触検出部Ｔｐとなる。

【００４９】

制御部１０は、グリップ検出エリアＡｒｇを設定したら、グリップ検出エリアＡｒｇよりも上側のＹ座標の所定の範囲を操作検出エリアＡｒｖと設定する。この場合、必要に応じて、グリップ検出エリアＡｒｇと隣接するＹ座標の所定の範囲を操作無効エリアＡｒivとして設定し、グリップ検出エリアＡｒｇをグリップ検出エリアＡｒｇから離間させた位置とする。

【００５０】

次に、図１１～図１３を用いて、運転者が親指または人差し指を用いてタッチセンサ２１に対して行う特定の入力操作の例を説明する。図１１（Ａ）～（Ｅ）は、タッチセンサ２１の運転者と対向する正面側または裏面側である半分を模式的な平面で示している。図１１（Ａ）～（Ｅ）に示す操作は、正面側であれ親指で、裏面側であれば人差し指で行われることになる。図１１（Ａ）において、D_Rは、親指または人差し指をタッチセンサ２１（操作検出エリアＡｒｖ）上で右方向に滑らせる右方向ドラッグであり、D_Lは親指または人差し指を右方向に滑らせる左方向ドラッグである。D_Uは親指または人差し指を上方向に滑らせる上方向ドラッグであり、D_Dは親指または人差し指をした方向に滑らせる下方向ドラッグである。

【００５１】

図１１（Ａ）において、右方向ドラッグD_R，左方向ドラッグD_L，上方向ドラッグD_U，下方向ドラッグD_Dの代わりに、親指または人差し指でそれぞれの方向にタッチセンサ２１をはじくフリックとしてもよい。

【００５２】

図１１（Ｂ）は、親指または人差し指でタッチセンサ２１をたたくタップＴを示している。図１１（Ｃ）は、親指または人差し指でタッチセンサ２１上に円弧を描くようにドラッグする円弧ドラッグD_Cを示している。図１１（Ｄ）は、親指または人差し指でタッチセンサ２１上にジグザグ状にドラッグするジグザグドラッグD_Zを示している。図１１（Ｅ）は、親指または人差し指で記号を書くようにドラッグする記号入力ドラッグD_Sを示している。図１１（Ｅ）は記号として数字の３を描いた状態を示している。記号としては、認識が比較的容易な数字やアルファベットを用いることが好ましい。

【００５３】

図１２（Ａ）～（Ｄ）は、タッチセンサ２１を開いてタッチセンサ２１の正面側の半分である正面部２１ｆと裏面側の半分である裏面部２１ｒとを模式的な平面で示している。正面部２１ｆは、図８，図９に示すＸ座標の０～１１の部分であり、裏面部２１ｒは、Ｘ座標の１２～２２の部分である。図８，図９に示す例では、厳密には正面部２１ｆと裏面部２１ｒとは均等の面積にはならないが、図１２（Ａ）～（Ｄ）では正面部２１ｆと裏面部２１ｒとを同じ面積で示している。図１２（Ａ）～（Ｄ）は理解を容易にするため、裏面部２１ｒは、裏面部２１ｒを円環状部２００ｒの裏面側から見た状態ではなく、正面部２１ｆから裏面部２１ｒを透視した状態を示している。

【００５４】

図１２（Ａ）～（Ｄ）に示すように、正面部２１ｆに対する親指による入力操作と裏面部２１ｒに対する人差し指による入力操作とを組み合わせたパターンをタッチセンサ２１に対する特定の入力操作としてもよい。図１２（Ａ）は、正面部２１ｆで親指を右方向に滑らせる右方向ドラッグD_{TR}と、裏面部２１ｒで人差し指を右方向に滑らせる右方向ドラッグD_{IR}との双方を行う例である。親指及び人差し指の双方を円環状部２００ｒの内周側から外周側へとドラッグすることにより、図１２（Ａ）が実現される。親指と人差し指の双方を、図１２（Ａ）とは逆方向にドラッグするパターンとしてもよい。

【００５５】
図１２（Ｂ）は、正面部２１ｆで親指を左方向に滑らせる左方向ドラッグD_{TL}と、裏面部２１ｒで人差し指を右方向に滑らせる右方向ドラッグD_{IR}との双方を行う例である。親指を円環状部２００ｒの外周側から内周側へとドラッグし、人差し指を円環状部２００ｒの内周側から外周側へとドラッグすることにより、図１２（Ｂ）が実現される。図１２（Ｃ）は、正面部２１ｆで親指を右方向に滑らせる右方向ドラッグD_{TR}と、裏面部２１ｒで人差し指を左方向に滑らせる左方向ドラッグD_{IL}との双方を行う例である。親指を円環状部２００ｒの内周側から外周側へとドラッグし、人差し指を円環状部２００ｒの外周側から内周側へとドラッグすることにより、図１２（Ｃ）が実現される。
【００５６】
図１２（Ｄ）は、正面部２１ｆで親指を上方向に滑らせる上方向ドラッグD_{TU}と、裏面部２１ｒで人差し指を下方向に滑らせる下方向ドラッグD_{ID}との双方を行う例である。親指を下方向、人差し指を上方向にドラッグとするパターンとしてもよく、親指と人差し指の双方を上方向または下方向にドラッグするパターンとしてもよい。ここでは、正面部２１ｆに対する親指による入力操作と裏面部２１ｒに対する人差し指による入力操作とを組み合わせた種々のパターンを示したが、入力操作のしやすさを考慮して適宜選択すればよい。
【００５７】
図１２（Ａ）～（Ｄ）に示すように、親指による入力操作と人差し指による入力操作とを組み合わせたパターンを、操作対象装置を制御するための特定の入力操作とすれば、さらに大幅に誤操作を低減させることが可能となる。
【００５８】
さらには、図３（Ａ），（Ｂ），（Ｄ），（Ｅ）や図４，図５のように、左右の手でタッチセンサ２１（２１ａ，２１ｂ）を操作できる場合に、左右の手による操作を組み合わせたパターンを、操作対象装置を制御するための特定の入力操作とすることも可能である。図１３（Ａ）～（Ｄ）は、図３（Ｂ）における左側のタッチセンサ２１を左側タッチセンサ２１Ｌとし、右側のタッチセンサ２１を右側タッチセンサ２１Ｒとした場合の、左右の手による操作を組み合わせたパターンの例を示している。ここでは、親指によって操作する図１２の正面部２１ｆに相当する面を模式的な平面で示している。
【００５９】
図１３（Ａ）は、左側タッチセンサ２１Ｌに対して親指を左方向に滑らせる左方向ドラッグD_{TL}と、右側タッチセンサ２１Ｒに対して親指を右方向に滑らせる右方向ドラッグD_{TR}とを組み合わせたパターンである。図１３（Ｂ）は、左側タッチセンサ２１Ｌに対して親指を右方向に滑らせる右方向ドラッグD_{TR}と、右側タッチセンサ２１Ｒに対して親指を左方向に滑らせる左方向ドラッグD_{TL}とを組み合わせたパターンである。
【００６０】
図１３（Ｃ）は、左側タッチセンサ２１Ｌと右側タッチセンサ２１Ｒの双方に対して、親指を上方向に滑らせる上方向ドラッグD_{TU}を組み合わせたパターンである。図１３（Ｄ）は、左側タッチセンサ２１Ｌと右側タッチセンサ２１Ｒの双方に対して、親指を下方向に滑らせる下方向ドラッグD_{TD}を組み合わせたパターンである。
【００６１】
左右の手による入力操作を組み合わせたパターンを、操作対象装置を制御するための特定の入力操作とすれば、運転者は円環状部２００ｒを両手で握ることになるので、安全運転に寄与することが可能である。特に、図３（Ｂ）の例は、円環状部２００ｒを両手で握る最も適切な位置にタッチセンサ２１を装着しているので、安全運転に寄与する点で最も好ましい。両手で左右のタッチセンサ２１を握っている場合に入力操作を受け付けるようにしてもよい。片手がタッチセンサ２１から離れた場合に入力操作を受け付けない状態としてもよい。片手がタッチセンサ２１から離れた場合には入力操作を受け付ける状態を継続してもよい。片手のみの特定の入力操作を用いる場合であっても、両手で左右のタッチセンサ２１を握っている場合に入力操作を受け付けるようにすれば、安全運転に寄与する

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【００６２】

運転者が通常の運転のために円環状部２００ｒを握っていて、操作対象装置を操作しようとする意思がない場合に、偶然に、親指による入力操作と人差し指による入力操作とを組み合わせた特定のパターンや、左右の手による入力操作を組み合わせた特定のパターンになってしまう可能性は比較的低いと考えられる。そこで、親指による入力操作と人差し指による入力操作とを組み合わせた特定のパターンや、左右の手による入力操作を組み合わせた特定のパターンのみを用いる場合には、上述した誤操作を回避するための工夫の一部または全てを省略してもよい。勿論、左右の手による入力操作を組み合わせた特定のパターンのみを用いる場合であっても、上述した誤操作を回避するための工夫を併せて採用することが好ましい。

【００６３】

記憶部１８は、以上説明した特定の入力操作または特定の入力操作を組み合わせたパターンと、操作対象装置に対する制御の種別とを対応させたテーブルを記憶している。制御部１０は、記憶部１８に記憶されたテーブルに従って、タッチセンサ２１に入力された操作に応じて操作対象装置を制御する。記憶部１８を制御部１０内に設けてもよい。

【００６４】

図１４のフローチャートを用いて、本実施形態において制御部１０で実行される処理について改めて説明する。図１３において、制御部１０は、ステップＳ１にて、センサデータ生成部２２から出力されるセンサデータを取得する。制御部１０は、ステップＳ２にて、検出部１０ａによる検出出力に基づいて、円環状部２００ｒが握られているか否かを判定する。円環状部２００ｒが握られていると判定されれば（YES）、制御部１０は、ステップＳ３に処理を移し、円環状部２００ｒが握られていると判定されなければ（NO）、制御部１０は、ステップＳ１に処理を戻す。

【００６５】

制御部１０は、ステップＳ３にて、検出部１０ａによる検出出力に基づいて、入力操作があったか否かを判定する。入力操作があったと判定されれば（YES）、制御部１０は、ステップＳ４に処理を移し、操作入力があったと判定されなければ（NO）、制御部１０は、ステップＳ１に処理を戻す。制御部１０は、ステップＳ４にて、ステップＳ３における入力操作によって操作対象装置に対する操作を許可するか否かを判定する。操作を許可すると判定されれば（YES）、制御部１０は、ステップＳ５に処理を移し、操作を許可すると判定されなければ（NO）、制御部１０は、ステップＳ１に処理を戻す。

【００６６】

上述のように、制御部１０は、操作検出エリアＡｒｖ内で特定の入力操作がなされた場合に操作対象装置に対する操作を許可し、操作無効エリアＡｒiv内で特定の入力操作がなされたとしても操作対象装置に対する操作を許可しない。また、制御部１０は、操作検出エリアＡｒｖ内で何らかの入力操作がなされたとしても、上述した特定の入力操作でない場合は操作対象装置に対する操作を許可せず、特定の入力操作がなされた場合のみ操作対象装置に対する操作を許可する。

【００６７】

制御部１０は、ステップＳ５にて、入力操作に基づいた操作を確定し、ステップＳ６にて、操作対象装置に対して、確定した操作に応じた制御を実行して、ステップＳ１に処理を戻す。

【００６８】

また、ステップＳ４では、車両が特定の状態にあるときに、操作対象装置に対する制御を許可しないようにする（即ち、無効にする）ことが好ましい。制御部１０には、操作対象装置に対する制御を許可するか否かを判断するためのステアリングホイール２００の回転角度が設定されている。図１５に示すように、ステアリングホイール２００を回転させていない状態を回転角度０°とし、例えば右方向に回転させたときをプラス、左方向に回転させたときをマイナスとして、一例として回転角度±３０°の範囲でタッチセンサ２１

に対する入力操作を有効として許可し、回転角度が±３０°を超えたらタッチセンサ２１に対する入力操作を無効として不許可とする。

【００６９】

回転角度が±３０°を超えた場合には、車両は右折または左折をしていたり、コーナリング走行していたりする特定の状態である。このような特定の状態で操作対象装置を制御しようとすれば誤操作が発生する可能性が高い。言い換えれば、このような特定の状態における操作入力は、ユーザの意図していない操作入力である可能性が高い。また安全性の上でも好ましくない。そこで、本実施形態では、車両が特定の状態にあるときには、操作対象装置に対する制御を無効とする。

【００７０】

前述のように、制御部１０にはステアリング角センサ３１によって検出されたステアリングホイール２００の回転角度が入力される。制御部１０は、ステアリング角センサ３１によって検出されたステアリングホイール２００の回転角度に応じて、タッチセンサ２１に対する入力操作を有効とする状態と無効とする状態とを切り換える。制御部１０には方向指示器センサ３２からの検出信号も入力される。そこで、制御部１０は、方向指示器センサ３２からの検出信号によって方向指示器３２０が操作された場合に、タッチセンサ２１に対する入力操作を無効としてもよい。方向指示器３２０が操作された場合は、ステアリングホイール２００が所定の回転角度を超えて回転される特定の状態になるとみなすことができる。なお、方向指示器３２０が右折または左折の合図以外の操作を兼用している場合があるが、ここでの方向指示器３２０の操作とは右折または左折の合図を行う操作である。

【００７１】

さらに、車両を後退させている最中にタッチセンサ２１に対して特定の入力操作を行って操作対象装置を制御することは好ましくない。誤操作が発生する可能性が高く、安全性の上でも好ましくない。そこで、制御部１０は、シフトレバーセンサ３３からの検出信号によって、シフトレバー３３０のシフト位置がリバースとなった場合にも、タッチセンサ２１に対する入力操作を無効とすることが好ましい。ステアリングホイール２００の回転角度が例えば±３０°の所定角度を超えた場合、または、方向指示器３２０が操作された場合に加えて、シフトレバー３３０のシフト位置がリバースとなった場合に操作対象装置に対する制御を無効とすることが好ましいが、一方のみとしてもよい。

【００７２】

なお、操作対象装置に対する制御を無効にするとは、仮に上述した特定の入力操作がなされたとしても特定の入力操作を無効として操作対象装置に対する制御を不許可とすることであってもよく、制御部１０に対してセンサデータ生成部２２から何らかのセンサデータが入力されても、制御部１０がセンサデータを無効することであってもよい。結果として、操作対象装置に対する制御を無効とすればよい。

【００７３】

図１６のフローチャートを用いて、図１４のステップＳ４の具体的な処理の例を説明する。図１６において、制御部１０は、ステップＳ４１にて、シフトレバー３３０のシフト位置がリバースであるか否かを判定する。シフト位置がリバースであれば（YES）、制御部１０は、ステップＳ４５にて、ステップＳ３での入力操作を不許可として、図１４のステップＳ１に移行させる。シフト位置がリバースでなければ（NO）、制御部１０は、ステップＳ４２にて、方向指示器３２０が操作されたか否かを判定する。方向指示器３２０が操作されたら（YES）、制御部１０は、ステップＳ４５にて、ステップＳ３での入力操作を不許可として、図１４のステップＳ１に移行させる。

【００７４】

方向指示器３２０が操作されなかったら（NO）、制御部１０は、ステップＳ４３にて、ステアリングホイール２００の回転角度が所定角度を超えたか否かを判定する。ステアリングホイール２００の回転角度が所定角度を超えたら（YES）、制御部１０は、ステップＳ４５にて、ステップＳ３での入力操作を不許可として、図１４のステップＳ１に移行さ

せる。ステアリングホイール２００の回転角度が所定角度を超えていなかったら（NO）、制御部１０は、ステップＳ４４にて、操作検出エリアＡｒｖ内で特定の入力操作がなされたか否かを判定する。特定の入力操作がなされなかったら（NO）、制御部１０は、ステップＳ４５にて、ステップＳ３での入力操作を不許可として、図１４のステップＳ１に移行させる。ステップＳ４５にて、入力操作を不許可とすれば、操作対象装置に対する制御が無効となる。特定の入力操作がなされたら（YES）、制御部１０は、ステップＳ４６にて、ステップＳ３での入力操作を許可して、図１４のステップＳ５に移行させる。

【００７５】

図１６に示す例では、ステップＳ４１，Ｓ４２，Ｓ４３の全てを設けたが、これらのステップの内の１つまたは２つのみとしてもよい。また、ステップＳ４１，Ｓ４２，Ｓ４３の全てまたはこれらのステップの内の２つを設ける場合、順番は任意である。なお、ここではシフトレバー３３０と称したが、車両の直進と後退の切り換え、変速機の変速比を変える操作部の形状は任意であり、フロアシフト，コラムシフト，パドルシフト等のいずれでもよい。これらは全てシフトレバーに含まれる。

【００７６】

以上のように、車両が右折，左折，コーナリング走行，後退等の特定の状態にあるときに、操作対象装置に対する制御を無効とすれば、運転者はこれらの特定の状態のときにタッチセンサ２１に対する入力操作を行わない。従って、安全性の向上に寄与する。

【００７７】

本実施形態による動作をまとめると、次の通りである。検出部１０ａ（第１の検出部）は、ステアリングホイール２００，２０１における運転者が握る握持部（円環状部２００ｒまたは直線部２０１ｓ）に装着されたタッチセンサ２１における第１のエリアが触られている状態であることを検出する。第１のエリアの例は、グリップ検出エリアＡｒｇである。検出部１０ａ（第２の検出部）は、第１のエリアが触られている状態で、タッチセンサ２１における第１のエリアよりも上側に位置する第２のエリアに対して特定の入力操作がなされたことを検出する。第２のエリアの例は、操作検出エリアＡｒｖである。運転時、親指または人差し指は手のひらよりも上方に位置するので、第１のエリアよりも上側を第２のエリアとすればよい。そして、第１のエリアが触られている状態であり、特定の入力操作がなされたら、タッチセンサ２１によって操作する対象の操作対象装置を特定の入力操作に応じて制御する。

【００７８】

上側に位置するエリアとは、ステアリングホイール２００を回転させていない状態で運転者が握持部を握った状態で、第１のエリアよりも上側に位置するエリアである。第１のエリアが所定の面積以上触られていることを検出した場合に、第１のエリアが触られている状態であるとすることが好ましい。

【００７９】

また、別の観点では、次の通りである。検出部１０ａ（第１の検出部）は、ステアリングホイール２００，２０１における運転者が握る握持部（円環状部２００ｒまたは直線部２０１ｓ）の所定の範囲に、握持部を覆うように装着されたタッチセンサ２１が、タッチセンサ２１上の第１のエリアにおいて、握持部をステアリングホイール２００，２０１の径方向に切断したときの断面における周方向の所定角度以上触られている状態であることを検出する。検出部１０ａ（第２の検出部）は、第１のエリアが所定角度以上触られている状態で、タッチセンサ２１における第１のエリアとは異なる第２のエリアに対して特定の入力操作がなされたことを検出する。第１のエリアが前記所定角度以上触られている状態であり、特定の入力操作がなされたら、タッチセンサ２１によって操作する対象の操作対象装置を特定の入力操作に応じて制御する。

【００８０】

第２のエリアは、第１のエリアよりも上側に位置するエリアであることが好ましい。上側に位置するエリアとは、ステアリングホイール２００を回転させていない状態で運転者が握持部を握った状態で、第１のエリアよりも上側に位置するエリアである。

【００８１】
図１７及び図１８は、タッチセンサ２１を操作したことを運転者に効果的に知らせるための構成例を示している。図１７及び図１８は、図９と同様、タッチセンサ２１を展開して矩形状に変換した模式図である。図１７は、タッチセンサ２１の下面側に発色物質を含む色変化シート４１を設けた例である。タッチセンサ２１に透明導電膜を用いることにより、運転者は、タッチセンサ２１を介して、タッチセンサ２１の下面に配置されている色変化シート４１の色を見ることができる。制御部１０による制御によって、タッチセンサ２１を触った部分の色変化シート４１の色を変化させることにより、運転者はタッチセンサ２１を操作したことを認識することができる。
【００８２】
図１８は、タッチセンサ２１の上面側に触覚（手触り）を変化させる触覚フィードバックシート４２を設けた例である。触覚フィードバックシート４２としては、例えば、フィンランドのSenseg社が開発した“E-Sense”と称されるシートを採用することができる。このシートは、フィルムを帯電させることで触覚のフィードバックを実現するものである。タッチセンサ２１の上面側に触覚フィードバックシート４２を設けても、タッチセンサ２１は指等の接触を検出することが可能である。触覚フィードバックシート４２を介してタッチセンサ２１を操作した場合に、制御部１０による制御によって、触覚フィードバックシート４２の触覚を変化させることにより、運転者はタッチセンサ２１を操作したことを認識することができる。
【００８３】
次に、図１９を用いてステアリングホイールの構成例について説明する。図１９に示すステアリングホイール２１０は、操作対象装置に対する制御信号をステアリングホイール２１０から出力させるように構成したものである。図１９において、図１，図２と同一部分には同一符号を付し、その説明を適宜省略する。図１９に示すように、ステアリングホイール２１０は、例えば円環状部２００ｒ以外の部分に、図１のセンサデータ生成部２２と同様のセンダデータ生成部２３と、制御部１０と同様の制御部２４を備えている。制御部２４は、検出部１０ａと同様の検出部２４ａと、制御信号発生部２４ｂを有する。
【００８４】
ステアリングホイール２１０を車両に装着した場合、制御信号発生部２４ｂは、タッチセンサ２１に対する特定の入力操作に応じて、操作対象装置を制御するための制御信号を発生する。制御信号発生部２４ｂより出力された制御信号はケーブル２５を介して出力端子２６へと出力される。出力端子２６を操作対象装置に接続すれば、制御信号によって操作対象装置を制御することが可能となる。特定の入力操作の例は図１１～図１３と同様である。制御信号発生部２４ｂが制御信号を発生する要件も上述と同様である。
【００８５】
本発明は以上説明した本実施形態に限定されるものではなく、本発明の要旨を逸脱しない範囲において種々変更可能である。タッチセンサ２１を、面ファスナを用いて円環状部２００ｒに着脱自在に装着するようにしてもよい。円環状部２００ｒを握持部としたが、握持部は必ずしも円環状でなくてもよい。
【００８６】
タッチセンサ２１は１枚のシートによって構成する必要はなく、複数のタッチセンサの片によってタッチセンサ２１を構成してもよい。複数のタッチセンサの片によってタッチセンサ２１を構成すれば、一つ一つのタッチセンサの片の形状を簡単な形にすることができるため、タッチセンサを生産する際に有利である。なお、複数のタッチセンサの片によってタッチセンサ２１を構成する場合、必ずしもタッチセンサの片を隙間なく配置しなくてもよい。本実施形態のタッチパネル２１は、握持部を覆うように装着されているが、本実施形態における、握持部を覆うように装着されているということは、複数のタッチセンサの片からなるタッチセンサ２１が、タッチセンサの片と片との間に隙間がある状態で、握持部を覆うように装着されていることも含むものとする。
【００８７】

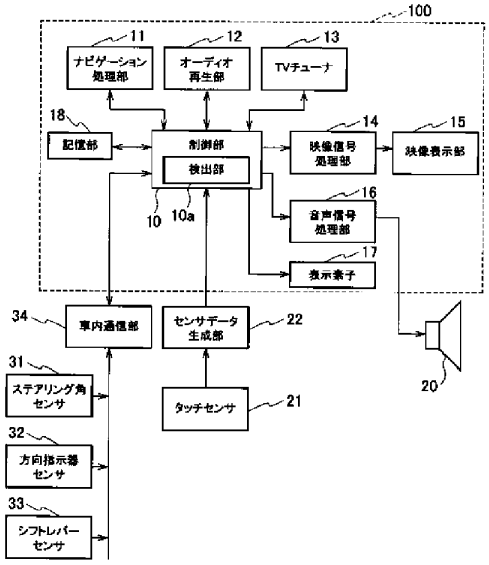
さらには、タッチセンサ２１を設ける範囲を、運転者が運転時に握る握持部（円環状部２００ｒまたは直線部２０１ｓ）に限定せず、例えばエアバッグ等が収納されるセンター部と円環状部２００ｒとの間を連結する連結部の表面まで広げてもよい。連結部は、図２においては、図2に示す状態で左右の手の間に位置する部分であり、図１９においては、センサデータ生成部２３及び制御部２４が設けられている部分である。このようにタッチセンサ２１を連結部の表面まで広げて、連結部における握持部に近い位置に操作検出エリアＡｒｖを設定してもよい。握持部に近い位置であれば、運転者が運転時に握持部から手を離したり、手を大きくずらしたりすることなく操作対象装置を操作することができる。よって、タッチセンサ２１を連結部の表面まで広げた構成としても、運転者がステアリングホイール２００，２０１，２１０を操作する際に支障となる可能性はほとんどない。

【符号の説明】

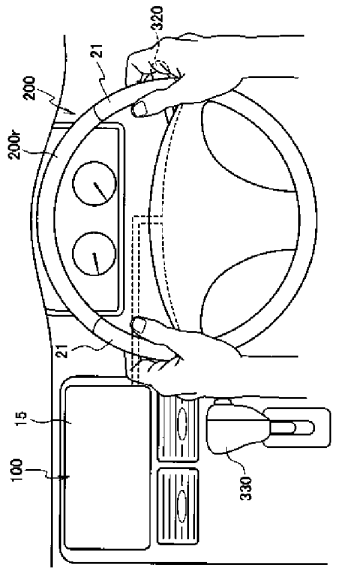
【００８８】

１０，２４　制御部
１０ａ，２４ａ　検出部
１１　ナビゲーション処理部
１２　オーディオ再生部
１３　テレビジョンチューナ
１４　映像信号処理部
１５　映像表示部
１６　音声信号処理部
１７　表示素子
１８　記憶部
２０　スピーカ
２１　タッチセンサ
２２，２３　センサデータ生成部
２４ｂ　制御信号発生部
２５　ケーブル
２６　出力端子
３１　ステアリング角センサ
３２　方向指示器センサ
３３　シフトレバーセンサ
３４　車内通信部
２００，２０１，２１０　ステアリングホイール
２００ｒ　円環状部（握持部）
２０１ｓ　直線部（握持部）

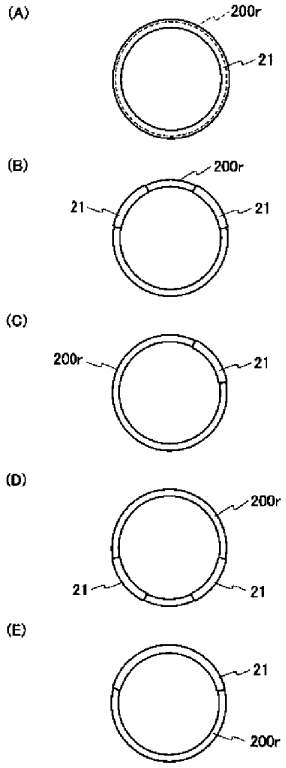
【図１】


100
11
ナビゲーション処理部
12
オーディオ再生部
13
TVチューナ
18
記憶部
制御部
検出部
14
映像信号処理部
15
映像表示部
10
10a
16
音声信号処理部
17
表示素子
20
34
車内通信部
センサデータ生成部
22
31
ステアリング角センサ
タッチセンサ
21
32
方向指示器センサ
33
シフトレバーセンサ

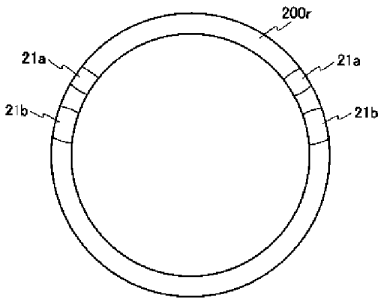
【図２】


320
21
200
200r
21
15
100
330

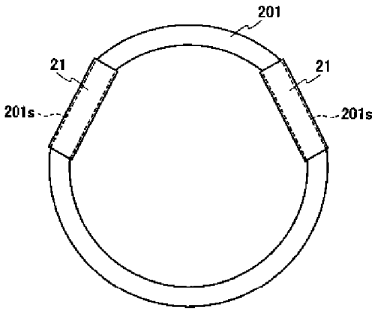
【図３】


(A)
200r
21
(B)
200r
21
21
(C)
200r
21
(D)
200r
21
21
(E)
21
200r

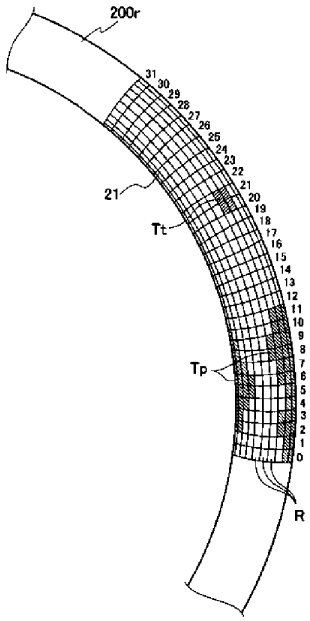
【図４】


200r
21a
21a
21b
21b

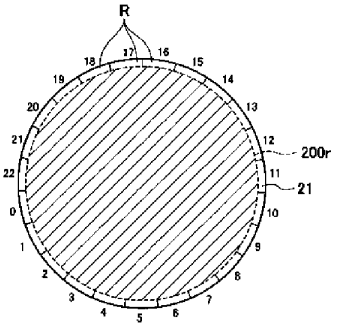
【図５】


201
21
21
201s
201s

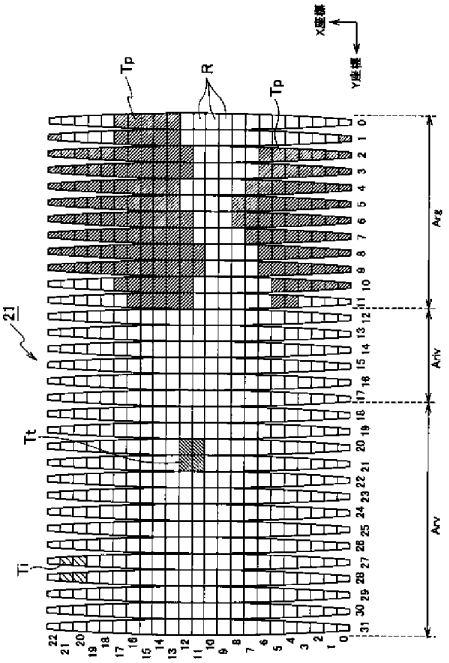
【図６】


200r
21
Tt
Tp
R

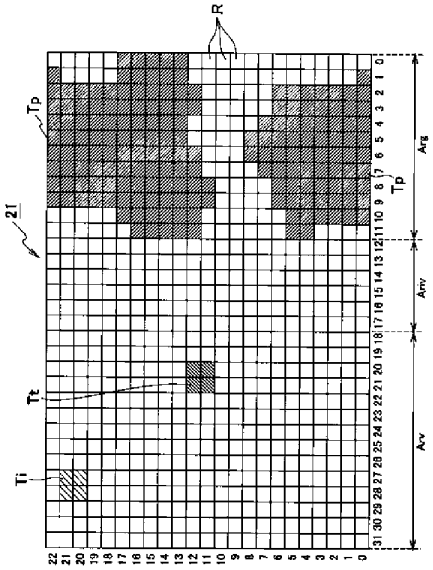
【図７】


R
200r
21

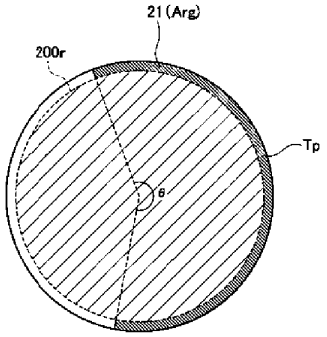
【図８】


X座標
Y座標
Tp
R
Tp
21
Tt
Ti
Arg
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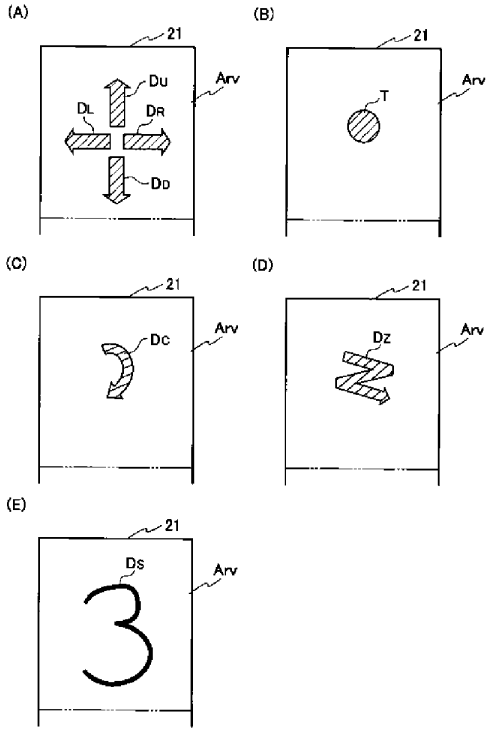
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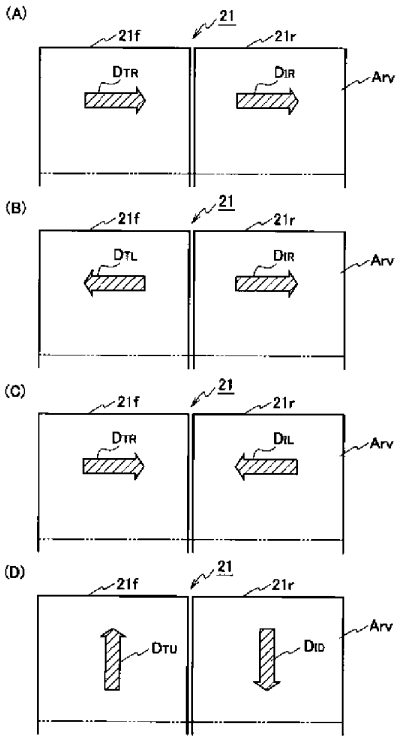
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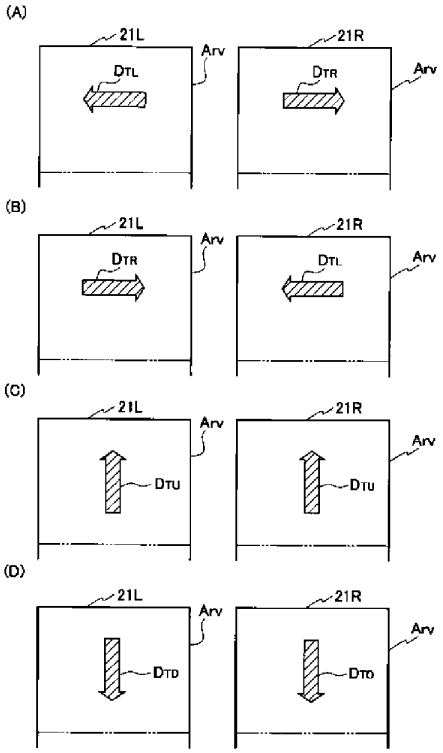
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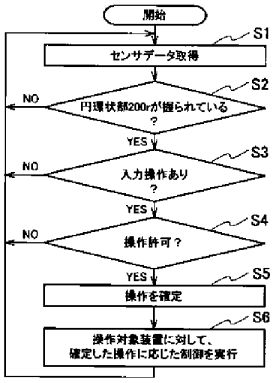
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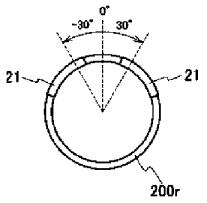
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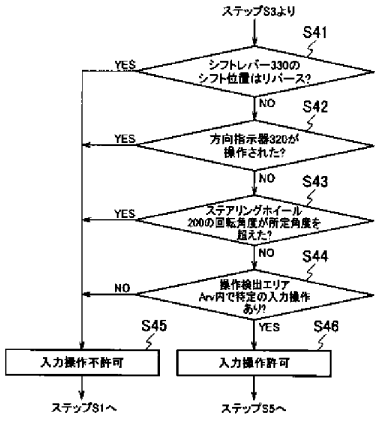
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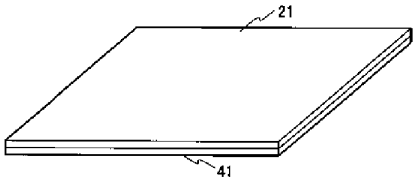
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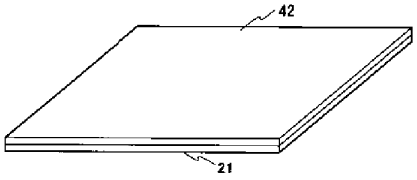
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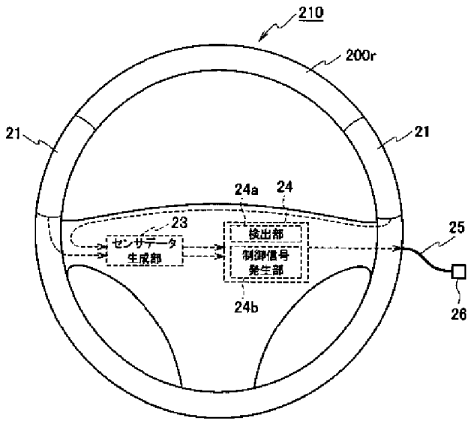
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特開２００７－０７６４９１（ＪＰ，Ａ）
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FLUID CONTROL DEVICES AND METHODS OF USING THE SAME

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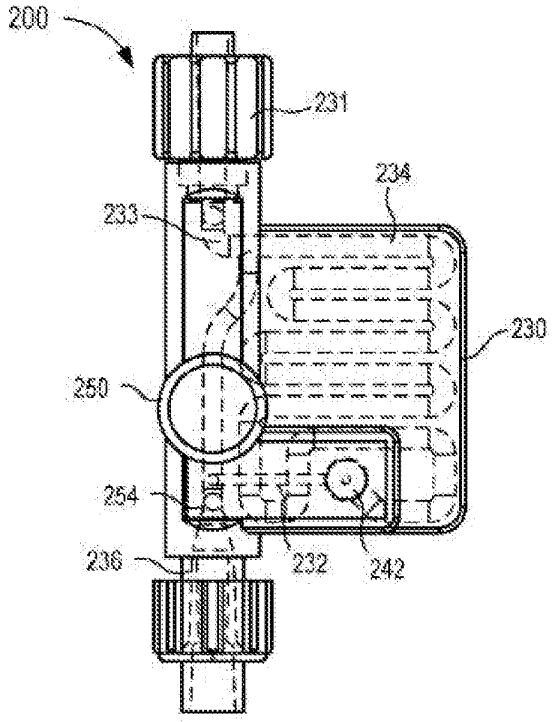
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Abstract of WO2019055487 (A1)

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

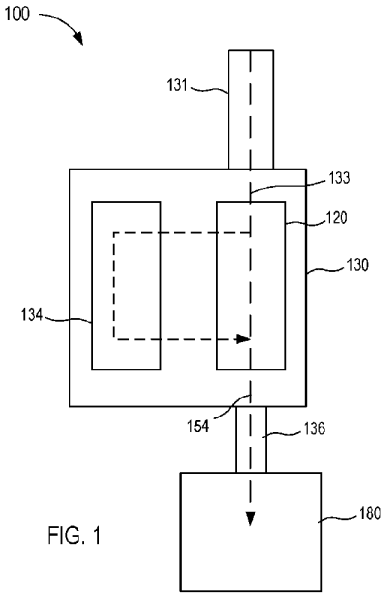


FIG. 1

(57) Abstract: A fluid control device includes an inlet configured to be placed directly or indirectly in fluid communication with a bodily fluid source and an outlet configured to be placed in fluid communication with a fluid collection device. The fluid control device has a first state in which a negative pressure differential produced from an external source such as the fluid collection device is applied to the fluid control device to draw an initial volume of bodily fluid from the bodily fluid source, through the inlet, and into a sequestration portion of the fluid control device. The fluid control device has a second state in which (1) the sequestration portion sequesters the initial volume, and (2) the negative pressure differential draws a subsequent volume of bodily fluid, being substantially free of contaminants, from the bodily fluid source, through the fluid control device, and into the fluid collection device.

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FLUID CONTROL DEVICES AND METHODS OF USING THE SAME

Cross-Reference to Related Applications

[1001] This application claims priority to and the benefit of U.S. Provisional Patent Application Serial No. 62/557,530 entitled, "Fluid Control Devices and Methods of Using the Same," filed September 12, 2017, the disclosure of which is incorporated herein by reference in its entirety.

[1002] This application also claims priority to and the benefit of U.S. Provisional Patent Application Serial No. 62/634,569 entitled, "Fluid Control Devices and Methods of Using the Same," filed February 23, 2018, the disclosure of which is incorporated herein by reference in its entirety.

[1003] This application also claims priority to and the benefit of U.S. Provisional Patent Application Serial No. 62/678,632 entitled, "Fluid Control Devices and Methods of Using the Same," filed May 31, 2018, the disclosure of which is incorporated herein by reference in its entirety.

Background

[1004] The invention relates generally to the parenteral procurement of bodily fluid samples, and more particularly to fluid diversion, sequestration, and/or isolation devices and methods for procuring bodily fluid samples with reduced contaminants such as dermally residing microbes and/or other contaminants exterior to the bodily fluid source.

[1005] Health care practitioners routinely perform various types of microbial as well as other broad diagnostic tests on patients using parenterally obtained bodily fluids. As advanced diagnostic technologies evolve and improve, the speed, accuracy (both sensitivity and specificity), and value of information that can be provided to clinicians continues to improve. Maintaining the integrity of the bodily fluid sample during and/or after collection also ensures that analytical diagnostic results are representative of the in vivo conditions of a patient. Examples of diagnostic technologies that are reliant on high quality, non-contaminated, and/or unadulterated bodily fluid samples include but are not limited to microbial detection, molecular diagnostics, genetic sequencing (e.g., deoxyribonucleic acid (DNA), ribonucleic acid (RNA), next-generation sequencing (NGS), etc.), biomarker identification, and the like. When biological matter, which can include cells external to the intended source for sample procurement, and/or other external contaminants are inadvertently included in the bodily fluid

sample that is to be analyzed, there is an opportunity for inaccurate test results to be derived. In short, when the purity of the sample intended to be derived or collected from a specific bodily fluid source is compromised during the specimen procurement process, resultant analytical test results may be inaccurate, distorted, adulterated, falsely positive, falsely negative, and/or otherwise not representative of the actual condition of the patient, which in turn, can inform faulty, inaccurate, confused, unsure, low-confidence, and/or otherwise undesired clinical decision making.

[1006] In some instances, patient samples (e.g., bodily fluids) are tested for the presence of one or more potentially undesirable microbes, such as bacteria, fungi, or yeast (e.g., Candida). In some instances, microbial testing may include incubating patient samples in one or more sterile and/or non-sterile vessels that may contain culture media, common additives, and/or other types of solutions that are conducive to microbial growth. In other instances, the sample in the vessel may be analyzed directly (i.e., not incubated) and may not contain culture media or additives associated with incubating the specimen. In still other instances, various technologies can be employed to assist in the detection of the presence of microbes as well as other types of biological matter, specific types of cells, biomarkers, proteins, antigens, enzymes, blood components, and/or the like during diagnostic testing. Examples include but are not limited to molecular polymerase chain reaction (PCR), magnetic resonance and other magnetic analytical platforms, automated microscopy, spatial clone isolation, flow cytometry, whole blood ("culture free") specimen analysis (e.g. NGS) and associated technologies, morphokinetic cellular analysis, and/or other common or evolving and advanced technologies utilized in the clinical laboratory environment to characterize patient specimens and/or to detect, identify, type, categorize, and/or characterize specific organisms, antibiotic susceptibilities, and/or the like.

[1007] In some instances, the detection of the presence of microbes includes allowing the microbes and/or organisms to grow for an amount of time (e.g., a variable amount of time from less than an hour to a few hours to several days – which can be longer or shorter depending on the diagnostic technology employed). The microbe and/or organism growth can then be detected by automated, continuous monitoring, and/or other methods specific to the analytical platform and technology used for detection, identification, and/or the like.

[1008] In culture testing, for example, when microbes are present in the patient sample, the microbes flourish over time in the culture medium and, in some instances, automated monitoring technologies can detect carbon dioxide produced by organism growth. The presence of microbes in the culture medium (as indicated by observation of carbon dioxide

and/or via other detection methods) suggests the presence of the same microbes in the patient sample which, in turn, suggests the presence of the same microbes in the bodily fluid of the patient from whom the sample was obtained. Accordingly, when microbes are determined to be present in the culture medium (or more generally in the sample used for testing), the patient may be diagnosed and prescribed one or more antibiotics or other treatments specifically designed to treat or otherwise remove the undesired microbes from the patient.

[1009] Patient samples, however, can become contaminated during procurement and/or otherwise can be susceptible to false positive or false negative results. For example, microbes from a bodily surface (e.g., dermally residing microbes) that are dislodged during the specimen procurement process (which can include needle insertion into a patient, specimen procurement via a lumen-containing device such as a peripheral IV catheter (PIV), a central line (PICC) and/or other indwelling catheter(s), collection with a syringe or any other suitable means employed to collect a patient specimen), either directly or indirectly via tissue fragments, hair follicles, sweat glands, and other skin adnexal structures, can be subsequently transferred to a culture medium, test vial, or other suitable specimen collection or transfer vessel with the patient sample and/or included in the specimen that is to be analyzed for non-culture based testing. Another possible source of contamination is from the person drawing the patient sample (e.g., a doctor, phlebotomist, nurse, technician, etc.). Specifically, equipment, supplies, and/or devices used during a patient sample procurement process often include multiple fluidic interfaces (by way of example, but not limited to, patient to needle, needle to transfer adapter, transfer adapter to sample vessel, catheter hub to syringe, syringe to transfer adapter, needle/tubing to sample vessels, and/or any other fluidic interface or any combination thereof) that can each introduce points of potential contamination. In some instances, such contaminants may thrive in a culture medium and/or may be identified by another non-culture based diagnostic technology and eventually may yield a false positive and/or a false negative microbial test result, which may inaccurately reflect the presence or lack of such microbes within the patient (i.e., in vivo).

[1010] Such inaccurate results because of contamination and/or other sources of adulteration that compromise the purity of the sample are a concern when attempting to diagnose or treat a wide range of suspected illnesses, diseases, infections, patient conditions or other maladies of concern. For example, false negative results from microbial tests may result in a misdiagnosis and/or delayed treatment of a patient illness, which, in some cases, could result in the death of the patient. Conversely, false positive results from microbial tests may result in the patient being unnecessarily subjected to one or more anti-microbial therapies,

which may cause serious side effects to the patient including, for example, death, as well as produce an unnecessary burden and expense to the health care system due to extended length of patient stay and/or other complications associated with erroneous treatments. The use of diagnostic imaging equipment attributable to these false positive results is also a concern from both a cost as well as patient safety perspective as unnecessary exposure to concentrated radiation associated with a variety of imaging procedures (e.g., CT scans) has many known adverse impacts on long-term patient health.

[1011] In some instances, devices and/or systems can be used to reduce the likelihood of contamination, adulteration, and/or the like of bodily fluid samples for testing. For example, some known devices can be configured to collect, divert, separate, and/or isolate or sequester an initial volume of bodily fluid that may be more likely to contain contaminants such as dermally residing microbes or the like. Some such devices, however, can be cumbersome, non-intuitive, perceived as difficult to use, inappropriate or unusable as intended for the target patient population, etc. In addition, some such devices can require training, user observation, intervention by more than one user, and/or can otherwise present challenges that can lead to limited efficacy based on variables including environmental, educational, clinician skill, patient condition, and/or the like. In some instances, such challenges can complicate the collection of consistently high quality samples that are non-contaminated, sterile, unadulterated, etc., which in turn, can impact the validity of test result outcomes.

[1012] On the other hand, some known passive diversion devices and/or systems (e.g., systems that do not specifically utilize or rely on direct user intervention, interaction, manipulation, and/or the like) may fail to adequately divert, sequester, and/or isolate a clinically desired and efficacious pre-sample volume of bodily fluid due to clinical realities such as, for example, the time required to fill a sequestration reservoir with a meaningful volume of fluid. In some instances, the operation of some known passive devices is dependent on a positive pressure applied by a bodily fluid source (e.g., a patient's blood pressure). The positive pressure applied by the bodily fluid source, however, may be insufficient to result in flow dynamics and/or flow rates that makes use of such devices practical in various clinical settings (including emergency rooms and other intensive settings). For example, the patient population with symptoms requiring diagnostic testing noted above commonly are in such physical condition that attaining vascular access and/or collection of bodily fluid samples can be difficult due to a hypotensive state (i.e., low blood pressure), hypovolemic state (i.e., low blood volume), and/or other physical challenges (e.g., severe dehydration, obesity, difficult and/or inaccessible vasculature, etc.). Such states or physical conditions can result in difficulty

in providing sufficient blood flow and/or pressure to achieve passive filling of a sequestration chamber, channel, reservoir, container (or other diversion volume) consistently with sufficient volume to meet clinically validated, evidence-based efficacy and results in diverting, sequestering, and/or isolating contaminants which otherwise can lead to distorted, inaccurate, falsely positive, falsely negative, and/or otherwise adulterated diagnostic test results. The challenges associated with this approach (e.g., relying on a positive pressure differential applied by the bodily fluid source without utilizing a specific external energy source and/or negative pressure to facilitate collection of an appropriate and clinically efficacious initial volume of bodily fluid) can render it impractical as failure rates can be unacceptably high for the fragile patient population from whom these samples are collected.

[1013] As such, a need exists for fluid diversion devices and methods for procuring bodily fluid samples with reduced contaminants such as dermally residing microbes and/or other contaminants exterior to the bodily fluid source that result in consistent bodily fluid collection (e.g., from a general patient population and/or a challenging patient population). Some such devices and methods can include, for example, bodily fluid collection with the assistance of various sources of external energy and/or negative pressure. Furthermore, a need exists for such devices that are user-friendly, demonstrate consistent efficacy, and address the challenges associated with collecting samples from patients with challenging health circumstances and/or physical characteristics that impact the ability to collect bodily fluid samples.

Summary

[1014] Devices and methods for procuring bodily fluid samples with reduced contaminants such as dermally residing microbes and/or other contaminants exterior to the bodily fluid source are described herein. In some embodiments, a system includes a housing, a flow controller, and a fluid collection device. The housing has an inlet and an outlet, and forms a sequestration portion. The inlet is configured to be placed in fluid communication with a bodily fluid source. The sequestration portion is configured to receive an initial volume of bodily fluid from the bodily fluid source. The flow controller is at least partially disposed in the sequestration portion of the housing and is configured to transition from a first state to a second state. The fluid collection device is configured to be fluidically coupled to the outlet to produce a negative pressure differential within at least a portion of the housing. The negative pressure differential is operable to draw the initial volume of bodily fluid into the sequestration portion when the flow controller is in the first state and is operable to draw the sample volume of bodily

fluid through the outlet and into the fluid collection device when the flow controller is in the second state.

Brief Description of the Drawings

[1015] FIG. 1 is a schematic illustration of a fluid control device according to an embodiment.

[1016] FIGS. 2-5 are various views of a fluid control device according to an embodiment.

[1017] FIGS. 6-8 are various views of a fluid control device according to an embodiment.

[1018] FIGS. 9 and 10 are front view illustrations of a fluid control device in a first operating mode and a second operating mode, respectively, according to an embodiment.

[1019] FIGS. 11 and 12 are front view illustrations of a fluid control device in a first operating mode and a second operating mode, respectively, according to an embodiment.

[1020] FIGS. 13-15B are various views of a fluid control device according to an embodiment.

[1021] FIGS. 16-18 are various views of a fluid control device according to an embodiment.

[1022] FIGS. 19-25 are various views of a fluid control device according to an embodiment.

[1023] FIGS. 26-28 are each a perspective view of a fluid control device according to different embodiments.

[1024] FIGS. 29-34 are various views of a fluid control device according to an embodiment.

[1025] FIGS. 35-40 are various views of a fluid control device according to an embodiment.

[1026] FIGS. 41-44 are various views of a fluid control device according to an embodiment.

[1027] FIGS. 45-50 are various views of a fluid control device according to an embodiment.

[1028] FIGS. 51 and 52 are cross-sectional views of a fluid control device according to an embodiment.

[1029] FIG. 53 is a flowchart illustrating a method of using a fluid control device according to an embodiment.

Detailed Description

[1030] Devices and methods for collecting, diverting, sequestering, isolating, etc. an initial volume of bodily fluid to reduce contamination in subsequently procured bodily fluid samples are described herein. Any of the fluid control devices described herein can be configured to receive, procure, and/or transfer a flow, bolus, volume, etc., of bodily fluid. A first reservoir, channel, flow path, or portion of the device can receive an initial amount of the bodily fluid flow, which then can be substantially or fully sequestered (e.g., contained or retained, circumvented, isolated, segregated, vapor-locked, separated, and/or the like) in or by the first reservoir or first portion of the device. In some instances, contaminants such as dermally residing microbes or the like can be included and/or entrained in the initial amount of the bodily fluid and likewise are sequestered in or by the first reservoir or first portion of the device. Once the initial amount is sequestered, any subsequent amount of the bodily fluid flow can be diverted, channeled, directed, flow controlled (e.g., manually, automatically, and/or semi-automatically) to a second reservoir, second portion of the device, and/or any additional flow path(s). Thus, with the initial amount sequestered, any additional and/or subsequent amount(s) of bodily fluid flow are substantially free from contaminants that may otherwise produce inaccurate, distorted, adulterated, falsely positive, falsely negative, etc., results in some diagnostics and/or testing. In some instances, the initial amount of bodily fluid also can be used, for example, in other testing such as those less affected by the presence of contaminants, can be discarded as a waste volume, can be infused back into the patient, and/or can be used for any other suitable clinical application.

[1031] In some embodiments, a feature of the fluid control devices and/or methods described herein is the use of an external negative pressure source (e.g., provided by a fluid collection device or any other suitable means) to (1) overcome physical patient challenges which can limit and/or prevent a sufficient pressure differential (e.g., a differential in blood pressure to ambient air pressure) to fully engage the sequestration chamber and/or to transition fluid flow to the fluid collection device; (2) result in proper filling of the sequestration chamber with a clinically validated and/or desirable volume of bodily fluid; (3) result in efficient, timely, and/or user-accepted consistency with bodily fluid collection process; and/or (4) provide a means of manipulating and/or automatically transitioning fluid flow (e.g., movement of physical components of the system or changing, switching, engaging, and/or otherwise employing or achieving desired fluid flow dynamics) to enable sequestration and/or isolation of the initial sample and collection of a subsequent sample.

[1032] In some embodiments, a fluid control device includes an inlet and an outlet. The inlet is configured to be placed in fluid communication with a bodily fluid source or an intermediary bodily fluid transfer device and the outlet is configured to be placed in fluid communication with a fluid collection device such as, for example, a sample reservoir, a syringe, a lumen-containing device, and/or any other suitable bodily fluid collection and/or transfer device. The fluid control device has a first state in which a negative pressure differential produced from an external source (e.g., the fluid collection device such as a sample reservoir, a syringe, a vessel, and/or any suitable intermediary fluid reservoir) is applied to the fluid control device to draw an initial volume of bodily fluid from the bodily fluid source, through the inlet, and into a sequestration and/or diversion portion of the fluid control device (which can be formed by or in the fluid control device or coupled thereto). The fluid control device has a second state in which (1) the sequestration chamber sequesters the initial volume, and (2) the negative pressure differential draws a subsequent volume of bodily fluid, being substantially free of contaminants, from the bodily fluid source, through the fluid control device, and into the fluid collection device.

[1033] In some embodiments, a system includes a housing, a flow controller, and a fluid collection device. The housing has an inlet and an outlet, and forms a sequestration portion. The inlet is configured to be placed in fluid communication with a bodily fluid source. The sequestration portion is configured to receive an initial volume of bodily fluid from the bodily fluid source. The flow controller is at least partially disposed in the sequestration portion of the housing and is configured to transition from a first state to a second state. The fluid collection device is configured to be fluidically coupled to the outlet to produce a negative pressure differential within at least a portion of the housing. The negative pressure differential is operable to draw the initial volume of bodily fluid into the sequestration portion when the flow controller is in the first state and is operable to draw the sample volume of bodily fluid through the outlet and into the fluid collection device when the flow controller is in the second state.

[1034] In some embodiments, an apparatus includes a housing and an actuator coupled to the housing. The housing has an inlet configured to be placed in fluid communication with a bodily fluid source and an outlet configured be placed in fluid communication with a fluid collection device. The housing forms a sequestration portion that is configured to receive an initial volume of bodily fluid from the bodily fluid source. The actuator has a first configuration in which a first fluid flow path places the inlet in fluid communication with the sequestration portion and a second configuration in which a second fluid flow path places the

inlet in fluid communication with the outlet. The fluid collection device is configured to be placed in fluid communication with the outlet to produce a negative pressure differential (1) within the first fluid flow path that is operable to draw the initial volume of bodily fluid into the sequestration portion when the actuator is in the first configuration, and (2) within the second fluid flow path that is operable to draw a sample volume of bodily fluid into the fluid collection device when the actuator is in the second configuration.

[1035] In some embodiments, a method of using a fluid control device to obtain a bodily fluid sample with reduced contamination includes establishing fluid communication between a bodily fluid source and an inlet of the fluid control device. A fluid collection device is coupled to an outlet of the fluid control device and is configured to produce a negative pressure differential within at least a portion of the fluid control device. An initial volume of bodily fluid is received from the inlet and into a sequestration portion of the fluid control device in response to the negative pressure differential. In response to contact with a portion of the initial volume of bodily fluid, a flow controller disposed in the sequestration portion is transitioned from a first state in which the flow controller allows a flow of a gas through the flow controller and prevents a flow of bodily fluid through the flow controller, to a second state in which the flow controller prevents a flow of gas and bodily fluid through the flow controller. The initial volume of bodily fluid is sequestered in the sequestration portion after the flow controller is transitioned to the second state and a subsequent volume of bodily fluid is transferred from the inlet to an outlet in fluid communication with a fluid collection device.

[1036] As used in this specification and the claims, the singular forms "a," "an" and "the" include plural referents unless the context clearly dictates otherwise. Thus, for example, the term "a member" is intended to mean a single member or a combination of members, "a material" is intended to mean one or more materials, or a combination thereof.

[1037] As used herein, the terms "about," "approximate," and/or "substantially" when used in connection with stated value and/or other geometric relationships is intended to convey that the structure so defined is nominally the value stated and/or the geometric relationship described. In some instances, the terms "about," "approximately," and/or "substantially" can generally mean and/or can generally contemplate plus or minus 10% of the value or relationship stated. For example, about 0.01 would include 0.009 and 0.011, about 0.5 would include 0.45 and 0.55, about 10 would include 9 to 11, and about 1000 would include 900 to 1100. While a value stated may be desirable, it should be understood that some variance may occur as a result of, for example, manufacturing tolerances or other practical considerations (such as, for example, the pressure or force applied through a portion of a device, conduit,

lumen, etc.). Accordingly, the terms "about," "approximately," and/or "substantially" can be used herein to account for such tolerances and/or considerations.

[1038] As used herein, "bodily fluid" can include any fluid obtained directly or indirectly from a body of a patient. For example, "bodily fluid" includes, but is not limited to, blood, cerebrospinal fluid, urine, bile, lymph, saliva, synovial fluid, serous fluid, pleural fluid, amniotic fluid, mucus, sputum, vitreous, air, and the like, or any combination thereof.

[1039] As used herein, the words "proximal" and "distal" refer to the direction closer to and away from, respectively, a user who would place the device into contact with a patient. Thus, for example, the end of a device first touching the body of the patient would be the distal end, while the opposite end of the device (e.g., the end of the device being manipulated by the user) would be the proximal end of the device.

[1040] As described in further detail herein, any of the devices and methods can be used to procure bodily fluid samples with reduced contamination by, for example, diverting a "pre-sample" volume of bodily fluid prior to collecting a "sample" volume of bodily fluid. Each of the terms "pre-sample," "first," and/or "initial," can be used interchangeably to describe and/or refer to an amount, portion, or volume of bodily fluid that is transferred, diverted, and/or sequestered prior to procuring the "sample" volume. In some embodiments, the terms "pre-sample," "first," and/or "initial" can refer to a predetermined, defined, desired, or given volume, portion, or amount of bodily fluid. For example, in some embodiments, a predetermined and/or desired pre-sample volume of bodily fluid can be about 0.1 milliliter (mL), about 0.2 mL, about 0.3 mL, about 0.4 mL, about 0.5 mL, about 1.0 mL, about 2.0 mL, about 3.0 mL, about 4.0 mL, about 5.0 mL, about 10.0 mL, about 20 mL, about 50 mL, and/or any volume or fraction of a volume therebetween. In other embodiments, the pre-sample volume can be greater than 50 mL or less than 0.1 mL. In some specific embodiments, a predetermined and/or desired pre-sample volume can be between about 0.1 mL and about 5.0 mL. In other embodiments, the pre-sample volume can be, for example, a drop of bodily fluid, a few drops of bodily fluid, a combined volume of any number of lumen that form, for example, a flow path (or portion thereof) from the bodily fluid source to an initial collection chamber, portion, reservoir, etc. (e.g., a sequestration chamber).

[1041] On the other hand, the terms "sample," "second," and/or "subsequent" when used in the context of a volume of bodily fluid can refer to a volume, portion, or amount of bodily fluid that is either a random volume or a predetermined or desired volume of bodily fluid collected after transferring, diverting, sequestering, and/or isolating the pre-sample volume of bodily fluid. For example, in some embodiments, a desired sample volume of bodily fluid can

be about 10 mL to about 60 mL. In other embodiments, a desired sample volume of bodily fluid can be less than 10 mL or greater than 60 mL. In some embodiments, for example, a sample volume can be at least partially based on one or more tests, assays, analyses, and/or processes to be performed on the sample volume.

[1042] The embodiments described herein can be configured to selectively transfer bodily fluid to one or more fluid collection device(s). In some embodiments, a fluid collection device can include, but is not limited to, any suitable vessel, container, reservoir, bottle, adapter, dish, vial, syringe, device, diagnostic and/or testing machine, and/or the like. By way of specific example, in some instances, any of the embodiments and/or methods described herein can be used to transfer a sample volume into a sample reservoir such as any of those described in detail in U.S. Patent No. 8,197,420 entitled, "Systems and Methods for Parenterally Procuring Bodily-Fluid Samples with Reduced Contamination," filed December 13, 2007 ("the '420 Patent"), the disclosure of which is incorporated herein by reference in its entirety.

[1043] In some embodiments, a sample reservoir can be a sample or culture bottle such as, for example, an aerobic culture bottle or an anaerobic culture bottle. In this manner, the culture bottle can receive a bodily fluid sample, which can then be tested (e.g., via in vitro diagnostic (IVD) tests, and/or any other suitable test) for the presence of, for example, Gram-Positive bacteria, Gram-Negative bacteria, yeast, fungi, and/or any other organism. In some instances, the culture bottle can receive a bodily fluid sample and the culture medium (disposed therein) can be tested for the presence of any suitable organism. If such a test of the culture medium yields a positive result, the culture medium can be subsequently tested using a PCR-based system to identify a specific organism. Moreover, as described in further detail herein, in some instances, diverting a pre-sample or initial volume of bodily fluid can reduce and/or substantially eliminate contaminants in the bodily fluid sample that may otherwise lead to inaccurate test results.

[1044] Any of the sample containers, reservoirs, bottles, dishes, vials, etc., described herein can be devoid of contents prior to receiving a sample volume of bodily fluid or can include, for example, any suitable additive, culture medium, substances, enzymes, oils, fluids, and/or the like. For example, in some embodiments, a sample reservoir can include an aerobic or anaerobic culture medium (e.g., a nutrient rich and/or environmentally controlled medium to promote growth, and/or other suitable medium(s)), which occupies at least a portion of the inner volume defined by the sample reservoir. In some embodiments, a sample reservoir can include, for example, any suitable additive or the like such as, heparin, citrate, ethylenediaminetetraacetic acid (EDTA), oxalate, SPS, and/or the like, which similarly

occupies at least a portion of the inner volume defined by the sample reservoir. In other embodiments, a sample reservoir can be any suitable container used to collect a specimen.

[1045] While the term "culture medium" can be used to describe a substance configured to react with organisms in a bodily fluid (e.g., microorganisms such as bacteria) and the term "additive" can be used to describe a substance configured to react with portions of the bodily fluid (e.g., constituent cells of blood, serum, synovial fluid, etc.), it should be understood that a sample reservoir can include any suitable substance, liquid, solid, powder, lyophilized compound, gas, etc. Moreover, when referring to an "additive" within a sample reservoir, it should be understood that the additive could be a culture medium, such as an aerobic culture medium and/or an anaerobic culture medium contained in a culture bottle, an additive and/or any other suitable substance or combination of substances contained in a culture bottle and/or any other suitable reservoir such as those described above. That is to say, the embodiments described herein can be used with any suitable fluid reservoir or the like containing any suitable substance. Furthermore, any of the embodiments and/or methods described herein can be used to transfer a volume of bodily fluid to a reservoir (or the like) that does not contain a culture medium, additive, and/or any other substance prior to receiving a flow of bodily fluid.

[1046] While some of the embodiments are described herein as being used for procuring bodily fluid for one or more culture sample testing, it should be understood that the embodiments are not limited to such a use. Any of the embodiments and/or methods described herein can be used to transfer a flow of bodily fluid to any suitable device that is placed in fluid communication therewith. Thus, while specific examples are described herein, the devices, methods, and/or concepts are not intended to be limited to such specific examples.

[1047] The embodiments described herein and/or portions thereof can be formed or constructed of one or more biocompatible materials. In some embodiments, the biocompatible materials can be selected based on one or more properties of the constituent material such as, for example, stiffness, toughness, durometer, bioreactivity, etc. Examples of suitable biocompatible materials include metals, glasses, ceramics, or polymers. Examples of suitable metals include pharmaceutical grade stainless steel, gold, titanium, nickel, iron, platinum, tin, chromium, copper, and/or alloys thereof. A polymer material may be biodegradable or non-biodegradable. Examples of suitable biodegradable polymers include polylactides, polyglycolides, polylactide-co-glycolides (PLGA), polyanhydrides, polyorthoesters, polyetheresters, polycaprolactones, polyesteramides, poly(butyric acid), poly(valeric acid), polyurethanes, and/or blends and copolymers thereof. Examples of non-biodegradable polymers include nylons, polyesters, polycarbonates, polyacrylates, polymers of ethylene-vinyl

acetates and other acyl substituted cellulose acetates, non-degradable polyurethanes, polystyrenes, polyvinyl chloride, polyvinyl fluoride, poly(vinyl imidazole), chlorosulphonate polyolefins, polyethylene oxide, and/or blends and copolymers thereof.

[1048] The embodiments described herein and/or portions thereof can include components formed of one or more parts, features, structures, etc. When referring to such components it should be understood that the components can be formed by a singular part having any number of sections, regions, portions, and/or characteristics, or can be formed by multiple parts or features. For example, when referring to a structure such as a wall or chamber, the structure can be considered as a single structure with multiple portions, or multiple, distinct substructures or the like coupled to form the structure. Thus, a monolithically constructed structure can include, for example, a set of substructures. Such a set of substructures may include multiple portions that are either continuous or discontinuous from each other. A set of substructures can also be fabricated from multiple items or components that are produced separately and are later joined together (e.g., via a weld, an adhesive, or any suitable method).

[1049] Referring now to the drawings, FIG. 1 is a schematic illustration of a fluid control device 100 according to an embodiment. Generally, the fluid control device 100 (also referred to herein as "control device" or "device") is configured to withdraw bodily fluid from a patient. A first portion or amount (e.g., an initial amount) of the withdrawn bodily fluid is sequestered from a second portion or amount (e.g., a subsequent amount) of the withdrawn bodily fluid which can be subsequently used for additional testing, discarded, and/or reinfused into the patient. In this manner, contaminants or the like can be sequestered within the first portion or amount, leaving the second portion or amount substantially free of contaminants. The second portion or amount of bodily fluid can then be used as a biological sample in one or more tests for the purpose of medical diagnosis and/or treatment (e.g., a blood culture test or the like), as described in more detail herein. The first portion or amount of bodily fluid can be discarded as waste or can be used in any suitable test that is less likely to produce false, inaccurate, distorted, inconsistent, and unreliable results as a result of potential contaminants contained therein. In other instances, the first portion or amount of bodily fluid can be infused back into the patient.

[1050] The control device 100 includes a housing 130 that has and/or forms an inlet 131, at least one outlet 136, and a sequestration chamber 134. The inlet 131 is configured to fluidically couple to a lumen-containing device, which in turn, can place the housing 130 in fluid communication with a bodily fluid source. For example, the housing 130 can be coupled to and/or can include a lumen-containing device that is in fluid communication with the inlet

131 and that is configured to be percutaneously disposed in a patient (e.g., a butterfly needle, intravenous (IV) catheter, peripherally inserted central catheter (PICC), syringe, sterile tubing, intermediary lumen-containing device, and/or bodily-fluid transfer device or the like). Thus, bodily fluid can be transferred from the patient and/or other bodily fluid source to the housing 130 via the inlet 131, as described in further detail herein. The outlet(s) 136 can be placed in fluid communication with a fluid collection device 180 (e.g., a fluid or sample reservoir, syringe, evacuated container, etc.). As such, the control device 100 can be used and/or manipulated to selectively transfer a volume of bodily fluid from a bodily fluid source, through the inlet 131, the housing 130, and the outlet(s) 136 to the fluid collection device 180, as described in further detail herein.

[1051] The housing 130 defines one or more fluid flow paths 133 between the inlet 131 and the sequestration chamber 134 and/or one or more fluid flow paths 154 between the inlet 131 and the outlet 136. The housing 130 of the device 100 can be any suitable shape, size, and/or configuration. For example, in some embodiments, the housing 130 can have a size that is at least partially based on a volume of bodily fluid at least temporarily stored, for example, in the sequestration chamber 134. As described in further detail herein, the control device 100 and/or the housing 130 can be configured to transition between operating modes such that bodily fluid flows through at least one of the fluid flow paths 133 and/or 154. Moreover, the control device 100 and/or the housing 130 can be configured to transition automatically (e.g., based on pressure differential, time, electronically, saturation of a membrane, an absorbent and/or barrier material, etc.) or via intervention (e.g., user intervention, mechanical intervention, or the like).

[1052] The sequestration chamber 134 is at least temporarily placed in fluid communication with the inlet 131 via the fluid flow path(s) 133. As described in further detail herein, the sequestration chamber 134 is configured to (1) receive a flow and/or volume of bodily fluid from the inlet 131 and (2) sequester (e.g., separate, segregate, contain, retain, isolate, etc.) the flow and/or volume of bodily fluid therein. The sequestration chamber 134 can have any suitable arrangement such as, for example, those described herein with respect to specific embodiments. It should be understood, however, that the control device 100 and/or the housing 130 can have a sequestration chamber 134 in any suitable arrangement and is not intended to be limited to those shown and described herein. For example, in some embodiments, the sequestration chamber 134 can be at least partially formed by the housing 130. In other embodiments, the sequestration chamber 134 can be a reservoir placed and/or disposed within a portion of the housing 130. In other embodiments, the sequestration chamber

134 can be formed and/or defined by a portion of the fluid flow path 133. That is to say, the housing 130 can define one or more lumens and/or can include one or more lumen defining device(s) configured to receive a flow of bodily fluid from the inlet 131, thereby defining the fluid flow path 133. In such embodiments, at least a portion of the lumen and/or a portion of the lumen defining device(s) can form and/or can define the sequestration chamber 134.

[1053] The sequestration chamber 134 can have any suitable volume and/or fluid capacity. For example, in some embodiments, the sequestration chamber 134 can have a volume and/or fluid capacity between about 0.25 mL and about 5.0 mL. In some embodiments, the sequestration chamber 134 can have a volume measured in terms of an amount of bodily fluid (e.g., the initial or first amount of bodily fluid) configured to be transferred in the sequestration chamber 134. For example, in some embodiments, the sequestration chamber 134 can have a volume sufficient to receive an initial volume of bodily fluid as small as a microliter or less of bodily fluid (e.g., a volume as small as 20 drops of bodily fluid, 10 drops of bodily fluid, 5 drops of bodily fluid, a single drop of bodily fluid, or any suitable volume therebetween). In other embodiments, the sequestration chamber 134 can have a volume sufficient to receive an initial volume of bodily fluid up to, for example, about 5.0 mL, 10.0 mL, 15 mL, 20 mL, 30 mL, 40 mL, 50 mL, or more. In some embodiments, the sequestration chamber 134 can have a volume that is equal to a fraction of and/or a multiple of at least some of the volumes of one or more lumen(s) placing the sequestration chamber 134 in fluid communication with the bodily fluid source.

[1054] Although not shown in FIG. 1, in some embodiments, the sequestration chamber 134 can include any suitable arrangement, configuration, and/or feature, and/or can be formed of one or more materials configured to interact with a portion of the bodily fluid transferred into the sequestration chamber 134. For example, in some embodiments, the housing 130 can include an absorbent and/or hydrophilic material disposed within the sequestration chamber 134. Accordingly, when bodily fluid is transferred into the sequestration chamber 134, the absorbent and/or hydrophilic material can absorb, attract, retain, expand, and/or otherwise interact with at least a portion of the bodily fluid, which in turn, can sequester and/or retain at least an initial portion of the bodily fluid within the sequestration chamber 134, as described in further detail herein. In other embodiments, the sequestration chamber 134 can include and/or can be formed of an expandable or collapsible material configured to transition between a first state (e.g., while an initial portion of the bodily fluid is being transferred into the sequestration chamber 134) to a second state (e.g., after the initial portion of the bodily fluid is transferred into the sequestration chamber 134). In some embodiments, a force associated with and/or

resulting from such a material expanding or collapsing can be operable to transition the housing 130 and/or the device 100 from a first state, position, configuration, etc. to a second state, position, configuration, etc. In some embodiments, the sequestration chamber 134 and/or any other suitable portion of the housing 130 can include one or more chemicals, compounds, and/or the like configured to chemically interact with bodily fluid transferred through a portion of the housing 130, which can be operable to transition the control device 100 and/or the housing 130 between the first state and the second state (e.g., via a force or any other suitable means).

[1055] In some embodiments, the control device 100 and/or the housing 130 can include and/or define a flow controller 120 configured to selectively control a flow of fluids (e.g., gas or liquids) through a portion of the control device 100. For example, in some embodiments, the flow controller 120 can control a flow of bodily fluid through the control device 100 (or housing 130) and/or otherwise selectively control a flow of bodily fluid through at least one of the fluid flow paths 133 and/or 154. The flow controller 120 can be, for example, a valve, a membrane, a diaphragm, a restrictor, a vent, a selectively permeable member (e.g., a fluid impermeable barrier or seal that at least selectively allows the passage of air or gas therethrough), a port, a junction, an actuator, and/or the like, or any suitable combination thereof. In some embodiments, the flow controller 120 can be configured to selectively control (at least in part) a flow of fluids into and/or out of the sequestration chamber 134 and/or any other suitable portion of the housing 130. In this context, the flow of fluids, for example, can be a liquid such as water, oil, dampening fluid, bodily fluid, and/or any other suitable liquid, and/or can be a gas such as air, oxygen, carbon dioxide, helium, nitrogen, ethylene oxide, and/or any other suitable gas. For example, in some embodiments, a wall or structure of the housing 130 can define an opening, aperture, port, orifice, and/or the like that is in fluid communication with the sequestration chamber 134. In such embodiments, the flow controller 120 can be, for example, a semi-permeable member or membrane disposed in or about the opening to selectively allow a flow of air or gas through the opening while limiting or substantially preventing a flow of fluid (e.g., bodily fluid such as blood) through the opening.

[1056] In some embodiments, one or more flow controllers 120 or the like can be configured to facilitate air (or other fluid) displacement through one or more portions of the control device 100, which in some instances, can result in a pressure differential across one or more portions of the control device 100 or can result in and/or allow for a pressure equalization across one or more portions of the housing 130. In some embodiments, the control device 100 can be configured to selectively transfer a volume of bodily fluid to the sequestration chamber

134 or to the outlet 136 based at least in part on a pressure differential between two or more portions of the control device 100. In some embodiments, the pressure differential can result from fluidically coupling the outlet 136 to the fluid collection device 180, which can define and/or can be configured to produce a negative pressure (e.g., an evacuated reservoir, a syringe, a pressure charged canister, and/or other source or potential energy to create a vacuum or pressure differential). In other embodiments, the pressure differential can result from a change in volume and/or temperature. In still other embodiments, the pressure differential can result from at least a portion of the control device 100, the housing 130, and/or other portions of the flow path being evacuated and/or charged (e.g., the sequestration chamber 134 and/or any other suitable portion). In some embodiments, the pressure differential can be established automatically or via direct or indirect intervention (e.g., by the user).

[1057] Moreover, a flow of a fluid (e.g., gas and/or liquid) resulting from a pressure differential can be selectively controlled via one or more flow controllers 120 that can, for example, transition between one or more operating conditions to control the fluid flow. In some embodiments, for example, the flow controller 120 can be an actuator or the like configured to transition between one or more operating conditions or states to establish fluid communication between one or more portions of the control device 100 and/or configured to sequester one or more portions of the control device 100 (e.g., the sequestration chamber 134). In some embodiments, the flow controller 120 can be member or device formed of an absorbent material configured to selectively allow fluid flow therethrough. For example, such an absorbent material can be transitioned from a first state in which the material allows a flow of gas (e.g., air) therethrough but prevents a flow of liquid (e.g., bodily fluid) therethrough, to a second state in which the material substantially prevents a flow of gas and liquid therethrough. In other embodiments, the flow controller 120 can include one or more valves, membranes, diaphragms, and/or the like. In some embodiments, the flow controller 120 can include any suitable combination of devices, members, and/or features. It should be understood that the flow controllers included in the embodiments described herein are presented by way of example and not limitation. Thus, while specific flow controllers are described herein, it should be understood that fluid flow can be controlled through the control device 100 by any suitable means.

[1058] The outlet(s) 136 is/are in fluid communication with and/or is/are configured to be placed in fluid communication with the fluid flow paths 133 and/or 154. As shown in FIG. 1, the outlet 136 can be any suitable outlet, opening, port, stopcock, lock, seal, coupler, valve (e.g. one-way, check valve, duckbill valve, umbrella valve, and/or the like), etc. and is configured

to be fluidically coupled to the fluid collection device 180 (e.g., a fluid reservoir, culture sample bottle, syringe, container, vial, dish, receptacle, pump, adapter, and/or any other suitable collection or transfer device). In some embodiments, the outlet 136 can be monolithically formed with the fluid collection device 180. In other embodiments, the outlet 136 can be at least temporarily coupled to the fluid collection device 180 via an adhesive, a resistance fit, a mechanical fastener, a threaded coupling, a piercing or puncturing arrangement, any number of mating recesses, and/or any other suitable coupling or combination thereof. Similarly stated, the outlet 136 can be physically (e.g., mechanically) and/or fluidically coupled to the fluid collection device 180 such that an interior volume defined by the fluid collection device 180 is in fluid communication with the outlet 136. In still other embodiments, the outlet 136 can be operably coupled to the fluid collection device 180 via an intervening structure (not shown in FIG. 1), such as a flexible sterile tubing. In some embodiments, the arrangement of the outlet 136 can be such that the outlet 136 is physically and/or fluidically sealed prior to coupling to the fluid collection device 180. In some embodiments, the outlet 136 can be transitioned from a sealed configuration to an unsealed configuration in response to being coupled to the fluid collection device 180 and/or in response to a negative pressure differential between an environment within the outlet 136 and/or housing 130 and an environment within the fluid collection device 180.

[1059] The fluid collection device 180 can be any suitable device for at least temporarily containing a bodily fluid, such as, for example, any of those described in detail above. For example, in some embodiments, the fluid collection device 180 can be a single-use disposable collection tube(s), a syringe, a vacuum-based collection tube(s), an intermediary bodily-fluid transfer device, and/or the like. In some embodiments, the fluid collection device 180 can be substantially similar to or the same as known sample containers such as, for example, a Vacutainer® (manufactured by BD), a BacT/ALERT ® SN or BacT/ALERT ® FA (manufactured by Biomerieux, Inc.), and/or any suitable reservoir, vial, microvial, microliter vial, nanoliter vial, container, microcontainer, nanocontainer, and/or the like. In some embodiments, the fluid collection device 180 can be a sample reservoir that includes a vacuum seal that maintains negative pressure conditions (vacuum conditions) inside the sample reservoir, which in turn, can facilitate withdrawal of bodily fluid from the patient, through the control device 100, and into the sample reservoir, via a vacuum or suction force, as described in further detail herein. In embodiments in which the fluid collection device 180 is an evacuated container or the like, the user can couple the fluid collection device 180 to the outlet 136 to initiate a flow of bodily fluid from the patient such that a first or initial portion of the

bodily fluid is transferred into and sequestered by the sequestration chamber 134 and such that any subsequent portion or volume of bodily fluid bypasses and/or is otherwise diverted away from the sequestration chamber 134 and flows into the fluid collection device 180, as described in further detail herein.

[1060] Although the outlet 136 of the control device 100 and/or the housing 130 is described above as being fluidically coupled to and/or otherwise placed in fluid communication with the fluid collection device 180, in other embodiments, the control device 100 can be used in conjunction with any suitable bodily fluid collection device and/or system. For example, in some embodiments, the control device 100 described herein can be used in any suitable fluid transfer device such as those described in U.S. Patent Publication No. 2015/0342510 entitled, "Sterile Bodily-Fluid Collection Device and Methods," filed June 2, 2015 (referred to herein as the "'510 publication"), the disclosure of which is incorporated herein by reference in its entirety. More particularly, the control device 100 can be used in an "all-in-one" or pre-assembled device (e.g., such as those described in the '510 publication) to receive and sequester an initial volume of bodily fluid such that contaminants in subsequent volumes of bodily fluid are reduced and/or eliminated.

[1061] As described above, the device 100 can be used to procure a bodily fluid sample having reduced contamination from microbes such as, for example, dermally residing microbes, and/or the like. For example, in some instances, a user such as a doctor, physician, nurse, phlebotomist, technician, etc. can manipulate the device 100 to establish fluid communication between the inlet 131 and the bodily fluid source (e.g., a vein of a patient, cerebral spinal fluid (CSF) from the spinal cavity, urine collection, and/or the like). As a specific example, in some instances, the inlet 131 can be coupled to and/or can include a needle or the like that can be manipulated to puncture the skin of the patient and to insert at least a portion of the needle in the vein of the patient, thereby placing the inlet 131 in fluid communication with the bodily fluid source (e.g., the vein, an IV catheter, a PICC, etc.).

[1062] In some embodiments, once the inlet 131 is placed in fluid communication with the bodily fluid source (e.g., the portion of the patient), the outlet 136 can be fluidically coupled to the fluid collection device 180. As described above, in some embodiments, the fluid collection device 180 can be any suitable reservoir, container, and/or device configured to receive a volume of bodily fluid. For example, the fluid collection device 180 can be an evacuated reservoir or container that defines a negative pressure and/or can be a syringe that can be manipulated to produce a negative pressure. In some instances, coupling the outlet 136 to the fluid collection device 180 selectively exposes at least a portion of the fluid flow paths 133

and/or 154 to the negative pressure, thereby resulting in a negative pressure differential operable in drawing bodily fluid from the bodily fluid source (e.g., the patient), through the inlet 131, and into the housing 130.

[1063] In some embodiments, the arrangement of the housing 130 is such that when a volume of bodily fluid is transferred to and/or through the inlet 131, an initial portion of the volume of bodily fluid (also referred to herein as an "initial volume" or a "first volume") flows from the inlet 131, through at least a portion of the fluid flow path 133, and into the sequestration chamber 134. That is to say, in some embodiments, the control device 100 and/or the housing 130 can be in first or initial state in which the initial portion or volume of bodily fluid can flow in or through at least a portion the fluid flow path 133 and into the sequestration chamber 134. For example, in some embodiments, the initial state of the control device 100 and/or the housing 130 can be one in which one or more flow controllers 120 (e.g., valves, membranes, diaphragms, restrictors, vents, air permeable and fluid impermeable barriers, ports, actuators, and/or the like, or a combination thereof) are in a first state in which the fluid flow path 133 is exposed to the negative pressure differential via the sequestration chamber 134. In other words, the negative pressure within or created by the fluid collection device 180 can result in a negative pressure (or negative pressure differential) within at least a portion of the sequestration chamber 134 that is operable in drawing an initial flow of bodily fluid into the sequestration chamber 134 when one or more flow controllers 120 is/are in a first or initial state.

[1064] For example, in some embodiments, the flow controller 120 can be an actuator or the like that includes a valve (e.g. one-way valve, check valve, duckbill valve, umbrella valve, and/or the like), a selectively permeable member (e.g., a fluid impermeable barrier or seal that allows at least selective passage of gas or air), a selectively permeable membrane, a diaphragm, and/or the like that is at least temporarily fluidically coupled to a flow path between the fluid collection device 180 and the sequestration chamber 134 (e.g., at least a portion of the fluid flow path 154). While in some embodiments the flow controller 120 examples noted above can be, for example, known off-the-shelf components that are used in medical devices to control the flow of fluids and air, in other embodiments, the flow controller 120 can be a custom, proprietary, and/or specifically tailored component integrated into the device 100. When the flow controller 120 is in the first or initial state, the flow controller 120 can allow a flow of fluid therethrough in response to the negative pressure of the fluid collection device 180. In some embodiments, the flow controller 120 or a portion or component thereof is configured to allow only a flow of air or gas through the flow controller 120 and is configured

to limit and/or substantially prevent a flow of liquid (e.g., bodily fluid) through the flow controller 120. As such, the fluid collection device 180 can produce a negative pressure differential within the sequestration chamber 134 that is operable to draw an initial portion and/or amount of bodily fluid into the sequestration chamber 134 when the flow controller 120 is in a first or initial state without allowing the initial portion of bodily fluid to flow into the fluid flow path 154 and/or otherwise out of the sequestration chamber 134.

[1065] Although not shown in FIG. 1, in some embodiments, the control device 100 and/or the housing 130 can include a member, device, mechanism, feature, etc. configured to modulate a magnitude of the negative pressure to which the sequestration chamber 134 is exposed. For example, in some embodiments, a housing can include a valve, a membrane, a porous material, a restrictor, an orifice, and/or any other suitable member, device, and/or feature configured to modulate pressure. In some embodiments, modulating and/or controlling a magnitude of the pressure to which the sequestration chamber 134 is exposed can, in turn, modulate a magnitude of pressure exerted on the bodily fluid and/or within a vein of a patient. In some instances, such pressure modulation can reduce, for example, hemolysis of a blood sample and/or a likelihood of collapsing a vein (e.g., which is particularly important in fragile patients needing microbial and/or other diagnostic testing associated with use of the control device 100). In addition, the modulation of the negative pressure can, for example, at least partially control a rate at which the control device 100 transitions between a first configuration or state and a second configuration or state. In some embodiments, modulating the negative pressure can act like a timer. For example, a time between the introduction of the negative pressure differential and the transitioning of the control device 100 from the first state to the second state can be known, predetermined, calculated, and/or controlled. As such, in some instances, modulating the negative pressure can at least partially control an amount or volume of bodily fluid transferred into the sequestration chamber 134 (i.e., can control a volume of the initial amount of bodily fluid).

[1066] The initial portion and/or amount of bodily fluid can be any suitable volume of bodily fluid, as described above. For example, in some instances, the control device 100 and/or the housing 130 can remain in the first state until a predetermined and/or desired volume (e.g., the initial volume) of bodily fluid is transferred to the sequestration chamber 134. In some embodiments, the initial volume can be associated with and/or at least partially based on a volume of the sequestration chamber 134. In other embodiments, the initial volume can be associated with and/or at least partially based on an amount or volume of bodily fluid that can be absorbed by an absorbent material, an expandable material, a hydrophilic material, a

wicking material, and/or other suitable material disposed in the sequestration chamber 134. In other embodiments, the initial volume of bodily fluid can be associated with and/or at least partially based on an amount or volume of bodily fluid that can be transferred into the sequestration chamber 134 in a predetermined time. In still other embodiments, the initial volume can be associated with and/or at least partially based on an amount or volume of bodily fluid that is sufficient to fully wet or saturate a semi-permeable member or membrane otherwise configured to selectively expose the sequestration chamber 134 to the negative pressure of the fluid collection device 180 (i.e., the flow controller 120 such as an air permeable and liquid impermeable member or membrane). In other words, in some embodiments, the initial volume of bodily fluid can be a volume sufficient to transition one or more flow controllers 120 to a second state (e.g., a saturated or fully wetted state). In still other embodiments, the control device 100 and/or the housing 130 can be configured to transfer a volume of bodily fluid (e.g., the initial volume) into the sequestration chamber 134 until a pressure differential between the sequestration chamber 134 and the fluid flow path 133 and/or the bodily fluid source is brought into substantial equilibrium and/or is otherwise reduced below a desired threshold.

[1067] After the initial volume of bodily fluid is transferred and/or diverted into the sequestration chamber 134, the initial volume is sequestered, segregated, retained, contained, isolated, etc. in the sequestration chamber 134. For example, in some embodiments, the transitioning of the one or more flow controllers 120 from a first state to a second state can be operable to sequester and/or retain the initial portion of the bodily fluid in the sequestration chamber 134. As described in further detail herein, in some instances, contaminants such as, for example, dermally residing microbes or the like dislodged during the venipuncture event, other external sources of contamination, colonization of catheters and PICC lines that are used to collect samples, and/or the like can be entrained and/or included in the initial volume of the bodily fluid and thus, are sequestered in the sequestration chamber 134 when the initial volume is sequestered therein.

[1068] With the initial volume transferred and/or diverted into the sequestration chamber 134, the device 100 can transition to the second state in which a subsequent volume(s) of bodily fluid can flow through at least a portion the fluid flow paths 133 and/or 154 from the inlet 131 to the outlet 136. In some embodiments, the control device 100 and/or the housing 130 can passively and/or automatically transition (e.g., without user intervention) from the first state to the second state once the initial volume of bodily fluid is sequestered in the sequestration chamber 134. For example, in some embodiments, filling the sequestration chamber 134 to capacity and/or fully saturating, wetting, and/or impregnating an absorbent or similar material

disposed between the sequestration chamber 134 and the fluid collection device 180 can be such that further transfer of bodily fluid into the sequestration chamber 134 is limited and/or substantially prevented due to a removal or diversion of the negative pressure. In other embodiments, the control device 100 and/or the housing 130 can be manually transitioned or transitioned in response to at least an indirect interaction by a user. For example, in some embodiments, a user can transition the control device 100 and/or the housing 130 from the first state to the second state by actuating an actuator or the like (e.g., actuating the flow controller 120 or a portion thereof). In still other embodiments, at least a portion of the initial volume of bodily fluid can transition the control device 100 and/or the housing 130 from the first state to the second state. For example, the control device 100 can include a flow controller 120 that is and/or that includes a bodily fluid activated switch, valve, port, and/or the like. In other embodiments, a volume of bodily fluid can move and/or displace one or more flow controller 120 (e.g., actuators or the like) that can, for example, open a port, flow path, and/or outlet. In still other embodiments, a user can manipulate such a flow controller 120 (e.g., switch, valve, port, actuator, etc.) to transition the control device 100 and/or the housing 130 from the first state to the second state.

[1069] With the fluid collection device 180 fluidically coupled to the outlet 136 and with the control device 100 and/or the housing 130 being in the second state (e.g., the initial volume of bodily fluid is sequestered in or by the sequestration chamber 134), any subsequent volume(s) of the bodily fluid can flow from the inlet 131, through at least one of the fluid flow paths 133 and/or 154, through the outlet 136, and into the fluid collection device 180. Thus, as described above, sequestering the initial volume of bodily fluid in the sequestration chamber 134 prior to collecting or procuring one or more sample volumes of bodily fluid reduces and/or substantially eliminates an amount of contaminants in the one or more sample volumes. Moreover, in some embodiments, the arrangement of the control device 100 and/or the housing 130 can be such that the control device 100 and/or the housing 130 cannot transition to the second state prior to collecting and sequestering the initial volume in the sequestration chamber 134.

[1070] FIGS. 2-5 illustrate a fluid control device 200 according to an embodiment. The fluid control device 200 can be similar in at least form and/or function to the fluid control device 100 described above with reference to FIG. 1. Accordingly, portions of the fluid control device 200 that can be similar to portions of the fluid control device 100 are not described in further detail herein.

[1071] As shown in FIGS. 2-5, the fluid control device 200 (also referred to herein as "control device" or "device") includes a housing 230 having an inlet 231, an outlet 236, and an actuator 250. As described above with reference to the control device 100, the inlet 231 is configured to be placed in fluid communication with a bodily fluid source to receive a flow of bodily fluid therefrom (e.g., via a lumen-containing device such as a needle, IV catheter, PICC line, or the like). The outlet 236 is configured to be fluidically coupled to a fluid collection device such as, for example, a sample reservoir, a syringe, and/or other intermediary bodily fluid transfer device or vessel (e.g., a transfer device similar to those described in the '510 publication), and/or the like.

[1072] As described above with reference to the housing 130, the housing 230 defines one or more fluid flow paths 233 between the inlet 231 and a sequestration chamber 234 and/or one or more fluid flow paths 254 between the inlet 231 and the outlet 236. The housing 230 of the device 200 can be any suitable shape, size, and/or configuration. For example, in some embodiments, the housing 230 can be substantially similar in at least form and/or function to the housing 130 described above with reference to FIG. 1. The sequestration chamber 234 of the housing 230 is at least temporarily placed in fluid communication with the inlet 231 via the fluid flow path(s) 233. Moreover, the sequestration chamber 234 can be selectively placed in fluid communication with the fluid flow path 254 such that at least air or gas can be transferred therebetween, as described in further detail herein.

[1073] As described in further detail herein, the sequestration chamber 234 is configured to (1) receive a flow and/or volume of bodily fluid from the inlet 231 and (2) sequester (e.g., separate, segregate, contain, retain, isolate, etc.) the flow and/or volume of bodily fluid therein. The sequestration chamber 234 can have any suitable shape, size, and/or configuration. For example, in some embodiments, the sequestration chamber 234 can have any suitable size, volume, and/or fluid capacity such as, for example, those described above with reference to the sequestration chamber 134. In the embodiment shown in FIGS. 2-5, the sequestration chamber 234 can be at least partially formed by the housing 230 that defines a lumen or flow path. In some embodiments, at least a portion of the fluid flow path 233 can extend through a portion of the housing 230 to form and/or define at least a portion of the sequestration chamber 234. As shown in FIGS. 2-5, the sequestration chamber 234 and/or a portion of the fluid flow path 233 forming the sequestration chamber 234 can have a serpentine configuration or the like. In other embodiments, the sequestration chamber 234 can have any suitable arrangement. For example, in some embodiments, a housing can include a sequestration chamber that is formed by a flexible tubing or the like that can be arranged in any suitable shape and/or configuration.

[1074] In some embodiments, the housing 230 and/or the sequestration chamber 234 can include, form, and/or define a flow controller 242. The flow controller 242 can be, for example, a valve, membrane, diaphragm, restrictor, vent, a selectively permeable member (e.g., a fluid impermeable barrier or seal that allows at least selective passage of gas or air such as, for example, a blood barrier and/or the like), port, etc. (collectively referred to herein as a "flow controller") configured to selectively control (at least in part) a flow of fluids into and/or out of the sequestration chamber 234 and/or any other suitable portion of the housing 230. More particularly, in the embodiment shown in FIGS. 2-5, the flow controller 242 is a selectively permeable fluid barrier (e.g., a blood barrier) that includes and/or is formed of a porous material configured to selectively allow a flow of gas therethrough but to prevent a flow of a liquid therethrough.

[1075] As shown, the flow controller 242 is positioned within the housing 230 to selectively establish fluid communication between the sequestration chamber 234 and the fluid flow path 254. Thus, with the flow controller 242 being configured as a semi-permeable member, the flow controller 242 can be configured to at least temporarily allow a gas or air to transfer between the fluid flow path 254 and the sequestration chamber 234 and can be configured to substantially prevent a flow of liquid between the fluid flow path 254 and the sequestration chamber 234, as described in further detail herein.

[1076] The outlet 236 of the housing 230 is in fluid communication with and/or is configured to be placed in fluid communication with the fluid flow paths 233 and/or 254. As shown in FIGS. 2-5, the outlet 236 can be any suitable outlet, opening, port, lock, seal, coupler, etc. and is configured to be fluidically coupled to a fluid collection device such as a sample reservoir, a syringe, container, and/or other sample vessel. In some embodiments, the outlet 236 can be monolithically formed with the fluid collection device or can be at least temporarily coupled to the fluid collection device, as described above with reference to the outlet 136 of the housing 130. The fluid collection device can be any suitable reservoir, container, and/or device for containing a bodily fluid, such as, for example, any of those described in detail above with reference to the fluid collection device 180. More particularly, in some embodiments, the outlet 236 can be configured to couple to an evacuated sample reservoir. As such, the user can couple the sample reservoir to the outlet 236 to initiate a flow of bodily fluid from the patient such that a first or initial portion of the bodily fluid is transferred into and sequestered by the sequestration chamber 234 and such that any subsequent portion or volume of bodily fluid bypasses and/or is otherwise diverted away from the sequestration chamber 234 and flows into the sample reservoir.

[1077] As shown in FIGS. 3-5, the housing 230 includes and/or is coupled to the actuator 250 configured to selectively control a flow of bodily fluid through the housing 230. More particularly, the actuator 250 is disposed, for example, between a portion of the fluid flow path 233 and a portion of the fluid flow path 254. While the actuator 250 is shown in FIGS. 3-5 as being positioned apart from, away from, and/or downstream of a junction between the fluid flow path 233 and the sequestration chamber 234, in other embodiments, the actuator 250 can be disposed at any suitable position within the housing 230. For example, in some embodiments, the actuator 250 can be positioned at and/or can form at least a portion of a junction between the fluid flow path 233, the sequestration chamber 234, and the fluid flow path 254.

[1078] The actuator 250 can be any suitable shape, size, and/or configuration. For example, in some embodiments, the actuator 250 can be any suitable member or device configured to transition between a first state and a second state. In the embodiment shown in FIGS. 2-5, the actuator 250 is configured to isolate, sequester, separate, and/or otherwise prevent fluid communication between the fluid flow path 233 and the fluid flow path 254 when in the first state and is configured to place the fluid flow path 233 in fluid communication with the fluid flow path 254 when in the second state. In some embodiments, for example, the actuator 250 can be a valve, plunger, seal, membrane, flap, plate, and/or the like. As shown, for example, in FIG. 5, the actuator 250 can include one or more seals 265 configured to selectively establish fluid communication between the fluid flow channels 233 and 254 when the actuator 250 is transitioned from a first state to a second state (e.g., pressed, rotated, moved, activated, switched, slid, etc.).

[1079] Although the actuator 250 is particularly shown in FIGS. 2-5 and described above, in other embodiments, the control device 200 can include any suitable actuator or device configured to selectively establish fluid communication between the fluid flow path 233 and 254. Thus, while particularly shown in FIGS. 2-5, it should be understood that the control device 200 is presented by way of example only and not limitation. For example, while the actuator 250 is shown in FIGS. 2-5 as being disposed in a given position, in other embodiments, the actuator 250 can be placed at any suitable position along the housing 230. By way of example, in some embodiments, the actuator 250 can be disposed at the junction between the fluid flow path 233, the sequestration chamber 234, and the inlet 231. In such embodiments, a flow of bodily fluid can flow directly from the inlet 231 and into the sequestration chamber 234 when the actuator 250 is in the first state and can flow directly from the inlet 231 to the fluid flow path 254 when the actuator 250 is in the second state. In other words, the actuator

250 can form a portion of the sequestration chamber 234 such that when the actuator 250 is in the first state, bodily fluid flows from the inlet directly into the sequestration chamber 234. When the actuator 250 is actuated, placed, and/or transitioned to the second state, the actuator 250 can, for example, allow bodily fluid to flow directly from the inlet 231 to the fluid flow path 233. In such embodiments, the actuator 250 can prevent the formation of a junction between the inlet 231, the sequestration chamber 234, and the fluid flow path 233. Moreover, when in the second state, the actuator 250 can be operable in at least partially sequestering the sequestration chamber 234 from the inlet 231 and/or the fluid flow path 233.

[1080] In addition, the actuator 250 can be actuated and/or transitioned in any suitable manner. For example, in some embodiments, the actuator 250 can transition between the first and the second state in response to a manual actuation by the user (e.g., exerting a manual force on a button, slider, switch, rotational member, etc.). In other embodiments, the actuator 250 can be configured to automatically transition between the first state and the second state in response to a pressure differential (or lack thereof), a change in potential or kinetic energy, a change in composition or configuration (e.g., a portion of the actuator could at least partially dissolve or transform), and/or the like. In still other embodiments, the actuator 250 can be mechanically and/or electrically actuated or transitioned based on a predetermined time, volumetric flow rate, flow velocity, etc. While examples of actuators and/or ways in which an actuator can transition are provided herein, it should be understood that they have been presented by way of example only and not limitation. Thus, a control device 200 can include any suitable actuator configured to transition in any suitable manner.

[1081] As described above, the device 200 can be used to procure a bodily fluid sample having reduced contamination from microbes such as, for example, dermally residing microbes, and/or the like. For example, in some instances, a user such as a doctor, physician, nurse, phlebotomist, technician, etc. can manipulate the device 200 to establish fluid communication between the inlet 231 and the bodily fluid source (e.g., a vein of a patient). Once the inlet 231 is placed in fluid communication with the bodily fluid source (e.g., the portion of the patient), the outlet 236 can be fluidically coupled to the fluid collection device. As described above, in the embodiment shown in FIGS. 2-5, the fluid collection device can be, for example, an evacuated reservoir or container that defines a negative pressure and/or can be any other suitable negative pressure source.

[1082] Coupling the outlet 236 to the fluid collection device selectively exposes at least a portion of the fluid flow path 254 to the negative pressure within the fluid collection device. As described above, the flow controller 242 is in fluid communication with the fluid flow path

254 and the sequestration chamber 234. Thus, coupling the outlet 236 to the fluid collection device exposes the sequestration chamber to the negative pressure of the fluid collection device, thereby resulting in a negative pressure differential operable in drawing bodily fluid from the bodily fluid source (e.g., the patient), through the inlet 231, and into the housing 230. As described above with reference to the control device 100, the arrangement of the housing 230 is such that when a volume of bodily fluid is transferred to and/or through the inlet 231, an initial portion of the volume of bodily fluid (also referred to herein as an "initial volume" or a "first volume") flows from the inlet 231, through at least a portion of the fluid flow path 233, and into the sequestration chamber 234. That is to say, in some embodiments, the control device 200 and/or the housing 230 can be in first or initial state in which the initial portion or volume of bodily fluid can flow in or through at least a portion the fluid flow path 233 and into the sequestration chamber 234.

[1083] As described above, the housing 230 and/or the control device 200 can be in the initial state when the flow controller 242 and the actuator 250 are in a first state, position, configuration, etc. As such, the actuator 250 isolates, separates, segregates, sequesters and/or otherwise prevents direct fluid communication between the fluid flow paths 233 and 254. In addition, the inlet 231 is exposed to the negative pressure differential via the sequestration chamber 234. In other words, the negative pressure within the fluid collection device can result in a negative pressure (or negative pressure differential) within at least a portion of the sequestration chamber 234 that is operable in drawing an initial flow of bodily fluid from the inlet 233 into the sequestration chamber 234 when the housing 230 and/or control device 200 is in the first or initial state.

[1084] When the flow controller 242 is in the first or initial state, the flow controller 242 can allow a flow of fluid (e.g., a gas or air) therethrough in response to the negative pressure of the fluid collection device (e.g., a sample reservoir, a syringe, or other source of potential energy used to create negative pressure), as described above with reference to the housing 130. In some instances, it may be desirable to modulate and/or control a magnitude of the negative pressure differential. In the embodiment shown in FIGS. 2-5, for example, the housing 230 defines a restricted flow path 232 that places the flow controller 242 in fluid communication with the fluid flow path 254. More specifically, the restricted flow path 232 is a fluid flow path having a smaller diameter than at least the fluid flow path 254.

[1085] For example, in some embodiments, the restricted flow path 232 can have a diameter of about 0.0005", about 0.001", about 0.003", about 0.005", about 0.01", about 0.1", about 0.5" or more. In other embodiments, the restricted flow path 232 can have a diameter

less than 0.0005" or greater than 0.5". In some embodiments, the restricted flow path 232 can have a predetermined and/or desired length of about 0.01", about 0.05", about 0.1", about 0.15", about 0.2", about 0.5", or more. In other embodiments, the restricted flow path 232 can have a predetermined and/or desired length that is less than 0.01" or more than about 0.5". Moreover, in some embodiments, a restricted flow path 232 can have any suitable combination of diameter and length to allow for and/or to provide a desired flow characteristic through at least a portion of the control device 200.

[1086] In this embodiment, the restricted flow path 232 having a smaller diameter results in a lower magnitude of negative pressure being applied through the sequestration chamber than a magnitude of negative pressure when the restricted flow path has a larger diameter. In some instances, modulating a magnitude of negative pressure can control a rate at which bodily fluid is transferred into the sequestration chamber 234. For example, in some embodiments, a fluid collection device and/or other suitable negative pressure source may produce a negative pressure differential having a magnitude (e.g., a negative magnitude) of about 0.5 pounds per square inch (PSI), about 1.0 PSI, about 2.0 PSI, about 3.0 PSI, about 4.0 PSI, about 5.0 PSI, about 10 PSI, about 12.5 PSI, or about 14.7 PSI (e.g., at or substantially at atmospheric pressure at about sea level). In some embodiments, a fluid collection device such as an evacuated container or the like can have a predetermined negative pressure of about 12.0 PSI. Accordingly, by controlling the diameter and/or length of the restricted flow path 232, the amount of negative pressure to which the sequestration chamber 234 is exposed and/or the rate at which the negative pressure is applied can be controlled, reduced, and/or otherwise modulated. In some instances, the use of the restricted flow path 232 can result in a delay or ramp up of the negative pressure exerted on or in the sequestration chamber.

[1087] Moreover, in this embodiment, the restricted flow path 232 is, for example, a gas flow path configured to receive a flow of gas or air but not a flow of a liquid (e.g., bodily fluid). In some embodiments, the diameter of the restricted flow path 232 can be sufficiently small to limit and/or prevent a flow of a liquid therethrough. In addition, the arrangement of the restricted flow path 232 being disposed between the fluid flow path 254 and the flow controller 242 is such that a flow of bodily fluid and/or any other liquid is substantially prevented by the flow controller 242 (e.g., a selectively permeable barrier or seal).

[1088] Although the pressure modulation is described above as being based on a diameter of the restricted flow path 232 (i.e., a single restricted flow path), it should be understood that this is presented by way of example only and not limitation. Other means of modulating the magnitude of negative pressure to which the sequestration chamber is exposed can include, for

example, a porous material, a valve, a membrane, a diaphragm, a specific restriction, a vent, a deformable member or flow path, and/or any other suitable means. In other embodiments, a control device can include any suitable number of restricted flow paths, each of which can have substantially the same diameter or can have varied diameters. For example, in some embodiments, a control device can include up to 100 restricted flow paths or more. In such embodiments, each of the restricted flow paths can have a diameter of between about 0.0005" and about 0.1", between about 0.0005" and about 0.05", or between about 0.0005" and about 0.01". In some embodiments, multiple restricted flow paths can be configured to (1) selectively provide a flow path between the outlet 236 and the sequestration chamber 234 that exposes the sequestration chamber 234 to the negative pressure differential, and (2) act as a flow controller configured to selectively allow the passage of a gas and/or air while substantially preventing the passage of a liquid (e.g., bodily fluid).

[1089] In some embodiments, modulating and/or controlling a magnitude of the pressure to which the sequestration chamber 234 is exposed can, in turn, modulate a magnitude of pressure exerted on the bodily fluid and/or within a vein of a patient. In some instances, such pressure modulation can reduce, for example, hemolysis of a blood sample and/or a likelihood of collapsing a vein. In some instances, the ability to modulate and/or control an amount or magnitude of negative pressure can allow the control device 200 to be used across a large spectrum of patients that may have physiological challenges whereby negative pressure is often needed to facilitate collection of bodily fluid such as, for example, blood (i.e. pressure differential between atmospheric pressure and a patient's vascular pressure is not sufficient to facilitate consistent and sufficiently forceful flow) but not so much pressure that a rapid force flattens, collapses, caves-in, and/or otherwise inhibits patency and ability to collect blood.

[1090] The initial portion and/or amount of bodily fluid can be any suitable volume of bodily fluid, as described in detail above with reference to the control device 100. For example, in some instances, the initial volume can be associated with and/or at least partially based on an amount or volume of bodily fluid that is sufficient to fully wet or saturate the flow controller 242. In other words, in some embodiments, the initial volume of bodily fluid can be a volume sufficient to transition the flow controller 242 to a second state (e.g., a saturated or fully wetted state). In some embodiments, the flow controller 242 is placed in a sealed configuration when transitioned to the second state. That is to say, saturating and/or fully wetting the flow controller 242 (e.g., the semi-permeable material) places the flow controller 242 in a sealed configuration in which the flow controller 242 substantially prevents a flow of a liquid and a gas therethrough. Thus, transitioning the flow controller 242 to the second state sequesters,

blocks, isolates, separates, segregates, and/or otherwise prevents flow through the flow controller 242 between the restricted flow path 232 and the sequestration chamber 234.

[1091] After the initial volume of bodily fluid is transferred and/or diverted into the sequestration chamber 234, the control device 200 and/or the housing 230 can be transitioned to its second state or operating mode to sequester, segregate, retain, contain, isolate, etc. the initial volume in the sequestration chamber 234. For example, as described above, the flow controller 242 is placed in the sealed configuration. In addition, the actuator 250 can be actuated to transition from its first state to its second state to establish fluid communication between the fluid flow paths 233 and 254. As such, the negative pressure otherwise exerted on or through the sequestration chamber 234 is now exerted on or through the fluid flow paths 233 and 254. In response, bodily fluid can flow from the inlet 231, through the fluid flow paths 233 and 254, through the outlet 236, and into the fluid collection device. In some embodiments, the transitioning of the flow controller 242 and the actuator 250 from their respective first states to their respective second states is operable to sequester and/or retain the initial portion of the bodily fluid in the sequestration chamber 234. As described in further detail herein, in some instances, contaminants such as, for example, dermally residing microbes or the like dislodged during the venipuncture event, can be entrained and/or included in the initial volume of the bodily fluid and thus, are sequestered in the sequestration chamber 234 when the initial volume is sequestered therein.

[1092] With the fluid collection device fluidically coupled to the outlet 236 and with the control device 200 and/or the housing 230 being in the second state (e.g., the initial volume of bodily fluid is sequestered in or by the sequestration chamber 234), any subsequent volume(s) of the bodily fluid can flow from the inlet 231, through the fluid flow paths 233 and 254, through the outlet 236, and into the fluid collection device. Thus, as described above, sequestering the initial volume of bodily fluid in the sequestration chamber 234 prior to collecting or procuring one or more sample volumes of bodily fluid reduces and/or substantially eliminates an amount of contaminants in the one or more sample volumes. Moreover, in some embodiments, the arrangement of the control device 200 and/or the housing 230 can be such that the control device 200 and/or the housing 230 cannot transition to the second state prior to collecting and sequestering the initial volume in the sequestration chamber 234.

[1093] While the control device 200 is described above with reference to FIGS. 2-5 as including the actuator 250 configured to be moved (e.g., via a force applied by a user) between the first state and the second state, in other embodiments, a control device can include any suitable member, device, mechanism, etc. configured to selectively establish fluid

communication between two or more fluid flow paths. For example, FIGS. 6-8 illustrate a fluid control device 300 according to an embodiment. The fluid control device 300 can be similar in at least form and/or function to the fluid control device 100 described above with reference to FIG. 1 and/or the fluid control device 200 described above with reference to FIGS. 2-5. Accordingly, portions of the fluid control device 300 that can be similar to portions of the fluid control devices 100 and/or 200 are not described in further detail herein.

[1094] As shown in FIGS. 6-8, the fluid control device 300 (also referred to herein as "control device" or "device") includes a housing 330 having an inlet 331 and an outlet 336, and including or being coupled to an actuator 350. As described above with reference to the control devices 100 and/or 200, the inlet 331 is configured to be placed in fluid communication with a bodily fluid source to receive a flow of bodily fluid therefrom (e.g., via a lumen-containing device such as a needle or the like). The outlet 336 is configured to be fluidically coupled to a fluid collection device (not shown in FIGS. 6-8).

[1095] As described above with reference to the housings 130 and/or 230, the housing 330 defines one or more fluid flow paths 333, 354A, and 354B configured to selectively place the inlet 331 in fluid communication with the sequestration chamber 334 and/or the outlet 336. The housing 330 of the device 300 can be any suitable shape, size, and/or configuration. For example, in some embodiments, the housing 330 can be substantially similar in at least form and/or function to the housings 130 and/or 230 described above. In some embodiments, the housing 330 can have a size that is at least partially based on a volume of bodily fluid at least temporarily stored, for example, in the sequestration chamber 334. The sequestration chamber 334 of the housing 330 is at least temporarily placed in fluid communication with the inlet 331 via the fluid flow path(s) 333. Moreover, the sequestration chamber 334 can be selectively placed in fluid communication with the fluid flow path 354A such that at least air or gas can be transferred therebetween, as described in further detail herein.

[1096] As described in further detail herein, the sequestration chamber 334 is configured to (1) receive a flow and/or volume of bodily fluid from the inlet 331 and (2) sequester (e.g., separate, segregate, contain, retain, isolate, etc.) the flow and/or volume of bodily fluid therein. The sequestration chamber 334 can have any suitable shape, size, and/or configuration. For example, in some embodiments, the sequestration chamber 334 can be substantially similar to the sequestration chamber 234 described above with reference to FIGS. 2-5 and thus, is not described in further detail herein. Likewise, the housing 330 and/or the sequestration chamber 334 include, form, and/or define a flow controller 342 that can be substantially similar to the flow controller 242 described above. As such, the flow controller 342 is positioned within the

housing 330 to selectively establish fluid communication between the sequestration chamber 334 and the fluid flow path 354A, as described in further detail herein.

[1097] The outlet 336 of the housing 330 is in fluid communication with and/or is configured to be placed in fluid communication with the fluid flow paths 333, 354A, and/or 354B. In addition, the outlet 336 is configured to be fluidically coupled to a fluid collection device such as, for example, a sample reservoir, container, vial, negative pressure source, syringe, and/or intermediate control and/or transfer device (not shown in FIGS. 6-8). The outlet 336 and the fluid collection device can each be substantially similar to the outlet 236 and fluid collection device, respectively, described above with reference to the control device 200. Thus, the outlet 336 and fluid collection device are not described in further detail herein.

[1098] As shown in FIGS. 6-8, the housing 330 includes and/or is coupled to the actuator 350, which is configured to selectively control a flow of bodily fluid through the housing 330. In some embodiments, the actuator 350 can be substantially similar in at least function to the actuator 250 described above with reference to FIGS. 2-5. In this embodiment, however, the actuator 350 is arranged as a plunger and includes a set of seals 365 disposed along an outer surface of the plunger. Moreover, the actuator 350 has a substantially annular shape and is configured to at least temporarily receive and/or otherwise be disposed about a portion of the flow controller 342, as shown in FIG. 8. As described above with reference to the actuator 250, the actuator 350 is configured to isolate, sequester, separate, and/or otherwise prevent fluid communication between the fluid flow path 333 and the fluid flow path 354B when in the first state and is configured to place the fluid flow path 333 in fluid communication with the fluid flow path 354B when in the second state.

[1099] As described above, the device 300 can be used to procure a bodily fluid sample having reduced contamination from microbes such as, for example, dermally residing microbes, and/or the like. For example, in some instances, a user such as a doctor, physician, nurse, phlebotomist, technician, etc. can manipulate the device 300 to establish fluid communication between the inlet 331 and the bodily fluid source (e.g., a vein of a patient). Once the inlet 331 is placed in fluid communication with the bodily fluid source (e.g., the portion of the patient), the outlet 336 can be fluidically coupled to the fluid collection device. As described above, in the embodiment shown in FIGS. 6-8, the fluid collection device can be, for example, an evacuated reservoir, a syringe, and/or any container that defines a negative pressure.

[1100] Coupling the outlet 336 to the fluid collection device selectively exposes at least a portion of the fluid flow paths 354A and 354B to the negative pressure within and/or produced

by the fluid collection device. The arrangement of the actuator 350 when in its first state, configuration, and/or position is such that the actuator 350 isolates the fluid flow path 354B from the fluid flow path 333 and as such, the fluid flow path 333 is not exposed to the negative pressure differential produced by the fluid collection device. As described above, the flow controller 342 is in fluid communication with the fluid flow path 354A and the sequestration chamber 334. More particularly, the annular arrangement of the actuator 350 allows the flow controller 342 to be in fluid communication with the fluid flow path 354A (see e.g., FIG. 8). Thus, coupling the outlet 336 to the fluid collection device exposes the sequestration chamber 334 to the negative pressure of the fluid collection device, thereby resulting in a negative pressure differential operable in drawing bodily fluid from the bodily fluid source (e.g., the patient), through the inlet 331, and into the housing 330. As described above with reference to the control devices 100 and 200, the arrangement of the housing 330 is such that when a volume of bodily fluid is transferred to and/or through the inlet 331, an initial portion of the volume of bodily fluid (also referred to herein as an "initial volume" or a "first volume") flows from the inlet 331 and into the sequestration chamber 334. That is to say, in some embodiments, the housing 330 can be in first or initial state in which the initial portion or volume of bodily fluid can flow from the inlet 331 and into the sequestration chamber 334.

[1101] As described above, the housing 330 and/or the control device 300 can be in the initial state when the flow controller 342 and the actuator 350 are in a first state, position, configuration, etc. As such, the actuator 350 isolates, separates, segregates, sequesters and/or otherwise prevents direct fluid communication between the fluid flow paths 333 and 354B. In addition, the inlet 331 is exposed to the negative pressure differential via the sequestration chamber 334. In other words, the negative pressure within or produced by the fluid collection device can result in a negative pressure (or negative pressure differential) within at least a portion of the sequestration chamber 334 that is operable in drawing an initial flow of bodily fluid from the inlet 331 into the sequestration chamber 334 when the housing 330 and/or control device 300 is in the first or initial state. As described in detail above, in some instances, it may be desirable to modulate and/or control a magnitude of the negative pressure differential by any suitable means such as those described herein.

[1102] The initial portion and/or amount of bodily fluid can be any suitable volume of bodily fluid, as described in detail above with reference to the control devices 100 and/or 200. For example, in some instances, the initial volume can be associated with and/or at least partially based on an amount or volume of bodily fluid that is sufficient to fully wet or saturate the flow controller 342. In other words, in some embodiments, the initial volume of bodily

fluid can be a volume sufficient to transition the flow controller 342 to a second state (e.g., a saturated or fully wetted state). As described above with reference to the flow controller 242, the flow controller 342 is placed in a sealed configuration when transitioned to the second state. Thus, transitioning the flow controller 342 to the second state sequesters, blocks, isolates, separates, segregates, and/or otherwise prevents flow through the flow controller 342.

[1103] After the initial volume of bodily fluid is transferred and/or diverted into the sequestration chamber 334, the control device 300 and/or the housing 330 can be transitioned to its second state or operating mode to sequester, segregate, retain, contain, isolate, etc. the initial volume in the sequestration chamber 334. As described above, the flow controller 342 is placed in the sealed configuration and thus, substantially prevents a flow of fluid therethrough. In this embodiment, the arrangement of the actuator 350 is such that when the flow controller 342 is placed in the sealed configuration, at least a portion of the negative pressure otherwise being exerted through the flow controller 342 is instead exerted on the actuator 350, which in turn, is sufficient to transition the actuator 350 from its first state to its second state. For example, in some embodiments, the negative pressure is operable to move the actuator 350 from a first position (e.g., the first state) to a second position (e.g., the second state), thereby establishing fluid communication between the fluid flow paths 333 and 354B.

[1104] More particularly, moving the actuator 350 to its second position (or otherwise transitioning the actuator 350 to its second state), moves and/or transitions the seals 365 relative to the fluid flow paths 333 and 354B such that fluid communication is established therebetween. As such, the negative pressure otherwise exerted on or through the sequestration chamber 334 is now exerted on or through the fluid flow paths 333 and 354B. In response, bodily fluid can flow from the inlet 331, through the fluid flow paths 333 and 354B, through the outlet 336, and into the fluid collection device. In some embodiments, the transitioning of the flow controller 342 and the actuator 350 from their respective first states to their respective second states is operable to sequester and/or retain the initial portion of the bodily fluid in the sequestration chamber 334. As described in further detail herein, in some instances, contaminants such as, for example, dermally residing microbes or the like dislodged during the venipuncture event, can be entrained and/or included in the initial volume of the bodily fluid and thus, are sequestered in the sequestration chamber 334 when the initial volume is sequestered therein.

[1105] With the fluid collection device fluidically coupled to the outlet 336 and with the control device 300 and/or the housing 330 being in the second state (e.g., the initial volume of bodily fluid is sequestered in or by the sequestration chamber 334), any subsequent volume(s)

of the bodily fluid can flow from the inlet 331, through the fluid flow paths 333 and 354B, through the outlet 336, and into the fluid collection device. Thus, as described above, sequestering the initial volume of bodily fluid in the sequestration chamber 334 prior to collecting or procuring one or more sample volumes of bodily fluid reduces and/or substantially eliminates an amount of contaminants in the one or more sample volumes. Moreover, in some embodiments, the arrangement of the housing 330 can be such that housing 330 cannot transition to the second state prior to collecting and sequestering the initial volume in the sequestration chamber 334.

[1106] FIGS. 9 and 10 illustrate a fluid control device 400 according to an embodiment. The fluid control device 400 can be similar in at least form and/or function to the fluid control device 100 described above with reference to FIG. 1, the fluid control device 200 described above with reference to FIGS. 2-5, and/or the fluid control device 300 described above with reference to FIGS. 6-8. Accordingly, portions of the fluid control device 400 that can be similar to portions of the fluid control devices 100, 200, and/or 300 are not described in further detail herein.

[1107] As shown in FIGS. 9 and 10, the fluid control device 400 (also referred to herein as "control device" or "device") includes a housing 430 having an inlet 431 and an outlet 436, and having and/or being coupled to an actuator 450. As described above with reference to the control devices 100, 200, and/or 300, the inlet 431 is configured to be placed in fluid communication with a bodily fluid source to receive a flow of bodily fluid therefrom (e.g., via a lumen-containing device such as a needle or the like). The outlet 436 is configured to be fluidically coupled to a fluid collection device (not shown in FIGS. 9 and 10).

[1108] As described above, the housing 430 of the control device 400 is configured to (1) receive a flow and/or volume of bodily fluid via the inlet 431 and (2) sequester (e.g., separate, segregate, contain, retain, isolate, etc.) the flow and/or volume of bodily fluid within the sequestration chamber 434. The housing 430 can be any suitable shape, size, and/or configuration. In some embodiments, the housing 430 can have a size that is at least partially based on a volume of bodily fluid at least temporarily stored, for example, in the sequestration chamber 434. For example, in the embodiment shown in FIGS. 9 and 10, the housing 430 is arranged (at least in part) as a syringe-like device or the like, as described in further detail herein.

[1109] The housing 430 defines fluid flow paths 433 and 454 that are selectively in fluid communication with the outlet 436 and that selectively receive a flow of fluid therethrough (e.g., a liquid and/or a gas). The outlet 436 of the housing 430 is in fluid communication with

and/or is configured to be placed in fluid communication with the fluid flow paths 433 and/or 454. In addition, the outlet 436 is configured to be fluidically coupled to a fluid collection device (not shown in FIGS. 9 and 10). The outlet 436 and the fluid collection device can each be substantially similar to the outlet 236 and fluid collection device, respectively, described above with reference to the control device 200. Thus, the outlet 436 and fluid collection device are not described in further detail herein.

[1110] The housing 430 includes and/or is coupled to the actuator 450 configured to selectively control a flow of bodily fluid through the housing 430. In this embodiment, the actuator 450 includes a first plunger 460 and a second plunger 461 movably disposed within the housing 430 and configured to at least partially define the sequestration chamber 434. More specifically, the actuator 450 is configured to move between a first state in which the inlet 431 is placed in fluid communication with the sequestration chamber 434 (FIG. 9) and a second state in which the inlet 431 is placed in fluid communication with the outlet 436 via the fluid flow path 454 (FIG. 10). In this embodiment, when the actuator 450 and/or housing 430 is in the first state, the inlet 431 is in fluid communication with a portion of the housing 430 defined between the first plunger 460 and the second plunger 461.

[1111] When in the first state, the first plunger 460 is disposed in a position such that a dampening chamber 437 is defined by the housing 430 on a side of the first plunger 460 opposite the sequestration chamber 434. As shown, the dampening chamber 437 is configured to be placed in fluid communication with the fluid flow path 433 via a port 435. The port 435 can be an opening, a valve, a membrane, a diaphragm, and/or any other suitable flow controller or the like configured to at least selectively establish fluid communication between the fluid flow path 433 and the dampening chamber 437. Furthermore, when the actuator 450 and/or the housing 430 is in the first state, the dampening chamber 437 includes and/or contains a dampening fluid 456 such as a gas (compressed or uncompressed) and/or a liquid (e.g., water, oil, dampening fluid, and/or any other suitable liquid).

[1112] When the actuator 450 and/or housing 430 are in the first state, the second plunger 461 is disposed in a position within the housing 430 such that one or more seals 465 formed by or coupled to the second plunger 461 fluidically isolate, separate, and/or sequester the inlet 431 from the fluid flow path 454. In addition, the second plunger 461 and/or the seals 465 formed by or coupled thereto fluidically isolate the fluid flow path 454 from the sequestration chamber 434. Thus, when the actuator 450 and/or control device 400 are in the first state, the inlet 431 is in fluid communication with the sequestration chamber 434 and is fluidically isolated from the fluid flow paths 433 and 454 as well as the outlet 436 (see FIG. 9). As

described in further detail herein, the actuator 450 and/or the control device 400 can be configured to transition to the second state in which the sequestration chamber 434 is sequestered within the housing 430 and the inlet 431 is placed in fluid communication with the fluid flow path 454 (see FIG. 10).

[1113] As described above, the device 400 can be used to procure a bodily fluid sample having reduced contamination from microbes such as, for example, dermally residing microbes, and/or the like. For example, in some instances, a user such as a doctor, physician, nurse, phlebotomist, technician, etc. can manipulate the device 400 to establish fluid communication between the inlet 431 and the bodily fluid source (e.g., a vein of a patient). Once the inlet 431 is placed in fluid communication with the bodily fluid source (e.g., the portion of the patient), the outlet 436 can be fluidically coupled to the fluid collection device. As described above, in the embodiment shown in FIGS. 9 and 10 the fluid collection device can be, for example, an evacuated reservoir or container that defines a negative pressure.

[1114] As shown in FIG. 9, the actuator 450 and/or the control device 400 can be in a first or initial state prior to coupling the outlet 436 to the fluid collection device. Thus, the fluid flow path 433 is in fluid communication with the dampening chamber 437 and the fluid flow path 454 is fluidically isolated from the inlet 431 and the sequestration chamber 434 (e.g., via the second plunger 461). As described above, coupling the outlet 436 to the fluid collection device exposes at least a portion of the fluid flow paths 433 and 454 to the negative pressure within the fluid collection device. When the actuator 450 and/or the control device 400 are in the first state, the second plunger 461 isolates the housing 430 and/or the sequestration chamber 434 from the negative pressure exerted via the fluid flow path 454. Conversely, the negative pressure exerted through the fluid flow path 433 can be operable in exerting at least a portion of the negative pressure on the dampening chamber 437 (e.g., via the port 435). In some embodiments, for example, the port 435 can be transitioned from a closed configuration to an open configuration in response to the negative pressure.

[1115] The negative pressure exerted through the fluid flow path 433 is operable in transitioning the actuator 450 from a first state to a second state. For example, in some embodiments, the negative pressure differential draws the dampening fluid 456 from the dampening chamber 437 and into the fluid flow path 433 or a secondary chamber or the like. Moreover, the negative pressure urges the first plunger 460 to transition and/or move relative to the housing 430 from a first configuration or position to a second configuration or position. In some embodiments, the transitioning and/or moving of the first plunger 460 can be such that a volume of the housing 430 defined between the first plunger 460 and the second plunger 461

is increased (i.e., a volume of the sequestration chamber 434 is increased). In some embodiments, the increase in the volume of the sequestration chamber 434 results in a negative pressure therein, which in turn, can be operable in drawing an initial volume of bodily fluid through the inlet 431 and into the sequestration chamber 434. In other words, the negative pressure of the fluid collection device indirectly results in a negative pressure differential between the inlet 431 and the sequestration chamber 434 that is operable in drawing the initial volume of bodily fluid into the sequestration chamber 434.

[1116] As shown in FIG. 10, movement of the first plunger 460 results in a similar movement of the second plunger 461. For example, in some embodiments, the arrangement of the actuator 450 is such that after the first plunger 460 has moved a predetermined amount (and/or after the volume of the sequestration chamber 434 has been increased a predetermined amount) and an initial volume of bodily fluid has been drawn into the sequestration chamber 434, the second plunger 461 is moved or transitioned from a first position and/or configuration to a second position and/or configuration. As such, the actuator 450 is placed in its second state in which the sequestration chamber 434 is sequestered from the inlet 431. In addition, the second plunger 461 and/or the seals 465 coupled thereto place the inlet 431 in fluid communication with the fluid flow path 454. Thus, the negative pressure otherwise exerted on or through the fluid flow path 433 is now exerted on or through the fluid flow path 454. In response, bodily fluid can flow from the inlet 431, through the fluid flow path 454, through the outlet 436, and into the fluid collection device.

[1117] In some embodiments, the transitioning of the actuator 450 from the first state to the second state is operable to sequester and/or retain the initial portion of the bodily fluid in the sequestration chamber 434. As described in further detail herein, in some instances, contaminants such as, for example, dermally residing microbes or the like dislodged during the venipuncture event, can be entrained and/or included in the initial volume of the bodily fluid and thus, are sequestered in the sequestration chamber 434 when the initial volume is sequestered therein. Thus, as described above, sequestering the initial volume of bodily fluid in the sequestration chamber 434 prior to collecting or procuring one or more sample volumes of bodily fluid reduces and/or substantially eliminates an amount of contaminants in the one or more sample volumes. Moreover, in some embodiments, the arrangement of the housing 430 can be such that housing 430 cannot transition to the second state prior to collecting and sequestering the initial volume in the sequestration chamber 434.

[1118] As described above with reference to the control devices 100, 200, and/or 300, the control device 400 is configured to modulate an amount of negative pressure exerted on the

first plunger 460 when the actuator 450 is in the first state. Specifically, in this embodiment, the dampening fluid 456 disposed in the dampening chamber 437 reduces a magnitude of the negative pressure exerted on the first plunger 460. As such, the rate at which the actuator 450 and/or control device 400 is transitioned from the first state to the second state can be controlled. Moreover, in some instances, exposing the housing 430 to the full magnitude of the negative pressure may result transitioning the actuator 450 and/or the control device 400 from the first state to the second state prior to receiving the initial volume of bodily fluid in the sequestration chamber 434. Thus, modulating the magnitude of the pressure can ensure a desired volume of bodily fluid is transferred into the sequestration chamber 434. Although shown in FIGS. 9 and 10 as modulating the negative pressure via the dampening fluid 456, it should be understood that this is presented by way of example only and not limitation. Any other suitable means of dampening and/or modulating a magnitude of the negative pressure can be used to control the transitioning of the actuator 450 and/or housing 430.

[1119] Although the housing 430 is shown in FIGS. 9 and 10 and described above as including the plungers 460 and 461 and being in a syringe-like configuration, in other embodiments, a housing can include any other suitable means for controlling fluid flow therethrough. For example, FIG. 11 and 12 illustrate a fluid control device 500 according to an embodiment. The fluid control device 500 can be similar in at least form and/or function to any of the fluid control devices 100, 200, 300, and/or 400. Accordingly, portions of the fluid control device 500 that can be similar to portions of the fluid control devices 100, 200, 300, and/or 400 are not described in further detail herein. As shown in FIGS. 11 and 12, the fluid control device 500 (also referred to herein as "control device" or "device") includes a housing 530 having an inlet 531 and an outlet 536, and having and/or being coupled to an actuator 550. As described above with reference to the control devices 100, 200, 300, and/or 400, the inlet 531 is configured to be placed in fluid communication with a bodily fluid source to receive a fluid of bodily fluid therefrom (e.g., via a lumen-containing device such as a needle or the like). The outlet 536 is configured to be fluidically coupled to a fluid collection device (not shown in FIGS. 11 and 12). The inlet 531, the outlet 536, and the fluid collection device can be substantially similar to those described above and thus, are not described in further detail herein.

[1120] As described above, the housing 530 of the control device 500 is configured to (1) receive a flow and/or volume of bodily fluid via the inlet 531 and (2) sequester (e.g., separate, segregate, contain, retain, isolate, etc.) the flow and/or volume of bodily fluid within the sequestration chamber 534. The housing 530 can be any suitable shape, size, and/or

configuration. In some embodiments, the housing 530 can have a size that is at least partially based on a volume of bodily fluid at least temporarily stored, for example, in the sequestration chamber 534. For example, in the embodiment shown in FIGS. 11 and 12, the housing 530 can be arranged in a substantially similar manner as the housing 430 described above with reference to FIGS. 9 and 10. As described in further detail herein, the housing 530 can differ from the housing 430, by arranging the actuator 550 as, for example, a diaphragm rather than one or more plungers.

[1121] The housing 530 defines a set of fluid flow paths 533 and 554 in fluid communication with the outlet 536 and configured to selectively receive a flow of fluid therethrough (e.g., a liquid and/or a gas). The housing 530 includes and/or is coupled to the actuator 550 configured to selectively control a flow of bodily fluid through the housing 530. In this embodiment, the actuator 550 includes a diaphragm 576 movably disposed within the housing 530 and configured to at least partially define the sequestration chamber 534. More specifically, the actuator 550 is configured to move between a first state in which the inlet 531 is placed in fluid communication with the sequestration chamber 534 (FIG. 11) and a second state in which the inlet 531 is placed in fluid communication with the outlet 536 via the fluid flow path 554 (FIG. 12).

[1122] As shown in FIG. 11, when the actuator 550 and/or control device 500 is in the first state, the inlet 531 is in fluid communication with a portion of the housing 530 defined between the diaphragm 576 and one or more seals 565. Moreover, the diaphragm 576 is disposed in a first state such that a dampening chamber 537 is defined by the housing 530 on a side of the diaphragm 576 opposite the sequestration chamber 534, as described above with reference to the housing 430. As shown, the dampening chamber 537 is configured to be placed in fluid communication with the fluid flow path 533 via a port 535. The port 535 can be an opening, a valve, a membrane, a diaphragm, and/or any other suitable flow controller or the like configured to at least selectively establish fluid communication between the fluid flow path 533 and the dampening chamber 537. Furthermore, when the actuator 550 and/or the control device 500 is in the first state, the dampening chamber 537 includes and/or contains a dampening fluid such as a gas (compressed or uncompressed) and/or a liquid (e.g., water, oil, dampening fluid, and/or any other suitable liquid). As described above with reference to the control devices 400, the arrangement of the dampening chamber 537, the dampening fluid, and the port 535 can be configured to modulate an amount of negative pressure exerted on the diaphragm 576 when the actuator 550 is in the first state. Although shown in FIGS. 11 and 12 as modulating the negative pressure via the dampening fluid, it should be understood that this

is presented by way of example only and not limitation. Any other suitable means of dampening and/or modulating a magnitude of the negative pressure can be used to control the transitioning of the actuator 550 and/or the control device 500.

[1123] As described above with reference to the actuator 450, when the actuator 550 and/or the control device 500 are in the first state, the one or more seals 565 are disposed in a position within the housing 530 such that the one or more seals 565 fluidically isolate, separate, and/or sequester the inlet 531 from the fluid flow path 554. In addition, the one or more seals 565 fluidically isolate the fluid flow path 554 from the sequestration chamber 534. Thus, when the actuator 550 and/or the control device 500 are in the first state, the inlet 531 is in fluid communication with the sequestration chamber 534 and fluidically isolated from the fluid flow paths 533 and 554 as well as the outlet 536 (see FIG. 11). As described in further detail herein, the actuator 550 and/or the control device 500 housing 530 can be configured to transition to the second state in which the sequestration chamber 534 is sequestered within the housing 530 and the inlet 531 is placed in fluid communication with the fluid flow path 554 (see FIG. 12).

[1124] As described in detail above, the device 500 can be used to procure a bodily fluid sample having reduced contamination from microbes such as, for example, dermally residing microbes, and/or the like. For example, in some instances, a user can place the inlet 531 in fluid communication with the bodily fluid source (e.g., the portion of the patient) and can fluidically couple the outlet 536 to the fluid collection device. As shown in FIG. 11, the actuator 550 and/or the device 500 can be in a first or initial state prior to coupling the outlet 536 to the fluid collection device. Thus, the fluid flow path 533 is in fluid communication with the dampening chamber 537 and the fluid flow path 554 is fluidically isolated from the inlet 531 and the sequestration chamber 534 (e.g., via the one or more seals 565), as described in detail above with reference to the control device 400 of FIGS. 9 and 10.

[1125] Coupling the outlet 536 to the fluid collection device selectively exposes at least a portion of the fluid flow paths 533 and 554 to the negative pressure within and/or produced by the fluid collection device. When the actuator 550 and/or the device 500 are in the first state, the one or more seals 565 isolate the housing 530 and/or the sequestration chamber 534 from the negative pressure exerted via the fluid flow path 554. Conversely, the negative pressure exerted through the fluid flow path 533 can be operable in exerting at least a portion of the negative pressure on the dampening chamber 537 (e.g., via the port 535). In some embodiments, for example, the port 535 can be transitioned from a closed configuration to an open configuration in response to the negative pressure. The negative pressure exerted through the fluid flow path 533 is operable in transitioning the actuator 550 from a first state to a second

state. For example, in some embodiments, the negative pressure differential draws the dampening fluid from the dampening chamber 537 and into the fluid flow path 533. Moreover, the negative pressure urges the diaphragm 576 to transition, flip, move, switch, deform, etc., from a first configuration or state (FIG. 11) to a second configuration or state (FIG. 12). As described above with reference to the actuator 450, the transitioning of the diaphragm 576 from the first state to the second state can be such that a volume of the housing 530 defined between the diaphragm 576 and the one or more seals 565 is increased (i.e., a volume of the sequestration chamber 534 is increased), which in turn, results in a negative pressure therein that can be operable in drawing an initial volume of bodily fluid through the inlet 531 and into the sequestration chamber 534.

[1126] As shown in FIG. 12, movement of the diaphragm 576 results in a similar movement of the one or more seals 565 such that the one or more seals 565 are disposed on the same side of the inlet 531 as the diaphragm 576. Thus, the sequestration chamber 534 is sequestered within the housing 530. In addition, moving the one or more seals 565 is such that fluid communication is established between the inlet 531 and the fluid flow path 554. Thus, the negative pressure otherwise exerted on or through the fluid flow path 533 is now exerted on or through the fluid flow path 554. In response, bodily fluid can flow from the inlet 531, through the fluid flow path 554, through the outlet 536, and into the fluid collection device, as described in detail above. In some embodiments, the transitioning of the actuator 550 from the first state to the second state is operable to sequester and/or retain the initial portion of the bodily fluid in the sequestration chamber 534, which can include contaminants such as, for example, dermally residing microbes or the like dislodged during the venipuncture event. Thus, as described above, sequestering the initial volume of bodily fluid in the sequestration chamber 534 prior to collecting or procuring one or more sample volumes of bodily fluid reduces and/or substantially eliminates an amount of contaminants in the one or more sample volumes. Moreover, in some embodiments, the arrangement of the control device 500 and/or the housing 530 can be such that the control device 500 and/or the housing 530 cannot transition to the second state prior to collecting and sequestering the initial volume in the sequestration chamber 534.

[1127] FIGS. 13-15 illustrate a fluid control device 600 according to an embodiment. The fluid control device 600 can be similar in at least form and/or function to any of the fluid control devices 100, 200, 300, 400, and/or 500. Accordingly, portions of the fluid control device 600 that can be similar to portions of the fluid control devices 100, 200, 300, 400, and/or 500 are not described in further detail herein. As shown in FIGS. 13-15, the fluid control device 600

(also referred to herein as "control device" or "device") includes a housing 630 having an inlet 631 and an outlet 636, and having and/or being coupled to an actuator 650. As described above with reference to the control devices 100, 200, 300, 500, and/or 500, the inlet 631 is configured to be placed in fluid communication with a bodily fluid source to receive a fluid of bodily fluid therefrom (e.g., via a lumen-containing device such as a needle or the like). The outlet 636 is configured to be fluidically coupled to a fluid collection device (not shown in FIGS. 13-15). The inlet 631, the outlet 636, and the fluid collection device can be substantially similar to those described above and thus, are not described in further detail herein.

[1128] As described above, the housing 630 of the control device 600 is configured to (1) receive a flow and/or volume of bodily fluid via the inlet 631 and (2) sequester (e.g., separate, segregate, contain, retain, isolate, etc.) the flow and/or volume of bodily fluid within a sequestration chamber 634 included in and/or at least partially formed by the housing 630. The housing 630 can be any suitable shape, size, and/or configuration. In some embodiments, the housing 630 can have a size that is at least partially based on a volume of bodily fluid at least temporarily stored, for example, in the sequestration chamber 634. For example, in the embodiment shown in FIGS. 13-15, the housing 630 can be arranged in a substantially similar manner as the housing 530 described above with reference to FIGS. 11 and 12. That is to say, the housing 630 includes an actuator 650 that is arranged as a diaphragm.

[1129] The housing 630 defines a set of fluid flow paths 633 and 654 in fluid communication with the outlet 636 and configured to selectively receive a flow of fluid therethrough (e.g., a liquid and/or a gas). The housing 630 includes and/or is coupled to the actuator 650 configured to selectively control a flow of bodily fluid through the housing 630. In this embodiment, the actuator 650 includes a diaphragm 676 movably disposed within the housing 630 and configured to at least partially define the sequestration chamber 634. More specifically, the actuator 650 is configured to move between a first state in which the inlet 631 is placed in fluid communication with the sequestration chamber 634 and a second state in which the inlet 631 is placed in fluid communication with the outlet 636 via the fluid flow path 654, as described in detail above with reference to the control device 500.

[1130] As shown in FIGS. 14 and 15, when the actuator 650 and/or the device 600 is in the first state, the inlet 631 is in fluid communication with a portion of the housing 630 defined between the diaphragm 676 and one or more seals 665. Moreover, the diaphragm 676 is disposed in a first state such that a dampening chamber 637 is defined by the housing 630 on a side of the diaphragm 676 opposite the sequestration chamber 634, as described above with reference to the housing 530. As shown, the dampening chamber 637 is configured to be placed

in fluid communication with the fluid flow path 654 via a port 635 (such as those described above). Although not shown, when the actuator 650 and/or the device 600 is in the first state, the dampening chamber 637 includes and/or contains a dampening fluid such as a gas (compressed or uncompressed) and/or a liquid (e.g., water, oil, dampening fluid, and/or any other suitable liquid), that can be configured to modulate an amount of negative pressure exerted on the diaphragm, as described in detail above with reference to the control device 500. Although described as modulating the negative pressure via the dampening fluid, it should be understood that this is presented by way of example only and not limitation. Any other suitable means of dampening and/or modulating a magnitude of the negative pressure can be used to control the transitioning of the actuator 650 and/or device 600.

[1131] As described above with reference to the actuator 550, when the actuator 650 and/or the device 600 are in the first state, the seal 665 is disposed in a position within the housing 630 such that the seal 665 fluidically isolates, separates, and/or sequesters the inlet 631 from the fluid flow path 654. In addition, the seal 665 fluidically isolates the fluid flow path 654 from the sequestration chamber 634. Thus, when the actuator 650 and/or the device 600 are in the first state, the inlet 631 is in fluid communication with the sequestration chamber 634 and fluidically isolated from the fluid flow path 654 as well as the outlet 636. The actuator 650 and/or the device 600 can be configured to transition to the second state in which the sequestration chamber 634 is sequestered within the housing 630 and the inlet 631 is placed in fluid communication with the fluid flow path 654. Accordingly, the device 600 can be used to procure a bodily fluid sample having reduced contamination from microbes (e.g., dermally residing microbes and/or the like), in a substantially similar manner as the device 500 described above with reference to FIGS. 11 and 12. Thus, the functioning of the device 600 is not described in further detail herein.

[1132] FIGS. 16-18 illustrate a fluid control device 700 according to an embodiment. The fluid control device 700 can be similar in at least form and/or function to any of the fluid control devices 100, 200, 300, 400, 500, and/or 600. Accordingly, portions of the fluid control device 700 that can be similar to portions of the fluid control devices 100, 200, 300, 400, 500, and/or 600 are not described in further detail herein. As shown in FIGS. 16-18, the fluid control device 700 (also referred to herein as "control device" or "device") includes a housing 730 having an inlet 731 and an outlet 736, and having or being coupled to an actuator 750. As described above with reference to the control devices 100, 200, 300, 400, 500, and/or 600, the inlet 731 is configured to be placed in fluid communication with a bodily fluid source to receive a fluid of bodily fluid therefrom (e.g., via a lumen-containing device such as a needle or the

like). The outlet 736 is configured to be fluidically coupled to a fluid collection device (not shown in FIGS. 16-18). The inlet 731, the outlet 736, and the fluid collection device can be substantially similar to those described above and thus, are not described in further detail herein.

[1133] As described above, the housing 730 of the control device 700 is configured to (1) receive a flow and/or volume of bodily fluid via the inlet 731 and (2) sequester (e.g., separate, segregate, contain, retain, isolate, etc.) the flow and/or volume of bodily fluid within the sequestration chamber 734. The housing 730 can be any suitable shape, size, and/or configuration. In some embodiments, the housing 730 can have a size that is at least partially based on a volume of bodily fluid at least temporarily stored, for example, in the sequestration chamber 734. For example, in the embodiment shown in FIGS. 16-18, the housing 730 can be arranged in a substantially similar manner as the housings 530 and/or 630. That is to say, the housing 530 includes and/or is coupled to the actuator 750 that is arranged as a diaphragm.

[1134] The housing 730 defines a set of fluid flow paths 733 and 754 in fluid communication with the outlet 736 (see e.g., FIGS. 17A and 17B) and configured to selectively receive a flow of fluid therethrough (e.g., a liquid and/or a gas). The housing 730 includes and/or is coupled to the actuator 750 configured to selectively control a flow of bodily fluid through the housing 730. In this embodiment, the actuator 750 includes a diaphragm 776 movably disposed within the housing 730 and configured to at least partially define the sequestration chamber 734. More specifically, the actuator 750 is configured to move between a first state in which the inlet 731 is placed in fluid communication with the sequestration chamber 734 and a second state in which the inlet 731 is placed in fluid communication with the outlet 736 via the fluid flow path 754, as described in detail above with reference to the control device 500.

[1135] In the embodiment shown in FIGS. 16-18, when the actuator 750 and/or the device 700 are in the first state, the inlet 731 is in fluid communication with the sequestration chamber 734 formed by a portion of the housing 730 defined between the diaphragm 776 and a flow controller 742 (e.g., a selectively permeable fluid barrier or seal, and/or any other flow controller such as any of those described above). Moreover, the diaphragm 776 is disposed in a first state such that the fluid flow path 733 is in fluid communication with the sequestration chamber 734. As described above with reference to the actuator 550, when in the actuator 750 and/or device 700 are in the first state, the diaphragm 776 and/or the seal 765 are disposed in a position within the housing 730 such that the diaphragm 776 and/or the seal 765 fluidically isolate, separate, and/or sequester the inlet 731 from the fluid flow path 754. In addition, the

diaphragm 776 and/or the seal 765 fluidically isolate the fluid flow path 754 from the sequestration chamber 734. Thus, when the actuator 750 and/or the device 700 are in the first state, the inlet 731 is in fluid communication with the sequestration chamber 734 and fluidically isolated from the fluid flow path 754.

[1136] As described above with reference to, for example, the control device 200, when the actuator 750 and/or the device 700 are in the first state, a negative pressure differential within the sequestration chamber 734 can result from the coupling of the fluid collection device to the outlet 736. More specifically, the fluid flow path 733 can be in fluid communication with the outlet 736 and the flow controller 742. When the flow controller 742 is in a first state, the flow controller 742 can allow a gas or air to pass therethrough. Thus, the negative pressure differential within the sequestration chamber 734 can result from the coupling of the fluid collection device to the outlet 736.

[1137] As shown in FIG. 18, the actuator 750 and/or the device 700 can be configured to transition to the second state in which the sequestration chamber 734 is sequestered within the housing 730 and the inlet 731 is placed in fluid communication with the fluid flow path 754, as described in detail above with reference to the control device 600. More particularly, an initial volume of bodily fluid can be transferred into the sequestration chamber 734, which in turn, can saturate, can wet, and/or otherwise can transition the flow controller 742 from the first or open state to a second or closed state. In some embodiments, the transitioning of the flow controller 742 from the first state to the second state is operable in isolating the fluid flow path 733 from the outlet 736. As such, a negative pressure exerted through the fluid flow path 754 can be operable in transitioning, switching, flipping, moving, deforming, and/or otherwise reconfiguring the diaphragm 776 such that the actuator 750 is placed in its second state. As such, the negative pressure of the fluid collection device can draw bodily fluid from the inlet 731, through the housing 730 (bypassing the sequestration chamber 734), through the fluid flow path 754 and the outlet 736, and into the fluid collection device, as described in detail above. Accordingly, the device 700 can be used to procure a bodily fluid sample having reduced contamination from microbes (e.g., dermally residing microbes and/or the like), in a manner substantially similar to one or more of the control devices 100, 200, 300, 400, 500, and/or 600 described in detail above. Thus, the functioning of the device 700 is not described in further detail herein.

[1138] In some embodiments, any of the control devices 100, 200, 300, 400, 500, 600, and/or 700 can be formed from any suitable components that can be manufactured, assembled, sterilized, and packaged as an assembly or integrated device. In such embodiments, a user can,

for example, open a packaging containing such an assembly or integrated device and can use the device as described above with reference to the control devices 100, 200, 300, 400, 500, 600, and/or 700. In some embodiments, any of the control devices can be monolithically formed in whole or at least in part.

[1139] In some embodiments any of the control devices can be physically coupled, attached, formed, and/or otherwise mated to a fluid collection device (e.g., a sample reservoir, a syringe, a blood culture bottle, a collection vial, a fluid transfer container, and/or any other suitable reservoir, collection device, and/or transfer device) during a manufacturing process. This can be done prior to sterilization so the collection pathway(s) and connection interface(s) (e.g., where the control device couples to the fluid collection device) maintain a closed-system, mechanical diversion device within a sterile environment that is not subject to touch-point contamination from external sources. In this manner, in order for a user to transfer a sample volume to the fluid collection device, the user would be forced first to sequester, segregate, and/or isolate at least a portion of the initial bodily fluid volume or flow. In some embodiments, the coupling, mating, and/or attachment of the fluid control device to the fluid collection device can be executed such that the control device can be removed (physically decoupled, removed with a specific "key," and/or any other approach used to separate the control device from the fluid collection device) after use to allow access to the fluid collection device, which can then be placed in an incubator and/or any other type of analytical machine, and accessed for analysis and/or otherwise further processed. In some embodiments, such decoupling may be blocked, limited, and/or substantially prevented prior to use and unblocked or allowed after use. In other embodiments, the fluid control device and the fluid collection device can be permanently coupled and/or monolithically formed (at least in part) to prevent such decoupling.

[1140] While described above as being coupled and/or assembled, for example, during manufacturing, in other embodiments, however, a control device can include one or more modular components that can be selected by a user based on a desired use, preference, patient, etc. In such embodiments, the user can couple one or more modular components (packaged together or packaged separately) to form the desired fluid control device. For example, FIGS. 19-25 illustrate a modular fluid control device 800 according to an embodiment. The fluid control device 800 can be similar in at least form and/or function to the fluid control devices described herein. More specifically, portions of the fluid control device 800 can be similar to and/or substantially the same as corresponding portions of the fluid control device 200 described above with reference to FIGS. 2-5. Accordingly, such portions of the fluid control device 800 are not described in further detail herein.

[1141] The fluid control device 800 (also referred to herein as "control device" or "device") includes a housing 830 and an actuator 850. As described above, the control device 800 can be at least partially monolithically formed or can be otherwise preassembled during manufacturing. In other embodiments, the control device 800 can be at least partially modular such that a user can physically and fluidically couple the housing 830 and the actuator 850 to form the control device 800. The housing 830 of the device 800 can be any suitable shape, size, and/or configuration. For example, in the embodiment shown in FIGS. 19-25, the housing 830 can be, for example, relatively thin and substantially rectangular. In some embodiments, portions of the housing 830 can be substantially similar in at least form and/or function to the housing 230 described above with reference to FIGS. 2-5. Thus, while such portions are identified, similar components, features, and/or functions are not described in further detail herein.

[1142] As shown in FIGS. 19 and 20, the housing 830 forms and/or defines a sequestration chamber 834 that is in selective fluid communication with a first port 845 and a second port 846. The first port 845 and the second port 846 are configured to be at least fluidically coupled to a portion of the actuator 850 to allow for selective fluid flow between the housing 830 and the actuator 850. As described in further detail herein, the sequestration chamber 834 is configured (1) to receive a selective flow and/or volume of bodily fluid from a portion of the actuator 850 via the first port 845, and (2) to sequester (e.g., separate, segregate, contain, retain, isolate, etc.) the flow and/or volume of bodily fluid (e.g., an initial or first flow and/or volume of bodily fluid or any portion thereof) within the sequestration chamber 834. The sequestration chamber 834 can have any suitable shape, size, and/or configuration. For example, in some embodiments, the sequestration chamber 834 can have any suitable size, volume, and/or fluid capacity such as, for example, those described above with reference to the sequestration chamber 134. In the embodiment shown in FIGS. 19-25, the sequestration chamber 834 can be, for example, a fluid flow path that extends through and/or that is defined by at least a portion of the housing 830. In some embodiments, the sequestration chamber 834 can be substantially similar in at least form and/or function to the sequestration chamber 234 described above with reference to FIGS. 2-5 and thus, is not described in further detail herein.

[1143] As shown in FIG. 20, the housing 830 includes and/or defines a flow controller 842 and a restricted flow path 832. The flow controller 842 can be, for example, a valve, membrane, diaphragm, restrictor, vent, a selectively permeable member, port, etc. configured to selectively control (at least in part) a flow of fluids into and/or out of the sequestration chamber 834 and/or any other suitable portion of the housing 830. For example, the flow controller 842 can be a

selectively permeable fluid barrier (e.g., a blood barrier) that includes and/or is formed of a porous material configured to selectively allow a flow of gas therethrough but to prevent a flow of a liquid therethrough. In some embodiments, the flow controller 842 can be substantially similar to the flow controller 242 described in detail above with reference to FIGS. 2-5 and thus, is not described in further detail herein.

[1144] As shown, the restricted flow path 832 defined by the housing 830 is in fluid communication with the second port 846 and is positioned between the second port 846 and the flow controller 842 (or a portion of the housing 830 receiving or housing the flow controller 842). As described above with reference to the restricted flow path 232 shown in FIGS. 2-5, the restricted flow path 832 is a fluid flow path having a smaller diameter than, for example, one or more other flow paths defined by the housing 830 and/or actuator 850. For example, in some embodiments, the restricted flow path 832 can have a diameter between about 0.0005" to about 0.5" and can have a length between about 0.01" and about 0.5", as described above with reference to the restricted flow path 232. As described above, the smaller diameter of the restricted flow path 832 results in a lower magnitude of negative pressure being applied through the sequestration chamber 834 than a magnitude of negative pressure when the restricted flow path 832 has a larger diameter. In other words, the restricted flow path 832 can be configured to modulate an amount of negative pressure to which the sequestration chamber 834 is exposed. In some instances, modulating the amount of negative pressure can control a rate at which bodily fluid is transferred into the sequestration chamber 834. Moreover, in this embodiment, the restricted flow path 832 is, for example, a gas flow path configured to receive a flow of gas or air but not a flow of a liquid (e.g., bodily fluid), which can allow for a negative pressure differential sufficient to successfully collect the initial volume of bodily fluid and/or sufficient to transition at least a portion of the control device 800 to a second state, while limiting and/or substantially preventing a portion of the initial or first volume of bodily fluid from being drawn through the sequestration chamber 834 and the second port 846.

[1145] As shown in FIGS. 19-24, the actuator 850 includes a body 851 and an actuator rod 862. The body 851 of the actuator 850 includes an inlet 852 and an outlet 853. The inlet 852 and the outlet 853 can be substantially similar in at least form and/or function to the inlet 231 and the outlet 236, respectively, described above with reference to FIGS. 2-5. Thus, the inlet 852 is configured to be placed in fluid communication with a bodily fluid source to receive a flow of bodily fluid therefrom (e.g., via a lumen-containing device such as a needle, IV catheter, PICC line, or the like). The outlet 853 is configured to be fluidically coupled to a fluid collection device 880 such as, for example, a sample reservoir, a syringe, and/or other

intermediary bodily fluid transfer device, adapter, or vessel (see e.g., FIG. 25) such as, for example, a transfer device similar to those described in the '510 publication.

[1146] As shown in FIG. 21, the body 851 of the actuator 850 includes and/or defines a first port 858 and a second port 859. The first port 858 is in fluid communication with the inlet 852 and the second port 859 is in fluid communication with the outlet 853. In addition, the first port 858 and the second port 859 are configured to be at least fluidically coupled to the first port 845 and the second port 846, respectively, of the housing 830. As described in further detail herein, the actuator 850 can be transitioned between a first operating mode or state and a second operating mode or state to selectively control fluid flow through the ports 858 and 859 of the actuator 850 and the ports 845 and 846 of the housing 830, which in turn, can selectively control a flow of bodily fluid into and/or out of the sequestration chamber 834 of the housing 830.

[1147] In some embodiments, the arrangement of the ports 858 and 859 of the actuator 850 and the ports 845 and 846 of the housing 830 can allow for and/or otherwise can provide a means of physically coupling the housing 830 to the actuator 850 as well as fluidically coupling the housing 830 to the actuator 850. For example, in some embodiments, the ports 858 and 859 of the actuator 850 and the ports 845 and 846 of the housing 830 can form a friction fit, a press fit, an interference fit, and/or the like. In other embodiments, the ports 858 and 859 of the actuator 850 can be coupled to the ports 845 and 846, respectively, of the housing 830 via an adhesive, a mechanical fastener, an elastomeric coupling, a gasket, an o-ring(s), and/or any other suitable coupling means. In still other embodiments, the ports 858 and 859 of the actuator 850 can be physically and fluidically coupled to the ports 845 and 846, respectively, of the housing 830 via an intervening structure such as, for example, one or more sterile, flexible tubing(s). As such, the device 800 can be and/or can have, for example, a modular configuration in which the housing 830 can be at least fluidically coupled to the actuator 850.

[1148] In some embodiments, such a modular arrangement can allow a user to select a housing (or actuator) with one or more desired characteristics based on, for example, the intended purpose and/or use of the assembled device. In other embodiments, the modular arrangement can allow and/or facilitate one or more components with desired characteristics to be coupled and/or assembled during manufacturing. For example, in some instances, it may be desirable to select a housing that includes and/or defines a sequestration chamber having a particular or desired volume. As a specific example, when the device is being used to procure bodily fluid from a pediatric patient and/or a very sick patient (for example), it may be desirable to select a housing that defines and/or includes a sequestration chamber with a smaller volume

than may otherwise be selected when the device is being used to procure bodily fluid from a seemingly healthy adult patient. Accordingly, such a modular arrangement can allow a user (e.g., a doctor, physician, nurse, technician, phlebotomist, etc.) to select a housing or an actuator having one or more desired characteristics based on, for example, the intended use of the device. In other instances, the modular arrangement can allow or facilitate assembly of a housing or an actuator having one or more desired characteristics during manufacturing without making significant changes to one or more manufacturing processes.

[1149] The actuator rod 862 of the actuator 850 is movably disposed within a portion of the body 851. The actuator rod 862 includes a first end portion 863 and a second end portion 864, at least one of which extends beyond the body 851 of the actuator 850 with the actuator rod 862 is disposed within the body 851 (see e.g., FIGS. 23 and 24). A portion of the actuator rod 862 includes and/or is coupled to a set of seals 865. The seals 865 can be, for example, o-rings, elastomeric over-molds, proud or raised dimensions or fittings, and/or the like. The arrangement of the actuator 862 and the body 851 of the actuator 850 can be such that an inner portion of the seals 865 forms a fluid tight seal with a surface of the actuator rod 862 and an outer portion of the seals 865 forms a fluid tight seal with an inner surface of the body 851. In other words, the seals 865 form one or more fluid tight seals between the actuator rod 862 and the inner surface of the body 851. As shown in FIGS. 23 and 24, the actuator rod 862 includes and/or is coupled to three seals 865 which form and/or define a first fluid flow path 833 within the body 851 of the actuator 850 and a second fluid flow path 854 within the body 851 of the actuator 850.

[1150] The actuator rod 862 is configured to be moved or transitioned relative to the body 851 between a first position or configuration and a second position or configuration. For example, in some instances, a force can be exerted on the first end portion 863 of the actuator rod 862 to place the actuator rod 862 in its first position and/or configuration, as shown in FIG. 23. The force exerted on the first end portion 863 of the actuator rod 862 can come from any suitable source. For example, a user can create the force with his or her hand or finger, a syringe, a positive or negative pressure source, and/or any other external energy source. When in the first position and/or configuration, the inlet 852 of the actuator 850 is in fluid communication with the first fluid flow path 833 and the outlet 853 of the actuator 850 is in fluid communication with the second fluid flow path 854. In some instances, a force can be exerted on the second end portion 864 of the actuator rod 862 to place the actuator rod 862 in its second position and/or configuration, as shown in FIG. 24. When in the second position and/or configuration, the inlet 852 and the outlet 853 of the actuator 850 are each in fluid

communication with the second fluid flow path 854 while the first fluid flow path is sequestered, isolated, and/or otherwise not in fluid communication with the inlet 852 and the outlet 853. Although not shown, the first port 858 of the actuator 850 is in fluid communication with the first fluid flow path 833 and the second port 859 of the actuator 850 is in fluid communication with the second fluid flow path 854. As such, moving and/or transitioning the actuator rod 862 (or the actuator 850 in general) between the first position and the second position can be operable in selectively controlling a flow of fluid (e.g., bodily fluid) between the inlet 852 of the actuator 850 and the housing 830, or between the inlet 852 of the actuator 850 and the outlet 853 of the actuator 850, as described in further detail herein.

[1151] As described above, the device 800 can be used to procure a bodily fluid sample having reduced contamination from microbes such as, for example, dermally residing microbes, microbes external to the bodily fluid source, and/or the like. For example, in some instances, a user such as a doctor, physician, nurse, phlebotomist, technician, etc. can manipulate the device 800 to establish fluid communication between the inlet 852 and the bodily fluid source (e.g., a vein of a patient). Once the inlet 852 is placed in fluid communication with the bodily fluid source (e.g., the portion of the patient), the outlet 853 can be fluidically coupled to the fluid collection device 880. In the embodiment shown in FIGS. 19-25, the fluid collection device 880 can be, for example, a syringe (as shown in FIG. 25), and/or any other suitable container or device configured to define or produce a negative pressure or energy source.

[1152] As described in detail above with reference to, for example, the device 200, coupling the outlet 853 to the fluid collection device 880 selectively exposes at least a portion of the control device 800 to a negative pressure within and/or produced by the fluid collection device 880. More specifically, in the embodiment shown in FIGS. 19-25, coupling the outlet 853 to the fluid collection device 880 exposes the outlet 853 of the actuator 850 and the second fluid flow path 854 to the negative pressure within and/or produced by the fluid collection device 880. In addition, the second port 859 of the actuator 850 is in fluid communication with the second fluid flow path 854 and the second port 846 of the housing 830. The second port 846 of the housing 830, in turn, is in selective fluid communication with the sequestration chamber 834 via the flow controller 842 and the restricted flow path 832. For example, the device 800 and/or the flow controller 842 can be in a first operating state or mode in which the flow controller 842 allows a flow of gas (e.g., air) through the flow controller 842 while limiting and/or preventing a flow of liquid (e.g., bodily fluid such as blood) through the flow controller 842. Thus, coupling the fluid collection device 880 to the outlet 853 results in a

negative pressure differential between the fluid collection device 880 (and/or any suitable negative pressure source) and the sequestration chamber 834.

[1153] As described above, the control device 800 can be in a first or initial state when the flow controller 842 and/or the actuator 850 are in a first state, position, configuration, etc. As such, the actuator rod 862 can be in its first position and/or configuration in which the first fluid flow path 833 is in fluid communication with the inlet 852. In addition, the first port 858 of the actuator 850 and the first port 845 of the housing 830 establish fluid communication between the sequestration chamber 834 and the first fluid flow path 833. Thus, the negative pressure within the fluid collection device 880 can result in a negative pressure (or negative pressure differential) within at least a portion of the sequestration chamber 834 that is operable in drawing an initial flow, portion, amount, or volume of bodily fluid from the inlet 852, through the first fluid flow path 833, and into the sequestration chamber 834 when the actuator 850 and/or control device 800 is in the first or initial state (e.g., when the actuator rod 862 is in its first state, position, and/or configuration). In some instances, the arrangement of the flow controller 842 and/or the restricted flow path 832 can be configured to restrict, limit, control, and/or otherwise modulate an amount or magnitude of negative pressure exerted on or through the sequestration chamber 834, as described in detail above with reference to the device 200.

[1154] The initial portion and/or amount of bodily fluid can be any suitable volume of bodily fluid, as described in detail above with reference to the control device 100. For example, in some instances, the initial volume can be associated with and/or at least partially based on an amount or volume of bodily fluid that is sufficient to fully wet or saturate the flow controller 842. In other words, in some embodiments, the initial volume of bodily fluid can be a volume sufficient to transition the flow controller 842 from a first state to a second state (e.g., a saturated or fully wetted state). In some embodiments, the flow controller 842 is placed in a sealed configuration when transitioned to the second state. That is to say, saturating and/or fully wetting the flow controller 842 (e.g., the semi-permeable material) places the flow controller 842 in a sealed configuration in which the flow controller 842 substantially prevents a flow of a liquid and a gas therethrough. Thus, transitioning the flow controller 842 to the second state sequesters, blocks, isolates, separates, segregates, and/or otherwise prevents flow through the flow controller 842 between the restricted flow path 832 and the sequestration chamber 834.

[1155] After the initial volume of bodily fluid is transferred and/or diverted into the sequestration chamber 834, the control device 800 and/or the actuator 850 can be transitioned to its second state or operating mode to sequester, segregate, retain, contain, isolate, etc. the

initial volume in the sequestration chamber 834. For example, the actuator 850 can be actuated to transition from its first state to its second state, for example, by exerting a force on the second end portion 864 of the actuator rod 862. As such, the actuator rod 862 is moved and/or transitioned to its second state, position, and/or configuration in which the first fluid flow path 833 is sequestered and/or isolated from the inlet 852. With the flow controller 842 in the sealed configuration in response to the initial volume of bodily fluid being disposed in the sequestration chamber 834 and with the initial fluid flow path 833 sequestered and/or isolated from the inlet 852, the initial volume of bodily fluid is sequestered in the sequestration chamber 834. As described in detail above, in some instances, contaminants such as, for example, dermally residing microbes or the like dislodged during the venipuncture event, can be entrained and/or included in the initial volume of the bodily fluid and thus, are sequestered in the sequestration chamber 834 when the initial volume is sequestered therein.

[1156] As shown in FIG. 24, moving and/or transitioning the control device 800 and/or the actuator 850 to its second state or configuration establishes fluid communication between the inlet 852 and the outlet 853 via the second fluid flow path 854. As such, the negative pressure otherwise exerted on or through the sequestration chamber 834 is now exerted on or through the fluid flow path 854. In response, bodily fluid can flow from the inlet 852, through the fluid flow path 854, through the outlet 853, and into the fluid collection device 880. Thus, as described above, sequestering the initial volume of bodily fluid in the sequestration chamber 834 prior to collecting or procuring one or more sample volumes of bodily fluid reduces and/or substantially eliminates an amount of contaminants in the one or more sample volumes. Moreover, in some embodiments, the arrangement of the control device 800 can be such that the control device 800 cannot transition to the second state prior to collecting and sequestering the initial volume in the sequestration chamber 834, thereby reducing the likelihood of contaminants being transferred to the fluid collection device 880.

[1157] In some instances, it may be desirable to isolate the negative pressure source (e.g., the fluid collection device 880 from the inlet 853 such as, for example, if it is desirable to collect multiple samples of bodily fluid using multiple fluid collection device 880 (e.g., syringes). For example, in some instances, after filling the fluid collection device 880 the user can engage the actuator 850 and exert a force on the first end portion 863 of the actuator rod 862 to move and/or transition the actuator rod 862 from its second position and/or configuration toward its first position and/or configuration. As such, the second fluid flow path 854 no longer places the inlet 852 in fluid communication with the outlet 853. Moreover, the flow controller 842 can remain in the sealed state or configuration (e.g., fully saturated, wetted, and/or

otherwise preventing flow therethrough) such that the outlet 853 is substantially sequestered or isolated from the rest of the control device 800. In some instances, the user can then remove the filled fluid collection device 880 (e.g., syringe) and can couple a new fluid collection device 880 (e.g., syringe) to the outlet 853. With the new fluid collection device 880 coupled to the outlet 853, the user can, for example, exert a force on the second end portion 864 of the actuator rod 862 to move and/or transition the actuator rod 862 back to its second position, state, and/or configuration, as described above.

[1158] While the fluid collection device 880 coupled to the device 800 is shown in FIG. 25 as being a syringe, in other embodiments, a control device can be physically and/or fluidically coupled to any suitable collection device. For example, FIG. 26 illustrates a fluid control device 900. As described above with reference to the control device 800, the fluid control device 900 includes a housing 930 and an actuator 950, which can be arranged, for example, in a modular configuration or the like. The actuator 950 includes an inlet 952 configured to be placed in fluid communication with a bodily fluid source and an outlet 953 configured to be coupled to a fluid collection device 980. In the embodiment shown in FIG. 26, the fluid collection device 980 is a transfer adapter configured to be coupled to one or more reservoirs such as, for example, an evacuated container, a sample bottle, a culture bottle, etc. In such embodiments, the reservoir can be sealed prior to being coupled to the transfer adapter (i.e., the fluid collection device 980) and once coupled the seal can be punctured, displaced, deformed, and/or otherwise unsealed to expose the outlet 953 to the negative pressure within the reservoir. Thus, the fluid control device 900 can function in a substantially similar manner to the control device 800 described above with reference to FIGS. 19-25.

[1159] While the fluid control device 800 is shown as including the actuator rod 862 that includes the first end portion 863 and the second portion 864 on which a force can be exerted to transition the device 800 between its first and second configurations, states, and/or positions, in other embodiments, a control device can include an actuator having any suitable configuration. For example, the fluid control device 900 includes an actuator rod 962 having only a single end portion that extends beyond the body 951 of the actuator 950, as shown in FIG. 26. In such embodiments, the device 900 can be used to fill a fluid collection device such as, for example, a sample reservoir, container, bottle, etc. and if it is desirable for more than one sample to be collected, the user can, for example, decouple the inlet 952 from a lumen-containing device and/or any suitable device otherwise placing the inlet 952 in fluid communication with the bodily fluid source. Once decoupled, the user can couple the inlet of a new control device 900 to the lumen-containing device and/or the like and can collect one or

more additional samples in a manner similar to that described above with reference to the control device 800.

[1160] As described above, some fluid control device described herein can be and/or can have a modular configuration in which one or more components can be coupled to collectively form a fluid control device having a desired set of characteristics or the like. For example, the fluid control device 800 shown in FIGS. 19-25 includes the housing 830 and the actuator 850 in one modular arrangement. It should be understood, however, that a control device can have any suitable modular arrangement. For example, FIG. 27 illustrates a modular fluid control device 1000 according to an embodiment. The fluid control device (also referred to herein as "device") includes a housing 1030 forming and/or defining a sequestration chamber 1034, and an actuator 1050 forming and/or having an inlet 1052 and an outlet 1053. The device 1000 can be substantially similar to the control device 800 described in detail above but can be arranged such that housing 1030 is disposed in different position and/or orientation relative to the actuator 1050. In some embodiments, varying the arrangement may, for example, enhance usability, visibility, and/or the like and/or may otherwise allow for a more compact design.

[1161] As another example, FIG. 28 illustrates a modular fluid control device 1100 according to an embodiment. The fluid control device (also referred to herein as "device") includes a housing 1130 forming and/or defining a sequestration chamber 1134, and an actuator 1150 forming and/or having an inlet 1152 and an outlet 1153. The device 1100 can be substantially similar to the control device 800 described in detail above but can be arranged such that housing 1130 is disposed in different position and/or orientation relative to the actuator 1150. Moreover, as shown in FIG. 28, the actuator 1150 can be arranged such that the inlet 1152 and the outlet 1153 are disposed in substantially perpendicular positions relative to one another. As described above, in some embodiments, varying the arrangement may, for example, enhance usability, visibility, and/or the like and/or may otherwise allow for a more compact design. While examples of modular fluid control devices are shown herein, it should be understood that such embodiments are presented by way of example and not limitation. Thus, while specific arrangements and/or orientations may be described herein, the devices and/or concepts described herein are not intended to be limited to those shown herein.

[1162] While the housings 230, 330, 830, 930, 1030, and 1130 have been shown and described herein as including and/or defining a sequestration chamber that is arranged in a serpentine-like configuration, in other embodiments, a housing and/or any other suitable portion of a control device can include and/or can define a sequestration chamber having any suitable configuration. For example, FIGS. 29-34 illustrate a fluid control device 1200

according to an embodiment. The fluid control device 1200 can be similar in at least form and/or function to the fluid control devices described herein. More specifically, portions of the fluid control device 1200 can be similar to and/or substantially the same as corresponding portions of the fluid control devices 200, 300, 800, 900, 1000, and/or 1100 described above. Accordingly, such portions of the fluid control device 1200 are not described in further detail herein.

[1163] The fluid control device 1200 (also referred to herein as "control device" or "device") includes a housing 1230 and an actuator 1250. As described above with reference to the control device 800, the control device 1200 can be arranged in a modular configuration such that the housing 1230 and the actuator 1250 can be physically and fluidically coupled to form the control device 1200. In other embodiments, the control device 1200 need not be modular. That is to say, in some embodiments, the control device 1200 can be assembled during manufacturing and delivered to a supplier and/or end user as an assembled device. In other embodiments, the control device can be monolithically formed and/or coupled to a fluid collection device in any suitable manner, as described in detail above.

[1164] The housing 1230 of the control device 1200 can be any suitable shape, size, and/or configuration. For example, in some embodiments, the housing 1230 can be substantially similar in at least form and/or function to the housing 830 described in detail above. Accordingly, such similar portions of the housing 1230 are identified below but may not be described in further detail herein.

[1165] As shown in FIGS. 29-31, the housing 1230 forms and/or defines a sequestration chamber 1234 that is in selective fluid communication with a first port 1245 and a second port 1246. The second port 1246 is configured to receive, include, and/or define a flow controller 1242 (see e.g., FIG. 30) and a restricted flow path 1232 (see e.g., FIG. 31). Although shown as including the restricted flow path 1232, in other embodiments, a housing need not include or receive a restricted flow path (e.g., when excessive negative pressure being applied to the sequestration chamber 1234 is unlikely or otherwise not intended such as when a fluid collection device is a syringe or the like). The first port 1245 and the second port 1246 are configured to be at least fluidically coupled to a portion of the actuator 1250 to allow for selective fluid flow between the housing 1230 and the actuator 1250. As described in further detail herein, the sequestration chamber 1234 is configured (1) to receive a selective flow and/or volume of bodily fluid from a portion of the actuator 1250 via the first port 1245, and (2) to sequester (e.g., separate, segregate, contain, retain, isolate, etc.) the flow and/or volume

of bodily fluid (e.g., an initial or first flow and/or volume of bodily fluid or any portion thereof) within the sequestration chamber 1234.

[1166] The sequestration chamber 1234 can have any suitable shape, size, and/or configuration. For example, in some embodiments, the sequestration chamber 1234 can have any suitable size, volume, and/or fluid capacity such as, for example, those described above with reference to the sequestration chamber 134. In the embodiment shown in FIGS. 29-34, the sequestration chamber 1234 can be, for example, a fluid flow path that extends through and/or that is defined by at least a portion of the housing 1230. In some embodiments, the sequestration chamber 1234 can be substantially similar in at least form and/or function to the sequestration chamber 834 described above with reference to FIGS. 19-25. The sequestration chamber 1234 and/or the housing 1230 can differ from the sequestration chamber 834 and/or the housing 830 by being arranged in a spiral configuration with the first port 1245 being in fluid communication with, for example, an inner portion of the spiraled sequestration chamber 1234 and the second port 1246 being in fluid communication with, for example, an outer portion of the spiraled sequestration chamber, as shown in FIG. 30. In some embodiments, the sequestration chamber 1234 can be, for example, a channel or the like formed in a portion of the housing 1230.

[1167] In some embodiments, the channel forming at least a portion of the sequestration chamber 1234 can have a relatively small cross-sectional shape and/or size that can reduce and/or substantially prevent a mixing of an initial volume of bodily fluid drawn into the sequestration chamber 1234 (channel) and a volume of air within the sequestration chamber 1234 (e.g., a volume of air that has not been vented or purged, as described in further detail herein). For example, in some instances, the relatively small cross-sectional shape and/or size of the sequestration chamber 1234 (channel), a surface tension associated with the bodily fluid flowing into the sequestration chamber 1234, and a contact angle between a surface of the housing 1230 forming the sequestration chamber 1234 and the bodily fluid flowing into the sequestration chamber 1234 can collectively limit and/or substantially prevent a mixing of the bodily fluid and a volume of air within the sequestration chamber 1234.

[1168] As shown in FIG. 30, the housing 1230 can include and/or can be coupled to a cover 1238 configured to enclose the channel, thereby forming the sequestration chamber 1234. The cover 1238 can be coupled to the housing 1230 in any suitable manner (e.g., via a friction fit, snap fit, interference fit, an adhesive, one or more mechanical fasteners, laser welding, ultrasonic welding, plasma techniques, annealing, heat boding and/or any other suitable coupling means or combination thereof). In other embodiments, the cover 1238 is

monolithically formed with and/or coupled to the housing 1230. Moreover, in some embodiments, the cover 1238 can be at least partially transparent to allow a user to visualize a flow of bodily fluid through the sequestration chamber 1234. In some embodiments, the arrangement of the housing 1230 and the cover 1238 can, for example, facilitate one or more manufacturing processes and/or can facilitate use of the control device 1200.

[1169] As shown in FIG. 30, the housing 1230 includes and/or defines a flow controller 1242 and a restricted flow path 1232. The flow controller 1242 can be, for example, a valve, membrane, diaphragm, restrictor, vent, a selectively permeable member, port, etc. configured to selectively control (at least in part) a flow of fluids into and/or out of the sequestration chamber 1234 and/or any other suitable portion of the housing 1230. For example, the flow controller 1242 can be a selectively permeable fluid barrier (e.g., a blood barrier) that includes and/or is formed of a porous material configured to selectively allow a flow of gas therethrough but to prevent a flow of a liquid therethrough. As such, the flow controller 1242 can be configured to vent and/or purge a volume of air within the sequestration chamber 1234 through the flow controller 1242 in response to a negative pressure differential within a portion of the control device 1200. Such a venting and/or purging of the volume of air within the sequestration chamber 1234 can result in a suction force and/or negative pressure differential being exerted and/or applied in or on the sequestration chamber 1234 that is operable to draw in the initial volume of bodily fluid. Moreover, the use of a selectively permeable fluid barrier can allow for the venting and/or purging of air without allowing a volume of bodily fluid to pass through the flow controller 1242. Accordingly, in some embodiments, the flow controller 1242 can be substantially similar to the flow controller 242 described in detail above with reference to FIGS. 2-5 and thus, is not described in further detail herein.

[1170] The actuator 1250 of the control device 1200 can be any suitable shape, size, and/or configuration. For example, in some embodiments, the actuator 1250 can be substantially similar in at least form and/or function to the actuator 850 described in detail above. Accordingly, such similar portions of the actuator 1250 are identified below but may not be described in further detail herein.

[1171] As shown in FIGS. 32-34, the actuator 1250 includes a body 1251 and an actuator rod 1262. The body 1251 of the actuator 1250 includes an inlet 1252 and an outlet 1253. The inlet 1252 and the outlet 1253 can be substantially similar in at least form and/or function to the inlet 852 and the outlet 853, respectively, described above with reference to FIGS. 19-25. Thus, the inlet 1252 is configured to be placed in fluid communication with a bodily fluid source to receive a flow of bodily fluid therefrom (e.g., via a lumen-containing device such as

a needle, IV catheter, PICC line, or the like). The outlet 1253 is configured to be fluidically coupled to a fluid collection device (not shown in FIGS. 29-34) such as, for example, a sample reservoir, a syringe, and/or other intermediary bodily fluid transfer device, adapter, or vessel such as, for example, a transfer device similar to those described in the '510 publication. In some embodiments, such a transfer device can provide a negative pressure and/or can act as an external energy source to enable desired functionality and fluid flow path dynamics/characteristics of the control device 1200.

[1172] The body 1251 of the actuator 1250 includes and/or defines a first port 1258 and a second port 1259. The first port 1258 is in fluid communication with the inlet 1252 and the second port 1259 is in fluid communication with the outlet 1252. In addition, the first port 1258 and the second port 1259 are configured to be at least fluidically coupled to the first port 1245 and the second port 1246, respectively, of the housing 1230. In some embodiments, the arrangement of the ports 1258 and 1259 of the actuator 1250 and the ports 1245 and 1246 of the housing 1230 can allow for and/or otherwise can provide a means of physically coupling the housing 1230 to the actuator 1250 as well as fluidically coupling the housing 1230 to the actuator 1250. That is to say, in some embodiments, the arrangement of the ports 1258 and 1259 of the actuator 1250 and the ports 1245 and 1246 of the housing 1230 can allow for a modular configuration or arrangement as described above with reference to the control device 800. In other embodiments, the housing 1230 and/or actuator 1250 need not be modular.

[1173] In some embodiments, the body 1251 and the actuator rod 1262 collectively include and/or collectively form a lock configured to at least temporarily lock the actuator 1250. For example, in some embodiments, the body 1251 and the actuator rod 1262 can each define an opening 1257 in or through which a locking member can be disposed. In such embodiments, when the locking member (not shown in FIG. 32) is disposed in the openings 1257, the locking member can limit and/or substantially prevent the actuator rod 1262 from being moved relative to the body 1251. On the other hand, removing the locking member from the openings 1257 can allow the actuator rod 1262 to be moved relative to the body 1251. While described as forming a lock, in some embodiments, the body 1251 and the actuator rod 1262 collectively include and/or collectively form a feature and/or arrangement that can limit and/or substantially prevent the actuator rod 1262 from being pulled out of the body 1251. In such embodiments, the feature can be a snap, a lock, a catch, and/or any other suitable feature and/or arrangement.

[1174] As shown in FIGS. 33 and 34, a portion of the actuator rod 1262 includes and/or is coupled to a set of seals 1265. The seals 1265 can be, for example, o-rings, over-molded elastomeric material, raised protrusions, and/or the like. The arrangement of the actuator 1262

and the body 1251 of the actuator 1250 can be such that the seals 1265 form one or more fluid tight seals between the actuator rod 1262 and the inner surface of the body 1251, as described above with reference to the actuator 850. In the embodiment shown in FIGS. 33 and 34, the actuator rod 1262 includes and/or is coupled to three seals 1265 which form and/or define a first fluid flow path 1233 within the body 1251 of the actuator 1250 and a second fluid flow path 1254 within the body 1251 of the actuator 1250. In other embodiments, any number of seals may be used to achieve desired performance.

[1175] As described above with reference to the device 800, the device 1200 can be used to procure a bodily fluid sample having reduced contamination from microbes such as, for example, dermally residing microbes, microbes external to the bodily fluid source, and/or the like. For example, the actuator rod 1262 is configured to be moved or transitioned relative to the body 1251 between a first position or configuration and a second position or configuration. In some embodiments, the transition of the actuator rod 1262 can be achieved by and/or can otherwise result from user interaction and manipulation of the actuator rod 1262, automatically in response to negative pressure and associated flow dynamics within the device 1200, and/or enacted by or in response to an external energy source which creates dynamics that result in the transitioning of the actuator rod 1262. As shown in FIG. 33, when in the first position and/or configuration, the inlet 1252 of the actuator 1250 is in fluid communication with the first fluid flow path 1233, which in turn, is in fluid communication with the first port 1258. The outlet 1253 of the actuator 1250 is in fluid communication with the second fluid flow path 1254, which in turn, is in fluid communication with the second port 1259. Thus, when in the actuator 1250 and/or actuator rod 1262 is in the first position and/or configuration (e.g., when the control device 1200 is in a first state or operating mode), the negative pressure within the fluid collection device (not shown in FIGS. 29-34) can result in a negative pressure (or negative pressure differential) within at least a portion of the sequestration chamber 1234 that is operable in drawing at least a portion of an initial flow, amount, or volume of bodily fluid from the inlet 1252, through the first fluid flow path 1233, and into the sequestration chamber 1234. Moreover, in some instances, the initial volume and/or flow of bodily fluid can be transferred into the sequestration chamber 1234 until, for example, the bodily fluid disposed within the sequestration chamber 1234 transitions the flow controller 1242 from an open or unsealed configuration or state (e.g., one in which a flow of gas or air can be drawn therethrough) to a sealed configuration or state (e.g., one in which a flow of gas and liquid cannot be drawn therethrough).

[1176] In some instances, a force can be exerted on the end portion 1263 of the actuator rod 1262 to place the actuator rod 1262 and/or actuator 1250 in its second position and/or configuration, as shown in FIG. 34. As described above, in some instances, prior to exerting the force on the end portion 1263 of the actuator rod 1262, the actuator 1250 may be transitioned from a locked configuration or state to an unlocked configuration or state. When the actuator rod 1262 and/or the actuator 1250 is placed in its second position and/or configuration (e.g., when the control device 1200 is transitioned to a second state or operating mode), the inlet 1252 and the outlet 1253 of the actuator 1250 are each in fluid communication with the second fluid flow path 1254 while the first fluid flow path 1233 is sequestered, isolated, and/or otherwise not in fluid communication with the inlet 1252 and the outlet 1253. As described in detail above, in some instances, contaminants such as, for example, dermally residing microbes or the like dislodged during the venipuncture event or throughout the bodily fluid collection process, can be entrained and/or included in the initial volume of the bodily fluid and thus, are sequestered in the sequestration chamber 1234 when the initial volume is sequestered therein. As such, the negative pressure otherwise exerted on or through the sequestration chamber 1234 is now exerted on or through the second fluid flow path 1254. In response, bodily fluid can flow from the inlet 1252, through the second fluid flow path 1254, through the outlet 1253, and into the fluid collection device coupled to the outlet 1253. Accordingly, the device 1200 can function in a manner substantially similar to that of the device 800 and thus, the function of the device 1200 is not described in further detail herein.

[1177] FIGS. 35-40 illustrate a fluid control device 1300 according to an embodiment. The fluid control device 1300 can be similar in at least form and/or function to the fluid control devices described herein. More specifically, portions of the fluid control device 1300 can be similar to and/or substantially the same as corresponding portions of the fluid control devices 200, 300, 800, 900, 1000, 1100, and/or 1200 described above. Accordingly, such portions of the fluid control device 1300 are not described in further detail herein.

[1178] The fluid control device 1300 (also referred to herein as "control device" or "device") includes a housing 1330 and an actuator 1350. As described above with reference to the control devices 800, the control device 1300 can be arranged in a modular configuration such that the housing 1330 and the actuator 1350 can be physically and fluidically coupled to form the control device 1300. In other embodiments, the control device 1300 need not be modular. That is to say, in some embodiments, the control device 1300 can be assembled during manufacturing and delivered to a supplier and/or end user as an assembled device. In

other embodiments, the device 1300 can be monolithically formed and/or collectively formed with, for example, a fluid collection device, as described above.

[1179] The housing 1330 of the control device 1300 can be any suitable shape, size, and/or configuration. As shown in FIGS. 35-37, the housing 1330 forms and/or defines a sequestration chamber 1334 that is in selective fluid communication with a first port 1345 and a second port 1346. The second port 1346 is configured to receive, include, and/or define a flow controller 1342 (see e.g., FIG. 36) and a restricted flow path 1332 (see e.g., FIG. 37). The first port 1345 and the second port 1346 are configured to be at least fluidically coupled to a portion of the actuator 1350 to allow for selective fluid flow between the housing 1330 and the actuator 1350. As described in further detail herein, the sequestration chamber 1334 is configured (1) to receive a selective flow and/or volume of bodily fluid from a portion of the actuator 1350 via the first port 1345, and (2) to sequester (e.g., separate, segregate, contain, retain, isolate, etc.) the flow and/or volume of bodily fluid (e.g., at least a portion of an initial or first flow and/or volume of bodily fluid) within the sequestration chamber 1334. The sequestration chamber 1334 can have any suitable shape, size, and/or configuration. For example, in some embodiments, the sequestration chamber 1334 can be, for example, a channel or the like formed in a portion of the housing 1330 and the housing 1330 can include and/or can be coupled to a cover 1338 configured to enclose the channel, thereby forming the sequestration chamber 1334. In some embodiments, the housing 1330 can be substantially similar in at least form and/or function to the housing 1230 described in detail above with reference to FIGS. 29-34. Accordingly, the housing 1330 is not described in further detail herein.

[1180] The actuator 1350 of the control device 1300 can be any suitable shape, size, and/or configuration. For example, in some embodiments, the actuator 1350 can be substantially similar in at least form and/or function to the actuators 850 and/or 1250 described in detail above. Accordingly, such similar portions of the actuator 1350 are identified below but may not be described in further detail herein.

[1181] As shown in FIGS. 38-40, the actuator 1350 includes a body 1351 and an actuator rod 1362. The body 1351 of the actuator 1350 includes an inlet 1352 and an outlet 1353. The inlet 1352 and the outlet 1353 can be substantially similar in at least form and/or function to the inlet 852 and the outlet 853, respectively, described above with reference to FIGS. 19-25. Thus, the inlet 1352 is configured to be placed in fluid communication with a bodily fluid source to receive a flow of bodily fluid therefrom (e.g., via a lumen-containing device such as a needle, IV catheter, surgical tubing, other standard bodily-fluid transfer device, PICC line, or

the like). The outlet 1353 is configured to be fluidically coupled to a fluid collection device (not shown in FIGS. 35-40) such as, for example, a sample reservoir, a syringe, and/or other intermediary bodily fluid transfer device, adapter, or vessel such as, for example, a transfer device similar to those described in the '510 publication.

[1182] The body 1351 of the actuator 1350 includes and/or defines a first port 1358 and a second port 1359. The first port 1358 is in fluid communication with the inlet 1352 and the second port 1359 is in fluid communication with the outlet 1353. In addition, the first port 1358 and the second port 1359 are configured to be at least fluidically coupled to the first port 1345 and the second port 1346, respectively, of the housing 1330. In some embodiments, the arrangement of the ports 1358 and 1359 of the actuator 1350 and the ports 1345 and 1346 of the housing 1330 can allow for and/or otherwise can provide a means of physically coupling the housing 1330 to the actuator 1350 as well as fluidically coupling the housing 1330 to the actuator 1350. That is to say, in some embodiments, the arrangement of the ports 1358 and 1359 of the actuator 1350 and the ports 1345 and 1346 of the housing 1330 can allow for a modular configuration or arrangement as described above with reference to the control device 800. In other embodiments, the housing 1330 and/or actuator 1350 need not be modular.

[1183] As shown in FIGS. 39 and 40, a portion of the actuator rod 1362 includes and/or is coupled to a set of seals 1365. The seals 1365 can be, for example, o-rings, elastomeric material, silicone or any other suitable material or configuration as described above with reference to the seals 1265. The arrangement of the actuator 1362 and the body 1351 of the actuator 1350 can be such that the seals 1365 form one or more fluid tight seals between the actuator rod 1362 and the inner surface of the body 1351, as described above with reference to the actuator 850. In the embodiment shown in FIGS. 33 and 34, the actuator rod 1362 includes and/or is coupled to three seals 1365 which form and/or define a first fluid flow path 1333 within the body 1351 of the actuator 1350 and a second fluid flow path 1354 within the body 1351 of the actuator 1350.

[1184] As described above with reference to the device 800, the device 1300 can be used to procure a bodily fluid sample having reduced contamination from microbes such as, for example, dermally residing microbes, microbes external to the bodily fluid source, and/or the like. For example, the actuator rod 1362 is configured to be moved or transitioned relative to the body 1351 between a first position or configuration and a second position or configuration. As shown in FIG. 39, when in the first position and/or configuration, the inlet 1352 of the actuator 1350 is in fluid communication with the first fluid flow path 1333, which in turn, is in fluid communication with the first port 1358. The outlet 1353 of the actuator 1350 is in fluid

communication with the second fluid flow path 1354, which in turn, is in fluid communication with the second port 1359. Thus, when in the actuator 1350 and/or actuator rod 1362 is in the first position and/or configuration (e.g., when the control device 1300 is in a first state or operating mode), the negative pressure within the fluid collection device (not shown in FIGS. 35-40) can result in a negative pressure (or negative pressure differential) within at least a portion of the sequestration chamber 1334 that is operable in drawing at least a portion of an initial flow, amount, or volume of bodily fluid from the inlet 1352, through the first fluid flow path 1333, and into the sequestration chamber 1334. Moreover, in some instances, the initial volume and/or flow of bodily fluid can be transferred into the sequestration chamber 1334 until, for example, the bodily fluid disposed within the sequestration chamber 1334 transitions the flow controller 1342 from an open or unsealed configuration or state (e.g., one in which a flow of gas or air can be drawn therethrough) to a sealed configuration or state (e.g., one in which a flow of gas and liquid cannot be drawn therethrough).

[1185] In some instances, a force can be exerted on a first end portion 1363 of the actuator rod 1362 to place the actuator rod 1362 and/or actuator 1350 in its second position, state, operating mode, and/or configuration, as shown in FIG. 35. As described above, in some instances, prior to exerting the force on the first end portion 1363 of the actuator rod 1362, the actuator 1350 may be transitioned from a locked configuration or state to an unlocked configuration or state. In some embodiments, the transition of the actuator rod 1362 can be achieved by and/or can otherwise result from user interaction and manipulation of the actuator rod 1362, automatically in response to negative pressure and associated flow dynamics within the device 1300, and/or enacted by or in response to an external energy source which creates dynamics that result in the transitioning of the actuator rod 1362.

[1186] When the actuator rod 1362 and/or the actuator 1350 is placed in its second position and/or configuration (e.g., when the control device 1300 is transitioned to a second state or operating mode), the inlet 1352 and the outlet 1353 of the actuator 1350 are each in fluid communication with the second fluid flow path 1354 while the first fluid flow path 1333 is sequestered, isolated, and/or otherwise not in fluid communication with the inlet 1352 and the outlet 1353. As described in detail above, in some instances, contaminants such as, for example, dermally residing microbes or the like dislodged during the venipuncture event or throughout the bodily-fluid collection process, can be entrained and/or included in the initial volume of the bodily fluid and thus, are sequestered in the sequestration chamber 1334 when the initial volume is sequestered therein. As such, the negative pressure otherwise exerted on or through the sequestration chamber 1334 is now exerted on or through the second fluid flow

path 1354. In response, bodily fluid can flow from the inlet 1352, through the second fluid flow path 1354, through the outlet 1353, and into the fluid collection device coupled to the outlet 1353. Accordingly, the device 1300 can function in a manner substantially similar to that of the device 800 and thus, the function of the device 1300 is not described in further detail herein.

[1187] In some instances, it may be desirable to isolate the negative pressure source (e.g., the fluid collection device from the inlet 1353 such as, for example, if it is desirable to collect multiple samples of bodily fluid using multiple fluid collection devices (e.g., syringes or the like). For example, in some instances, after filling the fluid collection device the user can engage the actuator 1350 and exert a force on a second end portion 1364 of the actuator rod 1362 to move and/or transition the actuator rod 1362 from its second position and/or configuration toward its first position and/or configuration. As such, the second fluid flow path 1354 no longer places the inlet 1352 in fluid communication with the outlet 1353. Moreover, the flow controller 1342 can remain in the sealed state or configuration (e.g., fully saturated, wetted, and/or otherwise preventing flow therethrough) such that the outlet 1353 is substantially sequestered or isolated from the rest of the control device 1300. In some instances, the user can then remove the filled fluid collection device and can couple a new fluid collection device to the outlet 1353. With the new fluid collection device coupled to the outlet 1353, the user can, for example, exert a force on the first end portion 1363 of the actuator rod 1362 to move and/or transition the actuator rod 1362 back to its second position, state, and/or configuration, as described above with reference to the actuator 850.

[1188] FIGS. 41-44 illustrate a fluid control device 1400 according to an embodiment. The fluid control device 1400 can be similar in at least form and/or function to the fluid control devices described herein. More specifically, portions of the fluid control device 1400 can be similar to and/or substantially the same as corresponding portions of the fluid control devices 200, 300, 800, 900, 1000, 1100, 1200, and/or 1300 described above. Accordingly, such portions of the fluid control device 1400 are not described in further detail herein.

[1189] The fluid control device 1400 (also referred to herein as "control device" or "device") includes a housing 1430 and an actuator 1450. As described above with reference to the control device 800, the control device 1400 can be arranged in a modular configuration such that the housing 1430 and the actuator 1450 can be physically and fluidically coupled to form the control device 1400. In other embodiments, the control device 1400 need not be modular. That is to say, in some embodiments, the control device 1400 can be assembled during manufacturing and delivered to a supplier and/or end user as an assembled device. In

other embodiments, the device 1400 can be monolithically formed and/or collectively formed with, for example, a fluid collection device, as described above.

[1190] The housing 1430 of the control device 1400 can be any suitable shape, size, and/or configuration. The housing 1430 is configured to be in selective fluid communication with a portion of the actuator 1450 via a first port 1458 and a second port 1459. As shown in FIGS. 43 and 44, the housing 1430 includes a bladder 1478 that can be transitioned from a first configuration and/or state to a second configuration and/or state to form and/or define a sequestration chamber 1434. As described in further detail herein, the bladder 1478 is configured to transition from the first configuration and/or state (FIG. 43) to the second configuration and/or state (FIG. 44) to form and/or define the sequestration chamber 1434, which in turn, is configured to receive a selective flow and/or volume of bodily fluid from a portion of the actuator 1450 via the first port 1458. After the bladder 1478 is placed in the second configuration and/or state, the sequestration chamber 1434 can sequester (e.g., separate, segregate, contain, retain, isolate, etc.) the flow and/or volume of bodily fluid (e.g., at least a portion of an initial or first flow and/or volume of bodily fluid) within the sequestration chamber 1434.

[1191] While the bladder 1478 is particularly shown in FIGS. 43 and 44, in other embodiments, the bladder 1478 can be any suitable shape, size, and/or configuration. Similarly, the bladder 1478 can be formed of any suitable material (e.g., any suitable biocompatible material such as those described herein and/or any other suitable material). In some embodiments, the bladder 1478 can be arranged and/or configured as, for example, a bellows, an expandable bag, a flexible pouch, and/or any other suitable reconfigurable container or the like. In addition, the sequestration chamber 1434 formed by the bladder 1478 can have any suitable shape, size, and/or configuration. In some embodiments, the housing 1430 can be substantially similar in at least form and/or function to the housing 1230 and/or 1330 described in detail above with reference to FIGS. 29-34 and FIGS. 35-40, respectively. Accordingly, the housing 1430 is not described in further detail herein.

[1192] The actuator 1450 of the control device 1400 can be any suitable shape, size, and/or configuration. For example, in some embodiments, the actuator 1450 can be substantially similar in at least form and/or function to the actuators 850, 1250, and/or 1350 described in detail above. Accordingly, such similar portions of the actuator 1450 are identified below but may not be described in further detail herein.

[1193] As shown in FIGS. 41-44, the actuator 1450 includes a body 1451 and an actuator rod 1462. The body 1451 of the actuator 1450 includes an inlet 1452 and an outlet 1453. The

inlet 1452 and the outlet 1453 can be substantially similar in at least form and/or function to the inlet 1252 and the outlet 1253, respectively, described above with reference to FIGS. 29-34. Thus, the inlet 1452 is configured to be placed in fluid communication with a bodily fluid source to receive a flow of bodily fluid therefrom (e.g., via a lumen-containing device such as a needle, IV catheter, surgical tubing, other standard bodily-fluid transfer device, PICC line, or the like). The outlet 1453 is configured to be fluidically coupled to a fluid collection device (not shown in FIGS. 41-44) such as, for example, a sample reservoir, a syringe, and/or other intermediary bodily fluid transfer device, adapter, or vessel such as, for example, a transfer device similar to those described in the '510 publication.

[1194] The body 1451 of the actuator 1450 includes and/or defines the first port 1458 and the second port 1459. Although not shown, the first port 1458 is configured to be in fluid communication with the inlet 1452 and the second port 1459 is configured to be in fluid communication with the outlet 1453. In addition, the first port 1458 is configured to be in fluid communication with the housing 1430 and more particularly, an inner volume or an inlet side of the bladder 1478 that forms the sequestration chamber 1434. The second port 1459 is configured to be in fluid communication with a portion of the housing 1430 defined between an inner surface of the housing 1430 and an outer surface of the bladder 1478. In other words, the second port 1459 is in fluid communication with a portion of the housing 1430 that is isolated and/or sequestered from the inner volume of the bladder 1478 that forms the sequestration chamber 1434. In some embodiments, the arrangement of the ports 1458 and 1459 of the actuator 1450 can allow for and/or otherwise can provide a means of physically coupling the housing 1430 to the actuator 1450 as well as fluidically coupling the housing 1430 to the actuator 1450. That is to say, in some embodiments, the arrangement of the ports 1458 and 1459 of the actuator 1450 can allow for a modular configuration or arrangement as described above with reference to the control device 800. In other embodiments, the housing 1430 and/or actuator 1450 need not be modular.

[1195] Although not shown in FIGS. 41-44, a portion of the actuator rod 1462 includes and/or is coupled to a set of seals. The seals can be, for example, o-rings, elastomeric material, silicone or any other suitable material or configuration as described above with reference to the seals 1265 and/or 1365. The arrangement of the actuator rod 1462 and the body 1451 of the actuator 1450 can be such that the seals form one or more fluid tight seals between the actuator rod 1462 and the inner surface of the body 1451, as described above with reference to the actuators 850, 1250, and/or 1350. Moreover, as described above with reference to the actuators 1250 and/or 1350, the actuator rod 1462 can include and/or can be coupled to a set seals which

selectively form and/or define a first fluid flow path configured to place the inlet 1452 of the actuator 1450 in fluid communication with the first port 1458 (e.g., when in a first position, state, operating mode, and/or configuration) and a second fluid flow path configured to place the inlet 1452 in fluid communication with the outlet 1453 (e.g., when in a second position, state, operating mode, and/or configuration).

[1196] As described above with reference to the devices 800, 1200, and/or 1300, the device 1400 can be used to procure a bodily fluid sample having reduced contamination from microbes such as, for example, dermally residing microbes, microbes external to the bodily fluid source, and/or the like. For example, as described above with reference to the devices 1200 and/or 1300, the actuator rod 1462 can be configured to be moved or transitioned relative to the body 1451 between a first position or configuration and a second position or configuration. When in the first position and/or configuration, the inlet 1452 of the actuator 1450 is in fluid communication with, for example, the first fluid flow path, which in turn, is in fluid communication with the first port 1458 (not shown in FIGS. 41-44). The outlet 1453 of the actuator 1450 is in fluid communication with the second fluid flow path 1454, which in turn, is in fluid communication with the second port 1459. Thus, when in the actuator 1450 and/or actuator rod 1462 is in the first position and/or configuration (e.g., when the control device 1400 is in a first state or operating mode), the negative pressure within the fluid collection device (not shown in FIGS. 41-44) can result in a negative pressure (or negative pressure differential) within the portion of the housing 1430 defined between the inner surface of the housing 1430 and the outer surface of the bladder 1478.

[1197] As shown in FIG. 43, the bladder 1478 can be in a first state and/or configuration prior to the fluid collection device being coupled to the outlet 1453. In some embodiments, for example, the bladder 1478 can have a flipped, inverted, collapsed, and/or empty configuration prior to coupling the fluid collection device to the outlet 1453. As shown in FIG. 44, the bladder 1478 can be configured to transition from the first state and/or configuration to a second state and/or configuration in response to the negative pressure differential resulting from the coupling of the fluid collection device to the outlet 1453. In other words, the negative pressure differential can be operable to transition the bladder 1478 from a collapsed or unexpanded configuration and/or state to an expanded configuration and/or state. For example, in some embodiments, the transitioning of the bladder 1478 can be similar to the transitioning and/or "flipping" of the diaphragm 576, described above with reference to FIGS. 11 and 12.

[1198] As described above, the bladder 1478 can be configured to transition from the first configuration and/or state to the second configuration and/or state to form and/or define the

sequestration chamber 1434. In some embodiments, the transitioning of the bladder 1478 results in an increase in an inner volume of the bladder 1478 (i.e., the sequestration chamber 1434). The increase in the inner volume can, in turn, result in a negative pressure differential between the sequestration chamber 1434 defined by the bladder 1478 and the inlet 1452 that is operable in drawing at least a portion of an initial flow, amount, or volume of bodily fluid from the inlet 1452, through the first port 1458, and into the sequestration chamber 1434. Moreover, in some instances, the initial volume and/or flow of bodily fluid can be transferred into the sequestration chamber 1434 until, for example, the bladder 1478 is fully expanded, and/or until the negative pressure differential is reduced and/or equalized.

[1199] Having transferred the initial volume of bodily fluid into the sequestration chamber 1434, a force can be exerted on a first end portion 1463 of the actuator rod 1462 to place the actuator rod 1462 and/or actuator 1450 in its second position, state, operating mode, and/or configuration, as described in detail above with reference to the devices 1200 and/or 1300. As described above, in some instances, prior to exerting the force on the first end portion 1463 of the actuator rod 1462, the actuator 1450 may be transitioned from a locked configuration or state to an unlocked configuration or state. In some embodiments, the transition of the actuator rod 1462 can be achieved by and/or can otherwise result from user interaction and manipulation of the actuator rod 1462, automatically in response to negative pressure and associated flow dynamics within the device 1400, and/or enacted by or in response to an external energy source which creates dynamics that result in the transitioning of the actuator rod 1462.

[1200] When the actuator rod 1462 and/or the actuator 1450 is placed in its second position and/or configuration (e.g., when the control device 1400 is transitioned to a second state or operating mode), the inlet 1452 and the outlet 1453 of the actuator 1450 are placed in fluid communication (e.g., via the second fluid flow path (not shown)) while the first fluid flow path (not shown) and/or the first port 1458 is sequestered, isolated, and/or otherwise not in fluid communication with the inlet 1452 and/or the outlet 1453. As described in detail above, in some instances, contaminants such as, for example, dermally residing microbes or the like dislodged during the venipuncture event or throughout the bodily-fluid collection process, can be entrained and/or included in the initial volume of the bodily fluid and thus, are sequestered in the sequestration chamber 1434 when the initial volume is sequestered therein. As such, the negative pressure otherwise exerted on or through the housing 1430 is now exerted on or through the outlet 1453 and the inlet 1452 via, for example, the second fluid flow path (not shown). In response, bodily fluid can flow from the inlet 1452, through the body 1451 of the actuator 1450, through the outlet 1453, and into the fluid collection device coupled to the outlet

1453. Accordingly, the device 1400 can function in a manner substantially similar to that of the devices 800, 1200, and/or 1300 and thus, the function of the device 1400 is not described in further detail herein.

[1201] While the device 1400 is described above as including the housing 1430 and the actuator 1450, in other embodiments, a fluid control device can have, for example, at least a partially integrated design. For example, FIGS. 45-50 illustrate a fluid control device 1500 according to an embodiment. The fluid control device 1500 can be similar in at least form and/or function to the fluid control devices described herein. More specifically, portions of the fluid control device 1500 can be similar to and/or substantially the same as corresponding portions of at least the fluid control device 1400 described above with reference to FIGS. 41-44. Accordingly, such portions of the fluid control device 1500 are not described in further detail herein.

[1202] The fluid control device 1500 (also referred to herein as "control device" or "device") includes an actuator 1550 having an actuator body 1551 and an actuator rod 1562. The actuator 1550 can be any suitable shape, size, and/or configuration. For example, in some embodiments, the actuator 1550 can be substantially similar in at least form and/or function to the actuators 850, 1250, 1350, and/or 1450 described in detail above. Accordingly, such similar portions of the actuator 1550 are identified below but may not be described in further detail herein.

[1203] As shown in FIGS. 45-50, the actuator 1550 includes an inlet 1552 and an outlet 1553, each of which is in fluid communication with the body 1551. The inlet 1552 and the outlet 1553 can be substantially similar in at least form and/or function to the inlet 1252 and the outlet 1253, respectively, described above with reference to FIGS. 29-34. Thus, the inlet 1552 is configured to be placed in fluid communication with a bodily fluid source to receive a flow of bodily fluid therefrom (e.g., via a lumen-containing device such as a needle, IV catheter, surgical tubing, other standard bodily-fluid transfer device, PICC line, or the like). The outlet 1553 is configured to be fluidically coupled to a fluid collection device (not shown in FIGS. 45-50) such as, for example, a sample reservoir, a syringe, and/or other intermediary bodily fluid transfer device, adapter, or vessel such as, for example, a transfer device similar to those described in the '510 publication.

[1204] As shown in FIGS. 48-50, the actuator 1550 includes a bladder 1578 that can be transitioned from a first configuration and/or state (FIG. 48) to a second configuration and/or state (FIG. 49) to form and/or define a sequestration chamber 1534. As described in further detail herein, the bladder 1578 is configured to transition from the first configuration and/or

state (FIG. 48) to the second configuration and/or state (FIGS. 49 and 50) to form and/or define the sequestration chamber 1534, which in turn, is configured to receive a selective flow and/or volume of bodily fluid from the inlet 1552. After the bladder 1578 is placed in the second configuration and/or state, the sequestration chamber 1534 can sequester (e.g., separate, segregate, contain, retain, isolate, etc.) the flow and/or volume of bodily fluid (e.g., at least a portion of an initial or first flow and/or volume of bodily fluid) within the sequestration chamber 1534. As such, the bladder 1578 can be substantially similar in at least form and/or function to the bladder 1478 described above with reference to FIGS. 41-44 and thus, is not described in further detail herein.

[1205] As shown in FIGS. 46 and 48-50, the body 1551 of the actuator 1550 includes and/or defines a port 1559 configured to be in fluid communication with the outlet 1553. In addition, the port 1559 defines a fluid flow path that is configured to be in fluid communication with a portion of the actuator 1550 defined between an inner surface of the body 1551 and an outer surface of the bladder 1578. In other words, the port 1559 is in fluid communication with a portion of the actuator 1550 that is isolated and/or sequestered from the inner volume of the bladder 1578 that forms and/or that is configured to form the sequestration chamber 1534.

[1206] As described above with reference to the devices 1200, 1300, and/or 1400, a portion of the actuator rod 1562 includes and/or is coupled to a set of seals 1565. The seals 1565 can be, for example, o-rings, elastomeric material, silicone or any other suitable material or configuration as described above with reference to the seals 1265 and/or 1365. The arrangement of the actuator rod 1562 and the body 1551 of the actuator 1550 can be such that the seals 1565 form one or more fluid tight seals between the actuator rod 1562 and the inner surface of the body 1551, as described above with reference to the actuators 850, 1250, and/or 1350. Moreover, as described above with reference to the actuators 1250 and/or 1350, the set seals 1565 can be arranged along the actuator rod 1562 to selectively form and/or define a fluid flow path 1554 that is sequestered from and/or fluidically isolated from the inlet 1552 when the actuator rod 1562 is in a first position and/or configuration and that is configured to place the inlet 1552 in fluid communication with the outlet 1553 when the actuator rod 1562 is in a second position and/or configuration.

[1207] As described above with reference to the devices 800, 1200, 1300, and/or 1400, the device 1500 can be used to procure a bodily fluid sample having reduced contamination from microbes such as, for example, dermally residing microbes, microbes external to the bodily fluid source, and/or the like. For example, as described above with reference to the devices 1200, 1300, and/or 1400, the actuator rod 1562 can be configured to be moved or transitioned

relative to the body 1551 between the first position or configuration and the second position or configuration. When in the first position and/or configuration, the inlet 1552 of the actuator 1550 is in fluid communication with a fluid flow path, which in turn, is in fluid communication with a portion of the body 1551 that is disposed on an inlet side of the bladder 1578. In other words, the fluid flow path establishes fluid communication between the inlet 1553 and the bladder 1578 and/or the sequestration chamber 1534 at least partially defined by the bladder 1578 when the bladder 1578 is transitioned to the second configuration and/or state. The outlet 1553 of the actuator 1550 is in fluid communication with the port 1559. Thus, when in the actuator 1550 and/or actuator rod 1562 is in the first position and/or configuration (e.g., when the control device 1500 is in a first state or operating mode), the negative pressure within the fluid collection device (not shown in FIGS. 45-50) can result in a negative pressure (or negative pressure differential) within the portion of the actuator body 1551 defined between the inner surface of the body 1551 and the outer surface of the bladder 1578, as described above with reference to the device 1400.

[1208] As shown in FIG. 48, the bladder 1578 can be in a first state and/or configuration prior to the fluid collection device being coupled to the outlet 1553. In some embodiments, for example, the bladder 1578 can have a flipped, inverted, collapsed, and/or empty configuration prior to coupling the fluid collection device to the outlet 1553. Moreover, when the actuator rod 1562 is in the first position and/or configuration, the fluid flow path 1554 is fluidically isolated from the inlet 1552. Accordingly, as shown in FIG. 49, the bladder 1578 can be configured to transition from the first state and/or configuration to a second state and/or configuration in response to the negative pressure differential resulting from the coupling of the fluid collection device to the outlet 1553. In other words, the negative pressure differential can be operable to transition the bladder 1578 from a collapsed or unexpanded configuration and/or state to an expanded configuration and/or state. For example, in some embodiments, the transitioning of the bladder 1578 can be similar to the transitioning and/or "flipping" of the diaphragm 576, described above with reference to FIGS. 11 and 12. In other embodiments, the bladder 1578 can be configured to transition between a first state and/or configuration to a second state and/or configuration in any suitable manner such as any of those described herein.

[1209] As described above, the bladder 1578 can be configured to transition from the first configuration and/or state to the second configuration and/or state to form and/or define the sequestration chamber 1534. In some embodiments, the transitioning of the bladder 1578 results in an increase in an inner volume of the bladder 1578 (i.e., the sequestration chamber 1534). The increase in the inner volume can, in turn, result in a negative pressure differential

between the sequestration chamber 1534 defined by the bladder 1578 and the inlet 1552 that is operable in drawing at least a portion of an initial flow, amount, or volume of bodily fluid from the inlet 1552 and a portion of the actuator body 1551, and into the sequestration chamber 1534. Moreover, in some instances, the initial volume and/or flow of bodily fluid can be transferred into the sequestration chamber 1534 until, for example, the bladder 1578 is fully expanded, and/or until the negative pressure differential is reduced and/or equalized.

[1210] Having transferred the initial volume of bodily fluid into the sequestration chamber 1534, a force can be exerted on a first end portion 1563 of the actuator rod 1562 to place the actuator rod 1562 and/or actuator 1550 in its second position, state, operating mode, and/or configuration, as described in detail above with reference to the devices 1200 and/or 1300. As described above, in some instances, prior to exerting the force on the first end portion 1563 of the actuator rod 1562, the actuator 1550 may be transitioned from a locked configuration or state to an unlocked configuration or state. In some embodiments, the transition of the actuator rod 1562 can be achieved by and/or can otherwise result from user interaction and manipulation of the actuator rod 1562, automatically in response to negative pressure and associated flow dynamics within the device 1500, and/or enacted by or in response to an external energy source which creates dynamics that result in the transitioning of the actuator rod 1562.

[1211] When the actuator rod 1562 and/or the actuator 1550 is placed in its second position and/or configuration (e.g., when the control device 1500 is transitioned to a second state or operating mode), the inlet 1552 and the outlet 1553 of the actuator 1550 are placed in fluid communication via the fluid flow path 1554 while the sequestration chamber 1534 is sequestered, isolated, and/or otherwise not in fluid communication with the inlet 1552 and/or the outlet 1553. As described in detail above, in some instances, contaminants such as, for example, dermally residing microbes or the like dislodged during the venipuncture event or throughout the bodily-fluid collection process, can be entrained and/or included in the initial volume of the bodily fluid and thus, are sequestered in the sequestration chamber 1534 when the initial volume is sequestered therein.

[1212] As described above with reference to the devices 1200 and/or 1300, transitioning the actuator rod 1562 to the second position and/or configuration is such that the fluid flow path 1554 places the inlet 1552 in fluid communication with the outlet 1553. For example, transitioning the actuator rod 1562 to the second position and/or configuration can move the seals 1565 relative to the inlet 1552 such that the fluid flow path 1554 is placed in fluid communication with both the inlet 1552 and the outlet 1553. As such, the negative pressure otherwise exerted on the outer surface of the bladder 1578 is now exerted on or through the

outlet 1553 and the inlet 1552 via the fluid flow path 1554. In response, bodily fluid can flow from the inlet 1552, through the fluid flow path 1554, through the outlet 1553, and into the fluid collection device coupled to the outlet 1553. Accordingly, the device 1500 can function in a manner substantially similar to that of the devices 800, 1200, 1300, and/or 1400 and thus, the function of the device 1500 is not described in further detail herein.

[1213] While the actuators 850, 1250, 1350, 1450, and 1550 have been described in detail above as being transitioned in response to an external force such as, for example, a force exerted by a user, in other embodiments, a fluid control device can include one or more actuators that can be transitioned in response to any suitable force, input, change of state or configuration, etc. For example, FIGS. 51 and 52 illustrate a portion of a fluid control device 1600 according to an embodiment. The fluid control device 1600 can be similar in at least form and/or function to the fluid control devices described herein. More specifically, portions of the fluid control device 1600 can be similar to and/or substantially the same as corresponding portions of at least the fluid control devices 500, 600, and/or 700 described above. Accordingly, such portions of the fluid control device 1600 are not described in further detail herein.

[1214] As shown in FIGS. 51 and 52, the fluid control device 1600 (also referred to herein as "control device" or "device") includes a housing 1630 having an inlet 1631 and an outlet 1636, and having and/or being coupled to an actuator 1650. As described in further detail herein, the housing 1630 defines a set of fluid flow paths 1633 and 1654 configured to establish fluid communication between one or more portions of the housing 1630 to selectively receive a flow of fluid therethrough (e.g., a liquid and/or a gas). The inlet 1631 is configured to be placed in fluid communication with a bodily fluid source to receive a flow of bodily fluid therefrom (e.g., via a lumen-containing device such as a needle or the like, as described in detail above). The outlet 1636 is configured to be fluidically coupled to a fluid collection device (not shown in FIGS. 51 and 52). The inlet 1631, the outlet 1636, and the fluid collection device can be substantially similar to those described above and thus, are not described in further detail herein.

[1215] The housing 1630 can be any suitable shape, size, and/or configuration. In some embodiments, the housing 1630 can have a size that is at least partially based on a volume of bodily fluid configured to be at least temporarily stored within one or more portions of the housing 1630. As described above, the housing 1630 of the control device 1600 is configured to (1) receive a flow and/or volume of bodily fluid via the inlet 1631 and (2) sequester (e.g., separate, segregate, contain, retain, isolate, etc.) the flow and/or volume of bodily fluid within a sequestration chamber 1634 included in and/or at least partially formed by the housing 1630.

In some embodiments, aspects of the housing 1630 can be substantially similar, for example, to aspects of the housings 630, 730, and/or 830. Accordingly, some portions and/or aspects of the housing 1630 are not described in further detail herein.

[1216] The housing 1630 includes and/or is coupled to the actuator 1650 configured to selectively control a flow of bodily fluid through the housing 1630. In this embodiment, the actuator 1650 includes a diaphragm 1676 and an actuator rod 1662 having a set of seals (e.g., seals 1665 and 1666). As described in further detail herein, the diaphragm 1676 and the actuator rod 1662 are configured to transition, move, and/or otherwise reconfigure within the housing 1630 in response to a negative pressure differential within at least a portion of the device. More specifically, the actuator 1650 is configured to move between a first state in which the inlet 1631 is placed in fluid communication with the sequestration chamber 1634 and a second state in which the inlet 1631 is placed in fluid communication with the outlet 1636 via the fluid flow path 1654, as described in detail above with reference to the control device 500.

[1217] In some embodiments, the diaphragm 1676 can be similar to, for example, the diaphragms 576, 676, and/or 776 described in detail above. Accordingly, the diaphragm 1676 can be at least partially disposed in a sequestration portion of the housing 1630 to define and/or to form at least a portion of the sequestration chamber 1634. As described in detail above, the diaphragm 1676 can be configured to transition, move, flip, and/or otherwise reconfigure from a first state to a second state in response to a negative pressure differential, which can be operable to draw an initial volume of bodily fluid into the sequestration chamber 1634 and/or to sequester the initial volume of bodily fluid in the sequestration chamber 1634 once disposed therein. Moreover, as shown in FIGS. 51 and 52, the diaphragm 1676 can include and/or can be coupled to a flow controller 1642. The flow controller 1642 can be any suitable flow controller such as any of those described herein. For example, in some embodiments, the flow controller 1642 can be a semi-permeable member or membrane such as an air permeable/liquid impermeable barrier (e.g., a blood barrier).

[1218] As described in detail above, the flow controller 1642 can be configured to transition from a first state in which the flow controller 1642 allows a flow of gas (e.g., air) to pass through the flow controller 1642 while preventing a flow of liquid (e.g., bodily fluid) to pass therethrough, to a second state in which the flow controller 1642 limits and/or substantially prevents a flow of gas and liquid to pass through the flow controller 1642. In some embodiments, the flow controller 1642 can be configured to transition from the first state to the second state in response to contact with, for example, the initial volume of bodily fluid

(e.g., at least a portion of the initial volume of bodily fluid can wet or saturate the flow controller 1642 to place the flow controller 1642 in the second state).

[1219] While the diaphragms 576, 676, and 776 are shown and described above as including a pin, rod, post, and/or the like that include and/or are coupled to one or more seals (e.g., the seals 565, 665, and 765, respectively), in the embodiment shown in FIGS. 51 and 52, the diaphragm 1676 includes a pin 1677 (e.g., a rod, an extension, a protrusion, a latch, a lock, and/or any other suitable feature, member, and/or mechanism) that does not include and/or is not coupled to a seal. For example, in this embodiment, the pin 1677 extends through a portion of the housing 1630 to selectively engage a portion of the actuator rod 1662, which in turn includes one or more seals (e.g., the seals 1665 and 1666), as described in further detail herein.

[1220] As shown in FIGS. 51 and 52, the actuator rod 1662 is movably disposed in, for example, an actuator portion 1639 of the housing 1630. The actuator rod 1662 includes a first seal 1665 and a second seal 1666 and is in contact with an energy storage member 1667 such as a spring or the like disposed within the actuator portion 1639 of the housing 1630. In the embodiment shown in FIGS. 51 and 52, the arrangement of the actuator 1650 can be such that a first end portion of the actuator rod 1662 is in selective contact with the pin 1677 of the diaphragm 1676 and a second end portion of the actuator rod 1662 (opposite the first end portion) is in contact with and/or otherwise is engaged with the energy storage member 1667.

[1221] As shown in FIG. 51, when the actuator 1650 is in a first state, the pin 1677 of the diaphragm 1676 can engage the actuator rod 1662 to maintain the actuator rod 1662 in a first or initial state and/or position in which the energy storage member 1667 has a relatively high potential energy (e.g., the energy storage member 1667 can be a spring maintained and/or held in a compressed state when in the first state). Furthermore, the first seal 1665 coupled to and/or disposed on the actuator 1662 is in a first or initial position in which the fluid flow path 1633 establishes fluid communication between the inlet 1631 and the sequestration chamber 1634 when the actuator 1650 is in the first state. As shown, the second seal 1666 coupled to and/or disposed on the actuator rod 1662 is likewise in a first or initial position in which the second seal 1666 is spaced apart from a seal surface 1640 formed by at least a portion of the actuator portion 1639 of the housing 1630.

[1222] In some embodiments, the separation of the second seal 1666 from the seal surface 1640 can be such that the fluid flow path 1654 places the outlet 1636 in fluid communication with the sequestration chamber 1634 via a restricted flow path 1632 (see FIG. 52). In some embodiments, the restricted flow path 1632 can be similar in at least form and/or function to any of the restricted flow paths described herein (e.g., the restricted flow paths 232, 832, 1232,

and/or 1332). As such, the restricted flow path 1632 can be configured to modulate a magnitude of a negative pressure differential applied on or in the sequestration chamber 1634 and/or a rate at which a negative pressure differential increases within the sequestration chamber 1634. In other embodiments, the outlet 1636 can be in fluid communication with the sequestration chamber 1634 via any suitable flow path, port, opening, valve, etc. In other words, in some embodiments, the control device 1600 need not include the restricted flow path 1632.

[1223] As shown in FIG. 51, when the actuator 1650 is in the first state, the actuator rod 1662 can be maintained in a first state or position in which the fluid flow path 1633 places the inlet 1631 in fluid communication with the sequestration chamber 1634, and the fluid flow path 1654 places the outlet 1636 in fluid communication with the sequestration chamber 1634 via the restricted flow path 1632. Accordingly, when a fluid collection device (such as those described herein) is coupled to the outlet 1636, a negative pressure defined in and/or otherwise produced by the fluid collection device can be operable to draw the initial volume of bodily fluid into the sequestration chamber 1634.

[1224] As described in detail above, the actuator 1650 can be transitioned to a second state and/or configuration in response to the initial volume being transferred into the sequestration chamber 1634. For example, in some embodiments, the initial volume of bodily fluid can be drawn into the sequestration chamber 1634 in response to a negative pressure being exerted through the flow controller 1642 (e.g., the selectively permeable membrane). In some instances, at least a portion of the bodily fluid drawn into the sequestration chamber 1634 can come into contact with the flow controller 1642, which in turn, can transition the flow controller 1642 from the first state to the second state (e.g., the flow controller 1642 limits and/or substantially prevents a flow of gas and liquid therethrough). As such, a negative pressure exerted on a surface of the diaphragm 1676 can build and can become sufficient to transition, move, and/or flip the diaphragm from a first state and/or configuration to a second state and/or configuration (see FIG. 52). In some embodiments, the transitioning of the diaphragm 1676 can correspond with and/or can be in response to the flow controller 1642 being transitioned from the first state to the second state (e.g., becoming fully wetted or the like, as described in detail above). In other embodiments, the diaphragm 1676 can transition before or after the flow controller 1642 has transitioned from the first state to the second state. In still other embodiments, the control device 1600 need not include the flow controller 1642 and the diaphragm 1676 can be configured to transition in response to being exposed to the negative pressure differential produced by the fluid collection device. In some such embodiments, the

diaphragm 1676 (and/or at least a portion thereof) can be configured to act in a similar manner to the flow controller 1642 by transitioning from the first state to the second state in a predictable and/or predetermined manner after being exposed to a predetermined negative pressure differential or a predetermined rate of change in negative pressure. Moreover, the transitioning of the diaphragm 1676 can be automatic (e.g., is not a result of user intervention).

[1225] As shown in FIG. 52, when the diaphragm 1676 is transitioned, moved, flipped, etc., the pin 1677 can be moved within the housing 1630 and relative to the actuator rod 1662. More particularly, the transitioning of the diaphragm 1676 can move the pin 1677 a sufficient amount that the pin 1677 is disengaged from the actuator rod 1662. As such, the energy storage member 1667 (e.g., spring) can be configured to release and/or convert at least a portion of its potential energy. As a specific example, in this embodiment, moving the pin 1677 can allow the spring 1667 to expand from a first or compressed state to a second or substantially uncompressed state. The transitioning of the energy storage member 1667 (e.g., spring) from the first state to the second state, in turn, moves the actuator rod 1662 within the actuator portion 1639 from a first state and/or position to a second state and/or position.

[1226] As shown in FIG. 52, when the actuator rod 1662 is in the second state and/or position, the first seal 1665 can be placed in a second or subsequent position in which the first seal 1665 sequesters the sequestration chamber 1634 from the inlet 1631. Similarly, the second seal 1666 can be placed in a second or subsequent position in which the second seal 1666 is pushed (e.g., by the energy storage member 1667) against the seal surface 1640, which in turn, sequesters the flow controller 1642 from the fluid flow path 1654. Furthermore, the placement of the first seal 1665 and the second seal 1666 when the actuator rod 1662 is in the second state and/or position is such that the fluid flow path 1633 is placed in fluid communication with the fluid flow path 1654. Thus, a negative pressure differential produced by the fluid collection device coupled to the outlet 1636 can be operable to draw a subsequent volume of bodily fluid from the inlet 1631, through the fluid flow path 1633 and 1654, through the outlet 1636, and into the fluid collection device. Moreover, the collecting and sequestering of the initial volume of bodily fluid can result in the subsequent volume(s) of bodily fluid being substantially free from contaminants, as described in detail above.

[1227] Referring now to FIG. 53, a flowchart is presented illustrating a method 10 of using a fluid control device to obtain a bodily fluid sample with reduced contamination according to an embodiment. The fluid control device can be similar to and/or substantially the same as any of the fluid control devices described in detail above. The method 10 includes establishing fluid communication between a bodily fluid source and an inlet of the fluid collection device,

at 11. For example, in some embodiments, a user can manipulate the fluid control device to physically and/or fluidically couple the inlet to a lumen-containing device (e.g., a needle, IV, PICC line, etc.) in fluid communication with a patient.

[1228] A fluid collection device is coupled to an outlet of the fluid control device, at 12. The coupling of the fluid collection device to the outlet is configured to produce a negative pressure differential within at least a portion of the fluid control device, as described in detail above. In some embodiments, for example, the fluid collection device can be a sample bottle or container that defines a negative pressure. In other embodiments, the fluid collection device can be a syringe or the like that can be manipulated to produce a negative pressure. Accordingly, a negative pressure differential can be produced within one or more portions of the fluid control device, as described above with reference to the control devices 100, 200, 300, 400, 500, 600, 700, 800, 900, 1000, 1100, 1200, 1300, 1400, 1500, and/or 1600.

[1229] An initial volume of bodily fluid is received from the inlet and into a sequestration portion of the fluid control device in response to the negative pressure differential, at 13. For example, in some embodiments, the sequestration portion can be similar to and/or substantially the same as the sequestration chamber 1234 described above with reference to FIGS. 29-34. In other embodiments, the sequestration portion can be similar to and/or substantially the same as the sequestration chamber 1634. In still other embodiments, the sequestration portion can be similar to and/or substantially the same as any of the sequestration chambers described herein. Furthermore, in some instances, the initial volume of bodily fluid can include contaminants entrained therein, which may otherwise result in false results during testing of a bodily fluid sample.

[1230] In response to contact with at least a portion of the initial volume of bodily fluid, a flow controller disposed in the sequestration portion is transitioned from a first state in which the flow controller allows a flow of a gas through the flow controller and prevents a flow of bodily fluid through the flow controller, to a second state in which the flow controller prevents a flow of gas and bodily fluid through the flow controller, at 14. For example, in some embodiments, the flow controller can be a selectively permeable member or membrane (e.g., a fluid or blood barrier and/or the like), as described above with reference to the flow controller 242. In other embodiments, the flow controller can be similar to and/or substantially the same as any of the flow controllers described herein. Thus, in some embodiments, the contact with at least the portion of the initial volume of bodily fluid can, for example, wet or saturate the flow controller such that the flow controller limits and/or substantially prevents a flow of gas and liquid (e.g., bodily fluid) therethrough. In other embodiments, the flow controller can be

a bladder and/or diaphragm that is configured to be transitioned in response to a negative pressure differential. For example, in such embodiments, a flow controller can be a substantially impermeable bladder or diaphragm that can transition from a first state to a second state when a negative pressure differential applied to a surface of the bladder and/or diaphragm exceeds a threshold amount of negative pressure.

[1231] The initial volume of bodily fluid is sequestered in the sequestration portion after the flow controller is transitioned to the second state, at 15. For example, in some embodiments, the fluid control device can include an actuator and/or any other suitable feature or mechanism configured to transition after the flow controller is placed in its second configuration to sequester the initial volume of bodily fluid. In some embodiments, the actuator can transition from a first state to a second state to automatically sequester the initial volume of bodily fluid in the sequestration portion, as described above with reference to, for example, the actuator 1650. In other embodiments, the actuator can transition from a first state to a second state in response to a force exerted by a user, as described above with reference to, for example, the actuator 850. In still other embodiments, the fluid control device can sequester the initial volume of bodily fluid in the sequestration portion in any suitable manner such as those described herein.

[1232] After sequestering the initial volume of bodily fluid, a subsequent volume of bodily fluid is transferred from the inlet, through the outlet, and into the fluid collection device, at 16. As described in detail above, in some instances, sequestering the initial volume of bodily fluid in the sequestration portion of the fluid control device can likewise sequester contaminants contained in the initial volume. Accordingly, contaminants in the subsequent volume of bodily fluid can be reduced or substantially eliminated.

[1233] While various embodiments have been described above, it should be understood that they have been presented by way of example only, and not limitation. Where schematics and/or embodiments described above indicate certain components arranged in certain orientations or positions, the arrangement of components may be modified. While the embodiments have been particularly shown and described, it will be understood that various changes in form and details may be made. For example, while the control devices 100, 200, 300, 400, 500, 600, 700, 800, 900, 1000, 1100, 1200, 1300, 1400, and/or 1500 are described as transferring a bodily fluid into the device as a result of a negative pressure within a fluid collection device, in other embodiments, the devices described herein can be used with any suitable device configured to establish a pressure differential (e.g., a negative pressure differential). For example, in some embodiments, an outlet of a control device can be coupled

to a syringe or pump. In other embodiments, a control device can include a pre-charged sequestration chamber, a vented sequestration chamber, a manually activated device configured to produce a negative pressure, an energy source (e.g., a chemical energy source, a kinetic energy source, and/or the like), and/or any other suitable means of defining and/or forming a pressure differential within a portion of the control device. Moreover, as described above, the control devices can be coupled to such collection devices by a user (e.g., doctor, nurse, technician, physician, etc.) or can be coupled or assembled during manufacturing. In some embodiments, pre-assembling a control device and a collection device (e.g., a sample container or syringe) can, for example, force compliance with a sample procurement protocol that calls for the sequestration of an initial amount of bodily fluid prior to collecting a sample volume of bodily fluid.

[1234] While some of the embodiments described above include a flow controller and/or an actuator having a particular configuration and/or arrangement, in other embodiments, a fluid control device can include any suitable flow controller and/or actuator configured to selectively control a flow of bodily fluid through one or more portions of the fluid control device. For example, while some embodiments include an actuator such as a diaphragm or the like having one or more seals arranged as an O-ring or an elastomeric over-mold, which is/are moved with the diaphragm and relative to a portion of the device (e.g., the inlet, the outlet, or any other suitable portion) when the diaphragm is transitioned or flipped from a first state to a second state, in other embodiments, a fluid control device can include one or more seals having any suitable configuration. For example, in some embodiments, a fluid control device can include one or more seals arranged as an elastomeric sheet or the like that is/are fixedly coupled to a portion of the control device. In such embodiments, a portion of an actuator such as a pin or rod extending from a diaphragm (see e.g., FIGS. 11 and 12) can extend through an opening defined in the one or more elastomeric sheets, which in turn, form a substantially fluid tight seal with an outer surface of the pin or rod. As such, when the actuator (e.g., diaphragm) is transitioned from a first state to a second state, the portion of the actuator (e.g., the pin or rod) can move through one or more of the elastomeric sheets. In other words, the portion of the actuator moves relative to the one or more elastomeric sheets, which in turn, remain in a substantially fixed position relative to the portion of the control device. In some embodiments, the removal or the portion of the actuator can allow a flow of fluid through the opening defined by the one or more elastomeric sheets that was otherwise occluded by the portion of the actuator. Accordingly, the one or more elastomeric sheets can function in a similar manner as any of the seals described herein. Moreover, in some embodiments, such an arrangement may,

for example, reduce an amount of friction associated with forming the desired fluid tight seals, which in turn, may obviate the use of a lubricant otherwise used to facilitate the movement of the seals within the control device.

[1235] While the diaphragms (e.g., diaphragms 576, 676, and 776) are described herein as being configured to transition, move, flip, and/or otherwise reconfigure in response to an amount of negative pressure exerted on a surface of the diaphragm exceeding a threshold amount of negative pressure, in other embodiments, a fluid control device can include any suitable actuator or the like configured to transition, move, flip, and/or otherwise reconfigure in response to being exposed to a desired and/or predetermined amount of negative pressure. For example, in some embodiments, a fluid control device can include an actuator including and/or arranged as a movable member, plug, plunger, occlusion member, seal, and/or the like configured to selectively control a flow of fluid through at least a portion of the fluid control device. More particularly, the movable member or the like can be transitioned from a first state and/or position in which the movable member or the like is disposed in and/or otherwise occludes an opening, to a second state and/or position in which the movable member or the like is removed from the opening. In such embodiments, a negative pressure can be exerted through a portion of the device to transfer, for example, an initial volume of bodily fluid into a sequestration portion and/or chamber.

[1236] As described in detail above, in some embodiments, a device can include a flow controller such as a selectively permeable member or membrane, that can be configured to transition from a first state to a second state in response to being wetted (or otherwise transitioned) by the initial volume of bodily fluid. After transferring the initial volume of bodily fluid and after the flow controller is transitioned to its second state, an amount of negative pressure exerted on a surface of the movable member or the like may build until a magnitude of the negative pressure is sufficient to pull or move the movable member out of the opening, thereby allowing a flow of bodily fluid through the opening that was otherwise occluded by the movable member. In this manner, the movable member can function similar to any of the diaphragms described herein (e.g., the diaphragm 576, 676, and/or 776) that are configured to transition or flip from a first state to a second state. In such embodiments, the movable member can be, for example, an elastomeric plug, cork, plunger, and/or any other suitable member that can be moved or "popped" out of such an opening or portion of a flow path.

[1237] While some of the embodiments described above include a flow controller and/or actuator that selectively establishes fluid communication between a sequestration chamber and

a fluid collection device (e.g., a sample reservoir, a syringe, and/or any other suitable source of negative pressure) in other embodiments, a control device can be arranged to transfer a flow of bodily fluid in response to negative pressure differentials resulting from any suitable portion(s) of the device. For example, while the control device 200 is described above as including the flow controller 242 and the restricted flow path 232 that selectively place the sequestration chamber 234 in fluid communication with the sample reservoir until the flow controller 242 is transitioned to a sealed or closed state (e.g., until the flow controller 242 is sufficiently wetted), in other embodiments, a control device can include a sequestration chamber that is a pre-sealed evacuated and/or charged chamber such that establishing fluid communication between an inlet and the sequestration chamber results in a negative pressure differential that is sufficient to draw an initial volume of bodily fluid into the sequestration chamber. In such embodiments, the control device can be configured to transfer bodily fluid to the sequestration chamber until the pressure differential is sufficiently reduced and/or until pressures otherwise substantially equalize. Moreover, in some such embodiments, the sequestration chamber and/or the inlet can include a coupler, an actuator, a needle, a septum, a port, and/or any other suitable member that can establish fluid communication therebetween (e.g., that can transition the sequestration chamber from a sealed to an unsealed configuration).

[1238] While some of the embodiments described above include a flow controller and/or actuator that physically and/or mechanically sequesters one or more portions of a fluid control device, in other embodiments, a fluid control device need not physically and/or mechanically sequester one or more portions of the fluid control device. For example, in some embodiments, an actuator such as the actuator 1250 can be transitioned from a first state in which an initial volume of bodily fluid can flow from an inlet to a sequestration chamber or portion, to a second state in which (1) the sequestration chamber or portion is physically and/or mechanically sequestered and (2) the inlet is in fluid communication with an outlet of the fluid control device. In other embodiments, however, an actuator and/or any other suitable portion of a fluid control device can transition from a first state in which an initial volume of bodily fluid can flow from an inlet to a sequestration chamber or portion, to a second state in which the inlet is placed in fluid communication with the outlet without physically and/or mechanically sequestering (or isolating) the sequestration chamber or portion. When such a control device is in the second state, one or more features and/or geometries of the control device can result in a preferential flow of bodily fluid from the inlet to the outlet and the initial volume of bodily fluid can be retained in the sequestration chamber or portion without physically and/or mechanically being sequestered or isolated.

[1239] While the restricted flow path 232 is described above as modulating and/or controlling a magnitude of negative pressure applied on or through at least a portion of the device 200, in other embodiments, a control device can include any suitable feature, mechanism, and/or device configured to modulate, create, and/or otherwise control one or more pressure differentials through at least a portion of the control device. For example, in some embodiments, a user can transition and/or move an actuator to change (e.g., reduce or increase) the size of one or more portions of a fluid flow path or fluid flow interface within a portion of the control device to manually modulate and/or otherwise control an amount or magnitude of negative pressure within one or more portions of a control device.

[1240] Although various embodiments have been described as having particular features, concepts, and/or combinations of components, other embodiments are possible having any combination or sub-combination of any features, concepts, and/or components from any of the embodiments described herein. For example, as described above, the device 700 includes concepts, features, and/or elements of the devices 200 and 600. As another example, any of the embodiments described herein can include a lock or other suitable feature configured to at least temporarily maintain one or more components in a desired position, state, arrangement, and/or configuration. As another example, any of the embodiments described herein can include and/or can define a sequestration chamber and/or portion that is configured similar to, for example, the sequestration chamber 1234 described above with reference to FIG. 30. In other words, any of the fluid control devices described herein can include a sequestration chamber that is arranged and/or formed as a channel. In some embodiments, a channel forming at least a portion of a sequestration chamber can have a relatively small cross-sectional shape and/or size that can reduce and/or substantially prevent mixing of air and bodily fluid as the initial volume of bodily fluid is drawn into the channel, as described above with reference to the sequestration chamber 1234. Moreover, such a channel can have a spiral shape and/or configuration similar to the sequestration chamber 1234 described above and/or can have any other suitable shape and/or configuration.

[1241] As another example, any of the control devices described herein can include a flow controller arranged as a selectively permeable member or membrane as described above, for example, with reference to the flow controller 242. More particularly, while the control device 600 is not described as including a flow controller, in other embodiments, a portion of the diaphragm 676 can include and/or can form a flow controller formed, at least in part, of a selectively permeable material. In such embodiments, the flow controller can be configured to allow a volume of the sequestration chamber and/or portion 634 to be vented in response to

being exposed to the negative pressure differential (as described above). In other words, a volume of air can be drawn out of (e.g., vented from or purged from) the sequestration chamber 634 via the flow controller in response to the negative pressure differential within a portion of the fluid control device 600. In some instances, such an arrangement can allow for a reduction in a size and/or volume of the sequestration chamber 634 because a volume of air otherwise occupying a portion of the sequestration chamber 634 is vented or purged through the flow controller in response to the negative pressure differential.

[1242] By way of another example, any of the embodiments described herein can include any suitable actuator and/or flow controller configured to selectively control fluid flow through at least a portion of the device. Specifically, a flow controller or the like can be one or more of a selectively permeable material or membrane, a valve, a diaphragm, and/or any other suitable flow controller. While some of the embodiments have been described as including an actuator rod configured to be transitioned from a first configuration or position to a second configuration or position (e.g., the actuator rod 1262 of the actuator 1250), in other embodiments, any actuator described herein can include an actuator rod configured to transition from between a first position and second position to at least temporarily isolate an outlet of the device from one or more other portions of the device (e.g., as described above with reference to the actuators 850 and/or 1350). In some embodiments, such an actuator can be configured for use with a given and/or predetermined collection device such as, for example, a syringe. In other embodiments, such an actuator can be used with any suitable collection device.

[1243] In some embodiments, the specific configurations of the various components can also be varied. For example, the size and specific shape of the various components can be different from the embodiments shown, while still providing the functions as described herein. For example, while a portion of the actuator body 1551, sequestration chamber 1534, and/or the bladder 1578 are shown in FIGS. 45-50 as being substantially tubular having a round or substantially semi-circular end portion, in other embodiments, the portion of the actuator body 1551, sequestration chamber 1534, and/or bladder 1578 can have any suitable shape and/or size. In some embodiments, varying the size and/or shape of such components may reduce an overall size of the device 1500 and/or may increase the ergonomics of the device 1500 without changing the function of the device 1500. As a specific example, a housing, sequestration chamber, and/or bladder may have a substantially cylindrical shape with a relatively flat end portion or the like. Moreover, in some embodiments, a control device can include a bladder that is configured to "flip" similar to the diaphragms described above in response to being exposed to a negative pressure differential. In other embodiments, a bladder can be configured

to gradually transition (e.g., unroll, unfold, unfurl, and/or otherwise reconfigure) from the first state to the second state. In some instances, controlling a rate at which a bladder is transitioned may allow for a modulation and/or control of a negative pressure differential produced within the sequestration chamber.

[1244] In other embodiments, a device may include a bladder (similar in form and/or function to the bladders 1478 and/or 1578) disposed in a housing having a size, shape, and/or profile similar to the housings 1230 and/or 1330. In some such embodiments, the bladder can define a volume that is similar in shape and/or size the overall size, and/or shape of the housing (e.g., cylindrical with a relatively low profile or height). In some instances, such an arrangement can allow at least a portion of an initial volume of bodily fluid to remain in contact with a surface of the bladder (or diaphragm or other actuator), which can provide a visual indication to the user regarding the bodily fluid being transferred into the sequestration chamber. In other embodiments, a housing similar to the housing 1230 can define a spiral channel or any other suitable channel and can include a bladder disposed within at least a portion of that channel. In such embodiments, the bladder can function similarly to the bladder 1578 in which the bladder expands, opens, and/or otherwise increases in volume in response to being exposed to a negative pressure differential. In some embodiments, a bladder can define an enclosed volume configured to receive an initial volume of bodily fluid. In other embodiments, the bladder and a portion of the housing (e.g., a surface defining the sequestration chamber and/or channel) can collectively define the volume configured to receive the initial volume of bodily fluid. In this manner, a fluid control device can include a bladder configured to conform to any suitable shape, feature, channel, and/or configuration of a housing in which it is disposed. In some embodiments, the size and shape of the various components can be specifically selected for a desired rate and/or volume of bodily fluid flow into a fluid reservoir.

[1245] In some embodiments, the size and/or shape of the various components can be specifically selected for a desired or intended usage. For example, in some embodiments, a device such as those described herein can be configured for use with or on seemingly healthy adult patients. In such embodiments, the device can include a sequestration chamber that has a first volume (e.g., about 0.5 ml to about 5.0 ml). In other embodiments, a device such as those described herein can be configured for use with or on, for example, very sick patients and/or pediatric patients. In such embodiments, the device can include a sequestration chamber that has a second volume that is less than the first volume (e.g., less than about 0.5 ml). Thus, it should be understood that the size, shape, and/or arrangement of the embodiments and/or

components thereof can be adapted for a given use unless the context explicitly states otherwise.

[1246] Although not shown, any of the devices described herein can include an opening, port, coupler, septum, Luer-Lok, gasket, valve, threaded connecter, standard fluidic interface, etc. (referred to for simplicity as a "port") in fluid communication with the sequestration chamber. In some such embodiments, the port can be configured to couple to any suitable device, reservoir, pressure source, etc. For example, in some embodiments, the port can be configured to couple to a reservoir, which in turn, can allow a greater volume of bodily fluid to be diverted and/or transferred into the sequestration chamber. In other embodiments, the port can be coupled to a negative pressure source such as an evacuated container, a pump, a syringe, and/or the like to collect a portion of or the full volume of bodily fluid in the sequestration chamber, channel, reservoir, etc. and use that volume of bodily fluid (e.g., the pre-sample volume) for additional clinical and/or in vitro diagnostic testing purposes. In other embodiments, the port can be configured to receive a probe, sampling tool, testing device, and/or the like that can be used to perform one or more tests (e.g., tests not sensitive to potential contamination) on the initial volume while the initial volume is disposed or sequestered in the sequestration chamber. In still other embodiments, the port can be coupled to any suitable pressure source or infusion device configured to infuse the initial volume of bodily fluid sequestered in the sequestration chamber back into the patient and/or bodily fluid source (e.g., in the case of pediatric patients, very sick patients, patients having a low blood volume, and/or the like). In other embodiments, the sequestration channel, chamber, and/or reservoir can be configured with the addition of other diagnostic testing components integrated into the chamber (e.g., a paper test) such that the initial bodily fluid is used for that test.

[1247] In still other embodiments, the sequestration chamber, channel, and/or reservoir can be designed, sized, and configured to be removable and compatible with testing equipment and/or specifically accessible for other types of bodily fluid tests commonly performed on patients with suspected conditions. By way of example, a patient with suspected sepsis commonly has blood samples collected for lactate testing, procalcitonin testing, and blood culture testing. All of the fluid control devices described herein can be configured such that the sequestration chamber, channel, reservoir, etc. can be removed (e.g., after receiving the initial volume of bodily fluid) and the bodily fluid contained therein can be used for these additional testing purposes before or after the subsequent sample is collected for microbial testing.

[1248] Although not shown, in some embodiments, a fluid control device can include one or more lumen, channels, flow paths, etc. configured to selectively allow for a "bypass" flow of bodily fluid, where an initial amount or volume of bodily fluid can flow from the inlet, through the lumen, cannel, flow path, etc. to bypass the sequestration chamber, and into the collection device. In some embodiments, the fluid control device can include an actuator having, for example, at least three states – a first in which bodily fluid can flow from the inlet to the sequestration chamber, a second in which bodily fluid can flow from the inlet to the outlet after the initial volume is sequestered in the sequestration chamber, and a third in which bodily fluid can flow from the inlet, through the bypass flow path, and to the outlet. In other embodiments, the control device can include a first actuator configured to transition the device between a first and second state, as described in detail above with reference to specific embodiments, and can include a second actuator configured to transition the device to a bypass configuration or the like. In still other embodiments, the control device can include any suitable device, feature, component, mechanism, actuator, controller, etc. configured to selectively place the fluid control device in a bypass configuration or state.

[1249] Any of the embodiments described herein can be used in conjunction with any suitable fluid transfer, fluid collection, and/or fluid storage device such as, for example, the fluid reservoirs described in the '420 patent. In some instances, any of the embodiments described herein can be used in conjunction with any suitable transfer adapter, fluid transfer device, fluid collection device, and/or fluid storage devices such as, for example, the devices described in the '510 Publication and/or any of the devices described in U.S. Patent Publication No. 2015/0246352 entitled, "Apparatus and Methods for Disinfection of a Specimen Container," filed March 3, 2015; U.S. Patent No. 8,535,241 entitled, "Fluid Diversion Mechanism for Bodily-Fluid Sampling," filed October 12, 2012; U.S. Patent No. 9,060,724 entitled, "Fluid Diversion Mechanism for Bodily-Fluid Sampling," filed May 29, 2013; U.S. Patent No. 9,155,495 entitled, "Syringe-Based Fluid Diversion Mechanism for Bodily-Fluid Sampling," filed December 2, 2013; U.S. Patent Publication No. 2016/0361006 entitled, "Devices and Methods for Syringe Based Fluid Transfer for Bodily-Fluid Sampling," filed June 13, 2016; U.S. Patent Publication No. 2018/0140240 entitled, "Systems and Methods for Sample Collection with Reduced Hemolysis," filed November 20, 2017; and/or U.S. Patent Publication No. 2017/0065733 entitled, "Apparatus and Methods for Maintaining Sterility of a Specimen Container," filed September 6, 2016, the disclosures of each of which are incorporated herein by reference in their entireties.

[1250] In some embodiments, a method of using a fluid control device such as those described herein can include the ordered steps of establishing fluid communication between a bodily fluid source (e.g., a vein of a patient or the like) and an inlet of a fluid control device. An outlet of the fluid control device is then placed in fluid communication with and/or otherwise engages a negative pressure source. Such a negative pressure source can be a sample reservoir, a syringe, an evacuated container, an intermediate transfer device, and/or the like. The fluid control device can be in a first state or operating mode when the outlet is coupled to the negative pressure source and, as such, a negative pressure differential is applied through the fluid control device that draws an initial volume of bodily fluid into a sequestration chamber of the fluid control device. For example, a negative pressure within a sample reservoir can be operable in drawing an initial volume of bodily fluid from a patient and into the sequestration chamber. Once the initial volume of bodily fluid is disposed in the sequestration chamber, the fluid control device is transitioned, either automatically or via user intervention, from the first state or operating mode to a second state or operating mode such that (1) the initial volume is sequestered in the sequestration chamber and (2) the fluid communication is established between the inlet and the outlet. The sequestration of the initial volume can be such that contaminants entrained in the flow of the initial volume are likewise sequestered within the sequestration chamber. With the initial volume of bodily fluid sequestered in the sequestration chamber and with fluid communication established between the inlet and the outlet, subsequent volumes of bodily fluid that are substantially free of contamination can be collected in one or more sample reservoirs.

[1251] While the method of using the fluid control device is explicitly described as including the recited ordered steps, in other embodiments, the ordering of certain events and/or procedures in any of the methods or processes described herein may be modified and such modifications are in accordance with the variations of the invention. Additionally, certain events and/or procedures may be performed concurrently in a parallel process when possible, as well as performed sequentially as described above. Certain steps may be partially completed or may be omitted before proceeding to subsequent steps. For example, while the devices are described herein as transitioning from a first state to a second state in a discrete operation or the like, it should be understood that the devices described herein can be configured to automatically and/or passively transition from the first state to the second state and that such a transitioning may occur over a period of time. In other words, the transitioning from the first state to the second state may, in some instances, be relatively gradual such that as a last portion of the initial volume of bodily fluid is being transferred into the sequestration chamber, the

housing begins to transition from the first state to the second state. In some instances, the rate of change when transitioning from the first state to the second state can be selectively controlled to achieve one or more desired characteristics associated with the transition. Moreover, in some such instances, the inflow of the last portion of the initial volume can limit and/or substantially prevent bodily fluid already disposed in the sequestration chamber from escaping therefrom. Accordingly, while the transitioning from the first state to the second state may occur over a given amount of time, the sequestration chamber can nonetheless sequester the volume of bodily fluid disposed therein.

What is claimed:

1. A system, comprising:

a housing having an inlet and an outlet, the inlet configured to be placed in fluid communication with a bodily fluid source, the housing forming a sequestration portion configured to receive an initial volume of bodily fluid from the bodily fluid source;

a flow controller at least partially disposed in the sequestration portion of the housing and configured to transition from a first state to a second state; and

a fluid collection device configured to be fluidically coupled to the outlet to produce a negative pressure differential within at least a portion of the housing, the negative pressure differential produced by the fluid collection device operable to draw the initial volume of bodily fluid into the sequestration portion when the flow controller is in the first state, the negative pressure differential produced by the fluid collection device operable to draw the sample volume of bodily fluid through the outlet and into the fluid collection device when the flow controller is in the second state.

2. The system of claim 1, wherein the flow controller is configured to transition from the first state to the second state automatically.

3. The system of claim 1, wherein the flow controller is configured to transition from the first state to the second state in response to contact with a portion of the initial volume of bodily fluid disposed in the sequestration portion.

4. The system of claim 1, wherein the flow controller includes a selectively permeable material.

5. The system of claim 4, wherein prior to being placed in the second state, the flow controller is configured to allow a flow of a gas through the flow controller and to prevent a flow of bodily fluid through the flow controller.

6. The system of claim 5, wherein the flow controller is configured to prevent a flow of gas and bodily fluid through the flow controller when in the second state.

7. The system of claim 6, wherein the flow controller is configured to be placed in the second state in response to a portion of the initial volume of bodily fluid saturating the selectively permeable material.

8. The system of claim 1, wherein the flow controller is configured to modulate a magnitude of negative pressure exerted on the sequestration portion of the housing prior to the flow controller transitioning to the second state.

9. The system of claim 1, wherein the fluid collection device is a sample reservoir that defines a negative pressure operable to produce the negative pressure differential within at least the portion of the housing when fluidically coupled to the outlet.

10. The system of claim 1, wherein the fluid collection device is a syringe configured to be manipulated by a user after being fluidically coupled to the outlet to produce the negative pressure differential within at least the portion of the housing.

11. The system of claim 1, wherein the housing defines a first fluid flow path and a second fluid flow path, the negative pressure differential is operable to draw the initial volume of bodily fluid through the first fluid flow path from the inlet to the sequestration portion when the flow controller is in the first state, the negative pressure differential is operable to draw the sample volume of bodily fluid through the second fluid flow path from the inlet to the outlet when the flow controller is in the second state.

12. The system of claim 11, further comprising:

an actuator coupled to the housing, the actuator having a first actuator state in which the negative pressure differential is applied to the first fluid flow path and a second actuator state in which the negative pressure differential is applied to the second fluid flow path.

13. The system of claim 12, wherein the actuator is in the first actuator state when the flow controller is in the first state, the actuator is configured to be transitioned from the first actuator state to the second actuator state after the flow controller is transitioned to the second state.

14. The system of claim 13, wherein the negative pressure differential automatically transitions the actuator from the first actuator state to the second actuator state after the flow controller is transitioned to the second state.

15. An apparatus, comprising:

a housing having an inlet configured to be placed in fluid communication with a bodily fluid source and an outlet configured be placed in fluid communication with a fluid collection device, the housing forming a sequestration portion configured to receive an initial volume of bodily fluid from the bodily fluid source; and

an actuator coupled to the housing, the actuator having a first configuration in which a first fluid flow path places the inlet in fluid communication with the sequestration portion and a second configuration in which a second fluid flow path places the inlet in fluid communication with the outlet,

wherein the fluid collection device is configured to be placed in fluid communication with the outlet to produce a negative pressure differential (1) within the first fluid flow path operable to draw the initial volume of bodily fluid into the sequestration portion when the actuator is in the first configuration, and (2) within the second fluid flow path operable to draw a sample volume of bodily fluid into the fluid collection device when the actuator is in the second configuration.

16. The apparatus of claim 15, wherein the initial volume of bodily fluid is sequestered in the sequestration portion when the actuator is in the second configuration.

17. The apparatus of claim 15, wherein sequestering the initial volume in the sequestration portion reduces contamination in the sample volume.

18. The apparatus of claim 15, wherein the fluid collection device is a sample reservoir that defines a negative pressure operable to produce the negative pressure differential within the first fluid flow path and the second fluid flow path.

19. The apparatus of claim 15, wherein the fluid collection device is a syringe configured to be manipulated by a user after being placed in fluid communication with the outlet to produce the negative pressure differential within the first fluid flow path and the second fluid flow path.

20. The apparatus of claim 15, wherein the actuator is configured to transition from the first configuration to the second configuration in response to a force applied by a user on a portion of the actuator.

21. The apparatus of claim 15, wherein the actuator includes at least one seal configured to define a portion of the first fluid flow path when the actuator is in the first configuration, the at least one seal is configured to define a portion of the second fluid flow path when the actuator is in the second configuration.

22. The apparatus of claim 15, wherein the actuator includes a diaphragm configured to transition from a first state to a second state when a negative pressure differential within a portion of the first fluid flow path is greater than a threshold amount of negative pressure.

23. The apparatus of claim 22, wherein the diaphragm is coupled to at least one seal configured to define a portion of the first fluid flow path when the diaphragm is in the first state and configured to define a portion of the second fluid flow path when the diaphragm is in the second state.

24. The apparatus of claim 15, further comprising:

a flow controller at least partially disposed in the sequestration portion of the housing, the flow controller is configured to establish selective fluid communication between the sequestration portion and the actuator.

25. The apparatus of claim 24, wherein the flow controller includes a selectively permeable material.

26. The apparatus of claim 25, wherein the flow controller is configured to transition from a first state in which the selective permeable material allows a flow of a gas through the flow controller and prevents a flow of bodily fluid through the flow controller, to a second state in which the selectively permeable material prevents a flow of gas and bodily fluid through the flow controller.

27. The apparatus of claim 26, wherein the flow controller is configured to be placed in the second state in response to at least a portion of the initial volume of bodily fluid saturating the selectively permeable material.

28. The apparatus of claim 26, wherein the actuator is configured to be transitioned to the second configuration after the flow controller is transitioned to the second state.

29. A method of using a fluid control device to obtain a bodily fluid sample with reduced contamination, the method comprising:

establishing fluid communication between a bodily fluid source and an inlet of the fluid control device;

coupling a fluid collection device to an outlet of the fluid control device, the coupling of the fluid collection device to the outlet configured to produce a negative pressure differential within at least a portion of the fluid control device;

receiving an initial volume of bodily fluid from the inlet and into a sequestration portion of the fluid control device in response to the negative pressure differential;

transitioning, in response to contact with at least a portion of the initial volume of bodily fluid, a flow controller disposed in the sequestration portion from a first state in which the flow controller allows a flow of a gas through the flow controller and prevents a flow of bodily fluid through the flow controller, to a second state in which the flow controller prevents a flow of gas and bodily fluid through the flow controller;

sequestering the initial volume of bodily fluid in the sequestration portion after the flow controller is transitioned to the second state; and

transferring a subsequent volume of bodily fluid from the inlet, through the outlet, and into the fluid collection device.

30. The method of claim 29, wherein the flow controller includes a selectively permeable material.

31. The method of claim 29, wherein the flow controller is configured to be placed in the second state in response to at least a portion of the initial volume of bodily fluid saturating the selectively permeable material.

32. The method of claim 29, wherein the flow controller is configured to automatically transition from the first state to the second state in response to contact with at least the portion of the initial volume of bodily fluid.

33. The method of claim 29, wherein the coupling the fluid collection device to the outlet includes coupling a fluid reservoir to the outlet to produce the negative pressure differential within at least the portion of the fluid control device, the fluid reservoir defining a negative pressure prior to the fluid reservoir being coupled to the outlet.

34. The method of claim 29, wherein coupling the fluid collection device to the outlet includes coupling a syringe to the outlet, the method further comprising:

manipulating the syringe, after coupling the syringe to the outlet, to produce the negative pressure differential within at least the portion of the fluid control device.

35. The method of claim 29, further comprising:

transitioning an actuator of the fluid control device from a first configuration to a second configuration after transitioning the flow controller from the first state to the second state, the actuator defining at least a portion of a first fluid flow path between the inlet and the sequestration portion when in the first configuration, the actuator defining at least a portion of a second fluid flow path between the inlet and the outlet when in the second configuration.

36. The method of claim 29, wherein the sequestering of the initial volume of bodily fluid sequesters contaminants within the sequestration portion such that the subsequent volume of bodily fluid is substantially free of contaminants.

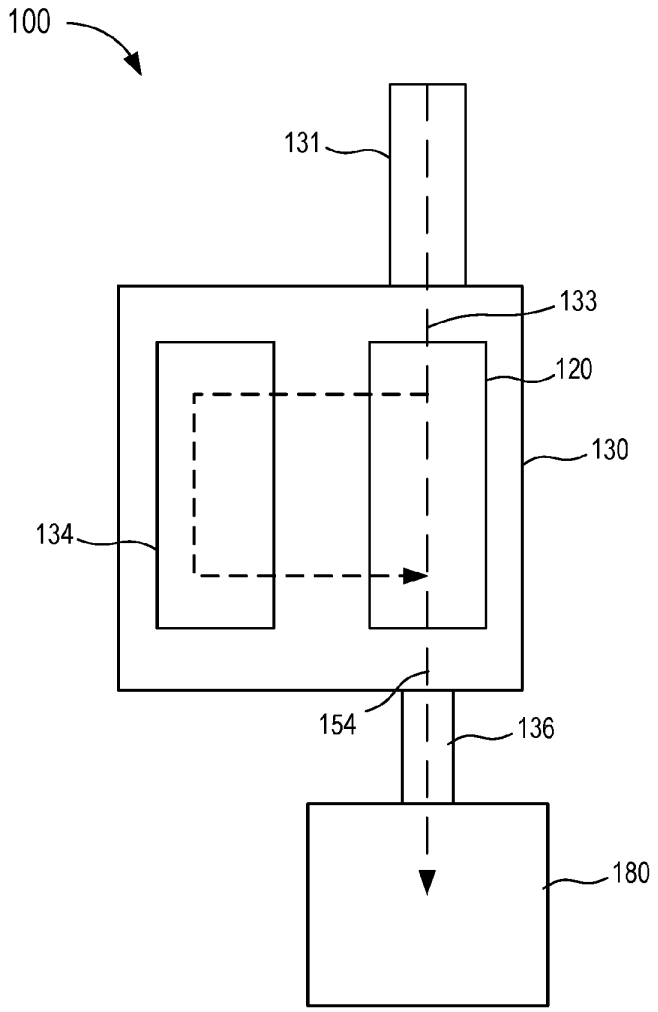


FIG. 1

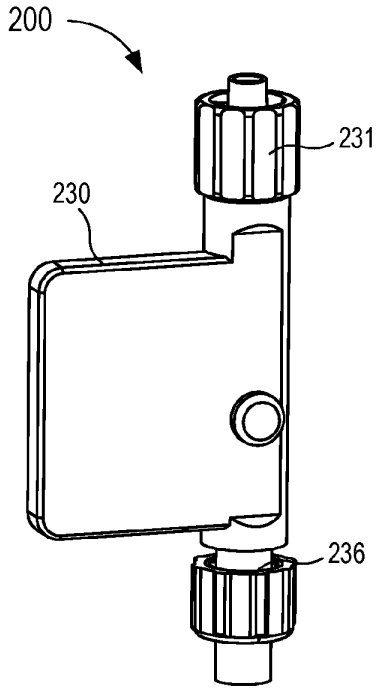


FIG. 2

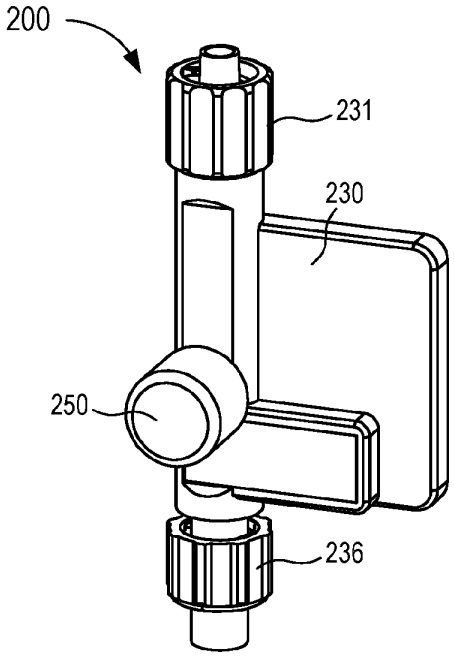


FIG. 3

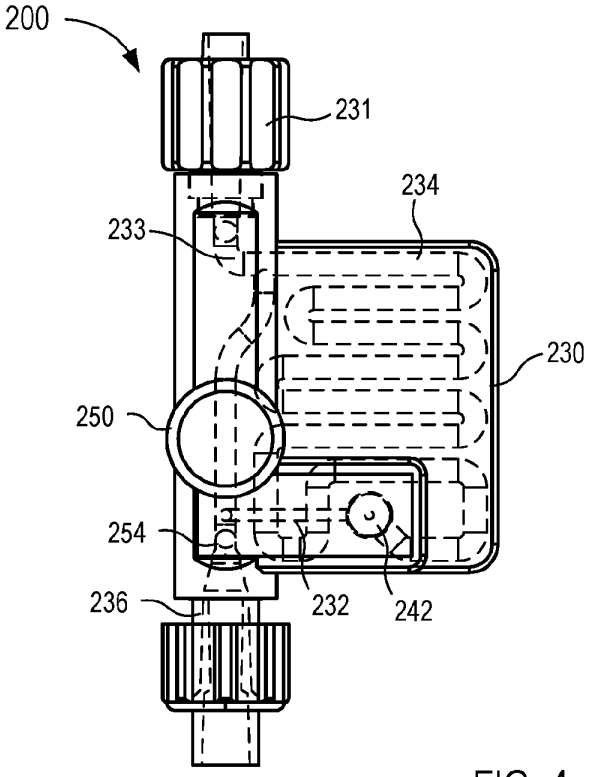


FIG. 4

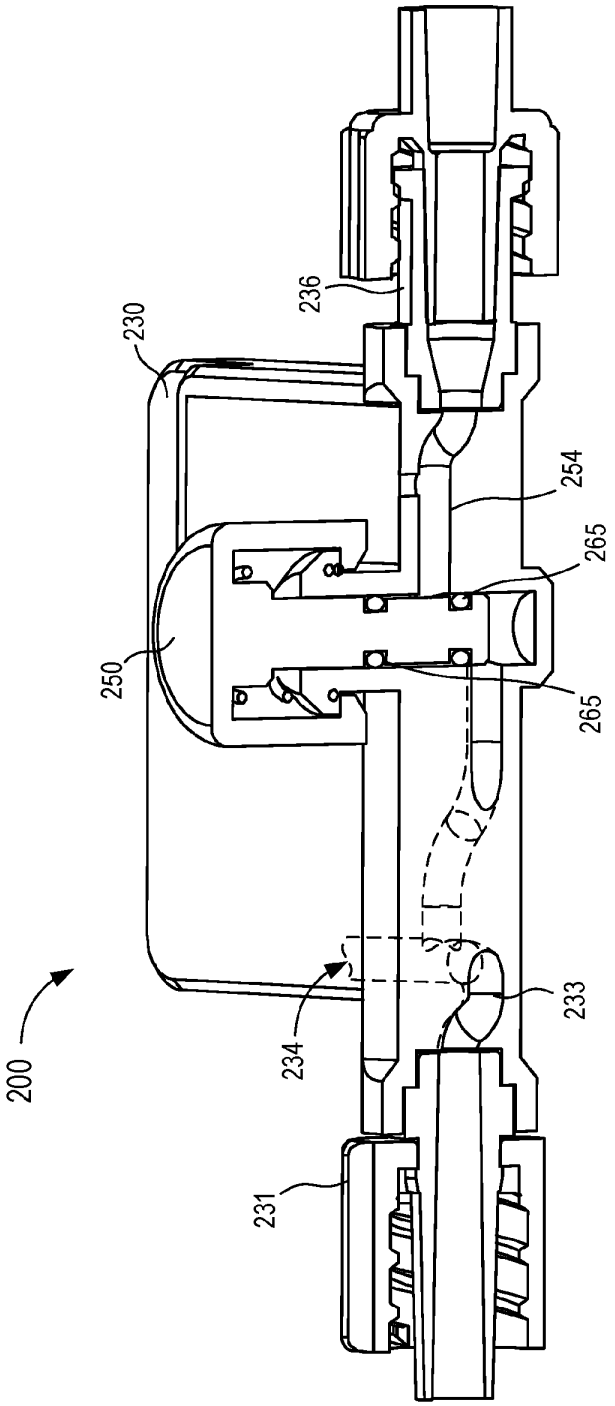


FIG. 5

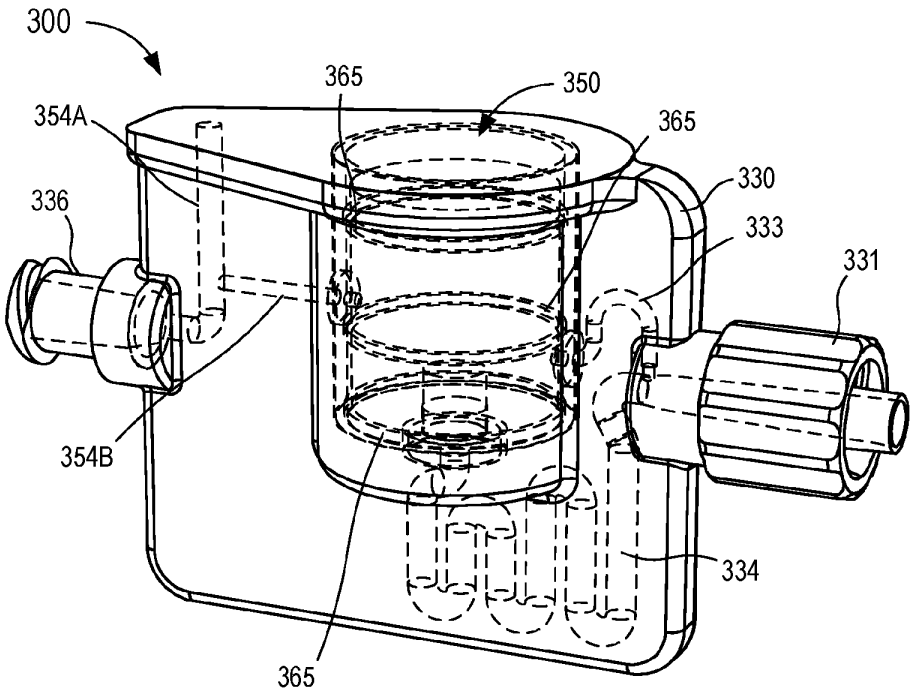

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FIG. 6

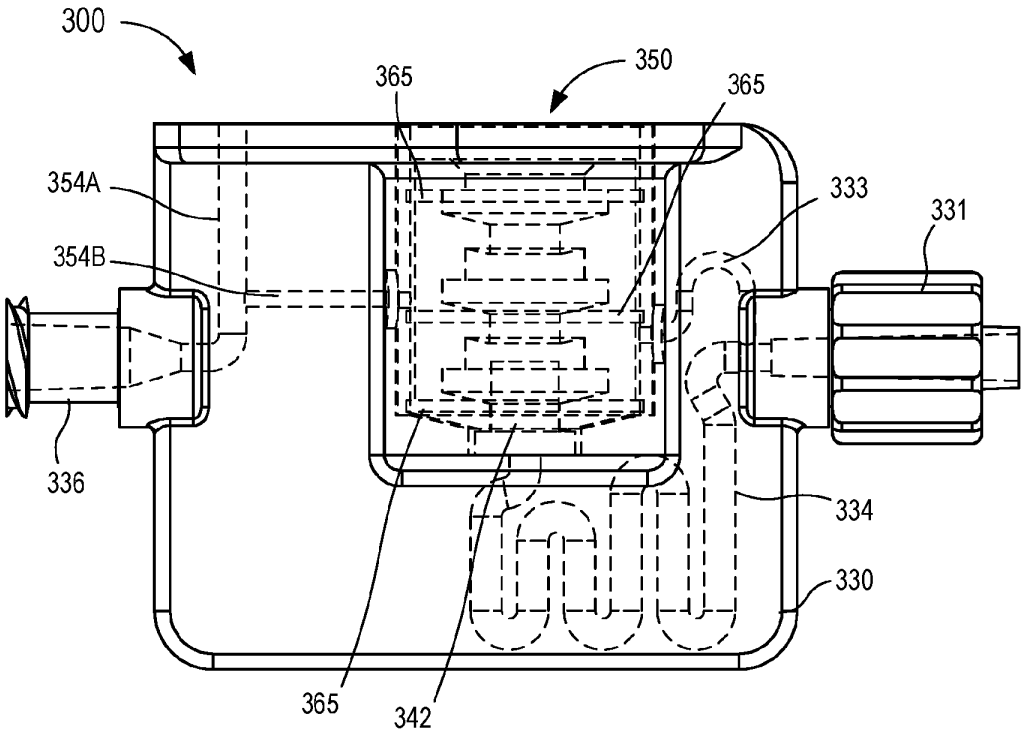

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FIG. 7

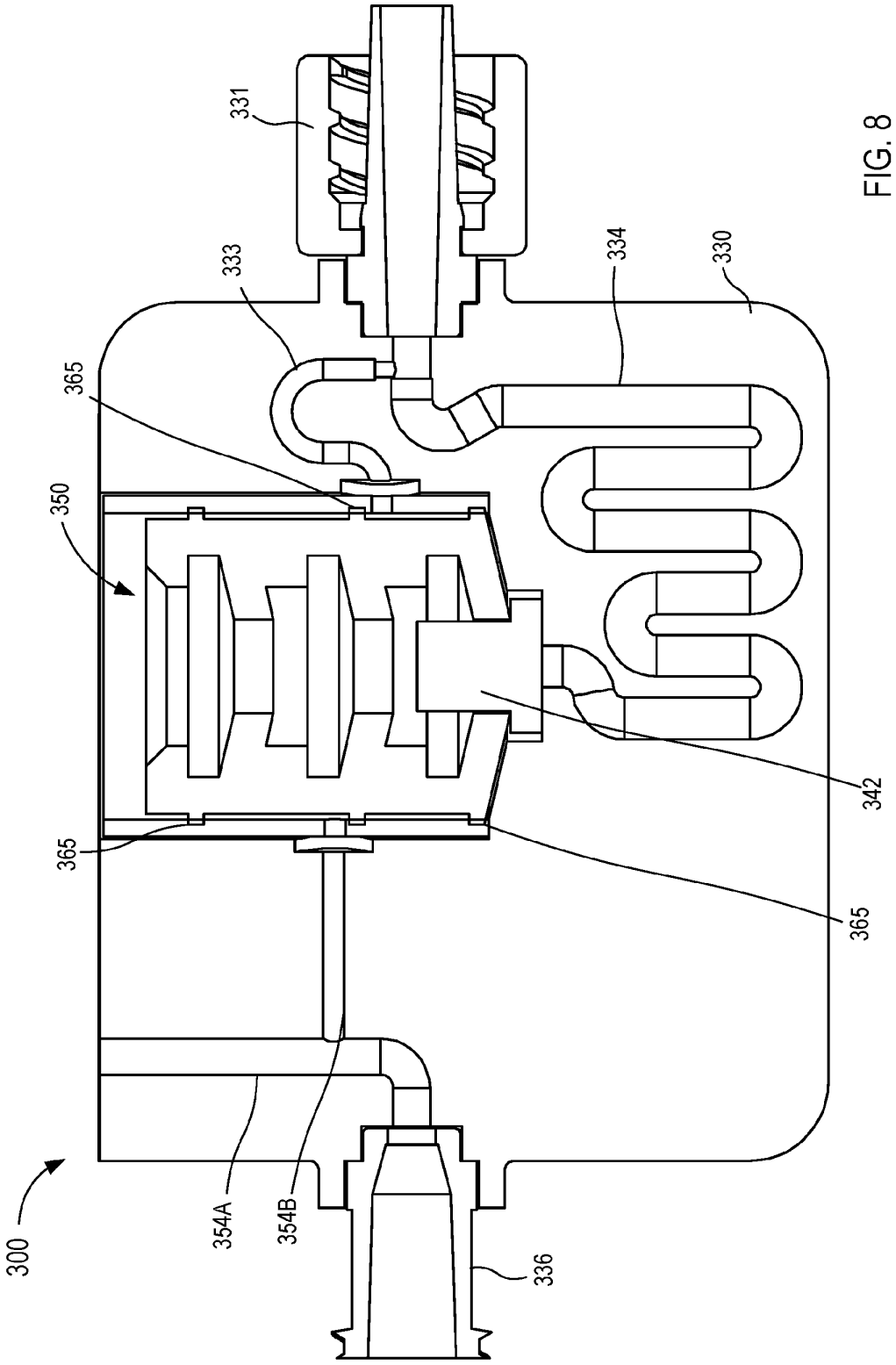


FIG. 8

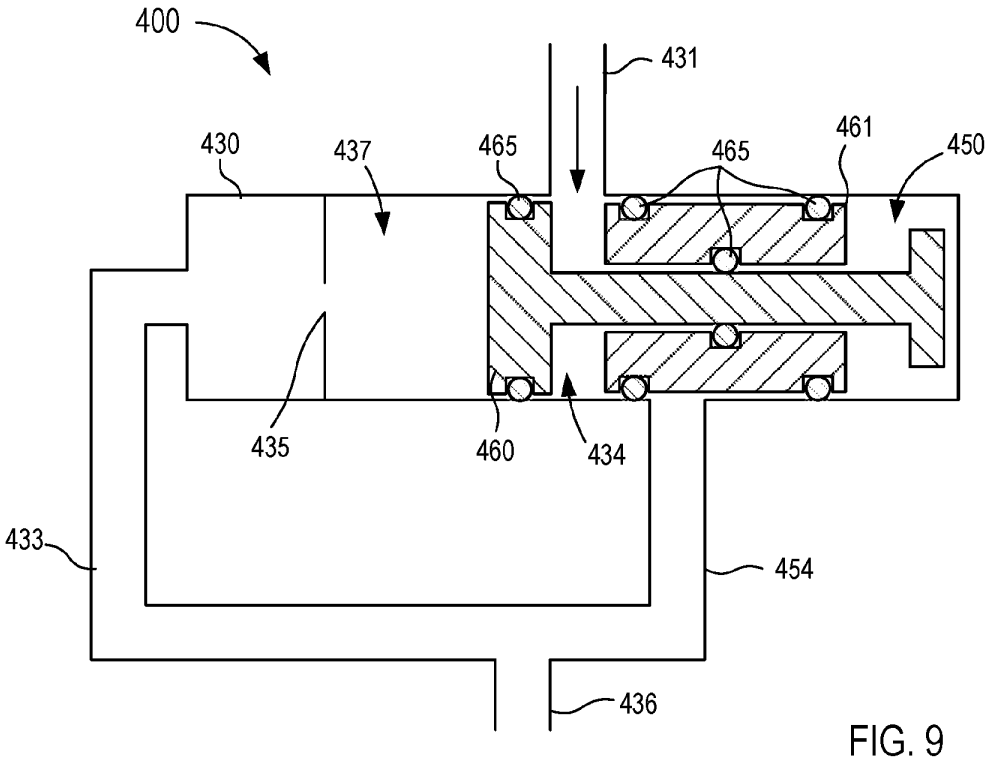

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FIG. 9

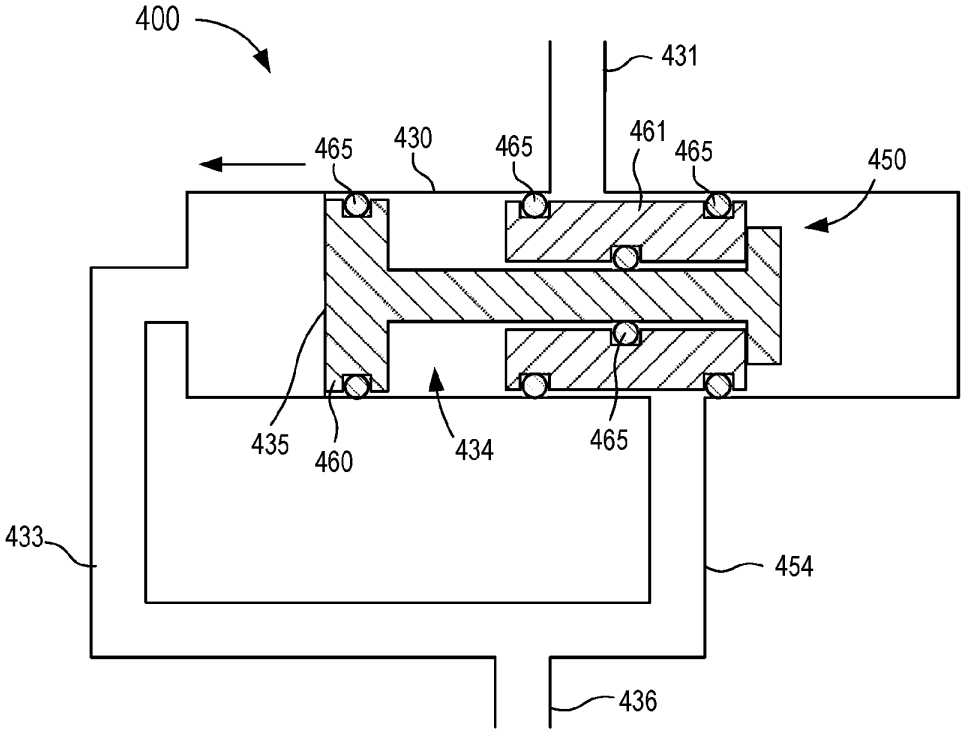

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FIG. 10

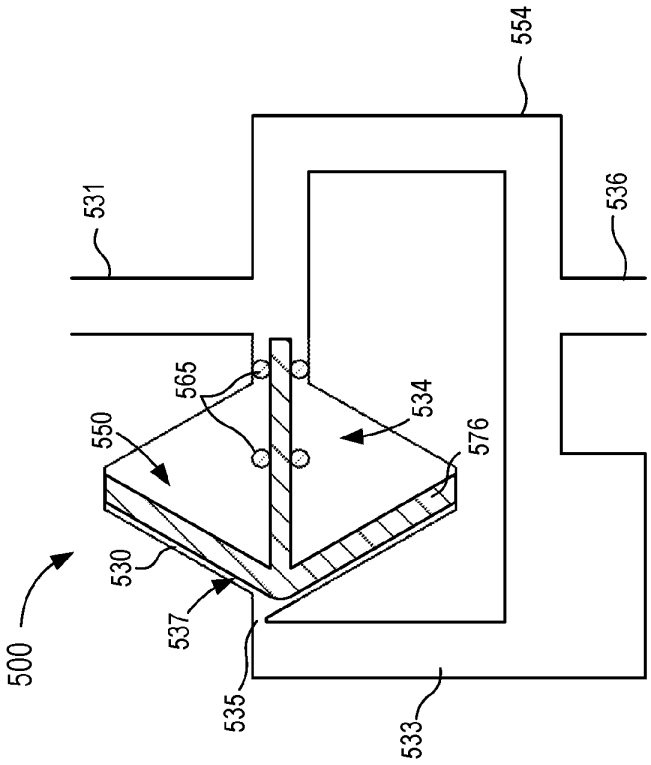

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FIG. 12

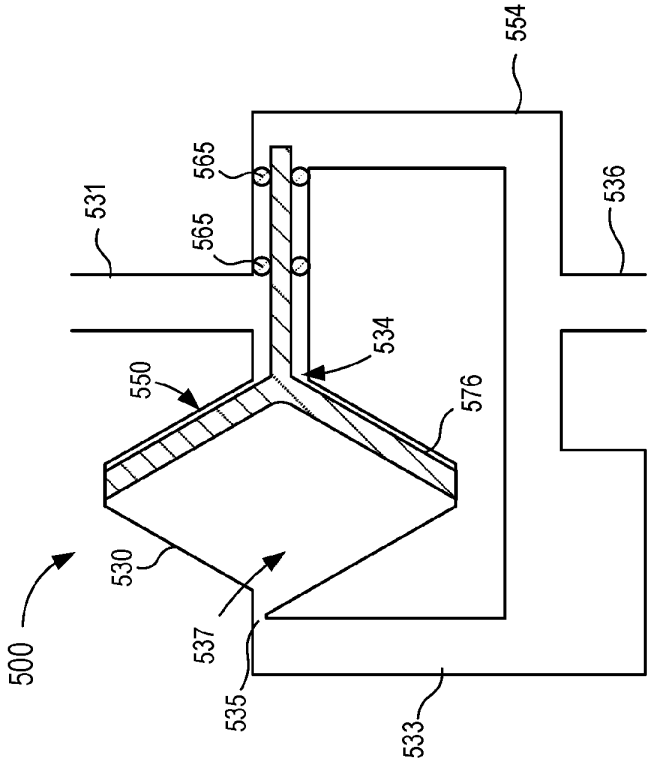

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FIG. 11

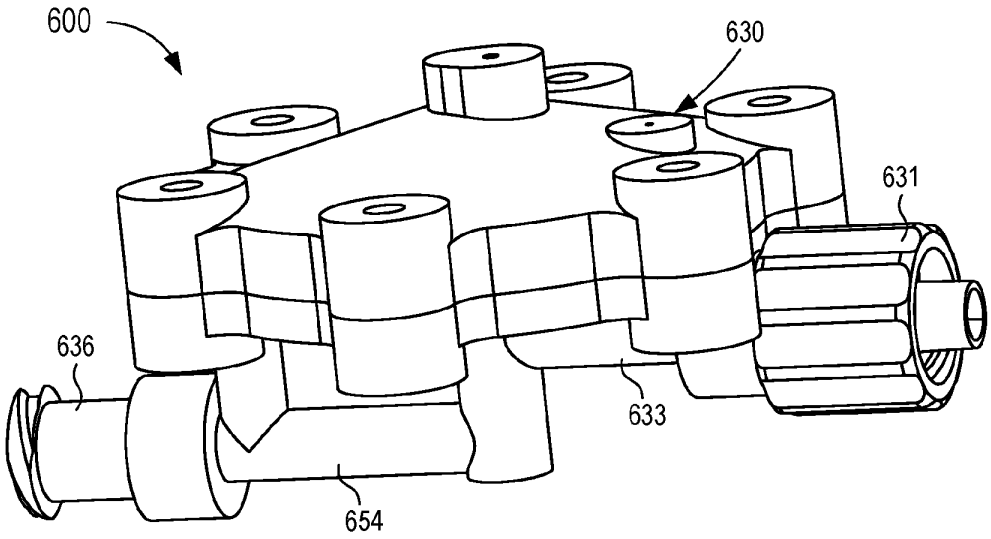

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FIG. 13

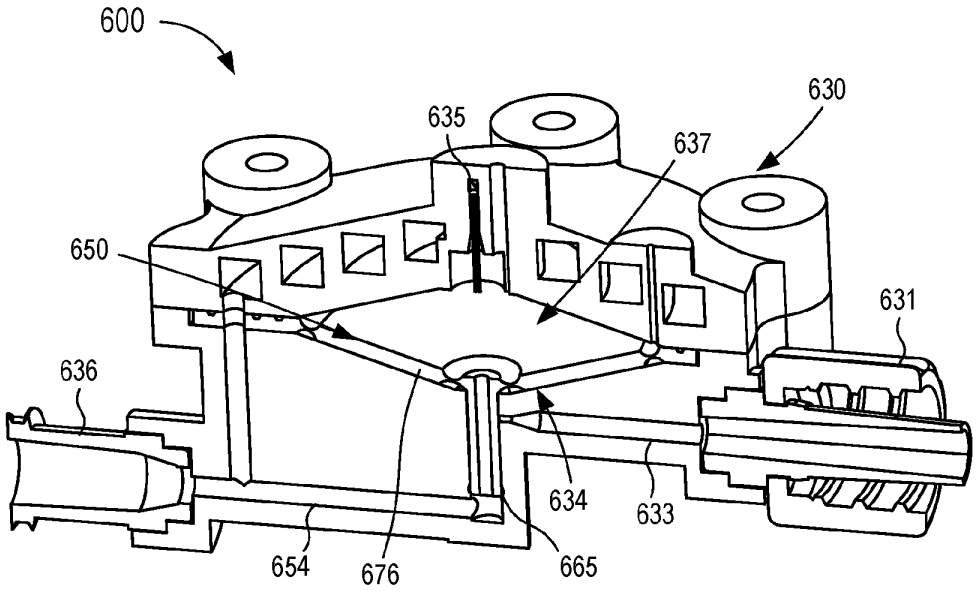

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FIG. 14

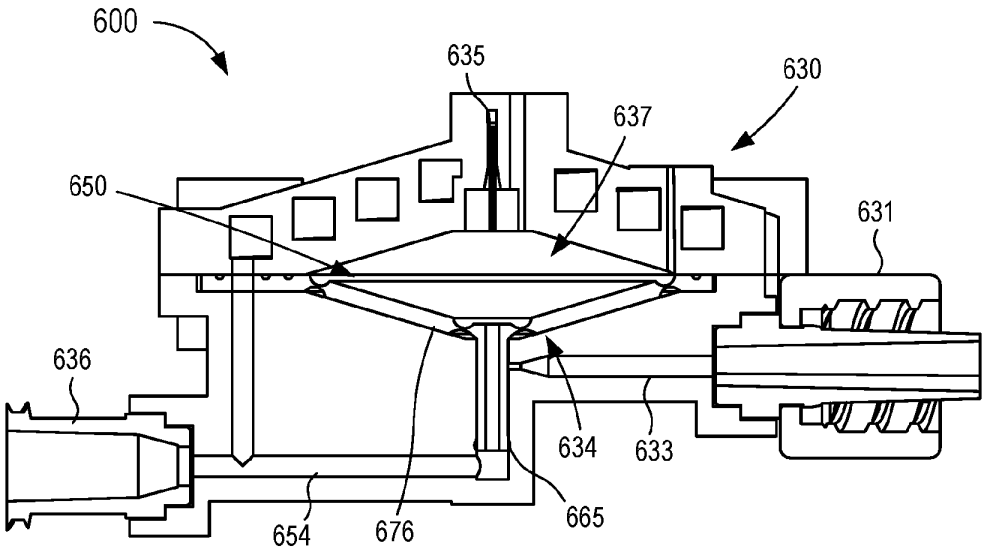


FIG. 15A

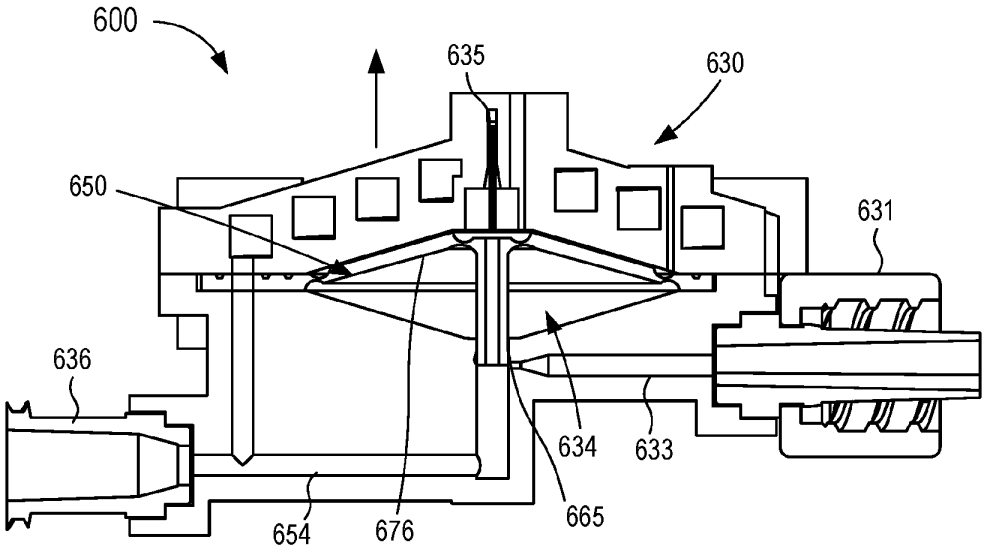


FIG. 15B

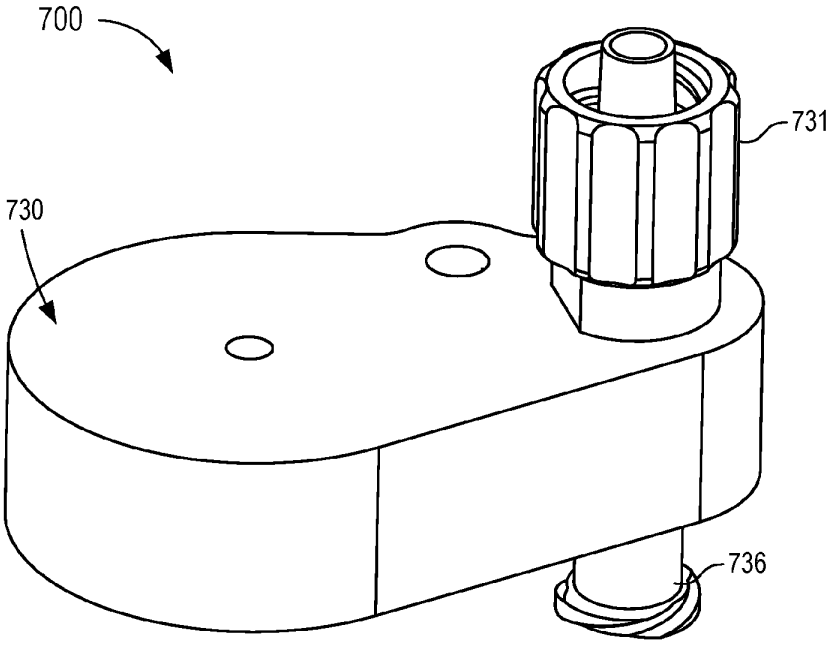


FIG. 16

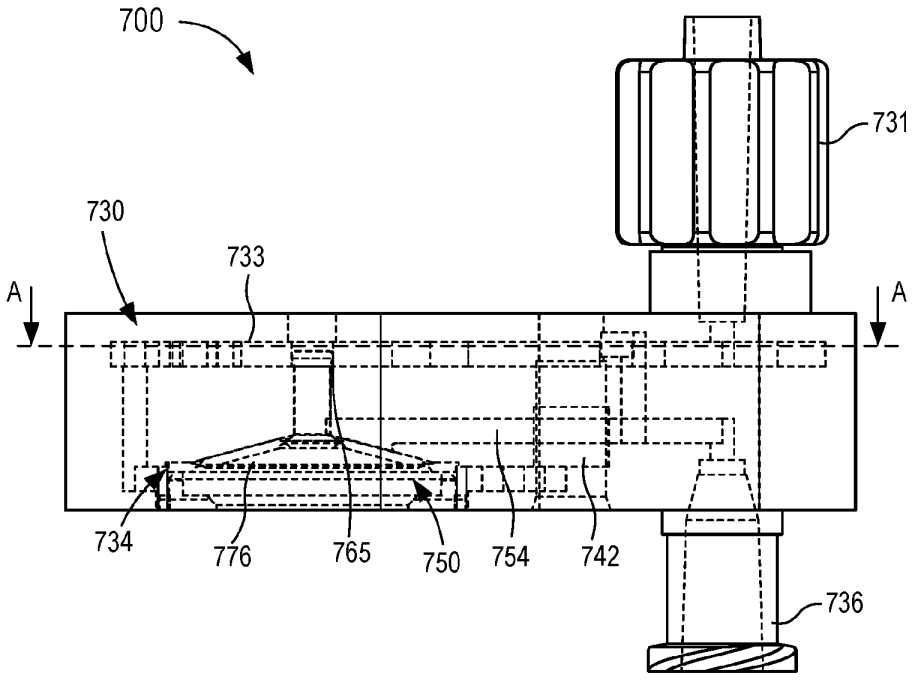


FIG. 17A

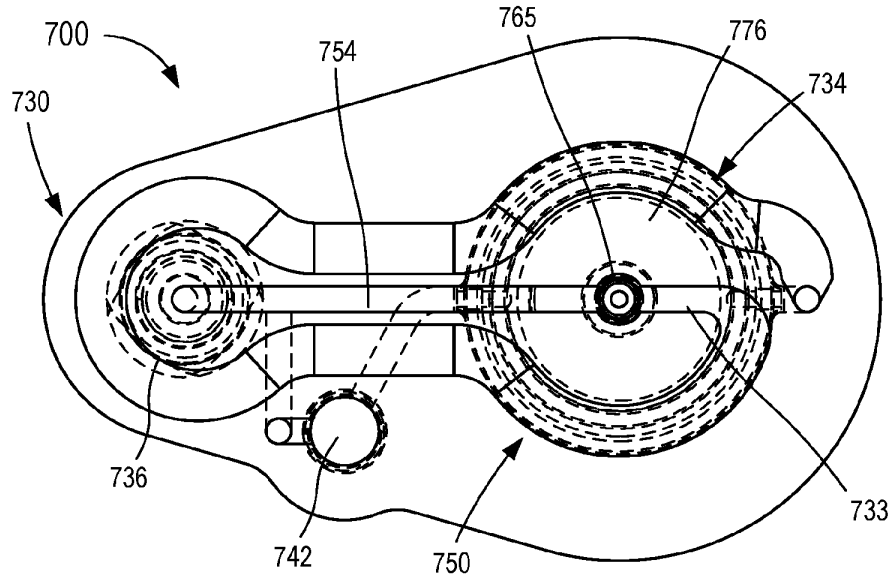


FIG. 17B

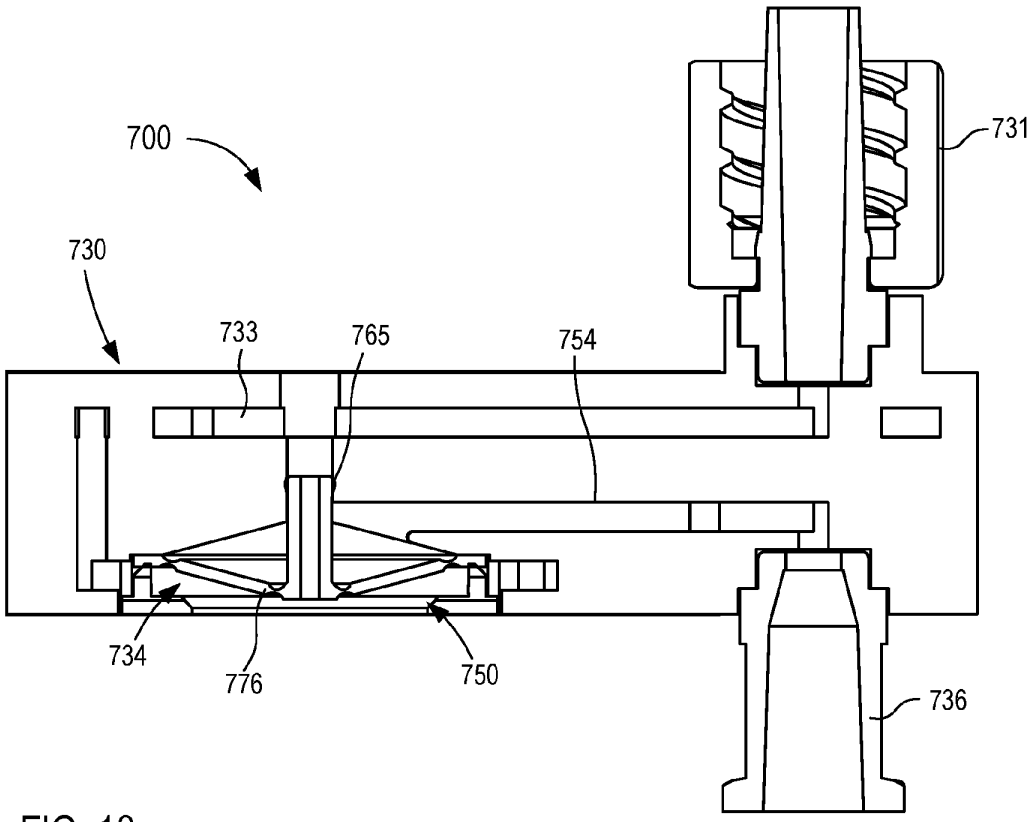


FIG. 18

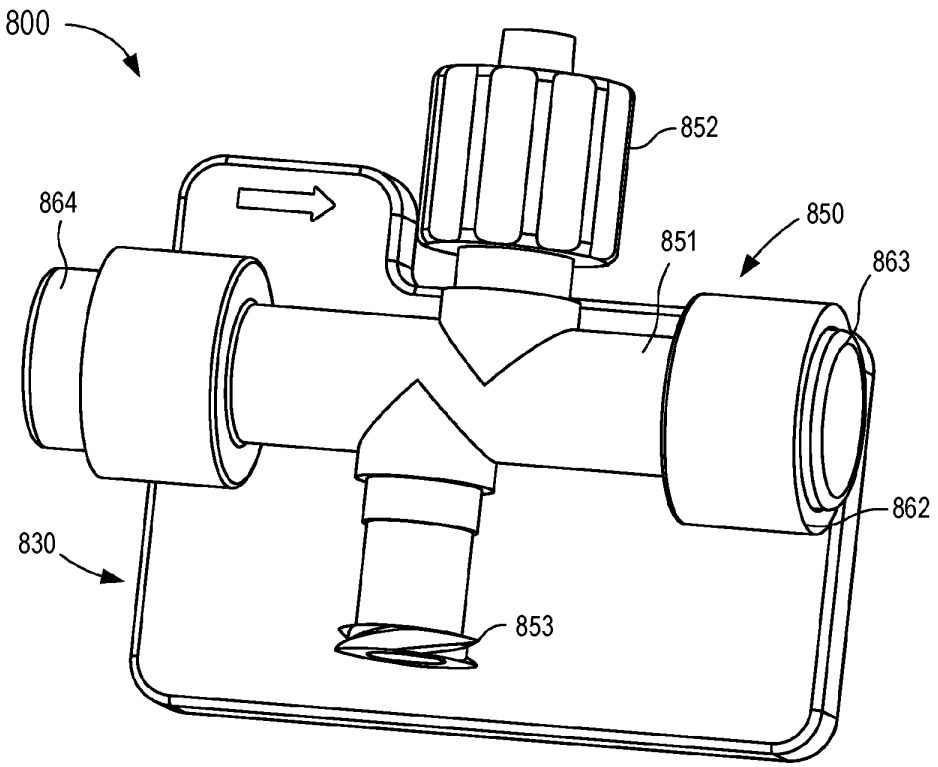


FIG. 19

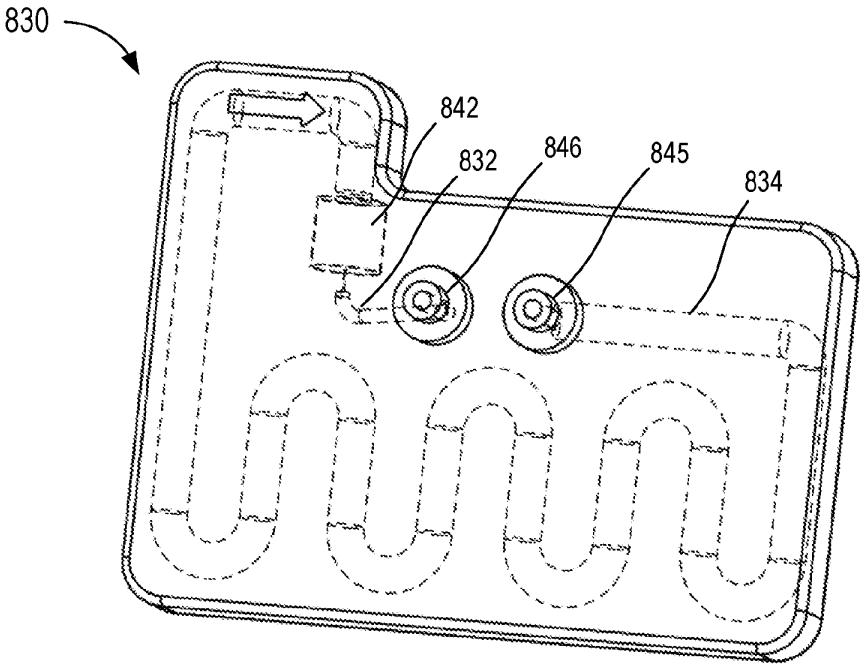


FIG. 20

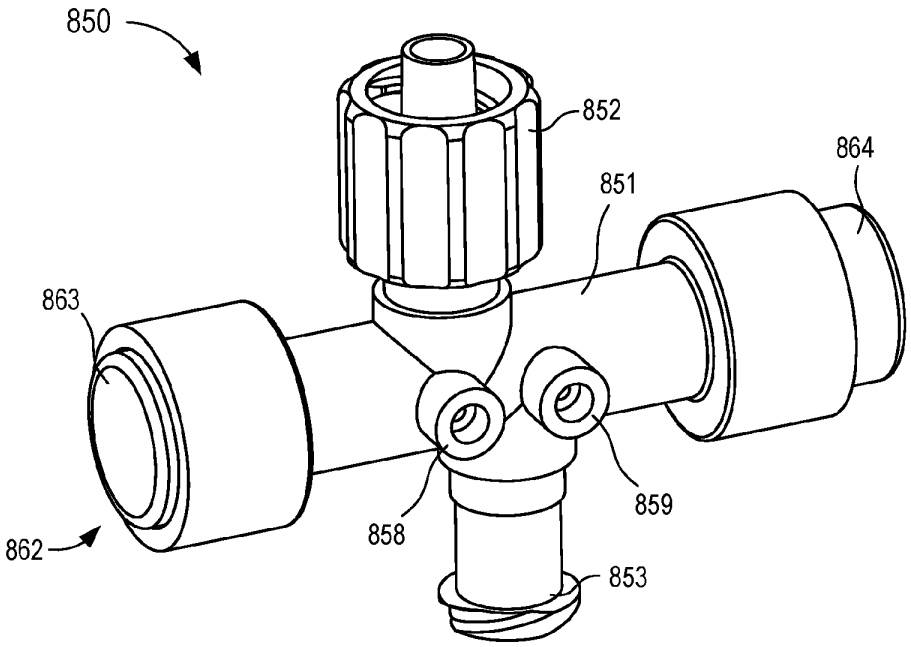


FIG. 21

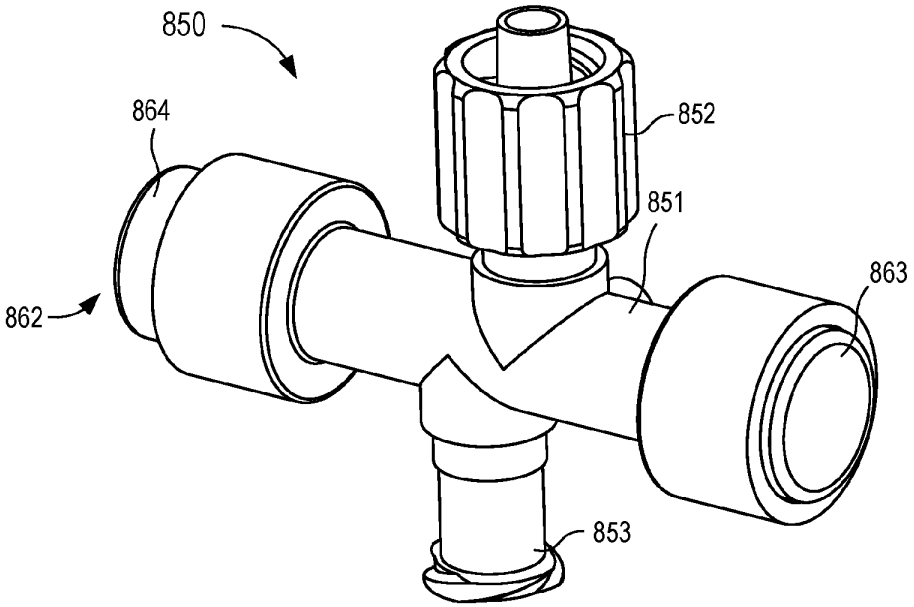


FIG. 22

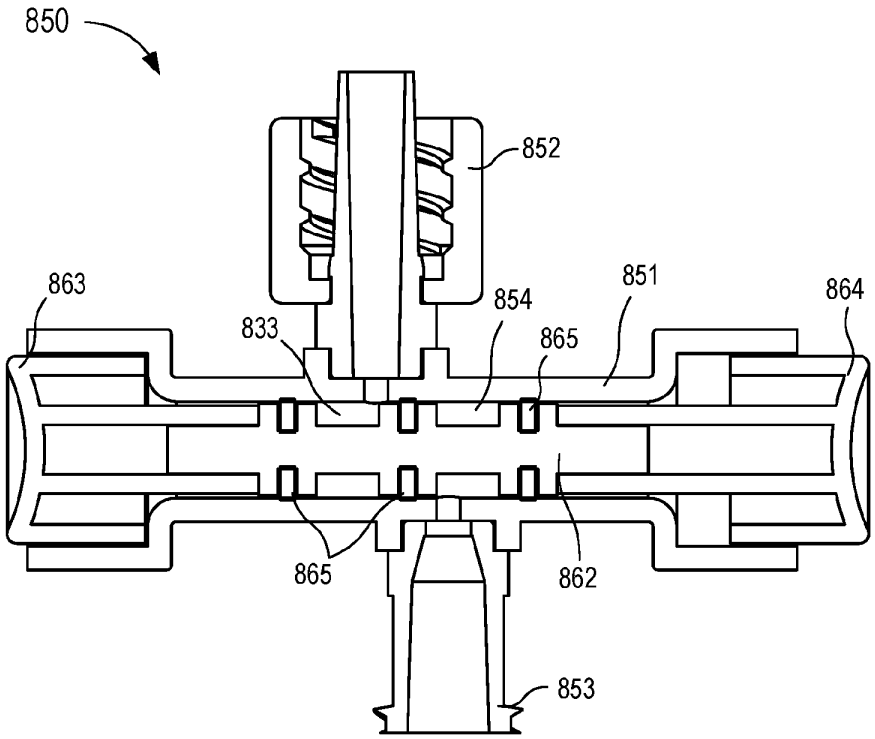

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FIG. 23

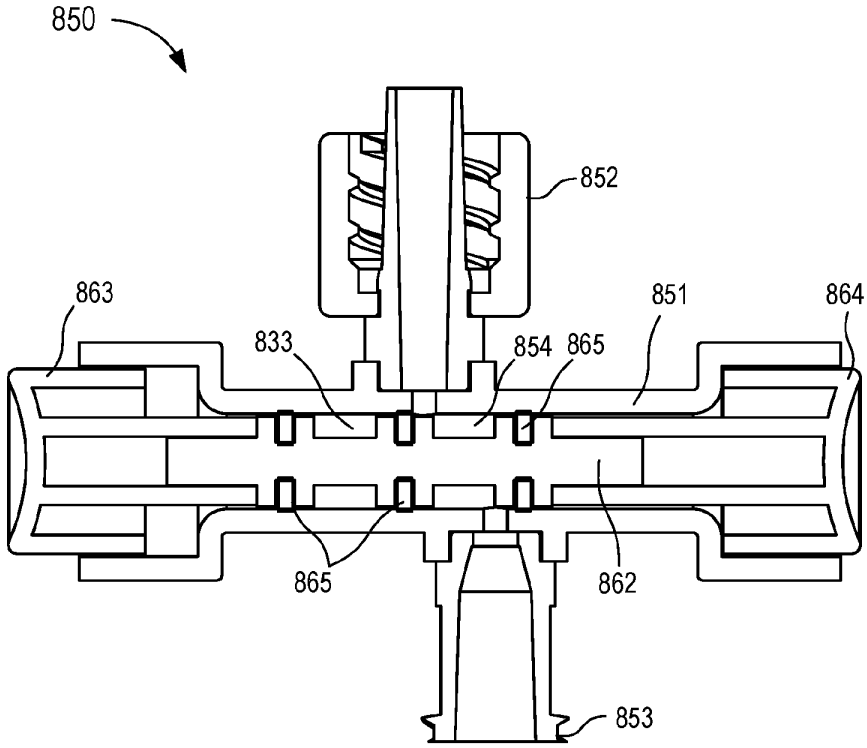

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FIG. 24

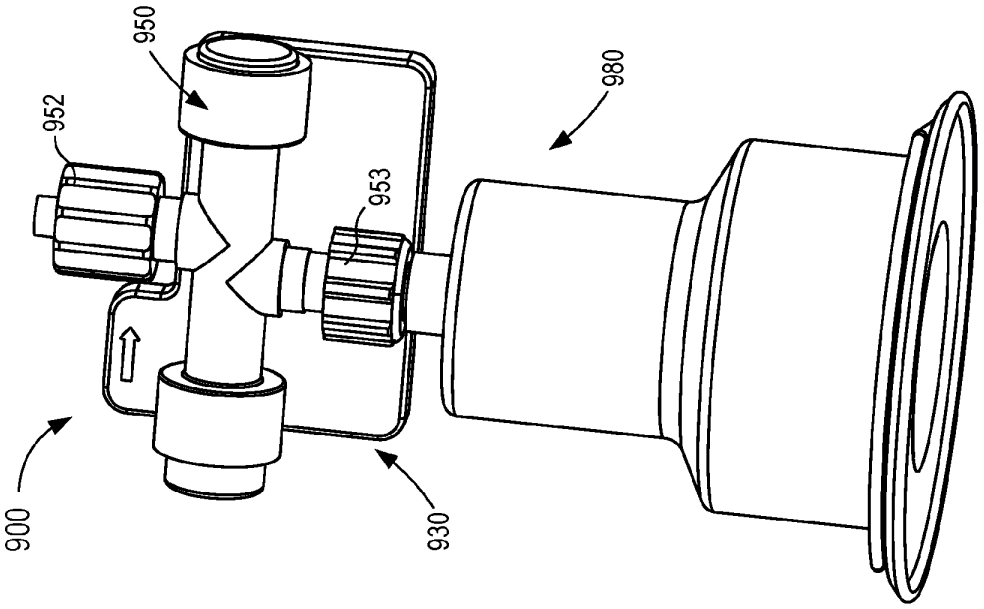


FIG. 26

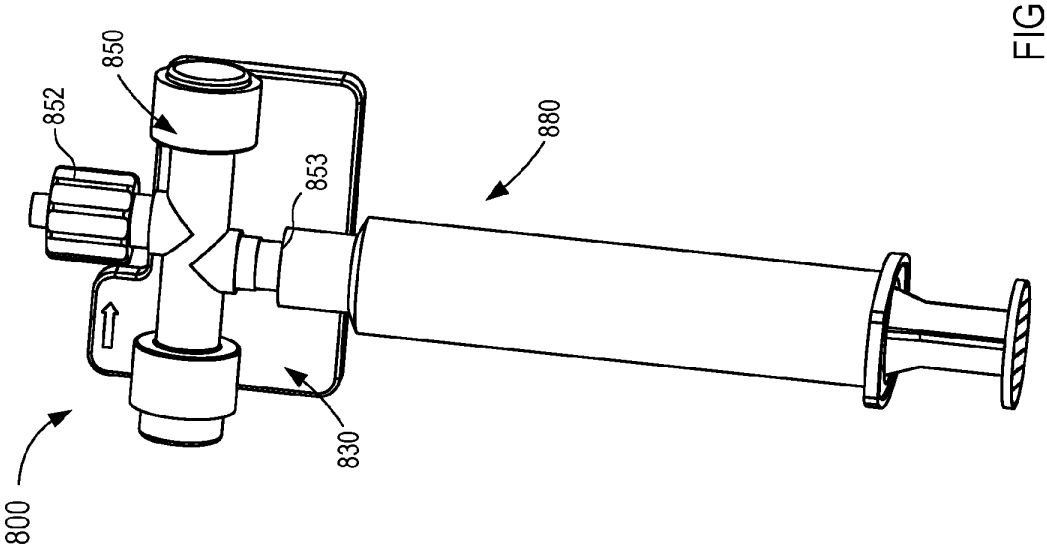


FIG. 25

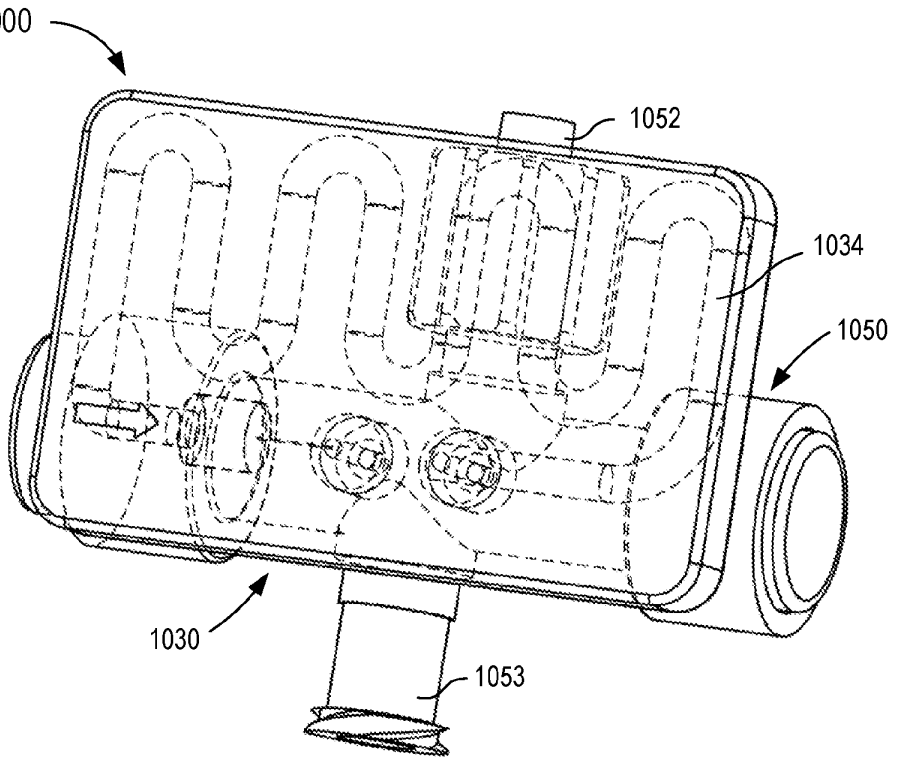


FIG. 27

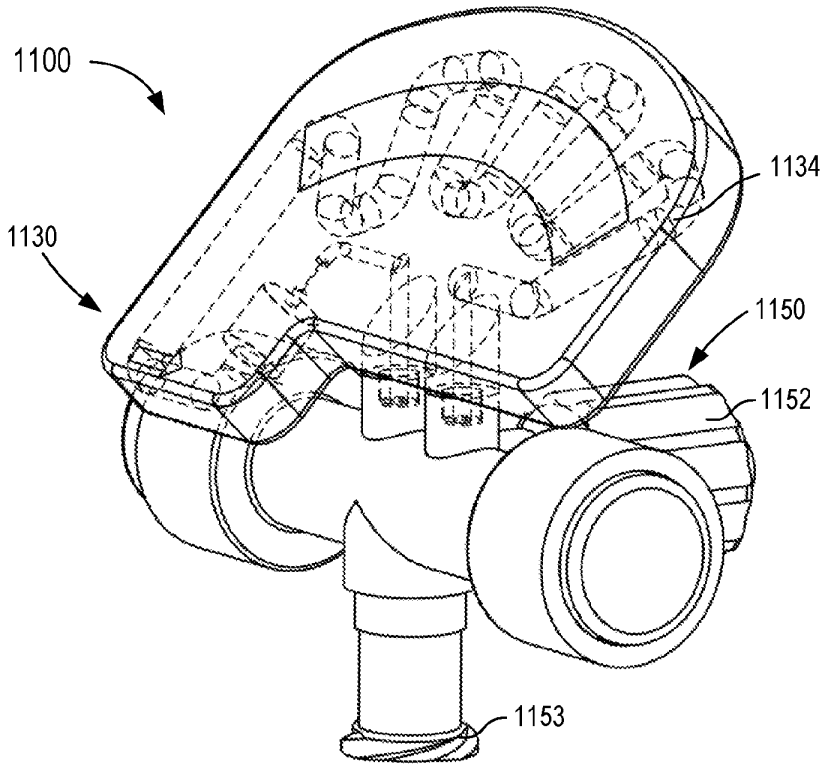


FIG. 28

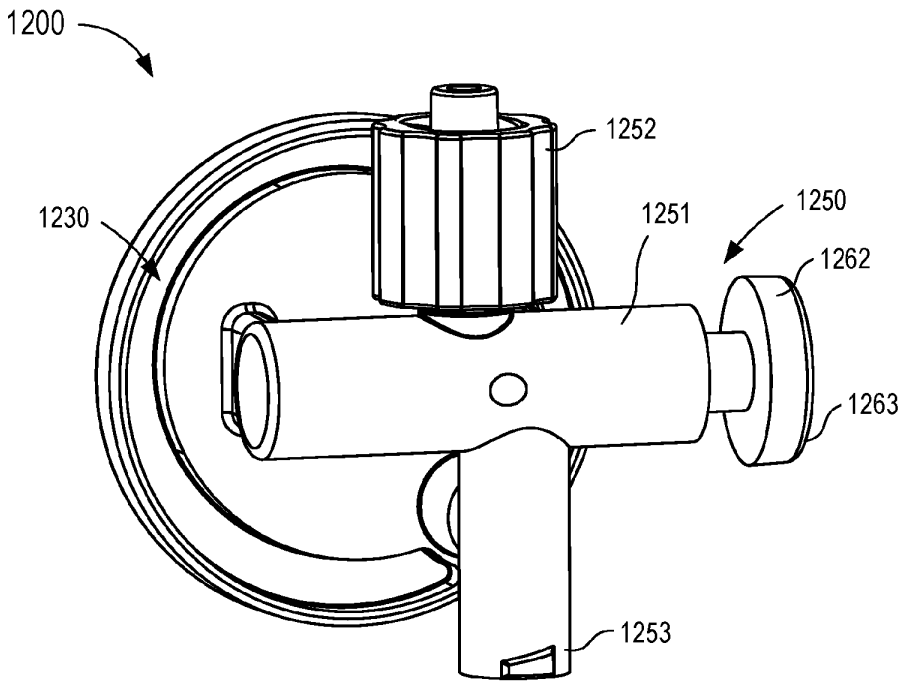

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FIG. 29

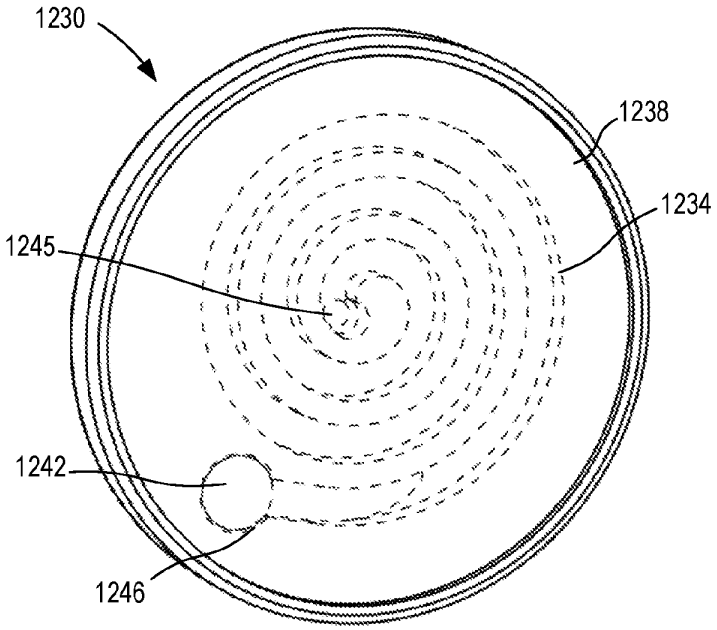

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FIG. 30

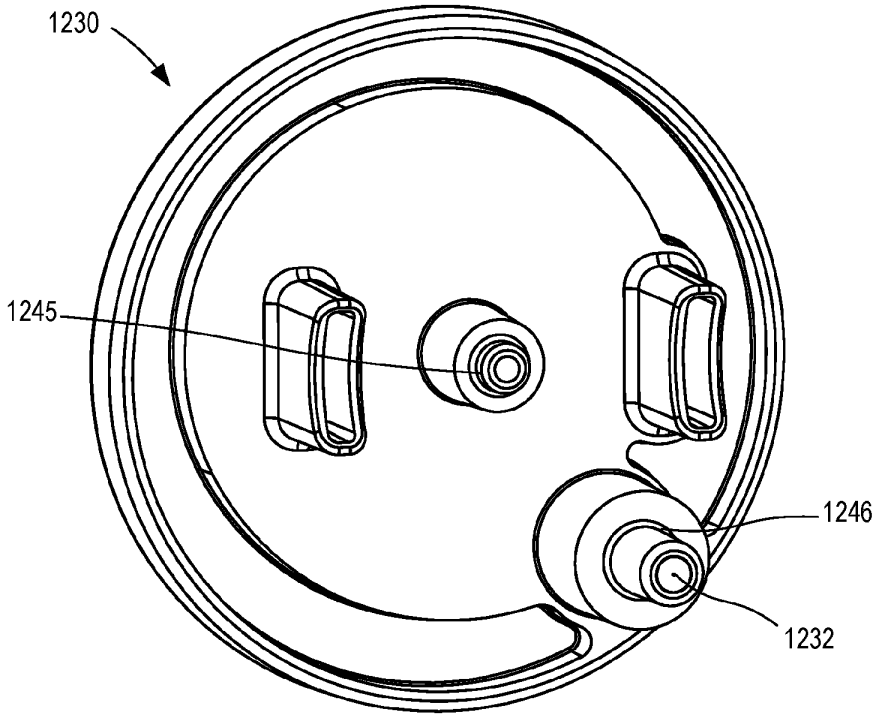

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FIG. 31

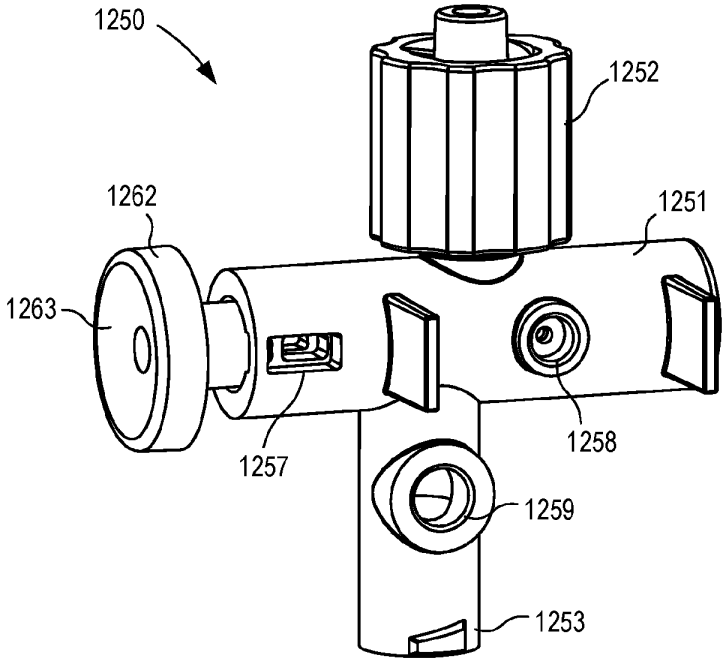

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FIG. 32

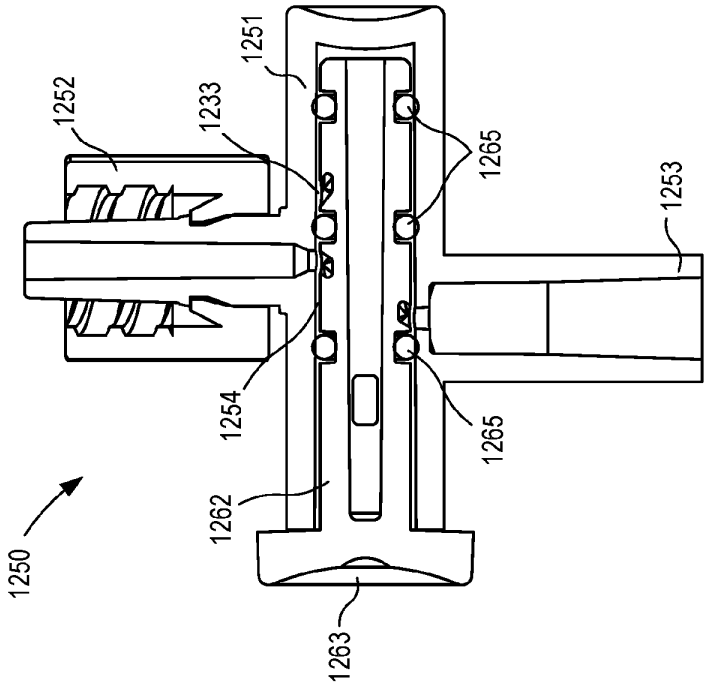

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FIG. 34

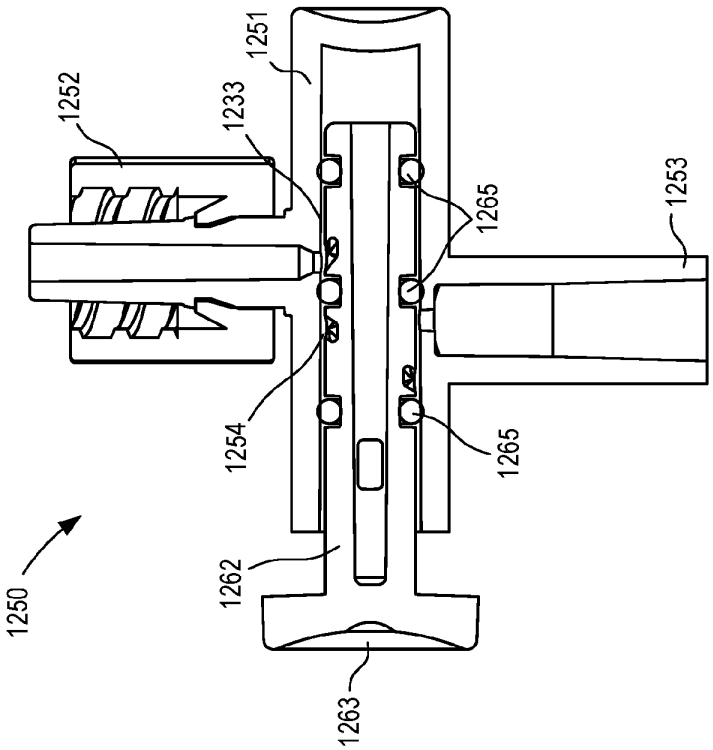

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FIG. 33

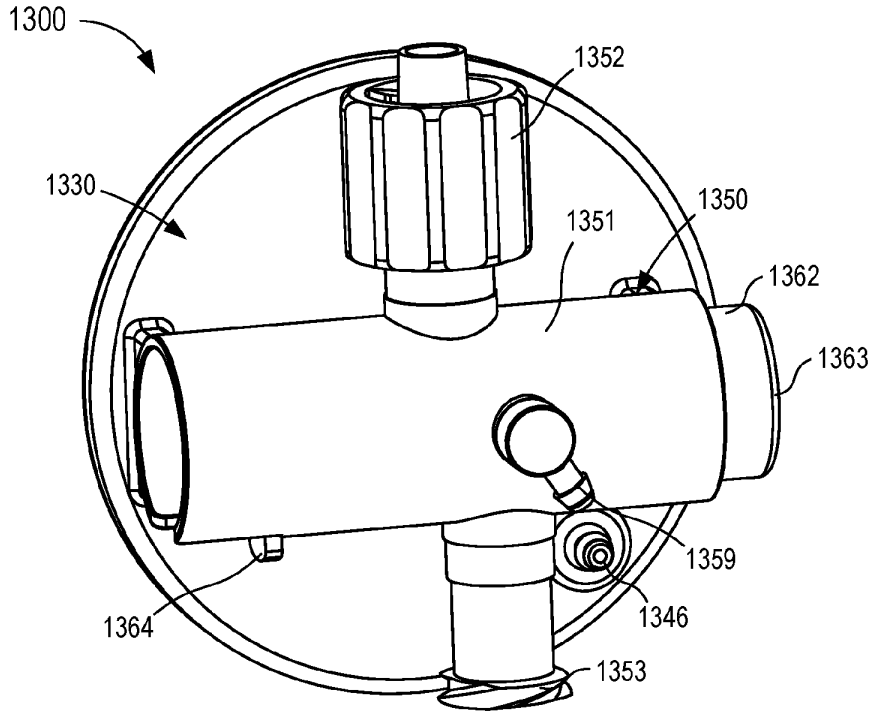

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FIG. 35

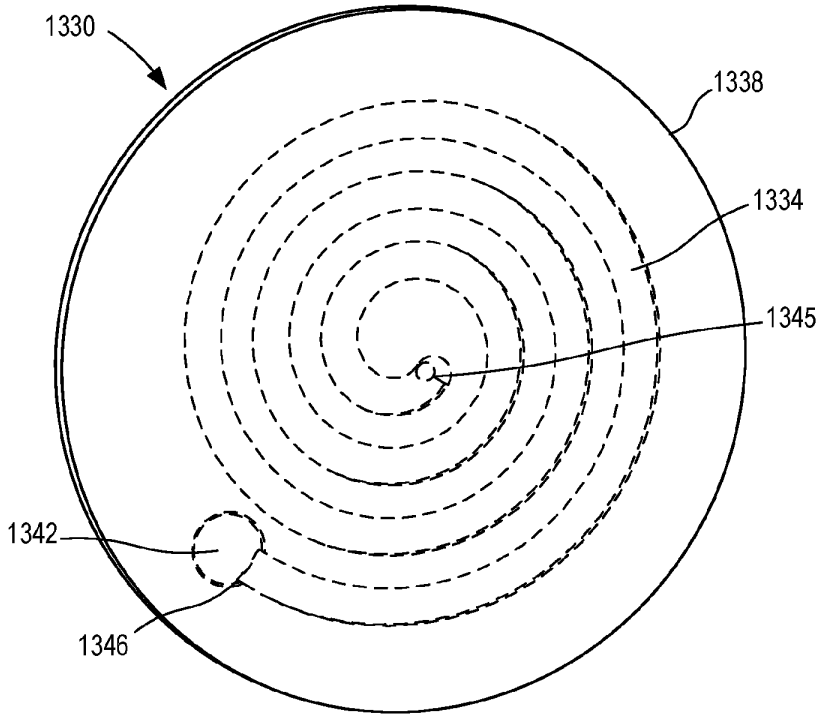

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FIG. 36

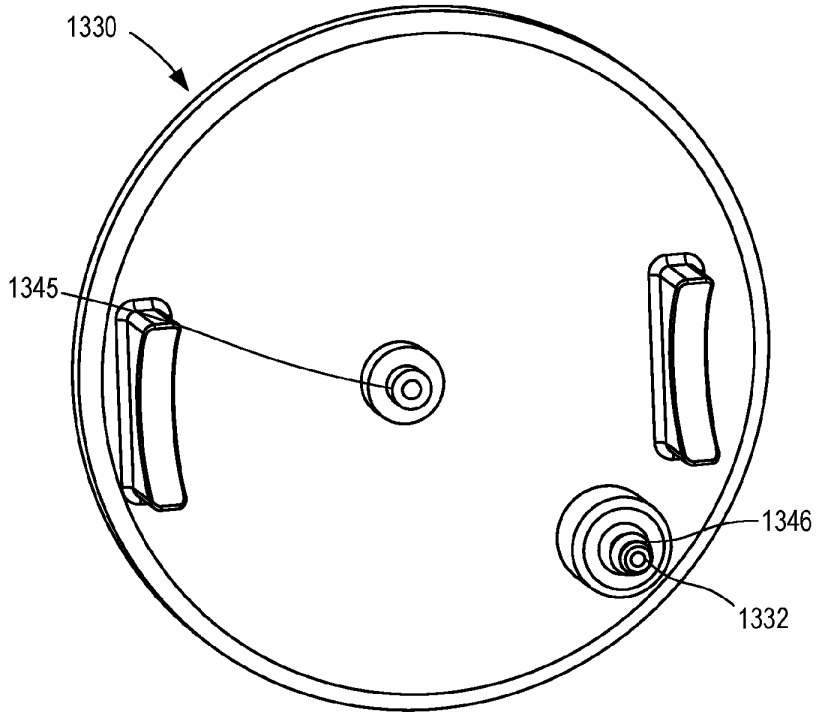


FIG. 37

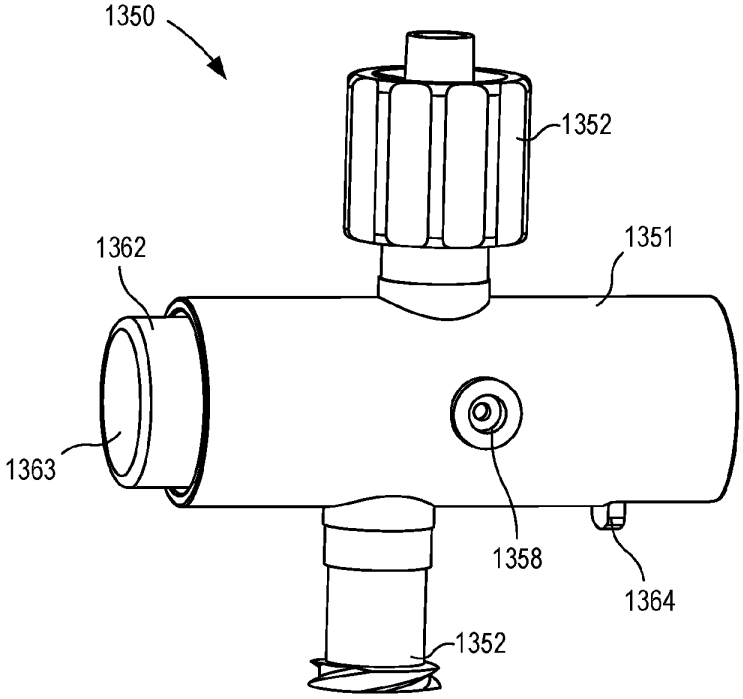


FIG. 38

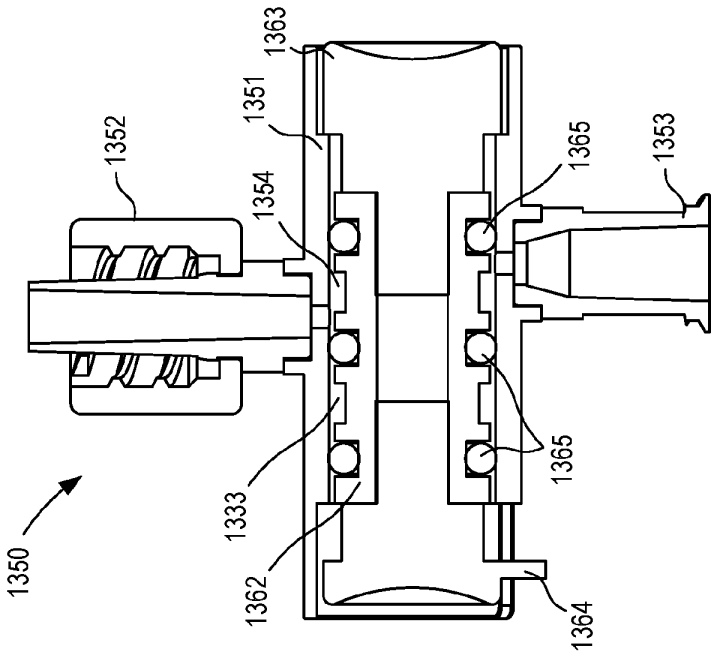

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FIG. 40

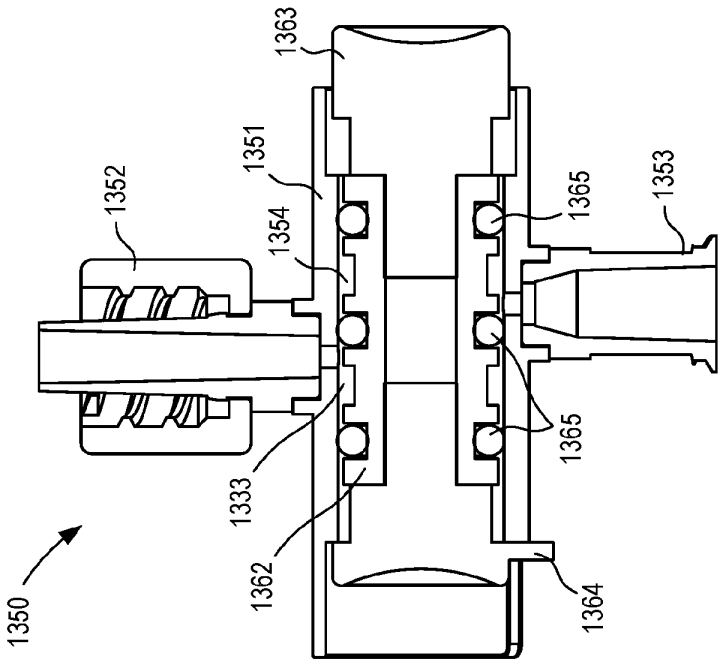

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FIG. 39

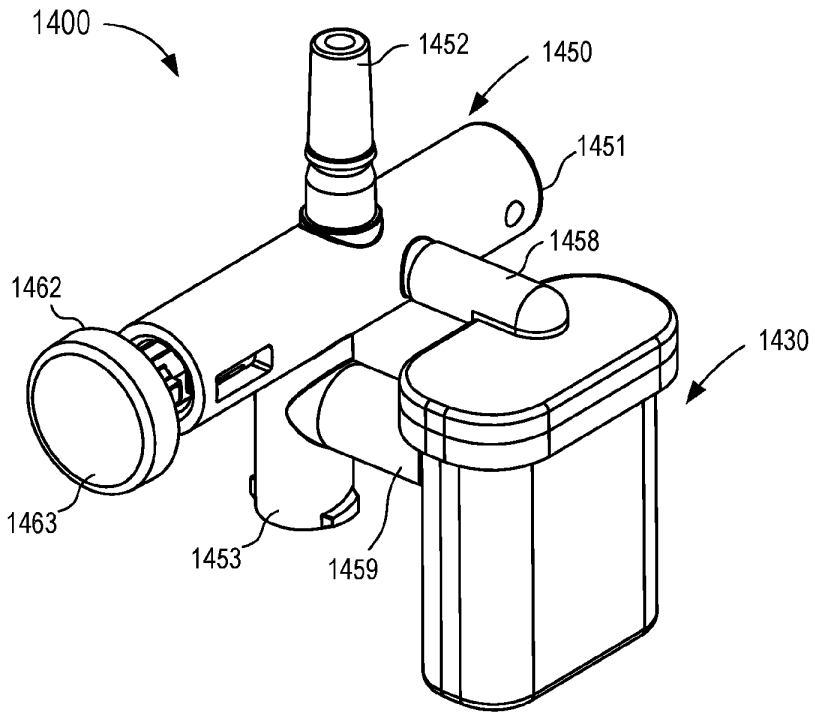

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FIG. 41

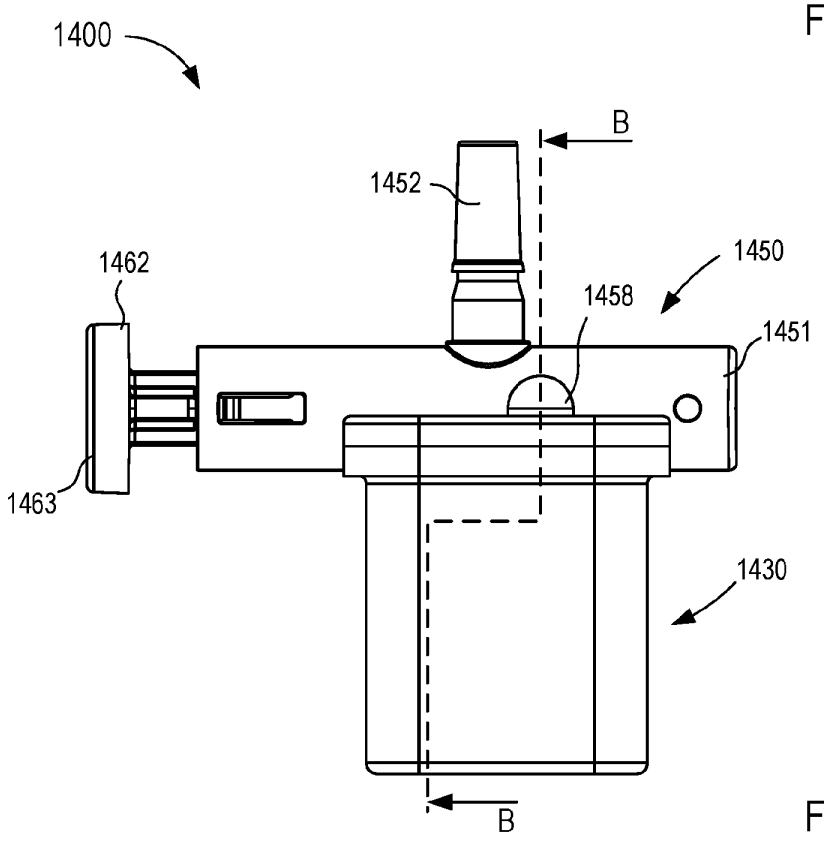

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FIG. 42

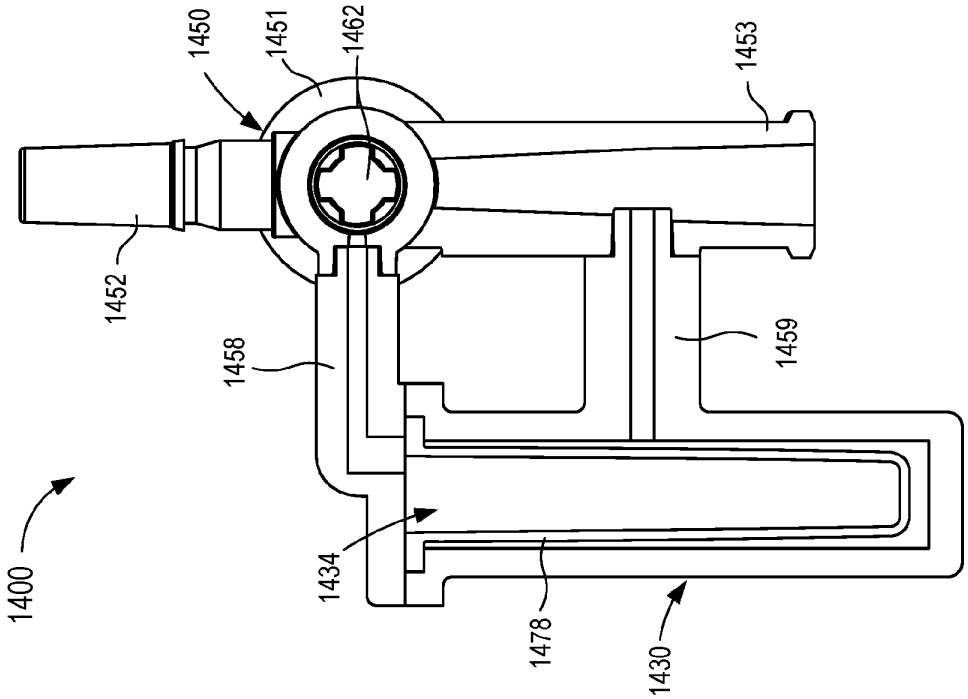

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SECTION B-B

FIG. 44

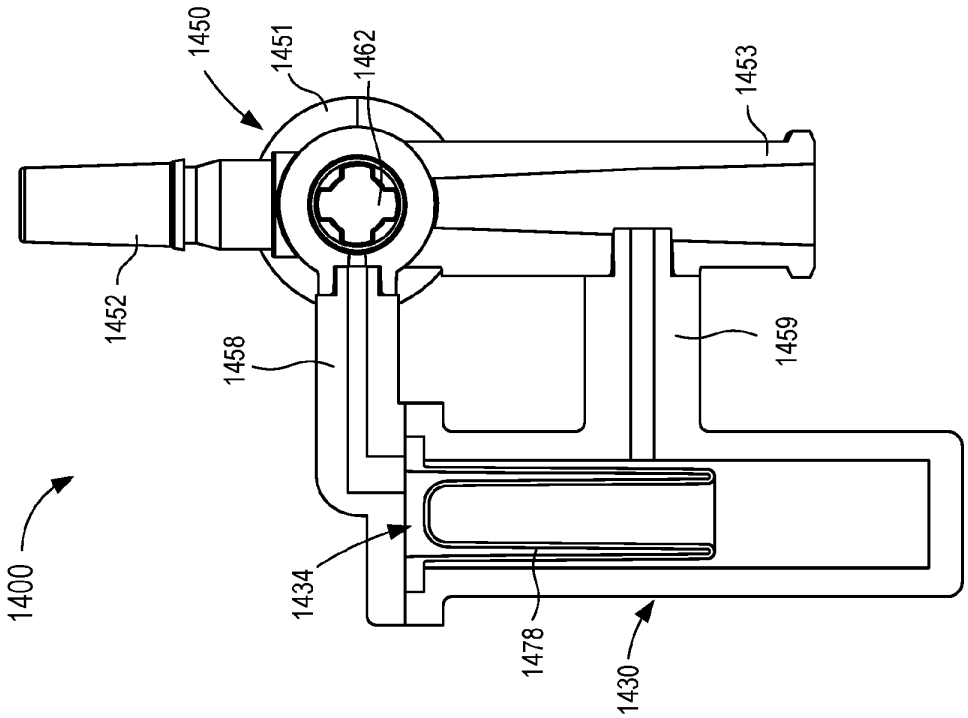

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SECTION B-B

FIG. 43

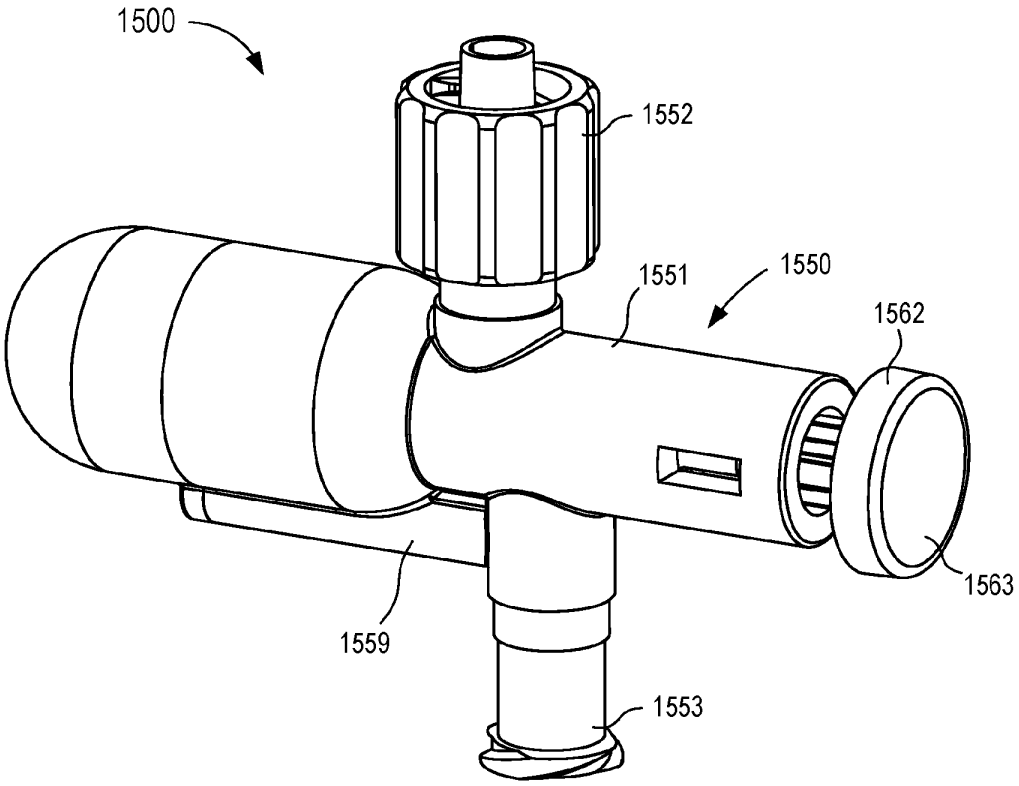

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FIG. 45

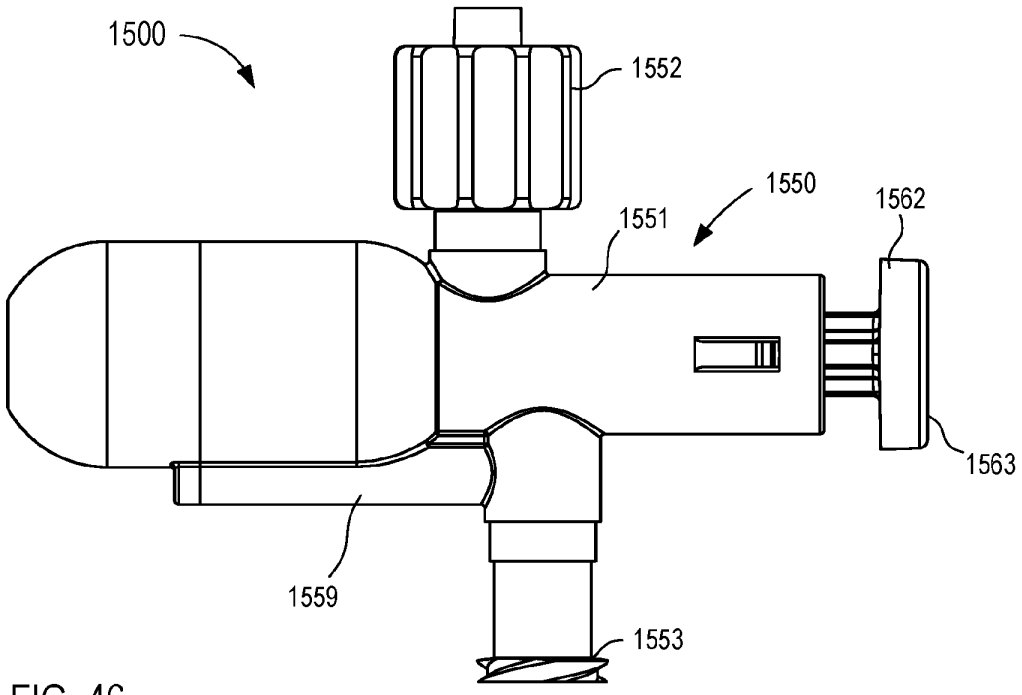

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FIG. 46

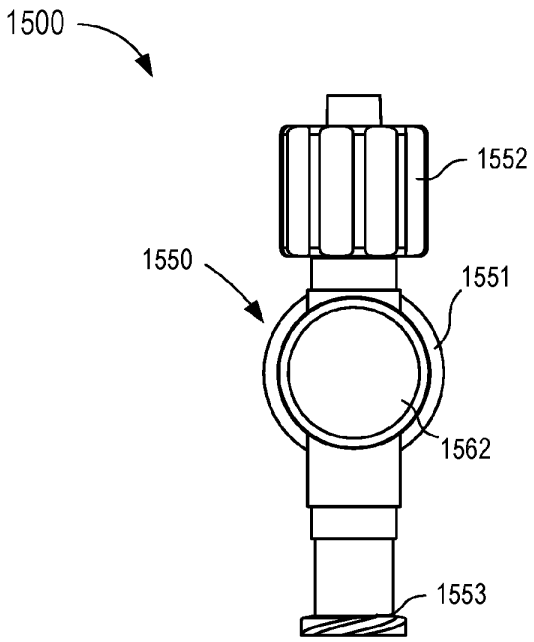

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FIG. 47

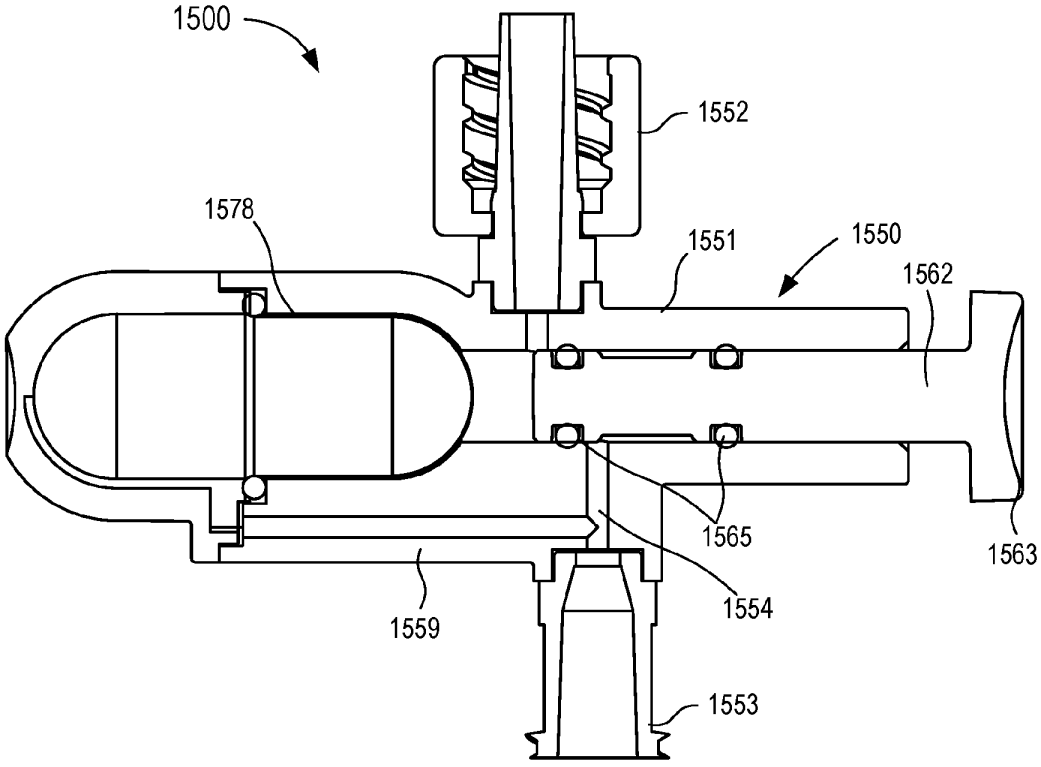

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FIG. 48

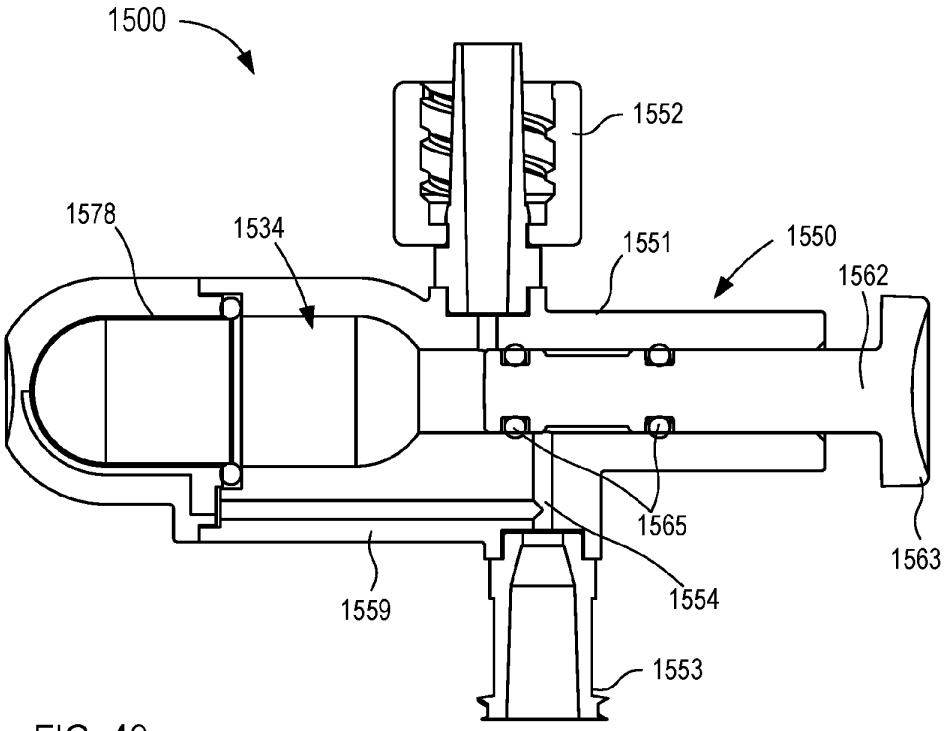

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FIG. 49

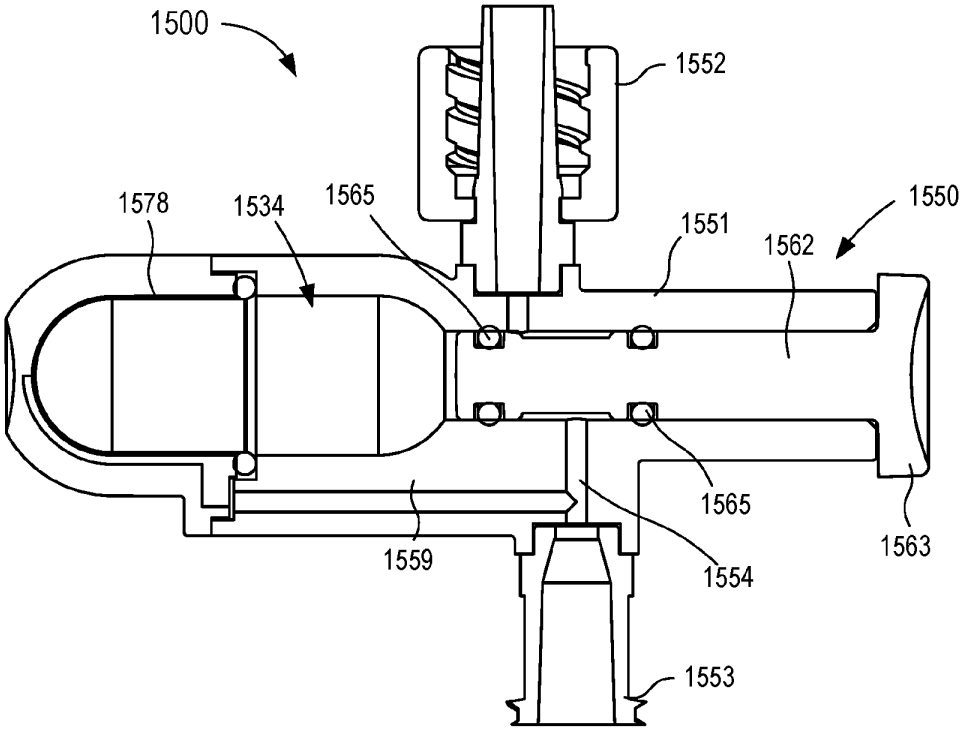

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FIG. 50

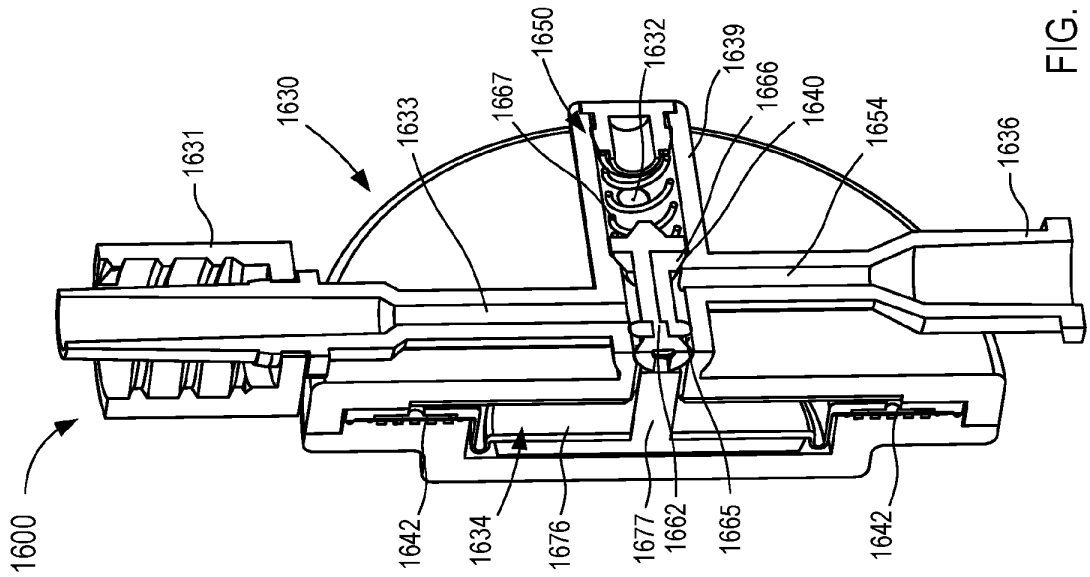

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FIG. 52

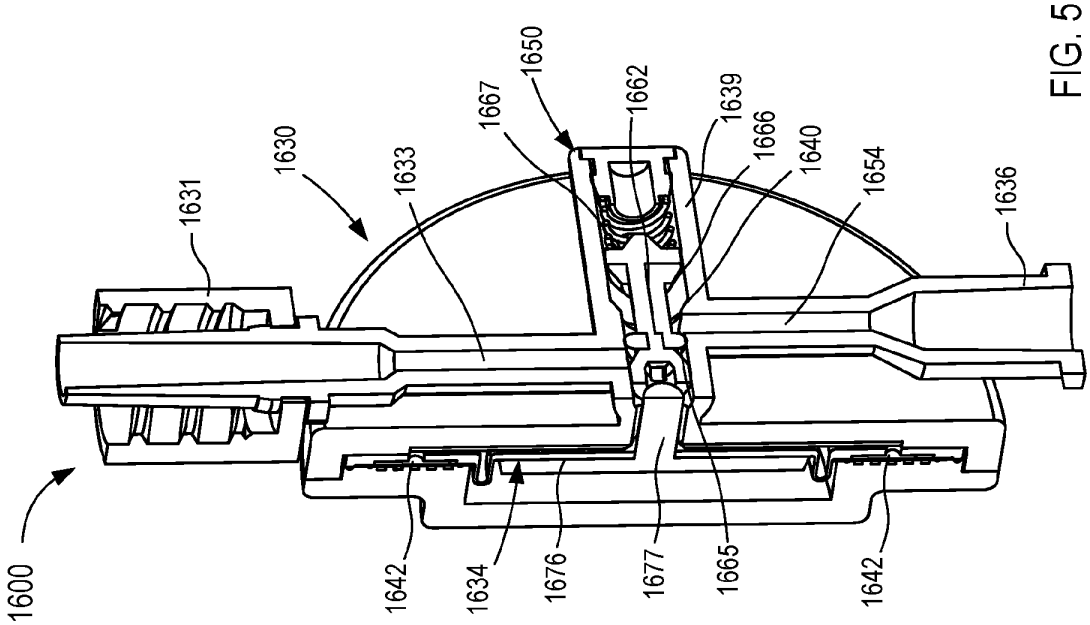

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FIG. 51

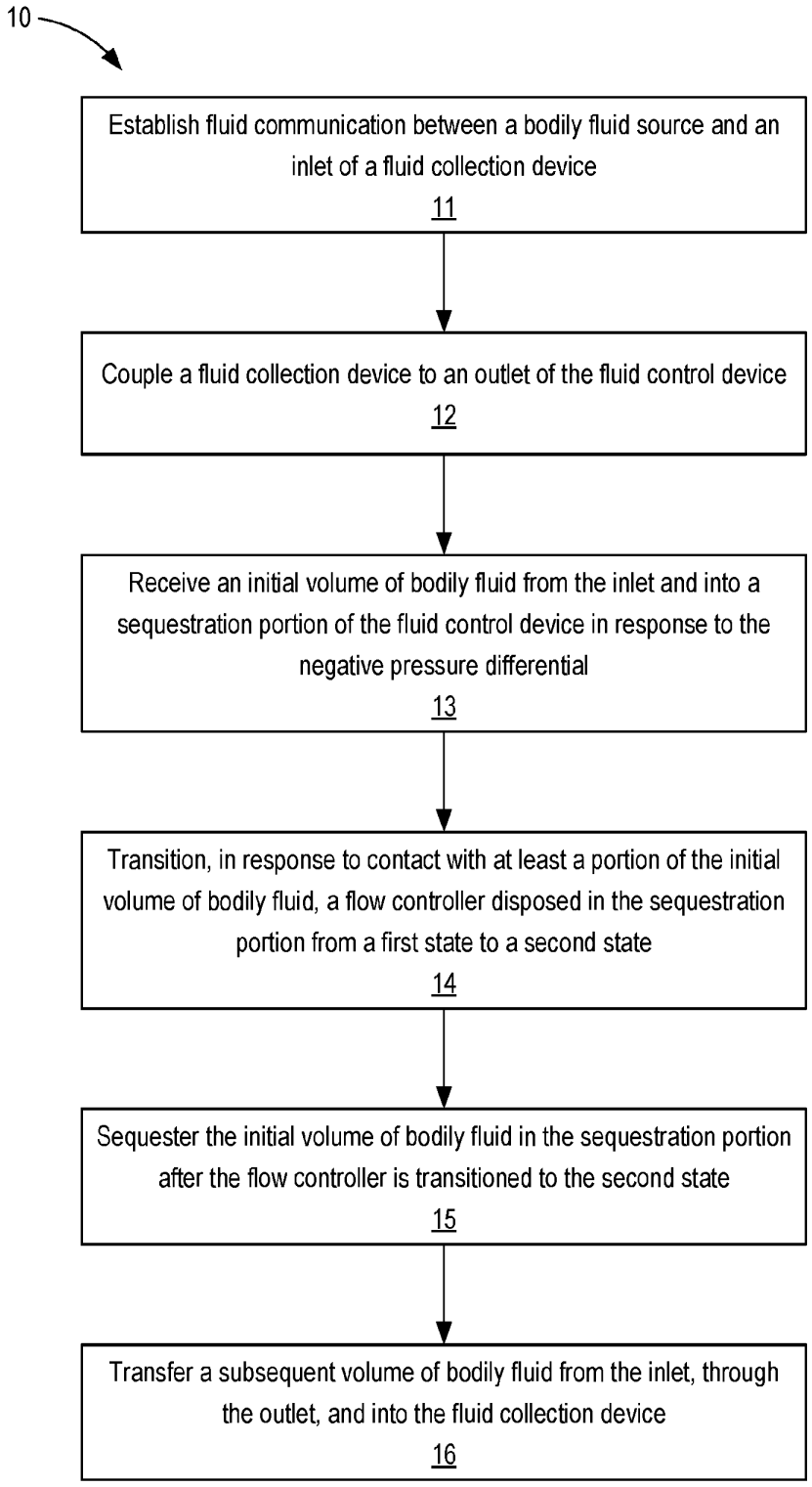

10
Establish fluid communication between a bodily fluid source and an inlet of a fluid collection device
11
Couple a fluid collection device to an outlet of the fluid control device
12
Receive an initial volume of bodily fluid from the inlet and into a sequestration portion of the fluid control device in response to the negative pressure differential
13
Transition, in response to contact with at least a portion of the initial volume of bodily fluid, a flow controller disposed in the sequestration portion from a first state to a second state
14
Sequester the initial volume of bodily fluid in the sequestration portion after the flow controller is transitioned to the second state
15
Transfer a subsequent volume of bodily fluid from the inlet, through the outlet, and into the fluid collection device
16

FIG. 53

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 18/50621

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - A61B 5/00, A61B 17/00, A61M 1/00, A61M 39/00 (2018.01)

CPC - A61B 5/00, A61B 5/02, A61B 5/03, A61B 5/06, A61B 5/14, A61B 5/1405, A61B 5/145, A61B 5/15, A61B 5/150007, A61B 5/150099, A61B 5/150206, A61B 5/150221, A61B 5/150251, A61B 5/150755, A61B 5/153, A61B 5/154, A61B 5/155, A61B 5/157, A61M 1/00, A61M 1/0001, A61M 1/0031, A61M 1/0035, A61M 1/0058, A61M 1/0066, A61M 1/10, A61M 1/1037, A61M 1/1086, A61M 1/34, A61M 1/36, A61M 39/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

See Search History Document

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

See Search History Document

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

See Search History Document

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- Y --- A	US 2014/0163419 A1 (MAGNOLIA MEDICAL TECHNOLOGIES, INC.) 12 June 2014 (12.06.2014), entire document, especially Figs. 11-15; paras [0079]-[0099])	1-3, 8-21, 24, 29, 32-36 --- 4-5, 25, 30 --- 6-7, 22-23, 26-28, 31
Y --- A	US 6,511,439 B1 (TABATA et al.) 28 January 2003 (28.01.2003), entire document, especially Fig. 1; col 4, ln 48-51; col 9; ln 48-51	4-5, 25, 30 --- 6-7, 22-23, 26-28, 31
A	US 8,876,734 B2 (MAGNOLIA MEDICAL TECHNOLOGIES, INC.) 4 November 2014 (04.11.2014), entire document	1-36
A	US 2014/0107564 A1 (MAGNOLIA MEDICAL TECHNOLOGIES, INC.) 17 April 2014 (17.04.2014), entire document	1-36
A	US 2013/0116599 A1 (BULLIUNGTON et al.) 9 May 2013 (09.05.2013), entire document	1-36
A	US 2015/0018715 A1 (WALTERSPIEL) 15 January 2015 (15.01.2015), entire document	1-36
A	US 2017/0020428 A1 (CALLIOPE SOLUTIONS, INC.) 26 January 2017 (26.01.2017), entire document	1-36

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:

"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
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)

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Literature display help

1 / 1 display

Japanese Patent Application Laid-Open No. 57-089869

Registration Gazette public notice Document unit PDF progress information OPD search key URLs

Display format of the document display screen:
text display PDF display

primary literature

The scope of the claims open

[Claims]

1. A single sample needle assembly adapted to recognize insertion of the needle into a blood vessel when collecting a blood sample from a patient into the evacuated vessel, the single sa mple needle assembly having at least a forward end, a rearward end and an interior chamber. a housing having a transparent portion surrounding the chamber so that a user can see the ch amber; a first opening formed in a front end of the housing and communicating with the cham ber; and a first opening extending outwardly into the chamber. a first puncture needle that co mmunicates and is inserted into a patient; a second opening that is formed in the rear end of the housing and communicates with the chamber; a second cannula closed and having two sp aced apart transverse holes, and a plug of air permeable blood impermeable material in fluid t ight sliding contact with the housing enclosing the chamber and the second puncture needle. said plug initially in a position covering a first side hole remote from said second opening and not covering the other second side hole from a first puncture needle under constant tournique t pressure; Blood entering the chamber is prevented by the plug from flowing out into the sec ond cannula, allowing only the air in the chamber to flow out so that the user can see through the transparent housing that the first needle has entered the blood vessel. , wherein a negativ e pressure gradient acting on the second opening causes the plug to slide to open the first lat

eral hole, allowing blood to flow from the chamber through the first lateral hole and the secon d cannula to the second opening. A single sample needle assembly, characterized in that it is collected externally.

2. 2. A needle assembly according to claim 1, wherein the distance between said lateral holes is greater than the longitudinal length of said plug so that said plug does not simultaneously c over said lateral holes.

3. 3. The needle assembly of claim 1, wherein only a portion of said plug outer surface is in fl uid tight contact with a housing enclosing a chamber.

4. The plug includes an air and blood impermeable material in combination with the air and bl ood impermeable material, the impermeable material being in fluid tight contact with the hou sing surrounding the chamber and the second cannula. of patent claimsThe needle assembly of claim 1.

5. 5. The needle assembly of claim 4, wherein only a portion of the outer surface of said impe rmeable plug material is in liquid-tight contact with the housing surrounding the chamber.

6. 6. The needle assembly of claim 5, wherein only a portion of the surface of said impermeab le plug material is in fluid tight contact with the second cannula.

7. 7. A needle assembly according to claim 6, wherein said impermeable material is a membe r surrounding the outside of the air permeable material and has at least one opening in which the air permeable material communicates directly with the chamber.

8. 8. The needle assembly of claim 7, wherein said impermeable material includes a plurality of apertures communicating air permeable material with the chamber.

9. 5. The needle assembly of claim 4, wherein said impermeable material is flexible.

10. 10. The needle assembly of claim 9, wherein said impermeable material is elastomeric.

11. 11. The needle assembly of claim 10, wherein said impermeable material is silicone rubbe r.

12. 3. A needle assembly as in claim 1, wherein said plug is in the shape of a hollow cylinder.

13. 3. The needle assembly of claim 1, wherein said plug material is porous.

14. 14. The needle assembly of claim 13, wherein said plug material is sintered polyethylene and the average pore diameter is about 10 microns.

15. 3. The needle assembly of claim 1, wherein the end of the second cannula extending into said chamber is sealed with an adhesive.

16. 3. The needle assembly of claim 1, including an exit needle in communication with said se cond cannula and extending outwardly from a second opening through a blood sample collecti on evacuated vessel.

17. 17. The needle assembly of claim 16, wherein said second cannula and exit needle are joi ned to form a unitary construction.

18. 4. The needle assembly of claim 1, wherein said entire housing is transparent.

19. 3. The needle assembly of claim 1, including a vacuum vessel holder connected to said ho using.

20. A single sample needle assembly adapted to be in fluid communication when collecting a f luid sample from a fluid supply to a vacuum collector, the assembly defining a chamber therei n and first and second openings communicating with the chamber. a housing having solution v iewing means and a second opening in communication with the vacuum collection device; a d evice for placing two openings in a closed relationship with a chamber and slidingly sealing sai d chamber to prevent liquid from flowing into one of the holes and permitting air to flow into o ne of the holes in a first position. a plug device for making the liquid within the chamber visibl e by visual means, said plug device being slidable by a negative pressure gradient acting on t he second opening to force the liquid through one of the holes at the second location within th e chamber. A single sample needle assembly, characterized in that the liquid is allowed to flow into the second opening and collect from the second opening.

21. A needle assembly adapted to be in fluid communication when collecting a fluid sample fr om a fluid supply into a vacuum collection device, the needle assembly defining a chamber th erein and first and second openings communicating with the chamber, the chamber contents. a housing having liquid viewing means and a second opening in communication with a vacuu m collection device; an extension device extending into said chamber for directing gas and liq uid to said second opening; and operatively sealing said chamber. a plug device for preventing liquid from flowing into the extension device and allowing gas to flow into the extension devic e at a first position within the chamber, the liquid within the chamber being visible by visual m eans, the plug device A needle assembly as characterized in that when moved to a second pos ition, fluid is allowed to flow into the extension device to allow fluid to be collected from the se cond opening.

22. A single sample needle assembly adapted to recognize a vascular puncture when collectin g a blood sample from a patient into an evacuated vessel, the assembly comprising a transpar ent housing having a front end, a rear end and an internal chamber; A first needle in commun ication extending outwardly from the front end of the housing for insertion into the patient, an d an outer portion extending outwardly from the rear end of the housing for penetrating the bl ood sample collection evacuated vessel. a second puncture needle with an inner portion exten ding into the chamber and having a closed end and two spaced apart transverse holes;and a plug slidable within the chamber as a composite member of an air permeable blood impermea ble material and an elastic impermeable material, the impermeable material forming an outer member surrounding the air permeable material. a plurality of apertures providing an air per meable material in direct communication with the chamber, said impermeable material being i n fluid tight contact with a housing surrounding the chamber and an inner portion of the seco nd needle; , the plug initially covers the first lateral hole furthest from the trailing end and op ens the other second lateral hole to the chamber, thereby providing a constant tourniquet pre ssure from the first needle. blood flowing into the chamber below is prevented by the plug fro m flowing into the second needle to allow room air flow to allow blood to be visualized throug h the transparent housing to indicate that the first needle has entered the vessel; The plug sli

des due to the negative pressure gradient acting on the second needle from the vacuum vess el to open the first lateral hole, and the blood that has flowed into the chamber is collected in the vacuum vessel through the first lateral hole and the second needle. A single sample needl e assembly, characterized in that:

detailed description open —

DETAILED DESCRIPTION OF THE INVENTION

The present invention relates to a needle assembly for collecting fluid from a patient, and mor e particularly to a needle assembly having means for collecting a single sample of blood from a patient and recognizing when the needle has entered the patient's blood vessel. Regarding s olids.

In collecting bodily fluids, such as blood, from a patient, a nurse or clinician must locate or ori entate the patient's blood vessels as the fluid is being collected, but even with the application of tourniquet pressure, the vessels are narrow. In some cases, or if the blood vessel is remote from the skin surface, it may not be possible to insert the needle directly into the patient's blo od vessel. In this case, the needle may be punctured at a location other than the location of t he blood vessel, or may penetrate the small vessel completely. As a result, the flow of blood t hrough the needle and into the evacuated blood collection tube is uncomfortable and extremel y slow because it does not flow out of the patient's blood vessel. Nurses have to start over an d often have to use another evacuated blood collection tube in this case, increasing equipmen t, cost and patient anxiety.

To reduce wastage of evacuated blood collection tubes when a nurse needs to locate a vessel, many blood collection devices have been proposed that have an indicator to show when the n eedle has entered the vessel. This visual indicator system usually has an antechamber and is i solated by some valve system from a needle through which blood is collected in an evacuated tube. When the nurse locates the vessel and the needle enters the vessel, it indicates that the blood has entered the antechamber through the needle and into the vessel in the correct posit ion. The blood collection process is now started, the evacuated blood collection tube is plugge d into the blood collection holder, the valve is opened and blood flows into the collection tube. Examples of blood collection devices with visual indicators are U.S. Pat. Nos. 4,166,450 and 3, 585,984.

In theory, antechamber structures for viewing blood flow are operable and sometimes work w ell, but there are inherent problems. That is, the anterior chamber is normally filled with air w hen the front end of the needle is inserted into the patient's blood vessel. Due to the valve clo sure between the second needle passing through the evacuated blood collection tube, the air i

n the antechamber has no escape and forms stagnant air. Thus, even if the nurse knows the l ocation of the vessel and the needle is well within the vessel, the constant tourniquet pressur e will not allow blood flow from the patient through the needle and into the antechamber. That is, the stagnant air in the anterior chamber prevents blood from entering the anterior chambe r through the needle even under constant tourniquet pressure. As a result, the nurse conclude s that the required endovascular insertion was not performed because no blood was visible in the anterior chamber. An unnecessary second vascular puncture is performed, which is not onl y uncomfortable for the patient, but also inefficient and wasteful.

Therefore, there is a need for new visual indicators for users of blood collection devices. Thus, there is a need for an improved blood collection device of the type that will know when the ne edle has been inserted into the patient's blood vessel prior to inserting the evacuated blood co llection tube into the blood collection holder, as per normal blood collection procedures.

A needle assembly capable of recognizing the arrival of liquid when collecting a liquid sample f rom a liquid source into a vacuum collection device in accordance with the present invention c omprises a housing having an interior chamber and a chamber in communication with the cha mber. and a first and second opening device. The housing includes means for viewing the cont ents of the chamber, and the second opening 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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SINGLE SAMPLE NEEDLE ASSEMBLAGE

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A needle assembly preferably suitable for single sample blood collection and for determining vein entry when collecting a blood sample from a patient into a vacuum collection device. This assembly includes a housing with an interior chamber with a blood inlet needle on one side of the housing and a blood outlet needle on the other. The outlet needle extends interiorly into the chamber, is closed at the end and includes a pair of holes each spaced preferably along an axial line. A slidable plug is operatively positioned in the chamber to prevent liquid from flowing into the side holes while allowing gas to flow into at least one of the side holes at a first position in the chamber whereby the prevented liquid may be viewed by a user through a transparent portion of the housing. The operative plug is movable to a second position in the chamber to allow liquid to flow into at least one of the side holes whereby liquid may be collected from the outlet needle of the assembly.

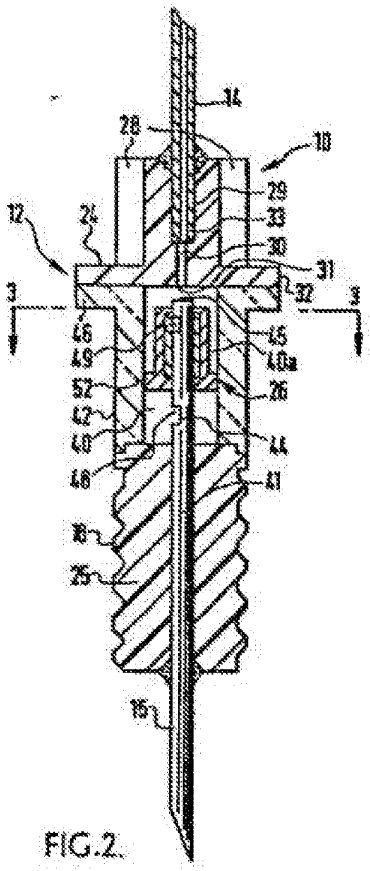

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FIG.2.

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⑤4単一サンプル針組立体

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㉛193054

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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５４、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５１の弾性を利用して押込む。空気透過部材６０を形成する材料の好適な例は焼結ポリエチレン等の多孔性材料とし、孔の直径はほぼ１０ミクロン程度とする。

第６図は本発明による針組立体１０をホルダ１９に連結した状態を示す。血液採集操業の第１段階では、真空の管１６は取付けないで穿刺針１４を患者Ｐ内に穿刺する。ここでプラグ２６は室４０内で室を囲むハウジング内壁と第２の針の内方部分４４とに液を通さない接触であり、第２図の位置にある。この位置では内方の横孔４９はプラグ２６によつて覆われ、下方の横孔４８は覆われない。第２の針１５内は真空でなく大気に連通するため、室４０、針１４、１５の内腔は大気圧であり、空気が存在する。第１の針１４が血管内に入れば、血液は通常の止血帯圧力によつて針１４内を通り室４０の前部部分４０ａに充満する。室４０の前部部分４０ａ内に存在した空気は、不透過性部材５１のスロット５９から空気透過部材６０を透過して逃げる。空気は横孔４８又は４９を通つて第２の針１５の先端部を通つて逃げる。その結果、血液は前部室４０ａに充満し、既知の装置のように空気の停留は生じない。不透過性部材５１が針１５及びハウジング内壁に対して液を通さない係合であり、空気透過部材６０は液を透過させないため、血液が第２の針１５内に流入することはない。前部室４０ａ内の血液は透明材料４２を通して使用者が見ることができ、第１の針１４が血管内に入つたことを示す。通常の止血帯圧力によつて室４０内に流入する血液による推力は小さく、プラグは第２図に示す最初の位置から滑動することはない。

使用者が目視で血管内に針が入つたことを確認すれば、真空管１６をホルダ１９に挿入し、第２の針１５はストッパ２１を貫通する。第７図は真空の血液採集管１６を挿入した状態を示す。第２の針１５が管１６内の真空スペースに連通すれば、横孔４８を経て負圧勾配が室４０内に作用する。この負圧はプラグ２６の下面に作用してプラグ２６は室４０内を第２の針１５の内方部分４４に沿つて管１６の方向に動く。第７図はプラグ２６の滑動によつて横孔４８を完全に覆つた状態を示したが、作用する真空条件に応じて横孔４８の一部又は全部が覆われないこともある。この滑動によつて横孔４９と室の前部部分４０ａとの間が連通し、前部室４０ａ内の血液は第２の針１５内に自由に流入する。血液は第２の針を通つて管１６内に流れ、所要量の血液サンプルが管１６に入つた時に第１の針１４を患者から抜き、血液サンプル収集手順は終了する。

上述によつて明らかにされた通り、本発明による針組立体は滑動可能のプラグを有し、プラグは容易に組込むことができ、最初の血管穿刺に際して空気が逃げるのを可能にして血管内に入つたことを確認できる。この空気の逃げを可能にしたため、血管を針が穿刺すれば血液は直ちに室内に流入し、使用者が血管に入つたことを視認する目視インジケータの特性を有する。この視認に基いて血液収集管を取付けて患者から血液サンプルを容易に採取できる。

4.〔図面の簡単な説明〕

第１図は本発明の好適な実施例による単一サン

プル針組立体とホルダと真空血液収集管とを示す分解斜視図、第2図は第1図の2－2線に沿う断面図、第3図は第2図の3－3線に沿う拡大断面図、第4図は第3図の4－4線に沿うプラグの拡大断面図、第5図は第4図のプラグ内の空気透過部材の拡大断面図、第6図は針組立体を患者の血管に穿刺した斜視図、第7図は第1図の7－7線に沿う使用状態を示す断面図である。

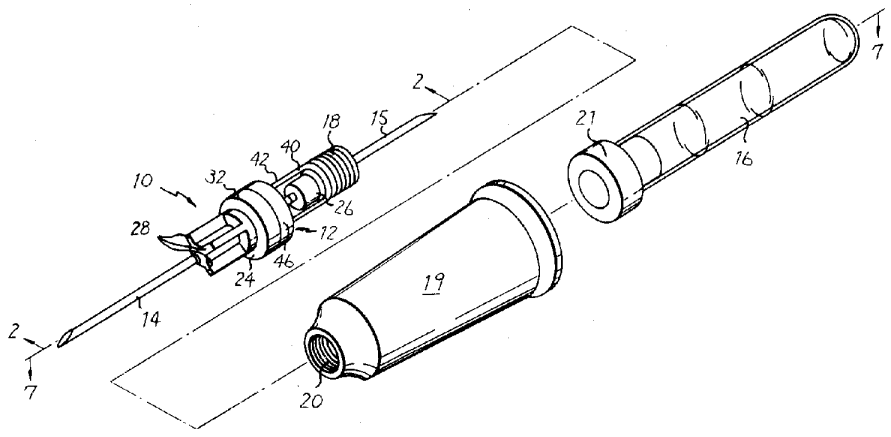
10---針組立体	12---ハウジング
14、15---針	16---真空容器
19---ホルダ	24---前端部
25---後端部	26---プラグ
40---室	44---内方部分
48、49---横孔	51---外側部材
59---開口	60---空気透過部材

特許出願人　ベクトン・デイツキンソン・アンド・カンパニー

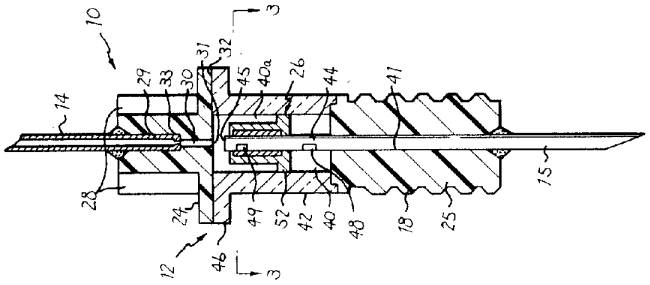
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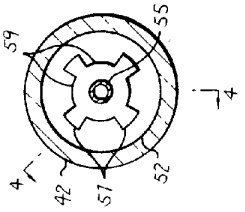
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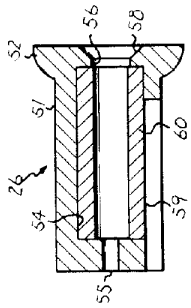
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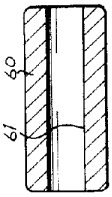
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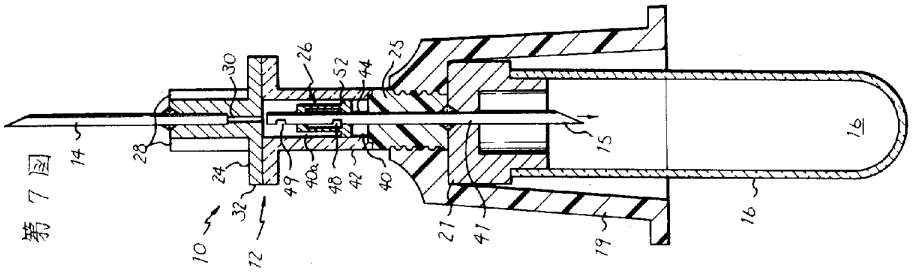
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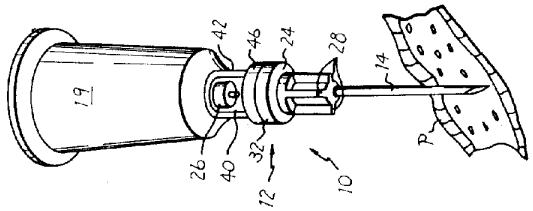
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Current Blood Culture Methods and Systems: Clinical Concepts, Technology, and Interpretation of Results

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Since the mid-1970s there has been a number of advances in blood culture practices and technology; these advances have been based largely on well-designed controlled clinical evaluations of blood culture systems and media. Thus, a sound scientific basis for the fundamental principles of blood culturing now exists. In this article, I will address issues of clinical and technical importance with regard to blood culturing; these issues include skin antisepsis, the number and timing of blood cultures, the appropriate volume of blood for culture, culture media and additives, length and atmosphere of incubation, and interpretation of positive blood culture results. Finally, I will discuss the currently available blood culture systems, with an emphasis on the newer continuous-monitoring blood culture systems.

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Detection of bacteremia and fungemia traditionally has been one of the most important functions of clinical microbiology laboratories. When blood cultures yield clinically important microorganisms, it is a sign that host defenses have failed to contain an infection at its primary site or that the clinician has failed to adequately eradicate the infectious process. During the past two decades, there has been a number of changes in blood culture practices; these changes have been based on clinical investigations that have established a stronger scientific basis for this diagnostic test. Moreover, manufacturers of blood culture systems and media have improved their products, and there has been a marked trend toward the use of automated systems—most recently, continuous-monitoring blood culture devices. In this review, I will focus on important clinical and technical issues related to blood culturing, as well as on the interpretation of positive blood cultures.

Clinical Issues

Skin antisepsis. The likelihood that a positive culture represents infection rather than contamination is, at least in part, a function of skin antisepsis at the time of culture. The recommended antiseptic preparations are 70% isopropyl alcohol, followed by an iodophor or iodine tincture [1]. Iodophors require 1.5–2 minutes of contact time for maximum antiseptic effect. Iodine tincture exerts its antiseptic effect more rapidly than do iodophors [2] and may lower contamination rates in institutions where these rates are high [3], including centers where house officers and medical students, who may not wait for the iodophor to exert its effect, obtain the blood samples for culture. In one study, a commercially available skin-preparation kit for blood cultures has been shown to reduce contamination [4].

Method of obtaining blood for culture. Venipuncture remains the method of choice for obtaining blood for culture; arterial blood cultures are not associated with higher diagnostic yields than are venous blood cultures [1]. Studies comparing contamination rates for blood cultures obtained from intravascular devices vs. those obtained by venipuncture have reported conflicting results [5–8]. My observations support those of Bryant and Strand [8], who noted significantly increased rates of contamination when blood for culture was obtained from intravenous catheters ($P < .001$).

Furthermore, the American College of Physicians guidelines also recommend that blood for culture not be obtained from intravascular devices [9]. Although blood may occasionally be obtained from intravenous lines, a culture of blood obtained from such a device should be paired with another culture of blood obtained by peripheral venipuncture. Finally, I am unaware of published data from systematic studies that support obtaining separate blood samples from different ports of triple-lumen catheters.

Several recent studies have documented that the two-needle technique, formerly recommended for blood cultures, is not associated with significantly lower contamination rates than is the single-needle technique [10–12]. Because the handling of any needle is associated with a small but finite risk of needlestick injury, the authors of these studies have recommended that the single-needle method become the standard. However, the results of a recently published meta-analysis have suggested that the two-needle method may reduce contamination rates slightly [13]. Nevertheless, pending further data, the single-needle method probably should continue to be the standard.

Number of blood cultures. Several studies have addressed the issue of the number of blood cultures needed to detect

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bacteremia and fungemia in adults. Washington [14] reported the cumulative yield from three 20-mL blood samples obtained in sequence and cultured with use of conventional manual methods; 64 (80%) of 80 bacteremic epidoses were detected with the first culture, 70 (88%) of 80 were detected with the first two cultures, and 79 (99%) of 80 were detected with three blood cultures. My colleagues and I also used conventional manual methods and found that the first blood culture detected 257 (91%) of 282 bacteremic episodes and that the first two blood cultures detected 281 (>99%) of 282 episodes [15].

More recently my colleagues and I used the BacT/Alert continuous-monitoring blood culture system (Organon Teknika, Durham, NC) and evaluated the yield of clinically important microorganisms from three consecutive 20-mL blood samples obtained and cultured during a 24-hour period [16]. During a 15-month period, three blood cultures were performed for 218 patients; the third blood culture was the only one positive on only six occasions, and only one of these positive cultures represented true sepsis. The conclusion that we drew from this small quality assurance study was that for the great majority of patients, two blood cultures should be sufficient to detect septicemia.

On the other hand, single blood cultures should be discouraged, if not forbidden altogether [9]. Not only will single blood cultures be insufficiently sensitive for detecting some bacteremias and fungemias, but they also may be difficult to interpret. For example, a single blood culture that yields a coagulase-negative staphylococcus may represent contamination or clinically important infection. However, if two samples obtained in sequence by separate venipunctures yield the same coagulase-negative staphylococcal species with the same antibiogram, the probability is high that the isolates represent true bacteremia.

On the basis of the concepts reviewed above, laboratories should recommend two blood cultures under routine circumstances. In institutions where phlebotomists or nurses obtain the blood for culture, two blood cultures should be performed automatically, even when the physician orders a single culture. On the other hand, ordering more than two blood cultures during any 24-hour period probably is unnecessary, except when the physician wishes to document the continuous bacteremia associated with an endovascular infection such as endocarditis. Therefore, it may be appropriate to require the approval of the laboratory director when more than two (or perhaps three) blood cultures are ordered during any 24-hour period.

Timing of blood cultures. Few studies have systematically evaluated the timing of blood cultures and the optimum interval between successive blood cultures. Strand [17] has arbitrarily recommended a 30- to 60-minute interval except for critically ill, septic patients, from whom specimens should be obtained minutes before initiating therapy. Li et al. [18] recently showed no difference in yield whether blood samples for cultures performed within a 24-hour period were drawn simultaneously or at spaced intervals [18]. However, drawing blood at intervals may be helpful if the clinician wishes to document continuous bacteremia in patients with suspected endovascular infections.

Technical Factors

Many technical factors affect the sensitivity of blood culture systems. Of these factors, the most important are probably the volume of blood cultured and the broth medium used for culture. Other important factors include the ratio of blood to broth, agitation during incubation, length of incubation, atmosphere of incubation, and additives to the media (e.g., those that neutralize the effect of antimicrobial agents present in the blood at the time the sample is drawn). These and other technical issues have been reviewed in detail elsewhere [1, 19, 20], and the reader is referred to those publications for additional discussion of these matters.

Volume of blood required for culture. During bloodstream infections, especially those in adults, there may be relatively few microorganisms present in a given volume of blood—often in the range of $<1-10$ cfu/mL. Moreover, in numerous studies of adult patients, a direct relationship between the diagnostic yield of blood cultures and the volume of blood cultured has been documented [21–24]. On the basis of this information, the recommended volume of blood per culture set for an adult is 10–30 mL [1], and the preferred volume is 20–30 mL. Blood volumes of >30 mL do not enhance the diagnostic yield and contribute to nosocomial anemia; as a practical matter, blood at these volumes may clot in the syringe, thereby making it impossible to inoculate the blood culture bottles.

The optimal volume of blood that should be obtained from children has not been defined with certainty [25]. However, for infants and small children, Szymczak et al. [26] concluded that the chance of failing to detect bacteremia was greater with blood volumes of <1 mL per culture than with blood volumes of ≥ 1 mL. On the basis of the available data, Paisley and Lauer [25] have recommended 1–2 mL of blood per culture for neonates, 2–3 mL for infants aged 1 month to 2 years, 3–5 mL for older children, and 10–20 mL for adolescents.

Culture media. All but one of the commercially available blood culture systems marketed in the United States are based on the inoculation of blood into broth culture media. No one medium or system is capable of detecting all microorganisms. Thus the results of innumerable clinical studies that evaluated different blood culture media and additives have been published. In general, most commercially marketed blood culture media perform well. However, many manufacturers supplement their base media with proprietary additives designed to enhance microbial growth, and it cannot be assumed that common generic media (e.g., supplemented soybean casein digest broth) from different manufacturers will perform in an equivalent manner. Decisions as to the choice of media formulations should be based on data from well-controlled field trials in which large numbers of cultures were assessed. The U.S. Food and Drug Administration has recently issued guidelines for

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manufacturers that sponsor such clinical field trials; these guidelines have been summarized by Wilson [27].

Blood-to-broth ratio. Human blood contains a number of substances (e.g., complement, lysozyme, and phagocytic WBCs) capable of inhibiting microbial growth. Moreover, nearly one-third of patients are receiving antimicrobial agents at the time blood for cultures is obtained (author's unpublished observations). Thus, to optimize the diagnostic yield, blood should be diluted adequately in the culture broth to minimize the effect of these substances. The results of studies that have addressed this issue have led to the recommendation that blood be diluted fivefold to tenfold [28–30]. Dilutions of <1:5 may result in a reduced yield; thus, filling blood culture bottles with more than the recommended amount of blood should be avoided. Dilutions of >1:10 may also be associated with a reduced yield that is not based on blood-to-broth ratio but rather on inadequate blood volume for culture.

Although commercially available blood culture bottles have a partial vacuum in the headspace, direct-draw techniques may result in overfilling and reduced blood-to-broth ratios. Collection of specimens with a needle and syringe provides greater control for inoculating blood culture bottles with the correct amount of blood and thus is preferred.

Neutralization and inactivation of antimicrobials. Given the frequency with which blood for cultures is obtained from patients already receiving antimicrobial agents, several manufacturers have marketed products designed to counteract the potential inhibitory effect on growth. These include the antimicrobial removal device (ARD; Becton Dickinson Microbiology Systems, Cockeysville, MD), BACTEC resin-containing media (Becton Dickinson Diagnostic Instrument Systems, Sparks, MD), and BacT/Alert FAN media (Organon Teknika).

The ARD, which was first introduced in 1980, has been the subject of many studies that have not defined a clear mandate for its use. By contrast, the results of studies of BACTEC resin media used with the semiautomated radiometric (BACTEC 460) and nonradiometric (BACTEC 660 and 730) systems generally were favorable [20]. In one study in which aerobic nonradiometric resin medium was used, the authors speculated that the improved yield of microorganisms might be due, at least in part, to factors other than the binding of antibiotics [31].

The resin medium is available for use in BACTEC continuous-monitoring blood culture devices (9240 and 9120). The manufacturer of the BacT/Alert continuous-monitoring blood culture instrument has recently marketed an aerobic medium, FAN, that uses activated charcoal in a proprietary substance (Ecosorb) to counter the potential inhibitory effects of antibiotics. Use of both the aerobic and the as yet unmarketed anaerobic formulations of the FAN media was associated with improved yields when they were compared with the standard BacT/Alert media [32–33]. The results of a comparative study of the FAN and BACTEC resin media suggest that the performance of these media is equivalent in the respective continuous-monitoring blood culture instruments [34].

Atmosphere of incubation. Traditional two-bottle blood culture systems have included one aerobic bottle and one anaerobic bottle, with the blood distributed equally between the two bottles. However, during the past two decades, the proportion of bacteremias due to obligate anaerobes has decreased substantially [35–37], leading some authorities to question the need for routine use of the anaerobic bottle. In fact, several recent studies of adults [35, 38, 39] and children [40] have concluded that the routine use of anaerobic blood culture bottles is not necessary and have recommended that these bottles be used only selectively for patients who are at high risk for bacteremia due to anaerobes.

Whether the data from these studies can be generalized to all institutions remains a subject of controversy for several reasons. Only a limited number of culture media and systems have been evaluated in these studies; for example, reports that assess the relative value of the BACTEC anaerobic resin or lytic media, the BacT/Alert anaerobic FAN medium, or the ESP anaerobic (80N) medium (Difco, Detroit) have not been published. Moreover, selective use of anaerobic bottles requires that certain logistic issues be addressed within each institution.

These issues include notifying physicians and staff of the change in procedure and the reasons the change was implemented; determining which, if any, nursing units (e.g., the gynecologic unit and the colon and rectal surgery unit) should be stocked routinely with anaerobic bottles; and, possibly, developing algorithms for the physicians ordering blood cultures or for the individuals obtaining the blood for culture (i.e., the phlebotomists, nurses, clinical care technicians, house officers, and medical students).

Indeed, an orderly and stepwise plan that includes both in-service education and postimplementation quality assurance evaluations to confirm that the recommended blood culture protocols are being followed should be developed at institutions where these changes are implemented.

Length of incubation of blood cultures. In routine circumstances, blood cultures need not be incubated for >7 days. Indeed, several recent studies in which instrumented blood culture systems were used have shown that 5-day incubation periods are sufficient for detecting the majority of pathogens [41–44]. Moreover, after 5 days most newly positive cultures represent contamination [44]. Incubation periods longer than 7 days may be useful when fungemia or bacteremia due to fastidious organisms such as the HACEK group of bacteria or species of *Legionella* or *Brucella* are suspected. Longer incubation periods may also be useful for patients with suspected endocarditis who have been treated with antimicrobial agents before blood cultures are performed. However, Washington [45] has noted that such extended incubation periods rarely increase yield. Mycobacterial blood cultures should be incubated for ≥4 weeks.

Microorganisms that Deserve Special Consideration

Yeasts and filamentous fungi. The incidence of fungemia has increased in recent decades because of the AIDS epidemic and

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because patients with malignancies survive longer, the number of patients with organ transplants has increased, and long-term indwelling intravascular devices are being used more frequently. The Isolator (Wampole Laboratories, Cranbury, NJ) lysis-centrifugation system continues to be the best system for detecting filamentous fungi. The Septi-Chek biphasic blood culture system (Becton Dickinson) also has performed well. Instrumented blood culture systems in which the newer media (e.g., the BACTEC aerobic resin, nonradiometric fungal media, and the BacT/Alert aerobic FAN medium) are used have performed well for the detection of yeasts other than *Cryptococcus neoformans* [32, 34, 46, 47].

Mycobacteria. Before the AIDS epidemic, blood cultures for detecting mycobacteria were rarely, if ever, performed. However, mycobacterial blood cultures are now commonly performed in many laboratories. The Isolator system and the BACTEC radiometric system with 13A media have excellent sensitivity and perform comparably [48, 49]. Manufacturers of continuous-monitoring blood culture systems are in various stages of evaluating these devices in terms of their utility for mycobacterial blood cultures, but no published data are yet available.

Blood Culture Systems that Are Currently Available

Manual blood culture systems. Conventional manual systems and media are available from many commercial sources. Aerobic blood culture bottles and (usually) anaerobic blood culture bottles are inoculated with blood and usually incubated for 7 days. Each bottle is examined daily for macroscopic evidence of microbial growth (e.g., hemolysis, turbidity of the media, gas production, or formation of discrete colonies). An aliquot of the contents of the aerobic bottle is gram stained and subcultured after the first overnight incubation. A terminal subculture is usually done at the end of the incubation period. Conventional manual systems are flexible and require no purchase of expensive instruments, but they are labor intensive.

The biphasic Septi-Chek system and the Opticult blood culture systems (Becton Dickinson) and the Oxoid Signal broth displacement blood culture system (Oxoid Unipath, Basingstoke, England) are labor-saving variations of the conventional manual method.

The Septi-Chek and Opticult systems utilize agar-coated paddles or slants attached to the broth-containing culture bottle and allow subcultures to be done daily or more frequently by inverting the blood-broth mixture so that it covers the agar. Microbial growth is often identified on the agar rather than in the broth, allowing for prompt preliminary identification and susceptibility testing. As mentioned earlier, comparative studies have shown that the Septi-Chek biphasic system performs well in detecting yeasts and other microorganisms [31, 50–52].

The Oxoid Signal system is a one-bottle system. After blood is inoculated into the bottle, a clear-plastic cylindrical signal device is attached to the top of the bottle; a long needle from the lower end of the device extends below the surface of the blood-broth mixture, creating a closed system. Gases produced as a by-product of microbial growth increase the pressure in the headspace and force some of the blood-broth mixture through the needle into the cylinder, thereby "signaling" a positive culture. Comparasons of this system with other manual systems and with the BACTEC radiometric system have yielded mixed results [53–56].

The Isolator is a unique manual blood culture system that is based on lysis of blood cells, centrifugation, and direct inoculation of the centrifugate into solid media. For children, from whom only small volumes of blood may be collected, the centrifugation step is deleted. Many studies that have compared the Isolator system with other systems have been reported (as reviewed by Doern [57]). Overall, the Isolator system performs well in the detection of most microorganisms—especially yeasts, filamentous fungi, mycobacteria, and opportunists such as *Bartonella (Rochalimaea) henselae.* Certain microorganisms, including *Streptococcus pneumoniae,* other streptococci, *Pseudomonas aeruginosa,* and anaerobic bacteria, may not be recovered optimally with this system. A potential advantage of the system is that it allows quantitation of the level of bacteremia or fungemia.

Disadvantages of the Isolator system include the following: the lysing solution is toxic for some microorganisms; specimens must be processed within 8 hours of blood collection (most microbiology laboratories are staffed for only one daily shift); substantial labor is required for the initial processing of Isolator cultures; and the contamination rates for this system are higher than those for conventional broth and automated systems.

Instrumented blood culture systems. Commercially available intsrumented blood culture methods were introduced in the 1970s. Until recently, the BACTEC instrumented systems were the only products commercially available in the United States; these systems were initially equipped with radiometric instruments and media, followed in the mid-1980s by the nonradiometric instruments and media. Both systems (as well as in the newer BACTEC and BacT/Alert continuous-monitoring devices) are based on the utilization of carbohydrate substrates in the culture media and subsequent production of CO_2 by growing microorganisms.

For the radiometric system, the instrument detects $^{14}CO_2$ in the bottle headspace, and for the nonradiometric system, CO_2 is detected by infrared spectrophotometry. For both systems, bottles are loaded onto the detection portion of the instrument, where needles perforate the bottle diaphragm and sample the gas contents of the headspace once or twice daily; a bottle is flagged as positive if the amount of CO_2 in the bottle exceeds a threshold value. The flagged bottle is then removed from the instrument, and an aliquot of its contents is gram-stained and subcultured for further testing. Numerous controlled clinical evaluations of the BACTEC radiometric and nonradiometric

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systems and media have been published; the advantages and disadvantages of these systems have been summarized recently by Wilson et al. [58].

Continuous-monitoring blood culture systems. With changes in health care financing, including the recognition that labor costs need to be better controlled, manufacturers are increasingly looking to the use of automation in clinical microbiology. The early-generation BACTEC instruments had the following disadvantages: culture bottles had to be manually manipulated, gas canisters were needed for every instrument; detection needles had to be changed periodically; sterilization of the needle devices occasionally failed, resulting in a false diagnosis of bacteremia (pseudobacteremia); cultures were sometimes instrument false-positive; and bottle throughput was relatively slow (35–60 seconds per bottle). Continuous-monitoring blood culture systems were developed in an effort to address these problems.

Three of these systems are currently available in the United States: the BACTEC 9000 series (Becton Dickinson), Difco ESP, and the BacT/Alert, which was the first to be marketed in 1991. All systems have several features in common including self-contained modular incubation; agitation; detection units, of which up to five or six can be controlled by a single computer; lack of the need for manual manipulation of culture bottles once they have been loaded into the instrument; instrument monitoring of microbial growth at 10- to 24-minute intervals; and culture bottles that each accept 10 mL of blood.

The BacT/Alert and BACTEC systems detect the production of CO_2 as change in pH; this is accomplished by means of colorimetry in the BacT/Alert system and by means of a fluorescent sensor in the BACTEC system. The ESP system detects changes in pressure, either as gases are used during early microbial growth or as they are produced later during growth. The BacT/Alert and BACTEC systems monitor every bottle at 10-minute intervals and gently rock all bottles 34 and 30 times a minute, respectively. The ESP system monitors aerobic bottles every 12 minutes and agitates them at 160 cycles per minute; anaerobic bottles are monitored every 24 minutes without agitation.

All comparative studies to date have shown that the three continuous-monitoring blood culture systems have detected growth sooner than earlier-generation BACTEC instruments and manual systems [46, 59–66]; these systems have been found to be comparable in terms of performance [66, 67]. All three systems have performed reliably in my laboratory.

Interpretation of Positive Blood Cultures

Since the presence of a bloodstream infection is important in terms of both diagnosis and prognosis, correct interpretation of the positive test result is crucial. Misinterpretation of positive results can be costly both to the institution and to the patient. Bates and colleagues [68] recently calculated that the excess cost associated with each blood culture contaminant was ~$4,500 [68]. Parameters that may be useful in interpreting results include the identity of the microorganism, the presence of more than one blood culture positive for the same microorganism, and the presence of the same microorganism as that found in the blood from another normally sterile site.

Microorganisms that almost always (>90% of isolates) represent true infection when isolated from the blood include *Staphylococcus aureus, Escherichia coli* and other Enterobacteriaceae, *P. aeruginosa, S. pneumoniae,* and *Candida albicans.* Isolates from blood that rarely (<5% of isolates) represent true infection include *Corynebacterium* species, *Bacillus* species, and *Propionibacterium acnes.*

Coagulase-negative staphylococci are particularly problematic, not only because they are so ubiquitous, but also because 12%–15% of the blood isolates are pathogens rather than contaminants [69]. Some authorities have suggested that the number of bottles positive in a culture set is a predictor of the clinical significance of an isolate. However, Mirrett and colleagues [70] and Peacock et al. [71] have found that this criterion is unreliable, at least for coagulase-negative staphylococci.

A useful interpretive concept is the number of culture sets found to be positive vs. the number obtained. If most or all cultures in a series are positive, regardless of the microorganism recovered, the probability that the organism is clinically important is high [15]. Of course, it is the physician who must ultimately make the final judgment, taking into account not only the laboratory findings but also the clinical presentation of the patient.

Limitations of Blood Cultures

Blood cultures, as described herein, currently represent the "gold standard" for diagnosis of septicemia. Nonetheless, they have limitations. Positive results require hours to days of incubation. No one culture medium or system in use has been shown to be best suited to the detection of all potential bloodstream pathogens. Some microorganisms grow poorly, or not at all, in conventional blood culture media and systems. Whether culture-based systems will remain the diagnostic methods of choice into the next century or be replaced by molecular techniques or other methods remains to be determined.

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DEVICE AND METHOD FOR PREPARING BLOOD

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The invention relates to a preparation device (100) for treating suspension samples, especially for preparing blood cryobanks. Said device comprises an arrangement of at least two containers for receiving suspension samples, sample parts and/or additives. Said containers are formed as chambers (13 to 15, 90) having fixed walls and are arranged in a fixed manner in relation to each other. A transfer device comprising at least one connecting line (22) is provided, by which means the chambers (13 to 15) can be interconnected.

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DESCRIPTION DE10134913A1

[0001]

13 The invention relates to a device for sample preparation, in particular a device for handling and treating blood samples, such as. B. for separating blood samples by centrifugation and for modifying blood samples by additives in preparation for cryopreservation of the blood samples, and methods for blood preparation, in particular for preparing blood samples for cryopreservation.

[0002]

21 It is known, for the cryopreservation of blood samples, to first prepare a blood unit from a blood donation for the state ready for freezing.

23 The preparation comprises in particular firstly a separation of the blood donation into an erythrocyte suspension which is to be cryopreserved and residual components and secondly the addition of a cryoadditive to the erythrocyte suspension. In conventional methods, blood samples are handled using flexible blood bags, as illustrated schematically in FIG. A blood donation is provided in a first blood bag 1' and centrifuged. After centrifugation, the blood donation is separated into the sediment and the supernatant (plasma). If necessary, the supernatant is drawn off into a waste container 4'. The erythrocyte suspension is transferred into another blood bag 2', to which a cryo-additive is added to provide the preserved product ready for freezing. The illustrated use of blood bags, described for example in DE 298 05 538 and WO 00/38762, has the following disadvantages.

[0003]

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

37 Since the blood bags do not have a fixed shape, careful handling of the blood bags must be

provided, in particular to preserve the phase boundary after centrifugation. In the conventional systems mentioned, devices for holding and transporting the blood bags are provided. However, these devices can only be automated to a very limited extent. The devices must be loaded manually and the operation must be continuously monitored. Furthermore, in the conventional devices, the blood bags are connected to one another via flexible hoses. To separate the erythrocyte suspension and the supernatant, the phase boundary on the blood bag or tube must be detected. Due to the flexibility of the respective containers, there is a risk of incorrect detection and thus a malfunction during preparation.

[0004]

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

50 The hose connections must be connected to the blood bags in a sterile manner and separated and sealed after the respective process step. In each step of the preparation, complex precautions must be taken to maintain the sterility and freedom from pyrogens of the blood samples. The conventional blood bag preparation is also problematic because of the risk of mix-ups. If a blood bag is mixed up during preparation or cross-contamination occurs between blood bags, the consequences for the recipient of the blood donation can be devastating. Extensive safety measures have to be implemented in conventional systems to rule out the risk of confusion.

[0005]

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

63 When separating stem cells from biological fluid samples, only a very small amount of stem cells has to be separated from the samples. This allows for the use of special centrifugation techniques and less sensitivity to the use of blood bags.

[0006]

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

71 Automating the preparation of the canned goods is necessary for the production of modern blood banks. Because of the need for automation, the applicability of conventional preparation devices is limited.

[0007]

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

79 There is also a corresponding need for sterile, automated and safe sample handling when

processing biological cell suspensions for therapeutic purposes.

[0008]

84 The object of the invention is to provide an improved device for the preparation of suspended biological samples, with which the disadvantages of conventional systems are overcome and which is particularly suitable for automated and safe handling of a large number of samples.

87 The object of the invention is in particular to provide an improved system for the preparation of cryopreserves such. B. Blood cryopreserves. The object of the invention is also to specify a novel method for handling biologically suspended samples which can be automated and carried out safely.

[0009]

94 These objects are achieved with a preparation device, a preparation station and a method having the features according to patent claims 1, 9 and 12.

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

[0010]

100 The basic idea of the invention is to provide a preparation device that has at least two containers for receiving the suspension samples to be treated, the containers, in contrast to conventional systems, being formed by chambers with fixed walls that are positioned stationary relative to one another.

104 The chambers are connected to one another via line connections that can be actuated individually or are equipped with connecting pieces for the optional formation of line connections between the chambers. According to a first embodiment, the preparation device according to the invention is formed by an integral structure in which the chambers are formed in a chamber body, at one end of which the line connections can be attached or adjusted. According to a second embodiment, the preparation device comprises a framework into which the chambers can be inserted individually. The connection pieces of the individual chambers are all on one (e.g. B. lower) side of the rack arranged. Depending on requirements, the connecting pieces, which are initially sealed with a septum, are opened and connected in pairs via line connections. According to a third embodiment, the design with individual chambers is such that the framework is equipped with a valve plate with line connections via which the individual chambers can be connected in pairs.

116 The design of the preparation device as an integral structure or as a frame structure with at least two chambers has the advantages that the preparation device represents an object that can be safely gripped and manipulated within the scope of an automated process sequence and that the sample handling, in particular the independent pre-filling of the chambers, the treatment of samples in the chambers and the transfer of the samples between the chambers, is simplified. When using the preparation device according to the invention for the production

of blood samples for cryopreservation, at least three chambers are preferably provided.

[0011]

126 According to said first embodiment of the invention, the chambers are preferably formed in the form of right circular cylinders in a plastic body, at one end of which is attached a valve plate which contains at least one line connection for coupling two chambers each.

129 The construction with an integral plastic body has the advantage that the preparation device can be manufactured as a disposable product, so that problems with sterility and mix-ups can be ruled out. A further advantage is the high stability of the preparation device, particularly during centrifugation processes.

[0012]

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

138 The chambers can be used as disposable products. An additional advantage is the relatively low weight of the frame construction.

[0013]

143 The transfer of samples between the chambers is preferably effected by hydrostatic pressure applied as gas pressure or preferably with plungers located in each chamber.

145 Alternatively, it is possible to transfer the pressure with a mechanically actuated piston (e.g. B. with a connecting rod rod). In this configuration, the chambers of the preparation device according to the invention form piston pressure generators, which are set up both to receive the respective samples and to transfer the samples to adjacent chambers.

[0014]

152 According to a further preferred embodiment, the preparation device, in particular the chambers as the main components, consists at least partially of a transparent plastic material.

154 If non-transparent material is used, the chambers preferably have at least one transparent window for optical detection. A reliable and reproducible optical detection of sample properties, in particular the position of the phase boundary after centrifugation, is made possible.

[0015]

160 The invention also relates to a preparation station that is equipped with the preparation device according to the invention and also has a pressure device for transferring samples between the chambers, a detector device for measuring sample properties in the chambers and an actuating device for selectively coupling chambers.

[0016]

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

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

171 The method is characterized in particular by the fact that all preparation steps are carried out with the entire preparation device, which contains different chambers for receiving samples at different stages of preparation.

[0017]

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

179 The preparation process is designed to increase productivity in canning, i. H. to achieve the highest possible canning throughput, can be automated, while at the same time increasing the production quality and maintaining it independently of the manual skills of an operator. A blood unit produced according to the invention already experiences an increase in quality through the use of the preparation device, without the preparation becoming significantly more expensive.

[0018]

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

190 It only comes into contact with the environment once during filling and emptying. For example, the pre-treatment of a preserve is absolutely sterile until it is ready for freezing. Advantageously, the opening, connecting and closing of bags and connecting tubes according to the conventional systems is avoided. The suspension sample does not leave the preparation device during the preparation steps. A mix-up e.g. B. blood from different donors or contamination by foreign blood or microorganisms are excluded. The identity of the donor blood is guaranteed. The preparation process is greatly accelerated, since work steps that may be necessary several times in conventional systems can be completely eliminated according to the invention. Partial or complete sample loss or contamination of the working environment, including the laboratory staff, through leaking tube connections are ruled out with the preparation device according to the invention.

[0019]

204 The preparation device according to the invention forms a solid container which, in comparison with conventionally used blood bags, enables the device and the valves and/or nozzles

attached to it to be gripped and manipulated in a defined and reproducible manner.

207 There is no need to grip or position and clamp connecting hoses if the at least one connecting line is integrated into the preparation device and thus enables the individual chambers to be connected repeatedly and reproducibly over the shortest possible route. The short distances and the choice of a suitable cross-section for the respective connecting line allow the transfer time for transferring samples between the chambers to be optimized. The construction of the device enables a defined positioning of the at least one connecting line. Accidental connection of currently non-cooperating chambers is excluded. Deformation or squeezing of the chambers is avoided according to the invention. a z. B. set by centrifugation phase separation of sample components can not be blurred by a gripping process.

[0020]

219 The fixed and preferably symmetrical arrangement of the chambers in a preparation device according to the invention enables rapid and defined positioning of the chamber of interest in a preparation system, independently of the process step.

222 All sensors and actuators are automatically positioned correctly. Increased, error-free throughput is achieved. For example, with a preparation device according to the invention, around three times as many cryopreserves can be prepared per unit of time. The preparation device allows a free choice of material and dimensioning of the outer shape of the chamber arrangement. Advantageously, the device can be readily used with conventional centrifuge equipment.

[0021]

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

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

[0022]

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

239 When using the preparation device according to the invention, there is no significant additional effort for blood donation services. No multiple bag systems are required. The preparation device can be coupled directly to a simple donation bag (single blood bag). The supernatant (plasma and buffy coat) which in conventional methods ends up in the waste or can only be obtained with great effort is available according to the invention as an additional end product if required. The preparation device also provides advantages when filling freezing bags after preparation. When docked to the preparation device, a filled freezing bag can be vented in a simple and sterile manner with this device by subjecting the respective chamber to negative pressure.

[0023]

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

253 Show it:

[0024]

257 1 shows a schematic phantom view of an embodiment of a preparation device according to the invention in a partially expanded state,

[0025]

262 FIG. 2 shows an illustration of the integration of the preparation device according to FIG. 1 into a device for the production of blood reserves,

[0026]

267 3 shows an enlarged partial view of a chamber end of the preparation device according to FIG. 1,

[0027]

272 4 illustration of a modified embodiment of a preparation device according to the invention,

[0028]

276 5 shows a schematic sectional view of a single chamber used according to the invention, and

[0029]

280 6 shows an illustration of a conventional preparation technique (prior art).

[0030]

284 1 shows an embodiment of a preparation device 100 according to the invention in a schematic phantom view.

286 The preparation device 100 comprises a chamber body 10, in which three chambers are formed for receiving suspension samples, a transfer device 20, consisting of a valve plate 21 and at least one connecting line 22, a stamp device 30 with several pressure stamps 31 to 33 and a cover plate 40, which upper end of the chamber body 10 forms.

290 The chamber body 10 is integrally formed of a transparent plastic material (e.g.
291 B. PMMA, cycloolefin copolymers, polyamide, polycarbonate, PCHP, polyester or polysulfone).
292 It has the external shape of a right circular cylinder with a flat upper side 11 and a flat lower side 12.
294 In the interior of the chamber body 10, the three cylindrical chambers 13, 14 and 15 for receiving samples are formed.
296 At the upper end of the chamber body 10, the chambers open out freely into the top 11.
297 At the lower end, each chamber has a taper 16 with a connecting piece 17, as illustrated in FIG. 3 on an enlarged scale. The connecting piece 17 opens into the underside 12 of the chamber body 10.

[0031]

303 For use in the preparation of blood samples, the preparation device 100 has, for example, a diameter of approximately 18 to 20 cm, the height of the chamber body 10 being approximately 10 to 12 cm and the chambers 13 to 15 each having an internal diameter of approximately 6 to own 8 cm.
307 A chamber preferably has a volume in the range 400 ml to 600 ml. The chambers 13 to 15 are preferably distributed symmetrically relative to the axis of the chamber body 10 .

[0032]

312 The transfer device 20 is set up to transfer samples between the chambers 13 to 15 .
313 The valve plate 21 is rotatably attached to the bottom 12 of the chamber body 10 . The connecting line 22, which forms an overflow channel, is integrated into the valve plate 21, which is also made of plastic material. Sealing rings made of an elastic material (e.g. B. PTFE) attached. In addition to the sealing function, the sealing rings (not shown) can also serve as latching devices. Upon rotation of the connecting plate 21, the sealing rings snap into place at the desired positions of the connecting pieces or the mouth of the connecting pipe 22 when these are straightly aligned with one another.

[0033]

323 The valve plate 21 has a valve function since liquid is generally only ever pumped in one direction from one chamber to the adjacent chamber.
325 To rule out incorrect operation, a device for forced specification of a specific direction of rotation and/or a repeat lock can be provided on the valve plate 21 or on the chamber body 10 . This device includes, for example, teeth that prevent reverse rotation and/or an additional locking aid.

[0034]

332 The structure of the valve plate 21 can be modified depending on the application (see FIG. 4).
333 Several connecting lines can be provided. The at least one connecting line can be equipped with a blocking or valve device. Additional through-openings for charging the chambers can preferably be provided in the valve plate. However, loading can also take place from the top.

[0035]

339 Pressure is applied to the samples to transport the samples between the chambers.
340 The sample is transferred via the overflow channel in the valve plate 21 under the effect of an overpressure in the chamber from which the transfer originates. The transfer pressure is applied with a pressure device which is part of the preparation station (see FIG. 2) in which the preparation device according to the invention is preferably used. According to an advantageous embodiment of the invention, the pressure is transmitted using a stamp device 30 which has a pressure stamp 31 to 33 in each of the chambers 13 to 15 . The plunger 31 to 33 consist of plastic bodies z. B. in the form of a cylinder, which are fitted in a form-fitting manner into the respective chamber. Each plunger has at least one circumferential sealing lip, which seals any gaps that may occur between the plungers and the inner walls of the chamber. The sealing lips prevent the piston from passing through the liquid samples when pressure is applied. The pistons with the sealing lips are made of a plastic material (e.g.
351 e.g. PTFE). The use of the plungers 31 to 33 in the chambers has the advantage that when the preparation device 100 moves, a sample movement in the chambers is prevented when the plungers are respectively placed on the liquids. After a centrifugation, the phase boundary between the fractions is advantageously avoided.

[0036]

358 According to a preferred embodiment, the plungers 31 to 33 can each have a central bore (shown in dashed lines) with a closure (e.g.
360 B. a septum). This allows access to the samples or supplemental liquids in the chambers from the top of the device 100.

[0037]

365 According to a modified embodiment of the invention, the use of the plunger can also be dispensed with.
367 In this case, the transfer pressure is applied directly to the liquid surface in the respective chamber. In this design, the upper ends of the chambers are preferably equipped with a sterile filter insert at the top, which is only suitable for the sterile pressure medium used (e.g. B. air, inert gas) is permeable. The structure without a plunger has the advantages of an increased internal volume and a simplified structure of the chambers and thus cost savings.

[0038]

375 The upper cover plate 40 serves to close off the preparation device 100.

376 It is fixedly mounted on the chamber body 10 and has through openings or ports 41 aligned with the upper ends of the chambers 13-15, respectively. The connecting pieces 41 serve to connect individual chambers or all chambers at the same time to the pressure device and/or charging devices.

[0039]

383 The process sequence for producing a blood cryopreservation using a preparation device according to the invention is explained below with reference to FIG.

385 FIG. 2 shows the preparation device 100 analogous to the representation according to FIG. 1 in combination with parts of the preparation station.

[0040]

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

[0041]

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

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

399 Alternatively, the pressure device 50 comprises a lever device with a connecting rod. The mechanical power transmission has the advantage that the positioning of the plunger can be done with increased precision. According to alternative embodiments of the invention, the pressure generator can also be supplied by a pressure source (e.g. B. compressed gas cylinder) are formed with a control valve.

[0042]

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

409 Depending on the application, the light-sensitive element 61 can be equipped with filter devices (not shown). A plurality of light-sensitive elements can also be arranged corresponding to the positions of the chambers. Depending on the application, other detectors for detecting sample properties can also be provided, as are known from analytics (e.g. B. spectrophotometer, resistivity meter for density determination). The chambers can also each have a scale extending over their length for optical control of the filling level, the position of the plunger or the position of the phase boundary. The detectors can also be attached to other components

of the preparation device, e.g. B. be provided on a connecting line in the valve plate.

[0043]

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

422 The actuating element 71 has the form of a plate with at least one projection 73 which cooperates with at least one corresponding recess (not shown) on the underside of the valve plate 21. The projection 73 engages in the recess and rotates the valve plate 21 into the desired position when the servomotor 72 is actuated, so that one chamber can be opened or emptied, two chambers are connected via the connecting line 22 or all three chambers are closed.

[0044]

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

432 Depending on the operating state and the detector signal supplied by the detector device 60, the pressure generator 50 and the actuating device 70 are actuated in the following manner. In the case of semi-automatic or manual operation, the corresponding steps are at least partially carried out by an operator.

[0045]

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

441 In the first chamber 13 there is a blood donation. The blood donation is poured into the first chamber 13 from a donor bag, which may be carried out with the application of a supporting negative pressure. The second chamber 14 is filled with a wash solution. A cryoadditive is located in the third chamber 15 . In the starting state, the first chamber 13 is completely filled, while the remaining chambers 14, 15 are only partially filled. There is as much free volume in these chambers as is required to take over the erythrocyte suspension after centrifugation (see below). After the starting state (all closed), the valve plate 21 is set in such a way that, for example, the first and second chambers 13, 14 are connected. Advantageously, there is essentially no liquid exchange via the connecting line despite the connection in the pressure-free state.

[0046]

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

456 The centrifugation device (not shown) has the design of a large centrifuge known per se with individual centrifuge buckets in which a large number of preparation devices can be

centrifuged at the same time. During centrifugation, the blood donation is only separated into fractions. The plungers 31 to 33 are not shifted. The chambers are sealed during centrifugation.

[0047]

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

465 In the first chamber 13, the formed fractions of the blood donation with the erythrocyte sediment 1 of the so-called "Buffy Coat" layer 2 and the plasma supernatant 3 illustrated. Depending on the operation, the erythrocyte sediment 1 comprises a volume proportion of approx. 45% of the chamber 13. The volume fraction depends in particular on the centrifugation speed. A higher speed results in a higher packing density of the erythrocytes and thus a lower volume fraction. The “buffy coat” layer 2 is a greyish-colored coating containing thrombocytes and leukocytes, which forms between the deep red erythrocyte sediment 1 and the bright red plasma supernatant 3 after centrifugation.

[0048]

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

477 The valve plate 21 is rotated between the first and second chambers 13, 14 in the passage direction. This is done manually, e.g. B. with a knob wrench or with the adjusting device 70 (see above). The first chamber 13 is pressurized. Under the action of hydrostatic or mechanical pressure, the plunger 31 moves downwards and the plunger 32 moves upwards. The separated blood donation is transferred to the second chamber 14 . This preparation step is terminated as soon as the detector device 60 arranged at the lower end of the first chamber 13 detects the "buffy coat" layer 2 . In this state it is ensured that only erythrocyte sediment is still present in the narrowed area 16 (see FIG. 3) and the connecting line. When the buffy coat layer 2 has been detected, the print transfer is stopped. Then the valve plate is brought into the closed position. This occurs either immediately upon detection of the layer 2 or with a time delay, so that concentrate residues from the narrowed area 16 can still get into the connecting line.

[0049]

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

493 The washing solution includes, for example, physiological saline. Another centrifugation follows, as a result of which the treated erythrocytes again collect as a concentrate in the lower part of the second chamber 14, while the remaining washing solution forms the supernatant.

[0050]

499 In a further preparation step, the washed erythrocyte sediment is transferred to the third

chamber 15 analogously to the manner described.

501 For this purpose, the valve plate 21 is rotated in such a way that the connecting line 22 is arranged between the second and third chambers 14 , 15 . In addition, the pressure distributor 56 is adjusted accordingly. The pressure transmission is in turn controlled as a function of the detector signal from the detector device 60 . A further sensor (not shown) can be provided on the second chamber 14 . Alternatively, it is possible to rotate the preparation device 100 towards the sensor 61 so that the phase boundary in the second chamber 14 can be detected.

[0051]

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

512 The additives known per se are used as cryoadditive. For example, the cryoadditive comprises a solution of water-soluble starch derivative.

[0052]

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

519 This is followed by the transfer to the container selected depending on the application, e.g. B. a cryobag in which the freezing process takes place. After completion of the preparation, the plasma supernatant is advantageously present in the first chamber 13 as a donor-specific residual product. Depending on the application, the plasma can be used for other purposes.

[0053]

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

528 The differences relate to the design of the valve plate 21. The lower side 12 of the chamber body 10 with the chambers 13 to 15 is illustrated in the top partial image of FIG. Each chamber has an inlet and outlet opening in the form of a connecting piece 17 (see FIG. 3). An O-ring seal 18 is provided on each connecting piece 17 . In the middle of the chamber body 10, corresponding to the cylinder axis, there is a threaded hole 19 for fastening the valve plate 21.

[0054]

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

537 In this design, two connecting lines (or overflow channels) 22, 23 are provided, which are arranged such that two chambers can be connected to one of the connecting lines 22 or 23, while the other connecting line 22 or 23 is closed. The use of two connecting lines has the advantage of shorter adjustment paths when setting the chamber connections in the individual preparation steps. Three inlet and outlet bores 24 are provided in the valve plate, which are

arranged in such a way that when one of the inlet and outlet bores 24 is aligned with one of the connecting pieces 17, the other connecting pieces remain closed.

[0055]

547 The valve plate 21 has a circumferential O-ring 25 which provides an additional seal against the underside 12 of the chamber body 10.

549 The reference number 26 refers to the axis of rotation and the bearing of the valve plate 21.

[0056]

553 In the lower partial image of FIG. 4, the valve plate 21 and the underside 12 of the chamber body 10 are shown in the assembled state.

555 If the valve plate 21 is turned to the left from the state shown, the chambers 13 and 14 are first connected to the connecting line 22 and the chambers 14 and 15 are connected via the connecting line 23 as the adjustment continues. The two preparation steps explained above can thus be carried out with a short travel distance.

[0057]

562 The embodiment of the invention illustrated in FIGS. 1 to 4 can be modified in many ways depending on the task at hand.

564 For example, further chambers for accommodating further additives can be provided in the chamber body in order to carry out further preparation steps. Instead of the 120° arrangement, the chambers can also be arranged differently in the chamber body or a frame (see below). Depending on the application, the chambers can be loaded from the top or bottom. This is preferably done using tubing or pipetting systems. According to a preferred embodiment of the invention, the inlet openings of the chambers are adapted to the outer diameter of standardized liquid pipettes or tube adapters, so that they can be easily attached and operated for loading. Depending on the application, the size of the preparation device can be scaled as desired. The transmission device with the valve plate can be replaced by a fixed arrangement of several connecting lines with valves that can be actuated.

[0058]

577 Additional gripping or fastening devices for handling the chamber body and/or for use in a centrifuge can be provided on the outside of the chamber body.

[0059]

582 According to the invention, the chamber body with the integrated chambers can be replaced by an arrangement of individual chambers in a frame.

584 This configuration has advantages with regard to separate filling of the individual chambers before composition for the preparation device and disposal of the chambers after use.

586 Any suitable structure can be used as the framework, into which the chambers can be inserted in a fixed manner in accordance with the desired arrangement and which has sufficient stability during centrifugation. Depending on the design of the chambers, the structure of the frame is adjusted.

[0060]

593 If ready-made plunger syringes with suitable plunger diameters are used as chambers, then the frame has recesses to accommodate the syringe plunger.

595 If the individual chambers are formed by straight tubular bodies, the recesses in the framework are adjusted accordingly. If necessary, conically preformed chamber floors are provided on the floor of the framework, as illustrated in FIG.

[0061]

601 5 shows a single chamber in a schematic sectional view.

602 Two or more such individual chambers (e.g. B. according to the above design three individual chambers) are provided on a frame (not shown). The single chamber 90 comprises a chamber wall 91 in the shape of a right circular cylinder and a tapered portion 92 which rests in a correspondingly shaped support base 93 which is part of the framework. Inside the single chamber 90 is the plunger (see above). In this configuration, the pressure ram is not cylindrical, but is designed as a ram plate 94 with a sealing ring 97 running around it on the outside. The stamp plate 94 consists of PMMA, for example. The sealing ring 97 is a z. B. made of PTFE molded part that is pulled positively over the outer edge of the stamp plate 94. The cross section of the sealing ring 97 has a U-shape, the open ends of which form two sealing lips. This shape ensures that the sealing lips lie tightly against the chamber wall. The upper side of the individual chamber 90 is closed with a cover plate 95, which has a passage opening 96 for the passage of the pressure medium.

[0062]

617 The individual chamber 90 has, for example, a volume of 470 ml with a diameter of approx. 80 mm, a length of the chamber wall 91 of approx. 110 mm and a height of the support base 93 of approx. 30 mm.

620 The partial area 92 delimits a partial volume of approximately 30 ml.

[0063]

624 In a method according to the invention for blood preparation, the following single-chamber centrifugation can be provided in deviation from the centrifugation of the entire preparation

device explained above.

627 The individual chamber of interest (e.g. B. according to FIG. 5) removed from the frame and centrifuged separately. Before or after centrifugation, the individual chamber is arranged in the frame for carrying out the remaining steps of sample preparation. This method is particularly advantageous if no suitable centrifuge is available for centrifugation.

[0064]

634 The features of the invention disclosed in the above description, the claims and the drawings can be important both individually and in any combination for the implementation of the invention in its various configurations.

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CLAIMS DE10134913A1

1.

13 Preparation device (100) for treating suspension samples, in particular for preparing cryopreserved blood, with an arrangement of at least two containers for holding suspension samples, sample parts and/or additives, characterized in that the containers are designed as chambers (13 to 15, 90) are formed with solid walls and are arranged in a fixed position relative to one another, a transmission device (20) having at least one connecting line (22) being provided, via which the chambers (13 to 15) can be connected to one another.

2.

22 Preparation device according to claim 1, wherein the chambers (13 to 15) are formed in a one-piece chamber body (10).

3.

27 Preparation device according to Claim 1, in which the chambers (90) are detachably fastened as individual chambers in a framework.

4.

32 Preparation device according to one of the preceding claims, in which the walls of the chambers or the chamber body (10) consist of a transparent material.

5.

37 Preparation device according to one of the preceding claims 1 or 2, in which the chambers (13

to 15) have the shape of straight hollow cylinders which run from an upper side (11) to an underside (12) of the chamber body (10), the underside (12) each chamber (13 to 15) has a connecting piece (17) to which one end of the at least one connecting line (22) can be connected.

6.

45 Preparation device according to one of the preceding claims, in which a pressure plunger (31 to 33) is provided in each chamber.

7.

50 Preparation device according to Claim 6, in which each pressure plunger (31 to 33) has a circumferential sealing lip.

8.

55 Preparation device according to one of the preceding claims, in which the transmission device (20) is formed by a valve plate (21) in which at least one connecting line (22) is integrated, the valve plate (21) being arranged rotatably.

9.

61 Preparation station for preparing suspension samples, comprising: at least one preparation device (100) according to one of the preceding claims, a printing device (50), a detector device (60), an actuating device (70), and a control device (80).

10.

67 Preparation station according to Claim 9, in which the pressure device (50) comprises a pneumatic pressure generator or a mechanical pressure generator with connecting rods.

11.

72 Preparation station according to Claim 9 or 10, in which the adjusting device (70) has an actuating element (71) with which the transmission device (20) can be adjusted in such a way that two chambers are connected via the at least one connecting line (22).

12.

78 A method for preparing suspension samples using a preparation device (100) according to any one of claims 1 to 8, in which treatment of a sample in at least one of the chambers (13 to 15,

90) and transfer of at least part of the sample between two chambers are alternated he follows.

13.

84 Method according to Claim 12, in which the sample treatment comprises centrifugation of the sample and/or treatment of the sample with additives.

14.

89 Method according to claim 13, in which the entire preparation device (100) or an individual chamber (90) is centrifuged during the centrifugation of the sample.

15.

94 A method according to any one of claims 12 to 14, in which a cryopreserved blood is prepared.

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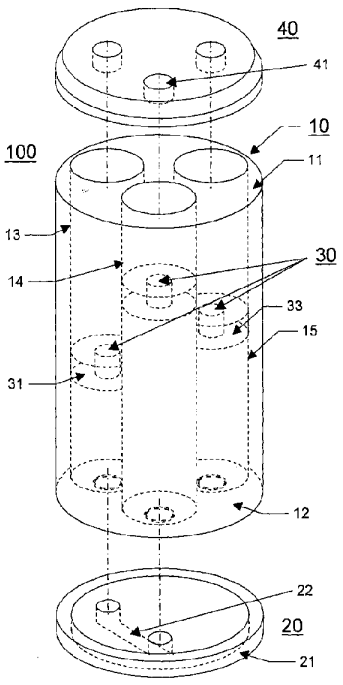
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Die folgenden Angaben sind den vom Anmelder eingereichten Unterlagen entnommen

Prüfungsantrag gem. § 44 PatG ist gestellt

(54) Vorrichtung und Verfahren zur Blutpräparation

(57) Es wird eine Präparationsvorrichtung (100) zur Behandlung von Suspensionsproben, insbesondere zur Präparation von Blut-Kryokonserven, mit einer Anordnung von mindestens zwei Behältnissen zur Aufnahme von Suspensionsproben, Probenteilen und/oder Zusatzstoffen beschrieben, wobei die Behältnisse als Kammern (13 bis 15, 90) mit festen Wänden gebildet und relativ zueinander ortsfest angeordnet sind, wobei eine Übertragungseinrichtung (20) mit mindestens einer Verbindungsleitung (22) vorgesehen ist, über die die Kammern (13 bis 15) miteinander verbunden werden können.



DE 101 34 913 A 1

Beschreibung

[0001] Die Erfindung betrifft eine Vorrichtung zur Probenpräparation, insbesondere eine Vorrichtung zur Handhabung und Behandlung von Blutproben, wie z. B. zum Trennen von Blutproben durch Zentrifugation und zur Modifizierung von Blutproben durch Zusatzstoffe zur Vorbereitung einer Kryokonservierung der Blutproben, und Verfahren zur Blutpräparation, insbesondere zur Vorbereitung von Blutproben für die Kryokonservierung.

[0002] Es ist bekannt, zur Kryokonservierung von Blutproben zunächst aus einer Blutspende eine Blutkonserve für den einfrierfertigen Zustand zu präparieren. Die Präparation umfasst insbesondere erstens eine Auftrennung der Blutspende in eine Erythrozytensuspension, die kryokonserviert werden soll, und Restbestandteile und zweitens den Zusatz eines Kryoadditives zur Erythrozytensuspension. Bei herkömmlichen Verfahren erfolgt die Handhabung der Blutproben unter Verwendung von flexiblen Blutbeuteln, wie es schematisch in **Fig.** 6 illustriert ist. Eine Blutspende wird in einem ersten Blutbeutel **1'** bereitgestellt und zentrifugiert. Nach dem Zentrifugieren ist die Blutspende in das Sediment und den Überstand (Plasma) getrennt. Der Überstand wird ggf. in einen Abfallbehälter **4'** abgezogen. Die Erythrozytensuspension wird in einen weiteren Blutbeutel **2'** umgefüllt, dem zur Bereitstellung der einfrierfertigen Konserve ein Kryoadditiv zugesetzt wird. Die illustrierte Verwendung von Blutbeuteln, die bspw. in DE 298 05 538 und WO 00/38762 beschrieben wird, besitzt die folgenden Nachteile.

[0003] Ein Hauptproblem betrifft die Handhabung der Blutbeutel. Da die Blutbeutel keine feste Form besitzen, muss insbesondere zur Erhaltung der Phasengrenze nach der Zentrifugation ein schonender Umgang mit den Blutbeuteln vorgesehen sein. Bei den genannten herkömmlichen Systemen sind zwar Vorrichtungen zur Halterung und zum Transport der Blutbeutel vorgesehen. Diese Vorrichtungen sind jedoch nur sehr eingeschränkt automatisierbar. Es müssen eine manuelle Beschickung der Vorrichtungen und eine laufende Überwachung des Betriebes erfolgen. Des Weiteren sind die Blutbeutel bei den herkömmlichen Vorrichtungen über flexible Schläuche miteinander verbunden. Zur Trennung von Erythrozytensuspension und Überstand muss die Phasengrenze am Blutbeutel oder am Schlauch detektiert werden. Wegen der Flexibilität der jeweiligen Behältnisse besteht das Risiko einer Fehldetektion und damit einer Fehlfunktion bei der Präparation.

[0004] Weitere Nachteile ergeben sich aus Sterilitätsproblemen beim Umgang mit den Blutbeuteln. Die Schlauchverbindungen müssen steril an die Blutbeutel angeschlossen und nach dem jeweiligen Verfahrensschritt abgetrennt und verschweißt werden. Bei jedem Präparationsschritt müssen aufwendige Vorkehrungen zur Erhaltung der Sterilität und Pyrogenfreiheit der Blutproben getroffen werden. Die herkömmliche Blutbeutelpräparation ist auch wegen der Verwechslungsgefahr problematisch. Wenn während der Präparation ein Blutbeutel verwechselt wird oder eine Kreuzkontamination zwischen Blutbeuteln auftritt, so kann dies verheerende Folgen für den Empfänger der Blutspende haben. Zum Ausschluss der Verwechslungsgefahr müssen bei herkömmlichen Systemen aufwendige Sicherheitsmaßnahmen realisiert werden.

[0005] Ein weiterer Nachteil der in WO 00/38762 beschriebenen Technik besteht in deren spezifischen Zuschnitt auf die Stammzellenpräparation. Bei der Trennung von Stammzellen aus biologischen Flüssigkeitsproben ist lediglich ein sehr geringer Stammzellengehalt aus den Proben abzutrennen. Dies ermöglicht den Einsatz spezieller Zentrifugationstechniken und eine geringere Empfindlichkeit in Bezug auf die Verwendung von Blutbeuteln.

[0006] In der modernen Medizin und im Katastrophenschutz besteht ein Interesse an vergrößerten Blutbanken mit einem breiten Spektrum verschiedenster Bluttypen. Zur Herstellung moderner Blutbanken ist eine Automatisierung der Konservenpräparation erforderlich. Wegen des Automatisierungsbedarfes ist die Anwendbarkeit herkömmlicher Präparationsvorrichtungen eingeschränkt.

[0007] Die illustrierten Probleme bei der Handhabung von Blutproben bestehen nicht nur bei der Vorbereitung von Konserven für die Kryokonservierung. Ein entsprechender Bedarf nach steriler, automatisierter und sicherer Probenhandhabung besteht auch bei der Bearbeitung von biologischen Zeilsuspensionen für therapeutische Zwecke.

[0008] Die Aufgabe der Erfindung ist es, eine verbesserte Vorrichtung zur Präparation suspendierter biologischer Proben bereitzustellen, mit der die Nachteile herkömmlichen Systeme überwunden werden und die insbesondere für eine automatisierbare und sichere Handhabung einer Vielzahl von Proben geeignet ist. Die Aufgabe der Erfindung besteht insbesondere in der Schaffung eines verbesserten Systems zur Präparation von Kryokonserven, wie z. B. Blut-Kryokonserven. Die Aufgabe der Erfindung ist es auch, ein neuartiges Verfahren zur Handhabung biologischer suspendierter Proben anzugeben, das insbesondere automatisierbar und sicher durchführbar ist.

[0009] Diese Aufgaben werden mit einer Präparationsvorrichtung, einer Präparationsstation und einem Verfahren mit den Merkmalen gemäß den Patentansprüchen 1, 9 und 12 gelöst. Vorteilhafte Ausführungsformen und Anwendungen der Erfindung ergeben sich aus den abhängigen Ansprüchen.

[0010] Die Grundidee der Erfindung ist es, eine Präparationsvorrichtung bereitzustellen, die mindestens zwei Behältnisse zur Aufnahme der zu behandelnden Suspensionsproben aufweist, wobei die Behältnisse im Unterschied zu herkömmlichen Systemen durch relativ zueinander ortsfest positionierte Kammern mit festen Wänden gebildet werden. Die Kammern sind über einzeln betätigbare Leitungsverbindungen miteinander verbunden oder mit Anschlussstücken zur optionalen Ausbildung von Leitungsverbindungen zwischen den Kammern ausgestattet. Die erfindungsgemäße Präparationsvorrichtung ist gemäß einer ersten Ausführungsform durch einen integralen Aufbau gebildet, bei dem die Kammern in einem Kammerkörper geformt sind, an dessen einem Ende die Leitungsverbindungen ansetzbar oder einstellbar sind. Gemäß einer zweiten Ausführungsform umfasst die Präparationsvorrichtung ein Rahmengestell, in das die Kammern einzeln einsetzbar sind. Die Anschlussstücke der einzelnen Kammern sind sämtlich auf einer (z. B. unteren) Seite des Rahmengestells angeordnet. Je nach Bedarf werden die zunächst mit einem Septum verschlossenen Anschlussstücke geöffnet und über Leitungsverbindungen paarweise in Verbindung gebracht. Die Gestaltung mit einzelnen Kammern ist gemäß einer dritten Ausführungsform derart ausgebildet, dass das Rahmengestell mit einer Ventilplatte mit Leitungsverbindungen ausgestattet ist, über die die einzelnen Kammern paarweise verbunden werden können. Die Ausbildung der Präparationsvorrichtung als integraler Aufbau oder als Gestellaufbau mit mindestens zwei Kammern besitzt die Vorteile, dass die Präparationsvorrichtung im Rahmen eines automatisierten Verfahrensablaufes einen sicher greif- und manipulierbaren Gegenstand darstellt und dass die Probenhandhabung, insbesondere die unabhängige Vorbefüllung der Kammern, die Behandlung von Proben in den Kammern und die Überführung der Proben zwischen den Kammern, vereinfacht wird. Bei Anwendung der erfindungsgemäßen Präparationsvorrichtung zur Her-

stellung von Blutproben für die Kryokonservierung sind vorzugsweise mindestens drei Kammern vorgesehen.

[0011] Gemäß der genannten ersten Ausführungsform der Erfindung sind die Kammern vorzugsweise in Form von geraden Kreiszylindern in einem Kunststoffkörper gebildet, an dessen einem Ende eine Ventilplatte angebracht ist, die mindestens eine Leitungsverbindung zur Kopplung von jeweils zwei Kammern enthält. Der Aufbau mit einem integralen Kunststoffkörper besitzt den Vorteil, dass die Präparationsvorrichtung als Einwegprodukt herstellbar ist, so dass Sterilitäts- und Verwechslungsprobleme ausgeschlossen werden können. Als weiterer Vorteil ergibt sich eine hohe Stabilität der Präparationsvorrichtung insbesondere bei Zentrifugationsvorgängen.

[0012] Die genannten zweiten und dritten Ausführungsformen der Erfindung stellen jeweils einen modularen Aufbau dar. Die Kammern können als Einwegprodukte verwendet werden. Als zusätzlicher Vorteil ergibt sich beim Rahmenaufbau ein relativ geringes Gewicht.

[0013] Die Übertragung von Proben zwischen den Kammern erfolgt vorzugsweise durch einen hydrostatischen Druck, der als Gasdruck oder vorzugsweise mit Druckstempeln ausgeübt wird, die jeweils in den Kammern angeordnet sind. Alternativ ist es möglich, den Druck mit einem mechanisch betätigbaren Kolben zu übertragen (z. B. mit einem Pleuelgestänge). Die Kammern der erfindungsgemäßen Präparationsvorrichtung bilden bei dieser Gestaltung Kolben-Druckerzeuger, die sowohl zur Aufnahme der jeweiligen Proben als auch zur Übertragung der Proben in benachbarte Kammern eingerichtet sind.

[0014] Gemäß einer weiteren bevorzugten Gestaltung besteht die Präparationsvorrichtung, insbesondere die Kammern als Hauptkomponenten, zumindest teilweise aus einem transparenten Kunststoffmaterial. Bei Verwendung von nicht-transparentem Material besitzen die Kammern vorzugsweise mindestens ein transparentes Fenster zur optischen Detektion. Es wird eine zuverlässige und reproduzierbare optische Detektion von Probeneigenschaften, insbesondere der Lage der Phasengrenze nach einer Zentrifugation, ermöglicht.

[0015] Gegenstand der Erfindung ist auch eine Präparationsstation, die mit der erfindungsgemäßen Präparationsvorrichtung ausgestattet ist und des Weiteren eine Druckeinrichtung zur Probenübertragung zwischen den Kammern, eine Detektoreinrichtung zur Messung von Probeneigenschaften in den Kammern und eine Stelleinrichtung zur selektiven Kopplung von Kammern aufweist.

[0016] Gegenstand der Erfindung ist auch ein Verfahren zur Präparation von Suspensionen, die biologisch relevante Komponenten, wie z. B. Zellen, Zellbestandteile oder Makromoleküle, enthalten, unter Verwendung der erfindungsgemäßen Präparationsvorrichtung. Das Verfahren zeichnet sich insbesondere dadurch aus, dass alle Präparationsschritte mit der gesamten Präparationsvorrichtung durchgeführt werden, die verschiedene Kammern zur Aufnahme von Proben in verschiedenen Präparationsstadien enthält.

[0017] Die Erfindung besitzt die folgenden Vorteile für die Probenpräparation, insbesondere für die Herstellung von Blut-Kryokonserven. Der Präparationsprozess ist zur Erhöhung der Produktivität bei der Konservenherstellung, d. h. zur Erzielung eines möglichst hohen Konservendurchsatzes, automatisierbar, wobei gleichzeitig die Herstellungsqualität gesteigert und unabhängig von der Handfertigkeit eines Bedieners aufrechterhalten wird. Eine erfindungsgemäß hergestellte Blutkonserve erfährt bereits durch die Verwendung der Präparationsvorrichtung eine Qualitätssteigerung, ohne dass die Präparation wesentlich verteuert wird.

[0018] Die erfindungsgemäße Präparationsvorrichtung ist während der Präparationsprozedur nach außen hin absolut abgeschlossen. Sie tritt lediglich einmalig jeweils beim Befüllen und beim Entleeren in Kontakt mit der Umgebung. Beispielsweise erfolgt die Vorbehandlung einer Konserve bis zum Erlangen des einfrierfertigen Zustandes absolut steril. Vorteilhafterweise wird das Öffnen, Verbinden und Verschließen von Beuteln und Verbindungsschläuchen entsprechend den herkömmlichen Systemen vermieden. Die Suspensionsprobe verlässt während der Präparationsschritte nicht die Präparationsvorrichtung. Eine Verwechslung z. B. von Blut verschiedener Spender oder eine Kontamination durch Fremdblut oder Mikroorganismen sind ausgeschlossen. Die Identität des Spenderblutes ist garantiert. Der Präparationsvorgang wird stark beschleunigt, da Arbeitsschritte, die bei herkömmlichen Systemen ggf. mehrfach notwendig sind, erfindungsgemäß vollständig entfallen können. Ein teilweiser oder vollständiger Probenverlust oder eine Kontamination der Arbeitsumgebung einschließlich des Laborpersonals durch undichte Schlauchverbindungen werden bei der erfindungsgemäßen Präparationsvorrichtung ausgeschlossen.

[0019] Die erfindungsgemäße Präparationsvorrichtung bildet ein festes Behältnis, das im Vergleich mit herkömmlich verwendeten Blutbeuteln ein definiertes und reproduzierbares Greifen und Handhaben der Vorrichtung und der an dieser angebrachten Ventile und/oder Stutzen ermöglicht. Das Greifen oder Positionieren und Klemmen von Verbindungsschläuchen entfällt, wenn die mindestens eine Verbindungsleitung in die Präparationsvorrichtung integriert ist und somit ein reproduzierbares und mehrfaches Verbinden der einzelnen Kammern auf kürzestem Weg ermöglicht. Durch die kurzen Wege und die Wahl eines geeigneten Querschnittes der jeweiligen Verbindungsleitung lässt sich die Transferzeit zur Übertragung von Proben zwischen den Kammern optimieren. Der Aufbau der Vorrichtung ermöglicht ein definiertes Positionieren der mindestens einen Verbindungsleitung. Ein verschentliches Verbinden von aktuell nicht kooperierenden Kammern wird ausgeschlossen. Ein Deformieren oder Quetschen der Kammern wird erfindungsgemäß vermieden. Eine z. B. durch Zentrifugation eingestellte Phasentrennung von Probenbestandteilen kann durch einen Greifvorgang nicht verwischt werden.

[0020] Die feste und vorzugsweise symmetrische Anordnung der Kammern in einer erfindungsgemäßen Präparationsvorrichtung ermöglicht ein schnelles und definiertes Positionieren der jeweils interessierenden Kammer in einem Präparationssystem unabhängig vom Verfahrensschritt. Alle Sensoren und Aktoren sind automatisch korrekt positioniert. Es wird ein erhöhter, fehlerfreier Durchsatz erzielt. Beispielsweise lassen sich mit einer erfindungsgemäß Präparationsvorrichtung rund dreifach mehr Kryokonserven pro Zeiteinheit präparieren. Die Präparationsvorrichtung ermöglicht eine freie Materialwahl und Dimensionierung der Außenform der Kammeranordnung. Vorteilhafterweise kann die Vorrichtung ohne Weiteres mit herkömmlichen Zentrifugiereinrichtungen verwendet werden.

[0021] Durch die Herstellung der Präparationsvorrichtung aus kostengünstigen Kunststoffmaterialien können große Stückzahlen der Vorrichtung in Spritzgieß- oder Extrusionstechniken hergestellt werden. Dies ist für die erfindungsgemäße Verwendung der fest bewandeten Kammern als Einwegprodukte von Vorteil.

[0022] Insbesondere bei der Präparation von Blutproben ergeben sich zusätzlich die folgenden Vorteile. Für Blutspendedienste entsteht bei Einsatz der erfindungsgemäßen Präparationsvorrichtung kein wesentlicher Zusatzaufwand. Es werden keine Mehrfachbeutelsysteme erforderlich. Die Präparationsvorrichtung kann direkt mit einem einfachen

Spendebeutel (Einfachblutbeutel) gekoppelt werden. Der bei herkömmlichen Verfahren ggf. in den Abfall gelangende oder nur mit großem Aufwand gewinnbare Überstand (Plasma und "Buffy Coat") steht erfindungsgemäß bei Bedarf als zusätzliches Endprodukt zur Verfügung. Die Präparationsvorrichtung liefert auch Vorteile bei der nach der Präparation vorgesehenen Befüllung von Einfrierbeuteln. Ein befüllter Einfrierbeutel kann im angedockten Zustand an der Präparationsvorrichtung mit dieser einfach und steril entlüftet werden, in dem die jeweilige Kammer mit einem Unterdruck beaufschlagt wird.

[0023] Weitere Vorteile und Einzelheiten der Erfindung ergeben sich aus der folgenden Beschreibung der beigefügten Zeichnungen. Es zeigen:

[0024] **Fig.** 1 eine schematische Phantomansicht einer Ausführungsform einer erfindungsgemäßen Präparationsvorrichtung in teilweise auseinander gezogenem Zustand,

[0025] **Fig.** 2 eine Illustration der Einbindung der Präparationsvorrichtung gemäß **Fig.** 1 in eine Vorrichtung zur Herstellung von Blutkonserven,

[0026] **Fig.** 3 eine vergrößerte Teilansicht eines Kammerendes der Präparationsvorrichtung gemäß **Fig.** 1,

[0027] **Fig.** 4 Illustration einer abgewandelten Ausführungsform einer erfindungsgemäßen Präparationsvorrichtung,

[0028] **Fig.** 5 eine schematische Schnittansicht einer erfindungsgemäß verwendeten Einzelkammer, und

[0029] **Fig.** 6 eine Illustration einer herkömmlichen Präparationstechnik (Stand der Technik).

[0030] In **Fig.** 1 ist eine Ausführungsform einer erfindungsgemäßen Präparationsvorrichtung **100** in schematischer Phantomansicht dargestellt. Die Präparationsvorrichtung **100** umfasst einen Kammerkörper **10**, in dem drei Kammern zur Aufnahme von Suspensionsproben gebildet sind, eine Übertragungseinrichtung **20**, bestehend aus einer Ventilplatte **21** und mindestens einer Verbindungsleitung **22**, eine Stempeleinrichtung **30** mit mehreren Druckstempeln **31** bis **33** und eine Deckplatte **40**, die den oberen Abschluss des Kammerkörpers **10** bildet. Der Kammerkörper **10** ist einstückig aus einem transparenten Kunststoffmaterial (z. B. PMMA, Cycloolefin-Copolymere, Polyamid, Polycarbonat, PCHP, Polyester oder Polysulfone) geformt. Er besitzt die äußere Form eines geraden Kreiszylinders mit einer ebenen Oberseite **11** und einer ebenen Unterseite **12**. Im Inneren des Kammerkörpers **10** sind die drei zylinderförmigen Kammern **13**, **14** und **15** zur Probenaufnahme gebildet. Am oberen Ende des Kammerkörpers **10** münden die Kammern frei in die Oberseite **11**. Am unteren Ende besitzt jede Kammer eine Verjüngung **16** mit einem Anschlussstutzen **17**, wie es vergrößert in **Fig.** 3 illustriert ist. Der Anschlussstutzen **17** mündet jeweils in die Unterseite **12** des Kammerköpers **10**.

[0031] Zur Anwendung bei der Präparation von Blutproben besitzt die Präparationsvorrichtung **100** bspw. einen Durchmesser von ca. 18 bis 20 cm, wobei die Höhe des Kammerkörpers **10** ca. 10 bis 12 cm beträgt und die Kammern **13** bis **15** jeweils einen Innendurchmesser von ca. 6 bis 8 cm besitzen. Eine Kammer besitzt vorzugsweise ein Volumen im Bereich von 400 ml bis 600 ml. Die Kammern **13** bis **15** sind vorzugsweise relativ zur Achse des Kammerkörpers **10** symmetrisch verteilt angeordnet.

[0032] Die Übertragungseinrichtung **20** ist zur Übertragung von Proben zwischen den Kammern **13** bis **15** eingerichtet. Die Ventilplatte **21** ist drehbar an der Unterseite **12** des Kammerkörpers **10** befestigt. In die ebenfalls aus Kunststoffmaterial hergestellte Ventilplatte **21** ist die Verbindungsleitung **22** integriert, die einen Überströmkanal bildet. An den Mündungen der Verbindungsleitungen **22** auf der inneren Seite der Verbindungsplatte **21**, die an die Unterseite **12** des Kammerkörpers **10** angrenzt, oder an den Anschlussstutzen **17** der einzelnen Kammern (siehe **Fig.** 3) sind Dichtungsringe aus einem elastischen Material (z. B. PTFE) angebracht. Neben der Dichtfunktion können die Dichtungsringe (nicht dargestellt) auch als Rasteinrichtungen dienen. Bei Drehung der Verbindungsplatte **21** rasten die Dichtungsringe an den gewünschten Positionen der Anschlussstutzen oder der Mündung der Verbindungsleitung **22** ein, wenn diese gerade zueinander ausgerichtet sind.

[0033] Die Ventilplatte **21** besitzt eine Ventilfunktion, da in der Regel Flüssigkeit immer nur in einer Richtung von einer Kammer zur benachbarten Kammer gepumpt wird. Zum Ausschluss einer Fehlbedienung kann an der Ventilplatte **21** oder am Kammerkörper **10** eine Vorrichtung zur erzwungenen Vorgabe einer bestimmten Drehrichtung und/oder eine Wiederholsperre vorgesehen sein. Diese Vorrichtung umfasst bspw. eine Verzahnung, die eine Rückwärtsdrehung ausschließt, und/oder eine zusätzliche Arretierhilfe.

[0034] Der Aufbau der Ventilplatte **21** kann anwendungsabhängig abgewandelt werden (siehe **Fig.** 4). Es können mehrere Verbindungsleitungen vorgesehen sein. Die mindestens eine Verbindungsleitung kann mit einer Sperr- oder Ventileinrichtung ausgestattet sein. In der Ventilplatte können vorzugsweise zusätzliche Durchgangsöffnungen zur Beschickung der Kammern vorgesehen sein. Die Beschikkung kann aber auch von der oberen Seite her erfolgen.

[0035] Zum Probentransport zwischen den Kammern werden die Proben mit einem Druck beaufschlagt. Unter der Wirkung eines Überdruckes in der Kammer, von der die Übertragung ausgeht, wird die Probe über den Überströmkanal in der Ventilplatte **21** übertragen. Der Übertragungsdruck wird mit einer Druckeinrichtung aufgebracht, die Teil der Präparationsstation (siehe **Fig.** 2) ist, in der die erfindungsgemäße Präparationsvorrichtung vorzugsweise verwendet wird. Gemäß einer vorteilhaften Ausführungsform der Erfindung wird der Druck mit einer Stempeleinrichtung **30** übertragen, die in den Kammern **13** bis **15** jeweils einen Druckstempel **31** bis **33** aufweist. Die Druckstempel **31** bis **33** bestehen aus Kunststoffkörpern z. B. in Zylinderform, die formschlüssig in die jeweilige Kammer eingepasst sind. Jeder Druckstempel weist mindestens eine umlaufende Dichtlippe auf, die ggf. auftretende Spalte zwischen den Druckstempeln und den Kammerinnenwänden abdichtet. Die Dichtlippen verhindern ein Durchlauf des Kolbens durch die flüssigen Proben bei Druckbeaufschlagung. Die Kolben mit den Dichtlippen bestehen aus einem Kunststoffmaterial (z. B. PTFE). Der Einsatz der Druckstempel **31** bis **33** in den Kammern besitzt den Vorteil, dass bei einer Bewegung der Präparationsvorrichtung **100** eine Probenbewegung in den Kammern verhindert wird, wenn die Druckstempel jeweils auf den Flüssigkeiten aufgesetzt sind. Nach einer Zentrifugation wird vorteilhafterweise eine Aufhebung der Phasengrenze zwischen den Fraktionen vermieden.

[0036] Die Druckstempel **31** bis **33** können gemäß einer bevorzugten Ausführungsform jeweils eine zentralen Bohrung (gestrichelt eingezeichnet) mit einem Verschluss (z. B. einem Septum) aufweisen. Dies ermöglicht einen Zugriff zu den Proben oder Zusatzflüssigkeiten in den Kammern von der Oberseite der Vorrichtung **100** her.

[0037] Gemäß einer abgewandelten Ausführungsform der Erfindung kann auf die Verwendung der Druckstempel auch verzichtet werden. In diesem Fall wird der Übertragungsdruck direkt auf die Flüssigkeitsoberfläche in der jeweiligen Kammer gegeben. Bei dieser Gestaltung sind die oberen Enden der Kammern an der Oberseite vorzugsweise mit einem Sterilfiltereinsatz ausgestattet, der nur für das jeweilig verwendete sterile Druckmedium (z. B. Luft, inertes Gas)

durchlässig ist. Der Aufbau ohne Druckstempel besitzt die Vorteile eines vergrößerten Innenvolumens und vereinfachten Aufbaus der Kammern und damit einer Kostenersparnis.

[0038] Die obere Deckplatte **40** dient dem Abschluss der Präparationsvorrichtung **100**. Sie ist fest auf dem Kammerkörper **10** angebracht und besitzt Durchtrittöffnungen oder Anschlussstutzen **41**, die jeweils mit den oberen Enden der Kammern **13** bis **15** ausgerichtet sind. Die Anschlussstutzen **41** dienen der Verbindung von einzelnen oder gleichzeitig allen Kammern mit der Druckeinrichtung und/oder Beschickungseinrichtungen.

[0039] Der Verfahrensablauf zur Herstellung einer Blut-Kryokonserve unter Verwendung einer erfindungsgemäßen Präparationsvorrichtung wird im Folgenden unter Bezug auf **Fig.** 2 erläutert. **Fig.** 2 zeigt die Präparationsvorrichtung **100** analog zur Darstellung gemäß **Fig.** 1 in Kombination mit Teilen der Präparationsstation.

[0040] Die Komponenten der Präparationsvorrichtung **100** sind mit den gleichen Bezugszeichen wie in **Fig.** 1 versehen.

[0041] Zur Präparationsstation gehören insbesondere die Druckeinrichtung **50**, eine Detektoreinrichtung **60**, eine Stelleinrichtung **70** und eine Steuereinrichtung **80**. Die Druckeinrichtung **50** umfasst vorzugsweise einen Druckerzeuger **51** mit einem Motor **52** und einem Pumpenteil **53**. Alternativ umfasst die Druckeinrichtung **50** eine Hebeleinrichtung mit einer Pleuelstange. Die mechanische Kraftübertragung besitzt den Vorteil, dass die Positionierung der Druckstempel mit einer erhöhten Präzision erfolgen kann. Gemäß alternativen Ausführungsformen der Erfindung kann der Druckerzeuger auch durch eine Druckquelle (z. B. Druckgasflasche) mit einem Regelventil gebildet werden.

[0042] Die Detektoreinrichtung **60** umfasst insbesondere mindestens ein lichtempfindliches Element **61** zur Erkennung der Phasengrenze. Das lichtempfindliche Element **61** kann anwendungsabhängig mit (nicht dargestellten) Filtereinrichtungen ausgestattet sein. Es können auch mehrere lichtempfindliche Elemente entsprechend den Positionen der Kammern angeordnet sein. Anwendungsabhängig können auch andere Detektoren zur Erfassung von Probeneigenschaften vorgesehen sein, wie sie an sich aus der Analytik bekannt sind (z. B. Spektralphotometer, Widerstandsmesser zur Dichtebestimmung). Die Kammern können auch eine sich jeweils über ihre Länge erstreckende Skalierung zur optischen Kontrolle des Füllstandes, der Position der Druckstempel oder der Position der Phasengrenze aufweisen. Die Detektoren können ferner an anderen Komponenten der Präparationsvorrichtung, z. B. an einer Verbindungsleitung in der Ventilplatte, vorgesehen sein.

[0043] Zur Verstellung der oben erläuterten Ventilplatte **21** umfasst die Stelleinrichtung **70** ein Betätigungselement **71** und einen Stellmotor **72**. Das Betätigungselement **71** besitzt die Form einer Platte mit mindestens einem Vorsprung **73**, der mit mindestens einer entsprechenden Ausnehmung (nicht dargestellt) auf der Unterseite der Ventilplatte **21** zusammenwirkt. Der Vorsprung **73** greift in die Ausnehmung ein und verdreht die Ventilplatte **21** bei Betätigung des Stellmotors **72** in die gewünschte Position, so dass jeweils eine Kammer geöffnet oder geleert werden kann, jeweils zwei Kammern über die Verbindungsleitung **22** verbunden sind oder alle drei Kammern verschlossen sind.

[0044] Die Steuereinrichtung **80** ist mit den Komponenten **50**, **60** und **70** des Präparationssystems verbunden. Je nach Betriebszustand und dem von der Detektoreinrichtung **60** gelieferten Detektorsignal werden in der folgenden Weise der Druckerzeuger **50** und die Stelleinrichtung **70** betätigt. Bei halbautomatischem oder manuellem Betrieb werden die entsprechenden Schritte zumindest teilweise durch einen Bediener durchgeführt.

[0045] In einem Startzustand sind die Kammern der erfindungsgemäßen Präparationsvorrichtung **100** wie folgt beschickt. In der ersten Kammer **13** befindet sich eine Blutspende. Die Blutspende wird aus einem Spenderbeutel in die erste Kammer **13** gefüllt, was ggf. unter Ausübung eines unterstützenden Unterdruckes erfolgt. Die zweite Kammer **14** ist mit einer Waschlösung gefüllt. In der dritten Kammer **15** befindet sich ein Kryoadditiv. Im Startzustand ist die erste Kammer **13** vollständig gefüllt, während die übrigen Kammern **14**, **15** lediglich teilweise befüllt sind. In diesen Kammern ist so viel Volumen frei, wie es zur Übernahme der Erythrozytensuspension nach der Zentrifugation (siehe unten) erforderlich ist. Die Ventilplatte **21** wird nach dem Startzustand (alle verschlossen) so eingestellt, dass bspw. die erste und zweite Kammer **13**, **14** verbunden sind. Vorteilhafterweise ist trotz der Verbindung im druckfreien Zustand über die Verbindungsleitung im Wesentlichen kein Flüssigkeitsaustausch gegeben.

[0046] In einem ersten Präparationsschritt wird der Kammerkörper mit den befüllten Kammern mit einer Zentrifugationseinrichtung zentrifugiert. Die (nicht dargestellte) Zentrifugationseinrichtung besitzt die Bauform einer an sich bekannten Großzentrifuge mit einzelnen Zentrifugenbechern, in denen eine Vielzahl von Präparationsvorrichtungen gleichzeitig zentrifugiert werden können. Während der Zentrifugation erfolgt lediglich die Auftrennung der Blutspende in die Fraktionen. Eine Verschiebung der Druckstempel **31** bis **33** erfolgt nicht. Während der Zentrifugation sind die Kammern verschlossen.

[0047] Der Zustand der Präparationsvorrichtung nach der Zentrifugation ist in **Fig.** 2 dargestellt. In der ersten Kammer **13** sind die gebildeten Fraktionen der Blutspende mit dem Erythrozytensediment **1** der sog. "Buffy Coat"-Schicht **2** und dem Plasmaüberstand **3** illustriert. Das Erythrozytensediment **1** umfasst betriebsabhängig einen Volumenanteil von ca. 45% der Kammer **13**. Der Volumenanteil hängt insbesondere von der Zentrifugationsgeschwindigkeit ab. Bei einer höheren Geschwindigkeit ergibt sich eine höhere Packungsdichte der Erythrozyten und damit ein geringerer Volumenanteil. Die "Buffy-Coat"-Schicht **2** ist ein thrombozyten- und leukozytenhaltiger Belag mit einer gräulichen Färbung, der sich nach der Zentrifugation zwischen den tiefroten Erythrozytensediment **1** und dem hellroten Plasmaüberstand **3** ausbildet.

[0048] Nach der Zentrifugation wird die Präparationsvorrichtung **100** in die Präparationsstation eingesetzt. Die Ventilplatte **21** wird in Durchlassrichtung zwischen die erste und zweite Kammer **13**, **14** gedreht. Dies erfolgt manuell, z. B. mit einem Noppenschlüssel oder mit der Stelleinrichtung **70** (siehe oben). Die erste Kammer **13** wird mit einem Überdruck beaufschlagt. Unter der hydrostatischen oder mechanischen Druckeinwirkung bewegen sich der Druckstempel **31** nach unten und der Druckstempel **32** nach oben. Die aufgetrennte Blutspende wird in die zweite Kammer **14** übertragen. Dieser Präparationsschritt wird beendet, sobald die am unteren Ende der ersten Kammer **13** angeordnete Detektoreinrichtung **60** die "Buffy Coat"-Schicht **2** erfasst. In diesem Zustand ist sichergestellt, dass in dem verjüngtem Bereich **16** (siehe **Fig.** 3) und der Verbindungsleitung noch ausschließlich Erythrozytensediment vorhanden ist. Wenn die "Buffy Coat"-Schicht **2** erfasst worden ist, wird die Druckübertragung gestoppt. Danach wird die Ventilplatte in Verschlussstellung gebracht. Dies erfolgt entweder unmittelbar bei Detektion der Schicht **2** oder zeitlich verzögert, so dass Konzentratreste aus dem verjüngten Bereich **16** noch in die Verbindungsleitung gelangen können.

[0049] Die in die zweite Kammer **14** übertragenen Ery-

throzyten vermengen sich mit der Waschlösung. Die Waschlösung umfasst bspw. physiologische Kochsalzlösung. Es folgt eine weitere Zentrifugation, in deren Ergebnis sich die behandelten Erythrozyten als Konzentrat wiederum im unteren Teil der zweiten Kammer **14** sammeln, während die übrige Waschlösung den Überstand bildet.

[0050] In einem weiteren Präparationsschritt wird analog zu der beschriebenen Weise das gewaschene Erythrozytensediment in die dritte Kammer **15** übertragen. Hierzu wird die Ventilplatte **21** so verdreht, dass die Verbindungsleitung **22** zwischen der zweiten und dritten Kammer **14**, **15** angeordnet ist. Außerdem wird der Druckverteiler **56** entsprechend verstellt. Die Druckübertragung wird wiederum in Abhängigkeit vom Detektorsignal der Detektoreinrichtung **60** gesteuert. Es kann an der zweiten Kammer **14** ein weiterer Sensor (nicht dargestellt) vorgesehen sein. Alternativ ist es möglich, die Präparationsvorrichtung **100** zu dem Sensor **61** hin zu verdrehen, so dass die Phasengrenze in der zweiten Kammer **14** erfasst werden kann.

[0051] Nach Übertragung des gewaschenen Erythrozytensedimentes in die dritte Kammer **15** erfolgt dort die Vermengung mit dem Kryoadditiv. Als Kryoadditiv werden die an sich bekannten Zusatzstoffe verwendet. Das Kryoadditiv umfasst bspw. eine Lösung aus wasserlöslichem Stärkederivat.

[0052] Nach Übertragung der gewaschenen Erythrozyten in die dritte Kammer **15** und Vermengung mit dem Kryoadditiv ist die Kryokonserve einfrierfertig. Es folgt die Übertragung in den anwendungsabhängig gewählten Behälter, z. B. einen Kryobeutel, in dem der Einfriervorgang erfolgt. Vorteilhafterweise ist nach Abschluss der Präparation in der ersten Kammer **13** der Plasmaüberstand als spenderspezifisches Restprodukt vorhanden. Anwendungsabhängig kann das Plasma einer weiteren Verwendung zugeführt werden.

[0053] Einzelheiten einer gegenüber **Fig.** 1 abgewandelten Gestaltung der erfindungsgemäßen Präparationsvorrichtung sind in **Fig.** 4 dargestellt. Die Unterschiede beziehen sich auf die Ausbildung der Ventilplatte **21**. Im obersten Teilbild von **Fig.** 4 ist die Unterseite **12** des Kammerkörpers **10** mit den Kammern **13** bis **15** illustriert. Jede Kammer besitzt eine Ein- und Auslassöffnung in Form eines Anschlussstutzens **17** (siehe **Fig.** 3). An jedem Anschlussstutzen **17** ist ein O-Dichtring **18** vorgesehen. In der Mitte des Kammerkörpers **10** befindet sich entsprechend der Zylinderachse eine Gewindebohrung **19** zur Befestigung der Ventilplatte **21**.

[0054] Im mittleren Teilbild von **Fig.** 4 ist die Ventilplatte **21** einzeln dargestellt. Bei dieser Gestaltung sind zwei Verbindungsleitungen (oder Überströmkanäle) **22**, **23** vorgesehen, die so angeordnet sind, dass mit einer der Verbindungsleitungen **22** oder **23** jeweils zwei Kammern verbunden werden können, während die jeweils andere Verbindungsleitung **22** oder **23** verschlossen ist. Die Verwendung von zwei Verbindungsleitungen besitzt den Vorteil geringerer Verstellwege bei der Einstellung der Kammerverbindungen bei den einzelnen Präparationsschritten. In der Ventilplatte sind drei Ein- und Auslassbohrungen **24** vorgesehen, die so angeordnet sind, dass wenn eine der Ein- und Auslassbohrungen **24** mit einem der Anschlussstutzen **17** ausgerichtet ist, die anderen Anschlussstutzen jeweils verschlossen bleiben.

[0055] Die Ventilplatte **21** besitzt einen umlaufenden O-Dichtring **25**, der eine zusätzliche Dichtung gegenüber der Unterseite **12** des Kammerkörpers **10** bereitstellt. Das Bezugszeichen **26** bezieht sich auf die Drehachse und das Lager der Ventilplatte **21**.

[0056] Im unteren Teilbild von **Fig.** 4 ist die Ventilplatte **21** und die Unterseite **12** des Kammerkörpers **10** im zusammenmontierten Zustand dargestellt. Wird die Ventilplatte **21** vom dargestellten Zustand nach links gedreht, so werden zunächst mit der Verbindungsleitung **22** die Kammern **13** und **14** verbunden und bei der weiteren Verstellung werden die Kammern **14** und **15** über die Verbindungsleitung **23** verbunden. Damit können mit einem kurzen Stellweg die beiden oben erläuterten Präparationsschritte ausgeführt werden.

[0057] Die in den **Fig.** 1 bis 4 illustrierte Ausführungsform der Erfindung kann je nach Aufgabenstellung vielfältig modifiziert werden. So können bspw. zur Durchführung weiterer Präparationsschritte im Kammerkörper weitere Kammern zur Aufnahme weiterer Zusatzstoffe vorgesehen sein. Anstelle der 120°-Anordnung können die Kammern auch anderweitig im Kammerkörper oder einem Rahmengestell (siehe unten) angeordnet werden. Die Beschickung der Kammern kann anwendungsabhängig von der Ober- oder Unterseite her erfolgen. Dies erfolgt vorzugsweise unter Verwendung von Schlauch- oder Pipettiersystemen. Gemäß einer bevorzugten Gestaltung der Erfindung sind die Einlassöffnungen der Kammern gerade an die Außendurchmesser von standardisierten Flüssigkeitspipetten oder Schlauchadapter angepasst, so dass diese zur Beschickung einfach angesetzt und betätigt werden können. Die Präparationsvorrichtung kann anwendungsabhängig in ihrer Größe beliebig skaliert werden. Die Übertragungseinrichtung mit der Ventilplatte kann durch eine fest eingestellte Anordnung mehrerer Verbindungsleitungen mit betätigbaren Ventilen ersetzt werden.

[0058] An der Außenseite des Kammerkörpers können zusätzliche Greif- oder Befestigungseinrichtungen zur Handhabung des Kammerkörpers und/oder zum Einsatz in eine Zentrifuge vorgesehen sein.

[0059] Der Kammerkörper mit den integrierten Kammern kann erfindungsgemäß durch eine Anordnung einzelner Kammern in einem Rahmengestell ersetzt werden. Diese Gestaltung besitzt Vorteile in Bezug auf eine separate Befüllung der einzelnen Kammern vor der Zusammensetzung zur Präparationsvorrichtung und die Entsorgung der Kammern nach Verwendung. Als Rahmengestell kann jede geeignete Struktur verwendet werden, in die die Kammern entsprechend der gewünschten Anordnung fixiert einsetzbar sind und die eine genügende Stabilität bei der Zentrifugation besitzt. Je nach der Gestaltung der Kammern ist die Struktur des Rahmengestells angepasst.

[0060] Werden als Kammern fertige Kolbenspritzen mit geeigneten Kolbendurchmessern verwendet, so besitzt das Rahmengestell Ausnehmungen zur Aufnahme der Spritzenkolben. Wenn die Einzelkammern durch gerade Rohrkörper gebildet sind, werden die Ausnehmungen des Rahmengestells entsprechend angepasst. Am Boden des Rahmengestells sind ggf. konisch vorgeformte Kammerböden vorgesehen, wie dies in **Fig.** 5 illustriert ist.

[0061] **Fig.** 5 zeigt eine Einzelkammer in schematischer Schnittansicht. Zwei oder mehr derartige Einzelkammern (z. B. entsprechend der obigen Gestaltung drei Einzelkammern) sind an einem Rahmengestell (nicht dargestellt) vorgesehen. Die Einzelkammer **90** umfasst eine Kammerwand **91** in Form eines geraden Kreiszylinders und einen sich verjüngenden Teilbereich **92**, der in einem entsprechend geformten Stützsockel **93** ruht, der Teil des Rahmengestells ist. Im Inneren der Einzelkammer **90** befindet sich der Druckstempel (siehe oben). Der Druckstempel ist bei dieser Gestaltung nicht zylinderförmig, sondern als Stempelplatte **94** mit einem außen umlaufenden Dichtring **97** ausgebildet. Die Stempelplatte **94** besteht beispielsweise aus PMMA. Der Dichtring **97** ist ein z. B. aus PTFE bestehendes Formteil, das formschlüssig über den äußeren Rand der Stempelplatte **94** gezogen ist. Der Querschnitt des Dichtringes **97** besitzt

eine U-Form, deren offenen Enden zwei Dichtlippen bilden. Durch diese Formgebung wird ein dichtendes Anlegen der Dichtlippen an die Kammerwand sicherstellt. Die Oberseite der Einzelkammer **90** ist mit einer Deckplatte **95** verschlossen, die eine Durchtrittsöffnung **96** zum Durchlass des Druckmediums aufweist.

[0062] Die Einzelkammer **90** besitzt bspw. ein Volumen von 470 ml bei einem Durchmesser von ca. 80 mm, einer Länge der Kammerwand **91** von ca. 110 mm und einer Höhe des Stützsockels **93** von ca. 30 mm. Der Teilbereich **92** grenzt ein Teilvolumen von ca. 30 ml ab.

[0063] Bei einem erfindungsgemäßen Verfahren zur Blutpräparation kann abweichend von der oben erläuterten Zentrifugation der gesamten Präparationsvorrichtung die folgende Einzelkammerzentrifugation vorgesehen sein. Dabei wird die jeweils interessierende Einzelkammer (z. B. gemäß **Fig. 5**) aus dem Rahmengestell entnommen und separat zentrifugiert. Vor oder nach der Zentrifugation ist die Einzelkammer im Rahmengestell zur Durchführung der übrigen Schritte der Probenpräparation angeordnet. Dieses Verfahren ist besonders vorteilhaft, falls zur Zentrifugation keine passende Zentrifuge zur Verfügung steht.

[0064] Die in der vorstehenden Beschreibung, den Ansprüchen und den Zeichnungen offenbarten Merkmale der Erfindung können sowohl einzeln als auch in beliebiger Kombination für die Verwirklichung der Erfindung in ihren verschiedenen Ausgestaltungen von Bedeutung sein.

Patentansprüche

1. Präparationsvorrichtung (**100**) zur Behandlung von Suspensionsproben, insbesondere zur Präparation von Blut-Kryokonserven, mit einer Anordnung von mindestens zwei Behältnissen zur Aufnahme von Suspensionsproben, Probenteilen und/oder Zusatzstoffen, **dadurch gekennzeichnet**, dass die Behältnisse als Kammern (**13** bis **15**, **90**) mit festen Wänden gebildet und relativ zueinander ortsfest angeordnet sind, wobei eine Übertragungseinrichtung (**20**) mit mindestens einer Verbindungsleitung (**22**) vorgesehen ist, über die die Kammern (**13** bis **15**) miteinander verbunden werden können.

2. Präparationsvorrichtung gemäß Anspruch 1, bei der die Kammern (**13** bis **15**) in einem einstückigen Kammerkörper (**10**) gebildet sind.

3. Präparationsvorrichtung gemäß Anspruch 1, bei dem die Kammern (**90**) als Einzelkammern lösbar in einem Rahmengestell befestigt sind.

4. Präparationsvorrichtung gemäß einem der vorhergehenden Ansprüche, bei der die Wände der Kammern oder der Kammerkörper (**10**) aus einem transparenten Material bestehen.

5. Präparationsvorrichtung gemäß einem der vorhergehenden Ansprüche 1 oder 2, bei der die Kammern (**13** bis **15**) die Gestalt gerader Hohlzylinder besitzen, die von einer Oberseite (**11**) bis zu einer Unterseite (**12**) des Kammerkörpers (**10**) verlaufen, wobei an der Unterseite (**12**) jede Kammer (**13** bis **15**) einen Anschlussstutzen (**17**) aufweist, mit dem jeweils ein Ende der mindestens einen Verbindungsleitung (**22**) verbunden werden kann.

6. Präparationsvorrichtung gemäß einem der vorhergehenden Ansprüche, bei der in jeder Kammer ein Druckstempel (**31** bis **33**) vorgesehen ist.

7. Präparationsvorrichtung gemäß Anspruch 6, bei der jeder Druckstempel (**31** bis **33**) eine umlaufende Dichtlippe aufweist.

8. Präparationsvorrichtung gemäß einem der vorhergehenden Ansprüche, bei der die Übertragungseinrichtung (**20**) durch eine Ventilplatte (**21**) gebildet wird, in der mindestens eine Verbindungsleitung (**22**) integriert ist, wobei die Ventilplatte (**21**) verdrehbar angeordnet ist.

9. Präparationsstation zur Präparation von Suspensionsproben, die umfasst:
mindestens eine Präparationsvorrichtung (**100**) gemäß einem der vorhergehenden Ansprüche,
eine Druckeinrichtung (**50**),
eine Detektoreinrichtung (**60**),
eine Stelleinrichtung (**70**), und
eine Steuereinrichtung (**80**).

10. Präparationsstation gemäß Anspruch 9, bei der die Druckeinrichtung (**50**) einen pneumatischen Druckerzeuger oder einen mechanischen Druckerzeuger mit Pleuelstangen umfasst.

11. Präparationsstation gemäß Anspruch 9 oder 10, bei der die Stelleinrichtung (**70**) ein Betätigungselement (**71**) aufweist, mit dem die Übertragungseinrichtung (**20**) derart einstellbar ist, dass jeweils zwei Kammern über die mindestens eine Verbindungsleitung (**22**) verbunden sind.

12. Verfahren zur Präparation von Suspensionsproben unter Verwendung einer Präparationsvorrichtung (**100**) gemäß einem der Ansprüche 1 bis 8, bei dem abwechselnd eine Behandlung einer Probe in mindestens einer der Kammern (**13** bis **15**, **90**) und eine Übertragung mindestens eines Teils der Probe zwischen zwei Kammern erfolgt.

13. Verfahren gemäß Anspruch 12, bei dem die Probenbehandlung eine Zentrifugation der Probe und/oder eine Behandlung der Probe mit Zusatzstoffen umfasst.

14. Verfahren gemäß Anspruch 13, bei dem bei der Zentifugation der Probe die gesamte Präparationsvorrichtung (**100**) oder eine Einzelkammer (**90**) zentrifugiert wird.

15. Verfahren gemäß einem der Ansprüche 12 bis 14, bei dem eine Blut-Kryokonserve herstellt wird.

Hierzu 5 Seite(n) Zeichnungen

Nummer: **DE 101 34 913 A1**
Int. Cl.[7]: **A 61 M 1/00**
Offenlegungstag: 20. Februar 2003

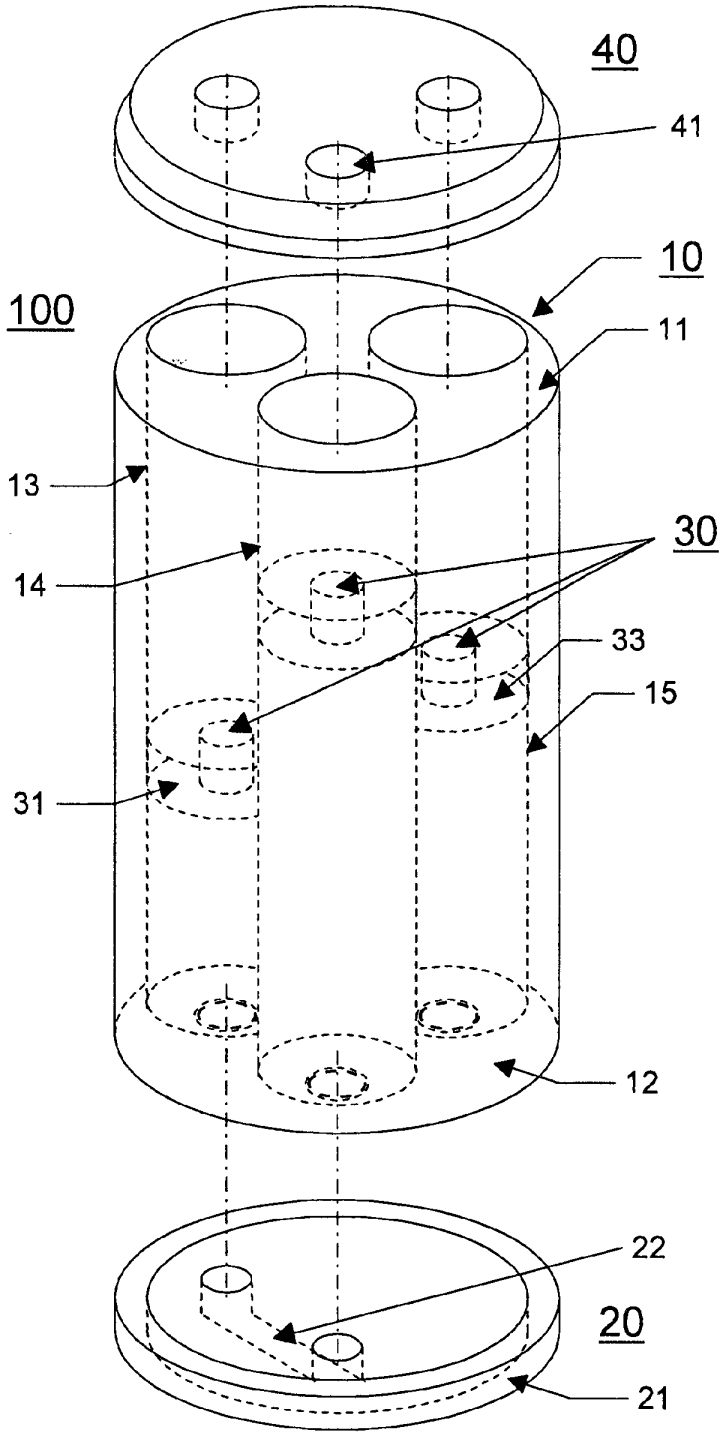


Fig. 1

Nummer: DE 101 34 913 A1
Int. Cl.[7]: A 61 M 1/00
Offenlegungstag: 20. Februar 2003

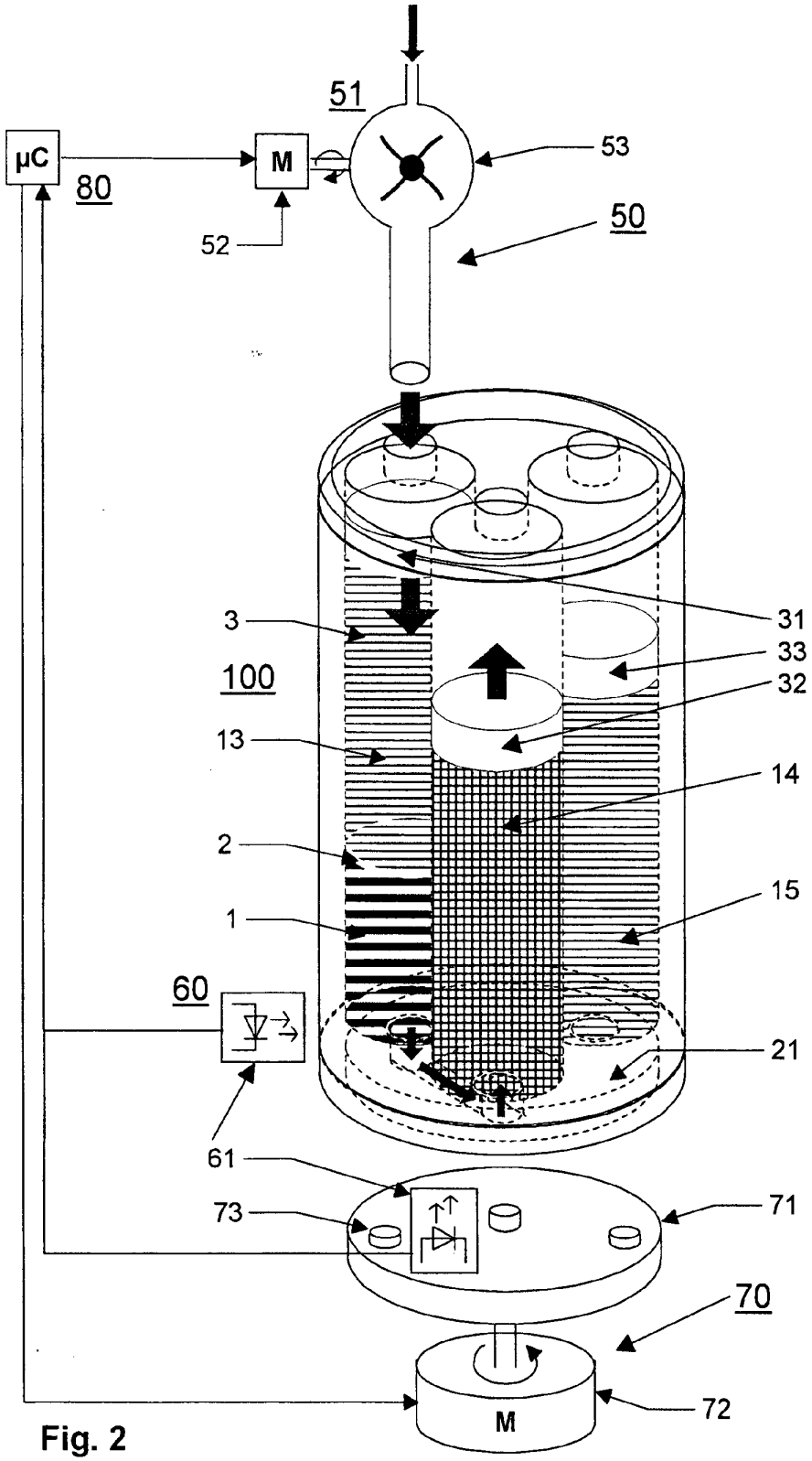


Fig. 2

102 680/59

Nummer: DE 101 34 913 A1
Int. Cl.[7]: A 61 M 1/00
Offenlegungstag: 20. Februar 2003

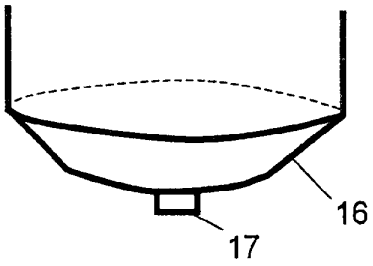


Fig. 3

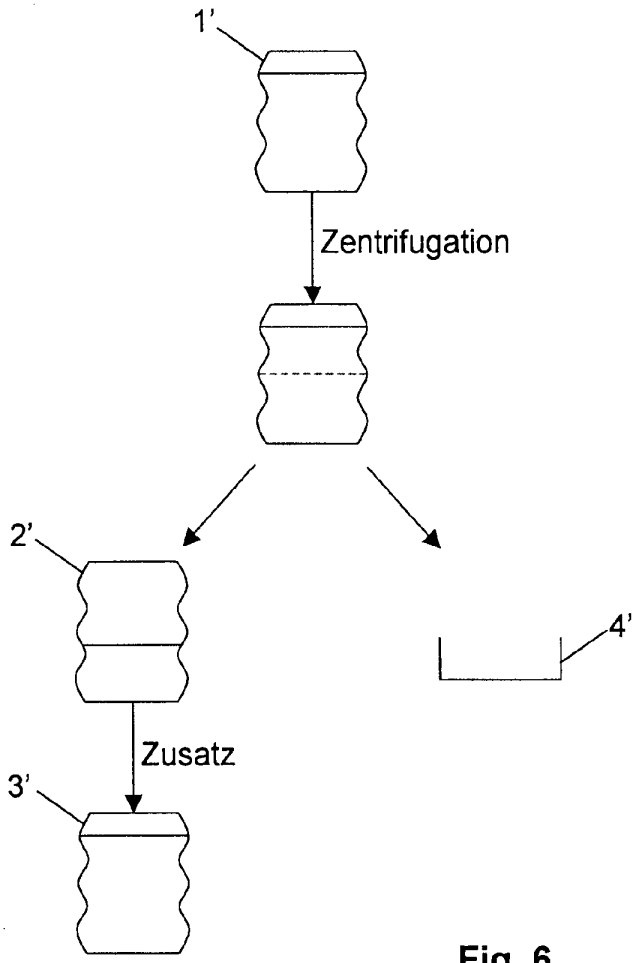
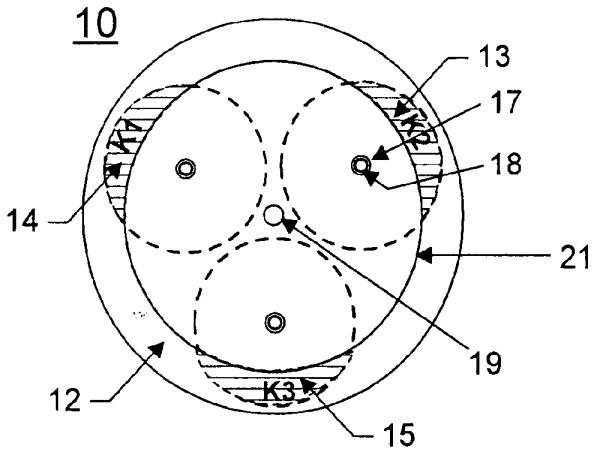
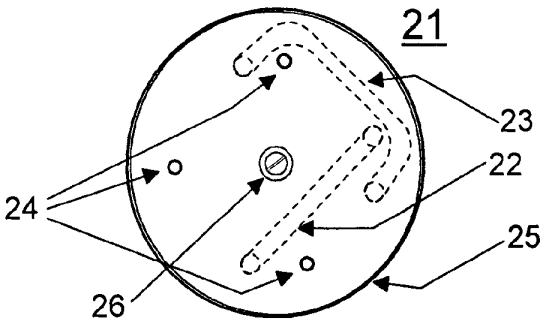


Fig. 6
(Stand der Technik)

Nummer: DE 101 34 913 A1
Int. Cl.[7]: A 61 M 1/00
Offenlegungstag: 20. Februar 2003





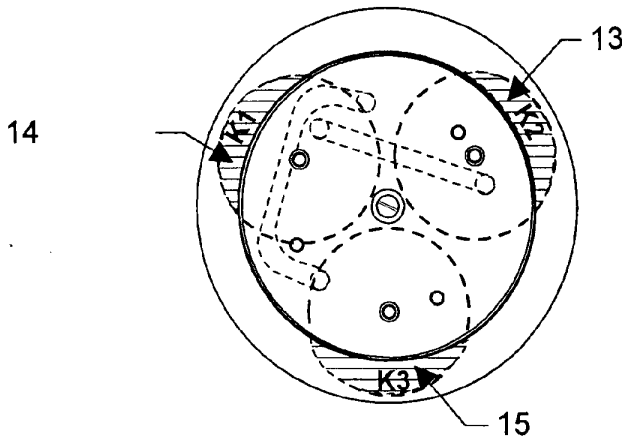


Fig. 4

102 680/59

Nummer: DE 101 34 913 A1
Int. Cl.[7]: A 61 M 1/00
Offenlegungstag: 20. Februar 2003

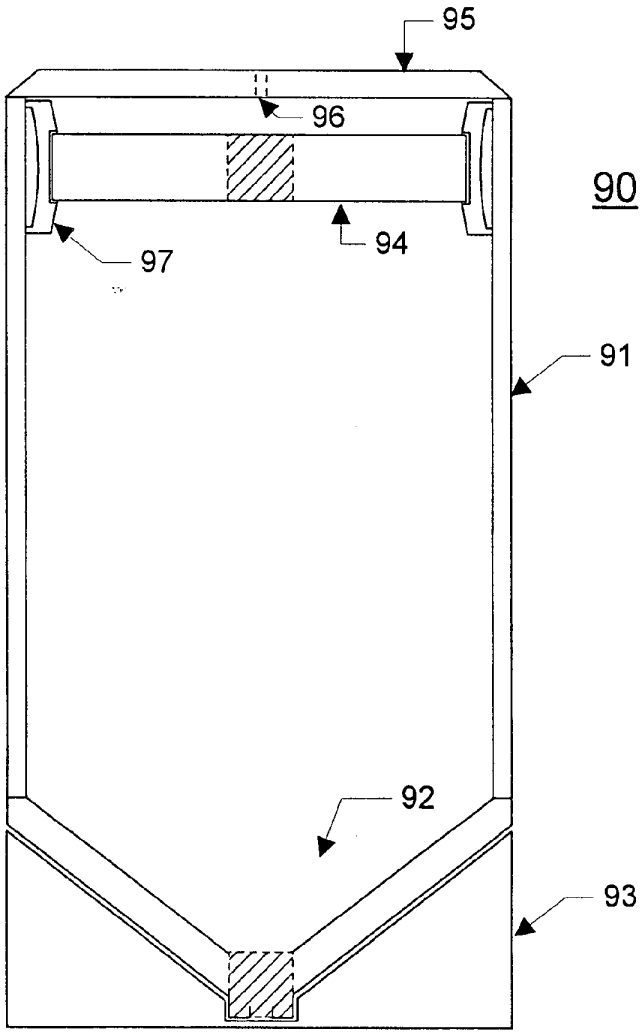


Fig. 5

Notice of Reasons for Refusal

Application number: Japanese Patent Application No. 2020-118498
Date of Drafting: Reiwa 3(2021) August 2
Patent examiner: OKAZAKI, Jun 3330 2Q00
Representative/Applicant: MIYOSHI, Hidekazu (other trinominal)
Applied Provisions: Article 29 (2) (Inventive Step) Article 36 (6) (ii) (Clarity Requirement)

This application should be refused for the reason mentioned below. If the applicant has any opinion(s) against the reason, a written opinion should be submitted within 3 months from the date on which this notification was dispatched.

Reason

1. (Inventive step) The claimed invention(s) listed below of this patent application shall not be granted a patent under the provision of Patent Act Article 29 (2) for the reason that the claimed invention(s) could have easily been made by persons who have common knowledge in the technical field to which the claimed invention(s) pertains, on the basis of the invention(s) described in the distributed publication listed below or made available to the public through electric telecommunication lines in Japan or other foreign countries prior to the filing of the patent application.

2. (Clarity) This patent application does not fulfill the requirement of the provision of Patent Act Article 36(6)(ii) in terms of the item(s) listed below regarding the statement of the scope of claims.

Note (For the cited documents, please refer to the list of cited documents below.)
- Reason 1 (Inventive step)

- Claim 1-10

- Cited Document, etc. 1-2

- Remarks

[About Claim 1]
Are the blood isolation device which was connected to the patient needles (first needle 508;[0038] etc.) which it was a blood sample optimization system for optimizing the blood samples ([0020] etc.) brought together in Cited document 1 ([0019]-[0055], Fig.5-8) with blood collecting machines (sample vessels 506;[0038] etc.) (sample-procurement system;[0038] etc.), and were constituted for a patient's venipuncture in order to be able to take out the first portions of a patient's blood sample and the aforementioned blood samples ([0021] etc.) which contain a pollutant

at least, and the aforementioned patient needle, and was connected to the aforementioned blood collecting course between the sample needle (refer to suggestion of Fig.5 etc.) constituted so that the aforementioned blood collecting machine might be accepted in order to collect the second portion of the aforementioned blood sample as the blood collecting course constituted so that the aforementioned blood sample might be carried, and the aforementioned patient needle and the aforementioned sample needle, and are connected to the inlet ports (sterile input tubing 514;[0039] etc.) constituted so that the aforementioned blood sample might be accepted, and the aforementioned inlet port, and are an isolation chamber and it accepts the first portion of the aforementioned blood sample (Refer to / etc / Fig.5]), The isolation chamber (pre-sample reservoirs 504;[0038] etc.) constituted so that a pollutant might be included in the first portion of the aforementioned blood sample, Including a sampling channel, and (second sterile output tubing 518;[0038], Fig.5), etc. which were constituted so that it might have a proximal edge connected to the aforementioned inlet port and the second portion of the aforementioned blood sample might be accepted, the aforementioned isolation chamber, [the aforementioned sampling channel and the aforementioned inlet port] Enable the second portion of the aforementioned blood sample to bypass the aforementioned isolation chamber, are constituted so that the second portion of the aforementioned blood sample may be made to go to the aforementioned exit port, and, [the aforementioned exit port] Blood sample optimization system , containing ([0038] etc.) blood isolation devices constituted so that the second portion of the aforementioned blood sample may be discharged in the aforementioned blood collecting machine is described.

Cited document 2 ([0012]-[0013] etc.) has disclosed the technology , which constitutes the housing (needle tube base material 2) which stores and demarcates the technology, the port, isolation chamber, and flow path which constitute the isolation chamber which is an isolation chamber which has a vent containing the air permeability blood barrier (air permeability blood impermeable component 23) in a blood sample optimization system (blood collecting needle), and drives out the air in an isolation chamber through a vent.

An invention described in Cited documents 1-2 belongs to the same technical field of the blood collecting field.
In an invention described in Cited document 1, it is easy for a person skilled in the art to constitute by referring to the technology of the description to Cited document 2, so that the same air permeability blood barrier and housing as an invention related to the Claim 1 of this application may be provided.

[About Claims 2 and 4]
Refer to [0012]-[0013] of Cited document 2.

[About Claim 3]
It can be called design matter to arrange sealant to a sample needle.

[About Claim 5]
Refer to [0011] of Cited document 2.

[About Claim 6]
Refer to the Fig.5 of Cited document 1.

[About Claims 7-10]
Refer to the explanation as stated above including the description of Cited document 1-2.

- Reason 2 (Clarity)

- The description of Claims 1-10 Claims 1-10 is indefinite in respect of the following. Therefore, The claimed invention in Claims 1-10 is not clear.

(1) About the description of Claim 1
As for a description with "the first portions of a patient's blood sample and the aforementioned blood sample which contains a pollutant at least" of Claim 1, what "a pollutant is included for at least" is indefinite considering whether the "blood sample" is started and whether "the first portion of the aforementioned blood sample" is started as Japanese. In dependent claim -- the same .

(2) About the description of Claims 4 and 7
The description with "the portion of succession of the aforementioned blood sample" of Claims 4 and 7 is indefinite in whether what "follows" what kind of portion is specified. In dependent claim -- the same .

<The list of cited documents etc.>
1.The description of US Publication of Unexamined Patent Application No. 2008/0145933
2.JP 2001-000424A

Record of the result of prior art search
- Technical fields searched:

IPC
A61B 5/00 - 5/398
DB name

- Prior art documents: JP S 58 - 025146A

JP H 09-504726A
JP H 02-224742A
The description of US Publication of Unexamined Patent Application No. 2011/0306899

This record of the result of prior art search does not constitute the reasons for refusal.

<Suggestions in amending>
(1) When making amendment to the description or the scope of claims, the amended

parts should be underlined so as to be clearly identified (please refer to Note 6 and 7 of Form 13, Regulations under the Patent Act).
(2) Correction must be performed within the scope of the matter described in the The translation of a document written in foreign language (or the after Amendment Description by Correction of Erroneous Translation, a scope of the claim, or Drawings) of this application. In addition, for the evidence of the legality of each amendment, allege the legality in a written opinion with clear indication of the corresponding parts in the translation (or the description, scope of the claims or drawings after amendment by Written Correction of Mistranslation).
(3) One should make sure not to perform any corrections that invoke a violation against Patent Act Article 17-2(4) when amending the scope of claims.

Please contact the following contact, if there is any inquiries about the contents of this Notification of Reasons for Refusal or a request for an intervew with the examiner. When sending of a draft amendment etc. is wished by E-mail etc., please inform me of that by telephone.

The First Examination Department analysis diagnosis (medicine diagnosis) Okazaki * TEL.03-3581-1101 Extension 3291

A Director(p.p.), an examiner, and assistant examiner OKUMA, Yasuo -- * ▲ tearing -- ▼ and 9710 3330

拒絶理由通知書

特許出願の番号	特願２０２０－１１８４９８
起案日	令和　３年　８月　２日
特許庁審査官	岡▲さき▼　潤　　３３３０　２Ｑ００
特許出願人代理人	三好　秀和（ほか　３名）　様
適用条文	第２９条第２項（進歩性） 第３６条第６項第２号（明確性）

この出願は、次の理由によって拒絶をすべきものです。これについて意見がありましたら、この通知書の発送の日から３か月以内に意見書を提出してください。

理由

１．（進歩性）この出願の下記の請求項に係る発明は、その出願前に日本国内又は外国において、頒布された下記の刊行物に記載された発明又は電気通信回線を通じて公衆に利用可能となった発明に基いて、その出願前にその発明の属する技術の分野における通常の知識を有する者が容易に発明をすることができたものであるから、特許法第２９条第２項の規定により特許を受けることができない。

２．（明確性）この出願は、特許請求の範囲の記載が下記の点で、特許法第３６条第６項第２号に規定する要件を満たしていない。

記　　（引用文献等については引用文献等一覧参照）

●理由１（進歩性）について

・請求項　１－１０

・引用文献等　１－２

・備考

[請求項１について]

引用文献１（[0019]-[0055],図5-8）には、

採血器（sample vessels 506;[0038]等）によって集められる血液サンプル（[0020]等）を最適化するための血液サンプル最適化システム（sample-procurement system;[0038]等）であって、

患者の血液サンプル、少なくとも汚染物質を含む（[0021]等）前記血液サンプルの第１の部分を取り出せるようにするために患者の静脈穿刺用に構成された患者針（first needle 508;[0038]等）と、

前記患者針に接続され、前記血液サンプルを運ぶように構成された採血経路と（図5等参照）、
前記血液サンプルの第２の部分を集めるために前記採血器を受け入れるように構成されたサンプル針（図5等の示唆参照）と、
前記患者針と前記サンプル針との間の前記採血経路に接続された血液隔離装置であって、
前記血液サンプルを受け入れるように構成された入口ポート（sterile input tubing 514;[0039]等）と、
前記入口ポートに接続され、隔離チャンバであって、前記血液サンプルの第１の部分を受け入れ、前記血液サンプルの第１の部分に汚染物質を含むように構成された隔離チャンバ（pre-sample reservoirs 504;[0038]等）と、
前記入口ポートに接続される近位端を有し、前記血液サンプルの第２の部分を受け入れるように構成されたサンプリング流路と（second sterile output tubing 518;[0038],図5等）を含み、
前記隔離チャンバ、前記サンプリング流路及び前記入口ポートは、前記血液サンプルの第２の部分が前記隔離チャンバを迂回することを可能にし、前記血液サンプルの第２の部分を前記出口ポートに向かわせるように構成され、前記出口ポートは、前記血液サンプルの第２の部分を前記採血器に排出するように構成される（[0038]等）、血液隔離装置とを含む、血液サンプル最適化システム、
が記載されている。

引用文献２（[0012]-[0013]等）には、血液サンプル最適化システム（採血針）において、空気透過性血液バリア（空気透過性血液不透過性部材２３）を含む通気口を有する隔離チャンバであって、通気口を通して隔離チャンバ内の空気を追い出す隔離チャンバを構成する技術、ポート、隔離チャンバ及び流路を収容及び画定するハウジング（針管支持体２）を構成する技術、が開示されている。

引用文献１-２に記載のものは、採血分野という同一の技術分野に属する。
引用文献１に記載のものにおいて、引用文献２に記載の技術を参考として、本願の請求項１に係る発明と同様の空気透過性血液バリアとハウジングを具備するよう構成することは、当業者にとって容易である。

［請求項２，４について］
引用文献２の[0012]-[0013]を参照。

［請求項３について］
サンプル針に密封材を配置することは、設計的な事項といえる。

［請求項５について］

引用文献２の[0011]参照。

［請求項６について］
引用文献１の図5を参照。

［請求項７－１０について］
引用文献１－２の記載を含め既述の説示を参照。

●理由２（明確性）について
・請求項　１－１０
請求項１－１０の記載は、以下の点で不明確である。よって、請求項１－１０に係る発明は、明確でない。

（１）請求項１の記載について
請求項１の「患者の血液サンプル、少なくとも汚染物質を含む前記血液サンプルの第１の部分」との記載は、「少なくとも汚染物質を含む」ことが「血液サンプル」に係っているのか、「前記血液サンプルの第１の部分」に係っているのか、日本語として不明確である。引用項においても同様。

（２）請求項４，７の記載について
請求項４，７の「前記血液サンプルの後続の部分」との記載は、いかなる部分に「後続」するものを特定しているのか不明確である。引用項においても同様。

＜引用文献等一覧＞
１．米国特許出願公開第２００８／０１４５９３３号明細書
２．特開２００１-０００４２４号公報

＜先行技術文献調査結果の記録＞
・調査した分野　　ＩＰＣ　Ａ６１Ｂ　　５／００　－　５／３９８
ＤＢ名
・先行技術文献　　特開昭５８-０２５１４６号公報
特表平０９-５０４７２６号公報
特開平０２-２２４７４２号公報
米国特許出願公開第２０１１／０３０６８９９号明細書

この先行技術文献調査結果の記録は、拒絶理由を構成するものではありません

。

＜補正をする際の注意＞
（１）明細書、特許請求の範囲について補正をする場合は、補正により記載を変更した個所に下線を引いてください（特許法施行規則様式第１３備考６、７）。
（２）補正は、この出願の外国語書面の翻訳文（又は誤訳訂正書による補正後の明細書、特許請求の範囲若しくは図面）に記載した事項の範囲内で行わなければなりません。また、意見書で、各補正事項について補正が適法なものである理由を、根拠となる翻訳文（又は誤訳訂正書による補正後の明細書、特許請求の範囲若しくは図面）の記載箇所を明確に示したうえで主張してください。
（３）特許請求の範囲について補正をする際には、特許法第１７条の２第４項に違反する補正とならないよう、注意してください。

この拒絶理由通知の内容に関するお問合せ又は面接のご希望がありましたら、次の連絡先までご連絡ください。電子メール等で補正案等の送付を希望される場合は、その旨を電話でお知らせください。

審査第一部分析診断（医学診断）　岡崎　潤
ＴＥＬ．０３-３５８１-１１０１　内線３２９１

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(全 4 頁)

⑤4ポリエステル系繊維構造物の処理方法

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明　細　書

1. 発明の名称

ポリエステル系繊維構造物の処理方法

2. 特許請求の範囲

(1) 芯成分がポリエステルから成り，鞘成分がアルカリに侵され難い成分から成る，一芯又は多芯の芯鞘型繊維と，アルカリ処理による見掛けの減量速度が，鞘成分除去後の該芯成分繊維より小さいポリエステル系繊維とを用いて繊維構造物と成し，該芯鞘型繊維の鞘成分を除去する前にアルカリ処理を施すに際し，あらかじめ，該鞘成分の軟化点以上，該芯成分ポリエステルの融点以下の温度で熱処理することを特徴とする，ポリエステル系繊維構造物の処理方法。

(2) 芯成分の単糸繊度が1.0デニール以下であることを特徴とする特許請求の範囲第1項記載のポリエステル系繊維構造物の処理方法。

3. 発明の詳細な説明

本発明は，アルカリ処理による見掛けの減量速度に差のある2種以上のポリエステル系繊維を含む繊維構造物の製造方法に関するものである。

ポリエステル系繊維構造物を，アルカリ処理することによつて，繊維間空隙を増大させ，シヤリ感のある柔軟で良好な風合を発現させることは，すでに知られている。

しかし，アルカリ処理による見掛の減量速度に差のある2種以上のポリエステル系繊維を含む繊維構造物においては，一方の繊維の強力低下が過大になり，満足すべき製品は得られなかつた。特に見掛の減量速度の大きい繊維が0.3デニール以下の場合には該極細糸がアルカリ処理によつて完全に溶解されることさえある。

これに対して見掛の減量速度の大きい繊維をアルカリに侵され難い成分で保護したまま処理することが検討されたが，期待に反して十分な効果は得られなかつた。たとえば，極細ポリエステルを芯とし，ポリスチレンを鞘とする一芯又は多芯の芯鞘繊維と普通繊度のポリエステルからなる布帛の鞘成分を溶出する前にアルカリで減量処理することも試みられたが，極細繊維の強度は極端に低

下するのである。本発明者はかかる問題について鋭意検討した結果，強度低下の原因が，該芯鞘繊維の製糸，製布工程で生じた鞘成分の欠陥によるものであることをつきとめ次の発明に到達したのである。つまり本発明は「芯成分がポリエステルから成り，鞘成分がアルカリに侵され難い成分から成る，一芯又は多芯の芯鞘型繊維とアルカリ処理による見掛けの減量速度が，鞘成分除去後の該芯成分繊維より小さいポリエステル系繊維とを用いて繊維構造物と成し，該芯鞘型繊維の鞘成分を除去する前にアルカリ処理を施すに際し，あらかじめ，該鞘成分の軟化点以上，該芯成分ポリエステルの融点以下の温度で熱処理することを特徴とするポリエステル系繊維構造物の処理方法」である。

以下，本発明をさらに詳細に説明する。

本発明における芯成分ポリエステル及びポリエステル系繊維とは，ポリエチレンテレフタレート，ポリブチレンテレフタレート等のポリエステル及び，それらを易染化，カチオン可染化，酸性可染

化，制電化，吸水吸湿化等をした改質ポリエステルをいう。

鞘成分として用いるアルカリに侵され難い成分とは，それ自身がアルカリによつて分解または溶解されないと同時に，アルカリを通しにくいものを指し，ポリスチレン，ポリオレフイン，及びそれらの共重合体などが挙げられる。

見掛けの減量速度とは，苛性ソーダ3％沸騰水溶液中で所定時間処理した時の減量率を測定し，時間を横軸，減量率を縦軸としてグラフを作成し，減量率20％までを最小二乗法で直線近似した場合の直線の傾きで表わされる。一般的には，減量率20％までは直線となるため，見掛けの減量速度は式Ⅰで表わされる。

$$V = \frac{\Delta W}{\tau} \quad \cdots\cdots\cdots\cdots \text{式 I}$$

V：見掛けの減量速度（sec^{-1}）

ΔW：繊維の減量率（％）

τ：処理時間（sec）

アルカリ減量速度の遅速は，一般的には式Ⅱで

示されるアルカリ溶解速度恒数で示されるが，本発明で使用する見掛けの減量速度とは異なるものである。すなわち，繊維を構成するポリマー，製糸方法及びアルカリ処理条件が同じであれば，アルカリ溶解速度恒数は一定であるが，それらが同じであつても，見掛けの減量速度は，繊度が異なれば変化する。例えば，繊度が4倍になれば，繊維表面積が1/2になるため，見掛けの減量速度は1/2になる。

つまり一般的な減量速度は次式による。

$$\sqrt{R} = -\frac{2.07\times10^{4}k}{\sqrt{D}}\tau + 10 \quad \cdots\cdots \text{式 II}$$

R：τ sec後の不溶解重量分率（％）

D：デニール

τ：処理時間（sec）

k：アルカリ溶解速度恒数（m／sec）

また，繊維を構成するポリマー，単糸繊度が同じであつても，製糸方法が異なれば，見掛けの減量速度は変化する。すなわち，芯鞘型の複合繊維の鞘を除去して得られた繊維は構成ポリマー，単

糸繊度が同じであつても，通常の製糸で得た繊維より見掛けの減量速度は大きくなる。

繊維構造物とは，織物，編物，不織布等の形態をいい，その構成繊維としては，芯成分がポリエステルから成り，鞘成分がアルカリに侵され難い成分から成る一芯又は多芯（の芯）鞘型繊維と，アルカリ処理による見掛けの減量速度が，鞘成分除去後の該芯繊維より小さいポリエステル系繊維とが，それぞれ10％以上含まれていればよく，それら2種の繊維の他に，見掛けの減量速度の異なるポリエステル系繊維，ポリアミド系繊維，ポリオレフイン系繊維等の合成繊維，綿，絹，羊毛等の天然繊維，アセテート等の半合成繊維，レーヨン等の再成繊維等が含まれていてもよい。またこれらの繊維以外に樹脂，接着剤，糊剤などが合浸，コーティング，スプレーなどの手段で付与されたものも含まれるものとする。

鞘成分除去の方法としては，例えば，ポリスチレン系ポリマーを用いた時は，各種の芳香族炭化水素や塩素化炭化水素，その他ポリエステルを溶

解しないような各種の有機溶剤を用いることができる。

アルカリ処理とは，苛性ソーダ，苛性カリ等の所謂アルカリ化合物及び炭酸ソーダ，炭酸カリ等のアルカリ性化合物を用いて，ポリエステルを加水分解させる処理であり，ポリエステルを加水分解できればどのような方法をとつてもよい。

本発明の一つのポイントは，前述したような芯鞘型繊維を用い，該鞘成分を除去する前にアルカリ処理を施すということである。すなわち，芯繊維を鞘成分によつてアルカリから保護し 他方のポリエステル系繊維のアルカリ減量処理を行なうわけである。しかし，芯繊維が鞘成分によつて完全に保護されていれば問題はないが，実際上，製糸やそれに続く工程，例えば製編織等，繊維構造物と成す工程において，鞘成分に多数の亀裂が生じているため，アルカリがその亀裂から侵入しまた，芯繊維の見掛けの減量速度が大きいこともあり，繊維は部分的にアルカリ加水分解を受け局部的脆化を起こす。

そこで，本発明の重要なポイントは，アルカリ処理前に，該鞘成分の軟化点以上，該芯成分ポリエステルの融点以下の温度で熱処理することである。すなわち，そのような熱処理によつて，鞘成分を流動させ，前述の亀裂を消滅させる効果を持つものである。従つて，該鞘成分の軟化点以下では亀裂をふさぐ効果は望めず，また，該芯成分の融点以上の温度では，該芯鞘型繊維が繊維としての形態をとどめないため，上述の範囲の熱処理が必須となる。なお，本発明でいう軟化点とは，ポリマーが流動を開始する温度で，明瞭な融点を持つ場合には，融点と一致する。

次に，本発明を実施例で詳しく説明するが，本発明はこれらに限定されるものではない。

実施例1

下記の糸を使用し，５枚朱子織物を２疋作つた。

(1) 経糸：１５０デニール，４８フイラメントのポリエチレンテレフタレート加工糸。

(2) 緯糸：２４５デニール，４０フイラメントの多芯芯鞘型繊維。芯数は３６芯／１フイラメン

トで芯成分は融点２５５℃のポリエチレンテレフタレート，鞘成分は軟化点１２０℃のポリスチレン，鞘成分の比率は２０％。鞘成分除去後の芯繊維の見掛けの減量速度は経糸の１４倍である。

この織物に通常のリラックス精練処理（９５℃）を施し，１疋はそのまま，他の１疋は１５０℃で乾熱処理し，アルカリ処理によつて，対織物重量比１０％の減量を実現させた。鞘成分をトリクレンで除去後，以後常法によつて染色仕上を行なつた。

１５０℃の乾熱処理を施した製品の緯糸強力は８１０ｇ／マルチフイラメント（強度4.1ｇ／ｄ強）であるのに対し，乾熱処理を施さなかつた製品の緯糸強力は半分以下の３９０ｇ／マルチフイラメント（強度2.0ｇ／ｄ弱）しかなく，毛羽立ちも見られた。

実施例2

下記の糸を使用し，ツイル織物を作つた。

(1) 経糸：１５０デニール，７２７フイラメントのポリエチレンテレフタレート糸。

(2) 緯糸：２００デニール，２４フイラメントの多芯芯鞘型繊維。芯数は３芯／１フイラメントで，芯成分は融点２３０℃の５－ナトリウムスルホイソフタル酸を3.8重量％共重合したポリエチレンテレフタレート，鞘成分は軟化点１０５℃のポリスチレン，鞘成分の比率は２５％。鞘成分除去後の芯繊維の見掛けの減量速度は，経糸の約１０倍である。

この織物に通常のリラックス精練処理（９５℃）を施し，１６０℃で乾熱処理し，アルカリ処理で対織物重量比１５％減量させた。鞘成分をトリクレンで除去後，以後常法によつて染色仕上を行なつた。

比較として，緯糸に１５０デニール，７２７フイラメントの５－ナトリウムスルホイソフタル酸を3.8重量％共重合したポリエチレンテレフタレート糸を使用し，同組織，密度の織物に同様の処理を施し，１５％減量させ，以後常法によつて，染色仕上を行なつた。

本発明法による緯糸強度は4.0ｇ／ｄあるのに

対し，比較法による緯糸強度は1.5ｇ／ｄしかなかつた。

特許出願人　東レ株式会社

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DISPOSABLE, CLOSED BLOOD SAMPLING SYSTEM FOR USE IN MEDICAL CONDUIT LINE

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- 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)

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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."

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(54) Title: DISPOSABLE, CLOSED BLOOD SAMPLING SYSTEM FOR USE IN MEDICAL CONDUIT LINE

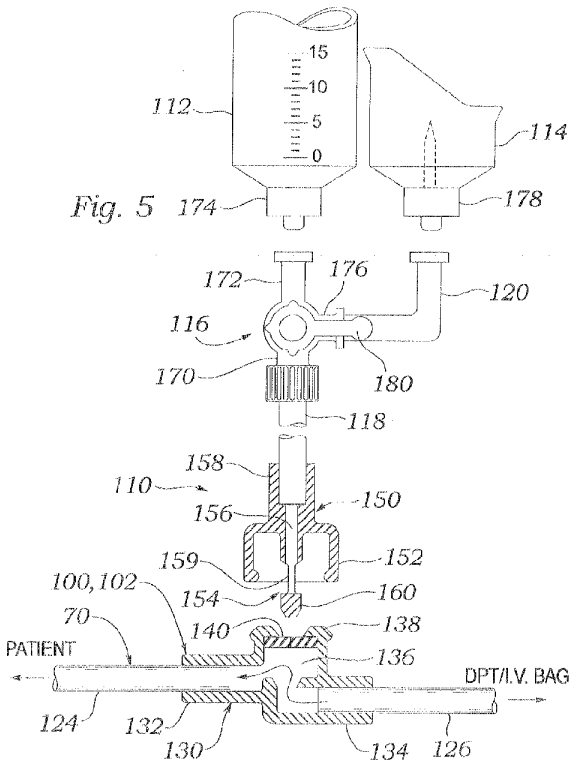


Fig. 5

(57) Abstract: 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."

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DISPOSABLE, CLOSED BLOOD SAMPLING SYSTEM FOR USE IN MEDICAL CONDUIT LINE

Field of the Invention

[0001] The present invention relates to blood sampling systems and, in particular, to a disposable blood sampling system in a medical conduit line such as a pressure monitoring line.

Background of the Invention

[0002] In a hospital setting there is always the need to monitor patient health through the evaluation of blood chemistry profile. The simplest method employed in the hospital is to use a syringe carrying a sharpened cannula at one end and insert that cannula into a vein or artery to extract a blood sample from the patient. Blood is drawn using a syringe or more easily into an evacuated vessel. Patients that are in the critical care units or the operating room sometimes require as many as twelve blood draws a day which can be quite uncomfortable. Moreover, such frequent sampling injections carry the risk to the clinician of needle sticks and blood exposure, and potentially subject the patient to airborne bacteria and viruses which can enter the bloodstream through the opening made by the sharpened cannula.

[0003] One way to obtain a blood sample is to draw the blood from a catheter that is already inserted in the patient, either in a central venous line, such as one placed in the right atrium, or in an arterial line. Typically, existing injection sites for arterial or venous drug infusion or pressure monitoring lines are used to take periodic blood samples from the patient. Conventional mechanisms for drawing blood from the lines used for infusion or pressure monitoring utilize a plurality of stopcock mechanisms that block flow from the infusion fluid supply or from the pressure column drip supply, while allowing blood to flow from the patient into a collecting syringe connected to a port formed in one of the stopcocks. Typically, a blunt cannula through a slit septum

is used to remove the danger of sticking the nurse or clinician, in a so-called "needle-less" system.

[0004] Most early systems required a two-step operation where a first sample of fluid, typically between 2-12 ml in volume for intensive care environments was withdrawn into the sampling syringe and discarded. This first sample potentially included some of the infusion fluid and thus would be an unreliable blood chemistry measurement sample. After the initial sample had been discharged, the second sample was pure blood from the artery or vein and was typically re-infused to the patient.

[0005] Of course, the possibility of discarding blood along with saline is a drawback, especially in anemic patients, and so-called closed systems that remain connected to the conduit line and preserve the initial fluid draw were developed. Examples of these can be seen in U.S. Patent No. 4,673,386 to Gordon, and more recently in U.S. Patent No. 5,961,472 to Swendson. Commercial closed systems such as the Edwards VAMP® and VAMP Plus® Venous Arterial blood Management Protection systems of Edwards Lifesciences in Irvine, CA feature a dedicated syringe-like reservoir incorporated in the tubing line from the patient that can draw fluid past a sampling port. The line continues past the reservoir to a proximal source of flushing fluid and a pressure transducer. (The standard directional nomenclature is that proximal is toward the clinician, or away from the patient, and distal is toward the patient). The clearing volume is held in the in-line reservoir, and not set aside in a syringe for discard or re-infusion later.

[0006] When a blood sample is to be taken, the flow of flushing or infusion fluid is halted by turning the handle of a reservoir stopcock valve. The nurse or clinician then withdraws an amount of fluid into the reservoir chamber and distal line sufficient to pull pure blood past one or more sampling sites and closes the reservoir stopcock. Desirably, the flow line includes a sampling site near the patient more often used in the ICU, and/or one farther away, close to the reservoir, and used in the OR when the space immediately around the patient is at a premium. To avoid needle sticks, blunt cannulas are used to draw

blood. Also, the sampling sites are desirably designed to ensure a complete flush after the sample is taken. The stopcock valve is then opened so that the volume within the reservoir can be re-infused back into the patient, and the flushing drip and pressure monitoring resumes.

[0007] In reservoir systems the nurse or technician must manipulate the reservoir, then let go of it to take the blood sample, and then grasp it again to re-infuse the prime volume, all of which is relatively inconvenient. Furthermore the continuing presence of the reservoir dangling from the pressure monitoring line is undesirable as it is only infrequently used and can become tangled with bedding or with other equipment. Finally, because the reservoir remains in place and is used multiple times, it must include a contamination shield to isolate the reservoir plunger, and such a device is costly compared to a simple syringe.

[0008] A minimum quality of system frequency response in the blood sampling/pressure monitoring systems described above is necessary for reliable blood pressure measurements. The pressure transducer typically includes a diaphragm exposed to the in-line fluid on one side and has a device for measuring deflection of the diaphragm on the other. Adding components to the flow line, such as sampling sites with elastomeric septums or a dedicated reservoir with a rubber-tipped plunger, and/or increasing the length of tubing contributes to signal degradation. Often only one sampling site is provided for the ICU or OR to avoid unduly degrading the signal response.

[0009] In view of the foregoing, there is a need for a blood sampling system, especially used in conjunction with a pressure transducer, that is more convenient and safer to use.

Summary of the Invention

[0010] In one aspect, the present invention provides a medical system for sampling of a fluid system of a patient for use with a conduit line. The conduit line includes a proximal segment adapted to be supplied with a

physiological fluid and a distal segment adapted to be in communication with the fluid system of a patient. A fluid sampling site in the conduit line defines a housing having a distal port connected to the distal segment and a proximal port connected to the proximal segment. Fluid may flow freely through a chamber in the housing between the proximal and distal ports, and the sampling site further defines a sampling port open to the chamber and closed from the exterior by an elastomeric seal. The medical system comprises a flowthrough bypass cannula having a body shaped to engage the sampling port. The cannula also has a bypass probe defining a throughbore and sized to pierce the elastomeric seal, project into the chamber and place the throughbore into fluid communication with the distal port of the sampling site while occluding the proximal port from the throughbore. Consequently, a fluid sample may be drawn into the bypass cannula from the distal segment of the conduit line to the exclusion of the proximal segment. In a preferred embodiment, the bypass cannula and sampling site include mating structure such that they engage with a positive snap fit.

[0011] In one embodiment, the bypass probe terminates in a tip that contacts a passageway opening in the fluid sampling site housing leading to one of the distal or proximal ports when the bypass cannula engages the sampling site, and the tip is tapered and matches the passageway opening. In another embodiment, the bypass probe terminates in a closed tip that contacts and occludes a passageway opening in the fluid sampling site housing leading to the proximal port when the bypass cannula engages the sampling site, and the bypass probe includes at least one side opening open to the chamber in the sampling site housing. The closed bypass probe tip may be at least partly compressible to enhance the seal between the tip and the passageway opening. Alternatively, the bypass probe defines a continuous tubular member and terminates in an open tip that contacts a passageway opening in the fluid sampling site housing leading to the distal port when the bypass cannula engages the sampling site. Furthermore, a sealing member may be positioned in

the passageway opening that contacts and seals against the open tip of the bypass probe to enhance the seal therebetween.

[0012] Another aspect of the present invention is a system for sampling fluid from a medical conduit line including a disposable subsystem. The system includes a conduit line with a proximal segment adapted to be supplied with a physiological fluid and a distal segment adapted to be in communication with a fluid system of a patient. A fluid sampling site in the conduit line defines an internal chamber in communication with all of: a proximal port connected to the proximal segment, a distal port connected to the distal segment, and a sampling port closed by an elastomeric seal. Further has a disposable sampling subsystem for engaging the fluid sampling site. The sampling subsystem includes a bypass cannula adapted to engage the sampling port of the sampling site and simultaneously occlude the proximal port therein. The sampling subsystem also includes a stopcock having three ports, a first port in communication with the bypass cannula, a fluid reservoir connected to a second port of the stopcock, and a fluid sampling vessel in fluid communication with the third port of the stopcock. Manipulating the stopcock into a first position enables fluid communication between the first and second ports so that fluid may be drawn into the reservoir from the distal segment. Manipulating the stopcock into a second position enables fluid communication between the first and third ports so that fluid may be drawn into the fluid sampling vessel from the distal segment. The system further may include a pressure transducer connected to the proximal segment of the conduit line for sensing the pressure of the fluid system of a patient through the fluid in the conduit line. An optional component of the system is a bubble trap connected to the bypass cannula between the sampling site and reservoir that prevents bubbles from entering the sampling site from the bypass cannula.

[0013] In one embodiment, the bypass cannula includes a bypass probe terminating in a closed tip that contacts and occludes a passageway opening in the fluid sampling site housing leading to the proximal port when the bypass cannula engages the sampling site, and the bypass probe includes at least one

side opening open to the chamber in the sampling site housing. In an alternative embodiment, the bypass cannula includes a continuous tubular bypass probe terminating in an open tip that contacts a passageway opening in the fluid sampling site housing leading to the distal port when the bypass cannula engages the sampling site. A still further alternative includes a stopcock positioned adjacent the proximal port of the sampling site for occluding the proximal port when fluid is drawn into and expelled from the reservoir and drawn into the fluid sampling container.

[0014] The present invention also provides a method for sampling blood from a medical fluid conduit line using a disposable subsystem, the conduit line having a proximal segment supplied with a physiological fluid and a distal segment in communication with the blood system of a patient. The conduit line also has a fluid sampling site defining an internal chamber in communication with all of: a proximal port connected to the proximal segment, a distal port connected to the distal segment, and a sampling port closed by an elastomeric seal. The method includes the steps of:

providing a disposable sampling subsystem for engaging the fluid sampling site including a flowthrough bypass cannula having a probe, a fluid reservoir, and a fluid sampling container;

engaging the bypass cannula with the sampling site so that the probe passes through the elastomeric seal;

opening fluid communication between the bypass cannula and reservoir while closing fluid communication between the bypass cannula and fluid sampling container;

closing fluid communication between the bypass cannula and proximal segment of the conduit line and drawing fluid into the reservoir from the distal segment through the bypass cannula until blood enters the sampling site;

opening fluid communication between the bypass cannula and fluid sampling vessel while closing fluid communication between the bypass cannula and reservoir;

drawing blood into the fluid sampling vessel from the distal segment;

maintaining the bypass cannula engaged with the sampling site until a sample of blood is drawn into the fluid sampling container; and

detaching the bypass cannula from the sampling site and disposing of the sampling subsystem.

[0015] The method desirably also includes providing a pressure transducer connected to the proximal segment of the conduit line and sensing the pressure of the fluid system of a patient through the fluid in the conduit line.

[0016] In one embodiment, the disposable sampling subsystem includes a stopcock having three ports, a first port in communication with the bypass cannula, a second ports in communication with the fluid reservoir, and a third port in communication with the fluid sampling container, wherein following steps of the method are enabled by manipulating the stopcock:

opening fluid communication between the bypass cannula and reservoir while closing fluid communication between the bypass cannula and fluid sampling container; and

opening fluid communication between the bypass cannula and fluid sampling vessel while closing fluid communication between the bypass cannula and reservoir.

[0017] In one version of the method the step of opening fluid communication between the bypass cannula and reservoir while closing fluid communication between the bypass cannula and fluid sampling vessel is accomplished by the step of engaging the bypass cannula with the sampling site. The probe of the bypass cannula may have a size sufficient to contact a passageway opening leading to the proximal port of the sampling site, and exclude fluid communication between the proximal port and the distal port by, for example, occluding the passageway opening.

[0018] The method may alternatively include providing a stopcock adjacent the proximal port of the sampling site for occluding the proximal port

when fluid is drawn into and expelled from the reservoir and drawn into the fluid sampling container.

[0019] A further understanding of the nature and advantages of the present invention are set forth in the following description and claims, particularly when considered in conjunction with the accompanying drawings in which like parts bear like reference numerals.

Brief Description of the Drawings

[0020] Features and advantages of the present invention will become appreciated as the same become better understood with reference to the specification, claims, and appended drawings wherein:

[0021] Figures 1A-1C are schematic diagrams of blood sampling systems within dedicated closed reservoirs within pressure monitoring lines of the prior art;

[0022] Figures 2A-2B are schematic diagrams of two different configurations of a blood sampling system of one embodiment of the present invention within a pressure monitoring line;

[0023] Figure 3 illustrates a typical hospital room setup of a pressure monitoring system for a patient incorporating two fluid sampling ports of one embodiment of the present invention;

[0024] Figure 4 schematically illustrate a fluid sampling system in conjunction with the fluid sampling ports of Figure 3;

[0025] Figure 5 is an exploded sectional view of the main fluid sampling components of one embodiment of the present invention;

[0026] Figure 6 is a partial sectional view of a flowthrough bypass cannula of the fluid sampling system of one embodiment of the present invention engaged with a fluid sampling site and illustrating the occlusion of a proximal segment of the pressure monitoring line;

[0027] Figures 7A-7E are schematic views illustrating a sequence of steps involved in taking a fluid sample in accordance with one embodiment of the present invention;

[0028] Figures 8A-8C are perspective assembled and exploded views of an exemplary bypass cannula and a sampling site combination of one embodiment of the present invention;

[0029] Figure 9A is a top plan view of the bypass cannula and sampling site combination of Figures 8A-8C;

[0030] Figures 9B and 9C are vertical sectional views along orthogonal axes through the centerline of the bypass cannula and sampling site combination, taken along respective section lines shown in Figure 9A;

[0031] Figure 10 is a vertical sectional view through an alternative bypass cannula and sampling site combination of one embodiment of the present invention;

[0032] Figure 11 is a vertical sectional view through another alternative bypass cannula and sampling site combination of one embodiment of the present invention;

[0033] Figures 12A and 12B illustrates a still further alternative bypass cannula and sampling site combination, as well as an exemplary bubble trap that may be used therewith; and

[0034] Figure 13 is an alternative disposable fluid sampling system of one embodiment of the present invention that permits fluid to be drawn into and expelled from a removable reservoir to and from a distal segment of a conduit line while occluding a proximal segment.

Detailed Description of the Preferred Embodiments

[0035] The present invention provides an improved blood sampling system, desirably for use in a pressure monitoring line. As mentioned above, continuous or periodic blood pressure monitoring is a common and extremely useful tool in the intensive care or operating room. However, it should be mentioned that the apparatuses and methods described herein could be utilized in conjunction with any fluid system of a patient which would benefit from pressure monitoring. For instance, intracranial pressures could be monitored and cerebrospinal fluid samples taken by placing the system described herein in

fluid communication with an intraventricular catheter. Therefore, the appended claims cover the sampling and monitoring of any fluid system within a patient unless otherwise specified. Additionally, certain aspects of the present invention may be useful for taking fluid samples in conduit lines connected to the patient that do not include pressure monitoring, such as from existing injection lines for arterial or venous drug infusion.

[0036] The present invention comprises an improved sampling system especially useful for sampling blood in the operating room (OR), intensive care unit (ICU) or critical care unit (CCU). The system is closed as some in prior systems, for example the VAMP Plus® Venous Arterial blood Management Protection system available from Edwards Lifesciences of Irvine, CA, because the prime volume drawn in to a reservoir may be returned to the patient. However, one embodiment of the present invention also provides an option of discarding the prime volume, and does not include a "dedicated" in-line reservoir.

[0037] Figures 1A-1C are schematic diagrams of closed blood sampling systems within pressure monitoring lines of the prior art. As explained above, a "closed" system typically features a dedicated in-line reservoir (i.e., one that remains connected), therefore avoiding "breaking" (or opening) the conduit line to pull the pure blood across the sampling site. This eliminates any potential contamination of the blood or contamination of the environment from the blood, such as if a removable syringe was used and set aside for later re-infusion. The systems illustrated in Figures 1A-1C all include a dedicated reservoir 20 mounted within a fluid conduit line or tubing connected to a fluid system of the patient P, much like the VAMP Plus® Venous Arterial blood Management Protection system available from Edwards Lifesciences.

[0038] Figure 1A illustrates a pressure monitoring system where the placement of the reservoir 20 defines a distal segment 22 and a proximal segment 24 of the conduit line. The conduit line is primarily medical grade pressure tubing. The system includes a disposable pressure transducer (DPT) 26 in the proximal segment 24 which measures pressure pulses within the fluid

column in the conduit line derived from a patient to which the distal segment 22 connects. Although not shown, the distal end of the distal segment 22 typically includes a luer connector which engages a mating luer connector on an in-dwelling catheter or cannula placed in a vein or artery of the patient. In this manner, the pulse and blood pressure of the patient transmits through the fluid column within the conduit line to the pressure transducer 26.

[0039] Pressure lines such as shown in Figure 1A typically make use of relatively stiff tubing primed with a suitable physiological fluid such as saline or 5% dextrose solution from a supply bag 30 (denoted "I.V.") as a pressure column. For adults, a bag pressurized with air surrounds the fluid supply bag to maintain a constant pressure differential in the line urging fluid toward the patient through a restrictor orifice. The slow drip of physiological fluid, as indicated by the flow arrows in Figure 1A, flushes the line to prevent clotting. Some transducers such as the TruWave® Disposable Pressure Transducer from Edwards Lifesciences include a flush device that also can be used for sending transient pressure waves through the line. A Snap-Tab™ device of the TruWave® is a rubber tab which when pulled and then released sends a square wave through the pressure column to check the inherent frequency response of the entire system, which includes the tubing and any components attached thereto.

[0040] When the pressure line is also used for fluid sampling it features at least one and preferably two sampling sites 32, 34 in the proximal segment 24. A proximal sampling site 32 is located near the reservoir 20, often 5 or 6 feet (152-178 cm) from the patient. The distal sampling site 34 is located close to the distal end of the conduit line. The operators (clinicians) who draw blood samples can be generally categorized in two groups: 1) OR nurses and anesthesiologists, and 2) CCU or ICU nurses. Each grouping has different requirements regarding position of the sampling sites. In the OR, access near the patient is limited; therefore the preferred sampling site location is near the IV pole, so the proximal sampling site 32 is preferred. On the other hand, in the

CCU or ICU nurses prefer to take blood as close to the patient as possible, so the distal sampling site 34 is preferred.

[0041] Figure 1B shows one step in operation of the sampling system wherein a prime volume of fluid has been drawn into the reservoir 20 from the distal segment 22 of the conduit line. The reservoir 20 has sufficient capacity to draw all of the saline and mixed saline and blood into its chamber such that pure blood extends from the patient past one or both of the sampling sites 32, 34. In the illustrated embodiment, enough prime volume has been drawn into the reservoir 20 such that a sample can be taken at the proximal sampling site 32, as indicated by the schematic sampling syringe 36, though of course a sample could be taken at the distal site 34. Prior to taking the sample, a stopcock 38 between the reservoir 20 and sampling site 32 is closed to prevent drawing any fluid into the sampling syringe 36 from the reservoir 20, thus insuring an undiluted sample. After taking a sample, the nurse withdraws the syringe 36 from the sample site 32, opens the stopcock 38, and depresses the plunger of the reservoir 20 so that the entire prime volume infuses back to the patient.

[0042] Figure 1C illustrates an alternative pressure monitoring/fluid sampling conduit line wherein a dedicated reservoir 20 is located close to the patient and there is only one sampling site 40. This system functions in a similar manner to the one described above, but is typically only used in the CCU or ICU because of the proximity of the sampling site 40 to the patient, which would get in the way in the OR.

[0043] Figures 2A and 2B are schematic views of a pressure monitoring/fluid sampling system of one embodiment of the present invention. As in the prior art systems, a conduit line 50 extends between an injection site in a vein or artery of the patient to a source of physiological fluid 52. A pressure transducer 54 connects to the fluid column within the conduit line 50 near the proximal end, and the system includes a proximal sampling site 56 and a distal sampling site 58, desirably at the same locations as those shown in Figure 1A.

[0044] The system of Figures 2A and 2B does not include a dedicated in-line reservoir or stopcock as described above. Instead, a removable fluid

sampling subsystem 60 is designed to engage either of the sampling sites 56, 58, but does not remain attached to the conduit line when not in use. Figure 2A illustrates engagement of the subsystem 60 with the proximal sampling site 56, while Figure 2B shows the subsystem 60 engaged with the distal sampling site 58. In this manner, the pressure monitoring function of the system is improved by removal of the dedicated reservoir 20 and stopcock 38 shown in Figures 1A-1C. That is, any reduction in signal fidelity caused by those dedicated components is removed. Also, elimination of an in-line reservoir dangling from the conduit line removes that potential cause of tangling with bedclothes or other such items. Furthermore, the fluid sampling aspect of the system is flexible such as that seen in Figure 1A, with both proximal and distal sampling sites provided for use in different hospital settings, depending on need.

[0045] Exemplary details of the components of the system of Figures 2A-2B will be described below, however the system enables a method for sampling fluid from a medical pressure monitoring conduit line without a dedicated reservoir, though with the closed functionality of such a reservoir, and greatly improved convenience. In essence, the system enables as-needed fluid sampling from the pressure monitoring line by temporary attachment of a fluid reservoir to one of the sampling sites, occlusion of fluid communication between the reservoir and the conduit line proximal to the sampling site, withdrawal of a prime volume from the distal segment into the reservoir, taking of a blood sample, re-introduction of the prime volume into the conduit line, and removal of the fluid reservoir from the conduit line.

[0046] Figure 3 illustrates an exemplary pressure monitoring system in a typical hospital room environment and connected to a patient P. The system shown in Figure 3 is absent the detachable/disposable blood sampling subsystem 60 of Figure 2, and therefore possesses a fairly low profile in the clinical setting which greatly enhances convenience when no blood sample is being taken. The pressure monitoring system comprises a conduit line 70 having a distal segment toward the patient and a proximal segment away from the patient. (As will be clear below, the terms proximal and distal segments will

be used relative to either of two blood sampling sites.) The distal segment may terminate in a male luer connector 72 for attaching to a female luer connector (not shown) of an injection site, or other conduit leading to the patient.

[0047] As mentioned above, the exemplary blood sampling system advantageously works in conjunction with the pressure monitoring system. The proximal segment of the conduit line terminates in a female luer connector 74 attached to a stopcock (not shown) of a pressure transducer 78, such as a TruWave™ Disposable Pressure Transducer available from Edwards Lifesciences of Irvine, CA. The pressure transducer 78 removably mounts to a bracket 80 which, in turn, may be secured to a conventional pole support 82 with the reservoir in a vertical orientation. A supply of flush solution 84 connects to a flush port 86 of the transducer 78 via tubing 88. Typically for adults, the flush solution 84 comprises a bag of physiological fluid such as saline surrounded by a pressurized sleeve that squeezes the fluid and forces it through the tubing 88. In addition, an infusion fluid supply (not shown) may be provided in communication with an infusion port of the stopcock 76. The pressure transducer 78 is thus placed in fluid communication with the arterial or venous system of the patient through the conduit line 70, and preferably includes a cable 92 and plug to connect to a suitable display monitor 94.

[0048] The blood sampling system 96 shown in Figure 4 comprises at least one and desirably both proximal and distal fluid sampling sites 100, 102 in the conduit line (also seen in Figure 3). Each sampling site 100, 102 defines a flow passage, preferably Z-shaped, adjacent a pre-slit septum (described below). With this configuration, a minimal amount of flush volume is needed to clear the line after sampling. The septum preferably comprises a split elastomeric disc which accepts a blunt cannula and reseals after each sample is drawn, reducing the potential for contamination and eliminating the danger of needle sticks. A similar sampling site is described in U.S. Patent No. 5,135,489 to Jepson, et al.

[0049] Figure 4 further illustrates an exploded packaged sterile kit that includes the aforementioned blood sampling subsystem 60 and integrates a

blood sampling collection vessel with a pull-back reservoir. This is a single use, disposable accessory used to sample blood at either the proximal (OR) sampling site 100 or distal (ICU/CCU) sampling site 102. The kit desirably consists of the following elements:

- ❑ Bypass cannula - 110
- ❑ Pull-back reservoir (shown as a simple syringe) - 112
- ❑ Sample collection vessel (Syringe or Vacutainer®) - 114
- ❑ 3-position valve, or stop-cock -116
- ❑ Short tube segment - 118
- ❑ Elbow - 120
- ❑ Sterile packaging - 122

[0050] Because the sterile kit described above works in conjunction with one of the two sampling sites 100, 102, and samples blood that is present in the conduit line 70, all of these components together make up the fluid sampling system 96 of one embodiment of the present invention. However, it should be understood that some of the elements above, such as the elbow 120, are optional.

[0051] Figure 4 best illustrates the disposable nature of most of the blood sampling system 96. Indeed, all of the disposable components of the system 96 are provided in the sterile package 122 for use at one of the two sample sites, and are then detached from the conduit line 70 and discarded. As mentioned, this greatly enhances the convenience of the system by eliminating the dedicated, in-line reservoir. However, as will be clear, the system remains closed during the sampling process and provides all of the safety benefits of a conventional dedicated reservoir. Moreover, as will be seen in greater detail below, the disposable components provided in the sterile package 122 are relatively simple, inexpensively produced items, which reduces the cost of the system even if multiple sterile packages 122 are used. Furthermore, because the reservoir 112 does not remain connected with conduit line 70, there is no need for a contamination sleeve or other special design to prevent blood stagnation.

[0052] Figure 5 is a close-up partial sectional view of an exemplary fluid sampling system 96 of one embodiment of the present invention. As mentioned, one of the two sampling sites 100, 102 within the conduit line 70 forms a part of the system 96. In the illustrated embodiment, the distal or patient segment 124 is to the left, while a proximal or pressure transducer/I.V. segment 126 is to the right. The sampling site 100, 102 is shown as a conventional "Z-site," so named because of the Z-shaped path taken by the fluid drip therethrough, as indicated. The sampling site 100, 102 includes a rigid housing 130 having a distal port 132 connected to the distal segment 124 and a proximal port 134 connected to the proximal segment 126, wherein fluid may flow freely through an inner chamber 136 in the housing between the proximal and distal ports. The sampling site 100, 102 further defines a sampling port 138 opening into the chamber 136 that is closed by an elastomeric septum or seal 140.

[0053] It should be emphasized at this point that although a particular blood sampling site (i.e., a Z-site configuration) is illustrated and described as a component of the blood sampling system, other in-line sampling sites could also be used. That is, the disposable blood sampling subsystem 60 described above may be designed to interact with other sampling sites than those illustrated. The disposable subsystem 60 is intended to be used with any flowthrough sampling site which includes a rigid housing having distal and proximal ports for connecting the sampling site within a fluid conduit line, and a sampling port to which the subsystem connects. The proximal, distal, and sampling ports all open to an internal chamber, and the sampling port is typically closed by an elastomeric seal or septum. As mentioned above, U.S. Patent No. 5,135,489 to Jepson, et al. exemplifies this type of sampling site, though another similar sampling site which could be used is disclosed in U.S. Patent No. 5,417,673 to Gordon.

[0054] As seen in Figure 5, the flowthrough bypass cannula 110 includes a generally tubular rigid body 150 defining a front fitting 152 shaped to engage the sampling port 138, and a bypass probe 154 that pierces the

elastomeric seal 140, projects into the chamber 136 and occludes the proximal port 134 of the sampling site. The bypass cannula 110 further defines a central throughbore 156 in communication with a rear fitting 158 opposite the front fitting 152. The throughbore 156 extends part way along the bypass probe 154 and opens within the front fitting 152 at at least one side passage 159. The terminal end of the probe 154 possesses an enlarged head or plug 160. The probe 154 may be configured in a number of ways, as will be seen, but includes a terminal end that mates with the opening to a passageway leading to one of the ports of the sampling site 100, 102, as seen in Figure 6. The exemplary probe 154 further includes at least one opening such as the side passage 159 providing fluid communication between the throughbore 156 and the chamber 136 of the sampling site. The probe 154 therefore may be configured as a tubular member having a solid terminal end at plug 160, and diametrically opposed side passages 159 just before the plug.

[0055] The front fitting 152 is illustrated as a female cap member that fits over the male sampling port 138 of the sampling site 100, 102. In this regard, opposed flanges or ribs (not numbered) ensure an interference or snap fit and positive coupling of the bypass cannula 110 to the sampling site. Of course, other arrangements such as a threaded (e.g., luer) coupling may be provided. One desirable feature of the system is to maintain a good seal between the plug 160 and passage within the sampling site 100, 102. This can be accomplished between various materials (rigid or compressible) using mechanical pressure by way of a snap fit or a threaded engagement between the bypass cannula 110 to the sampling site 100, 102. Any such connection desirably provides constant mechanical force and accommodates tolerance variations typical of manufacturing processes.

[0056] The stopcock 116 connects to the rear fitting 158 of the bypass cannula 110. In this regard, the stopcock 116 may attach directly to the fitting 158, or via the intermediate tubing segment 118. A transparent tubing segment 118 is preferably utilized so that the clinician can monitor the formation of any bubbles within the aspirated fluid created by the suction of the reservoir 112.

The short tubing segment 118 is included as a safety precaution against air bubble infusion. Because the syringe-type reservoir 112, bypass cannula 110, and tubing 118 are often not purged of air prior to sampling, an air pocket between the reservoir plunger and fluid may form during the draw back step. In the unlikely event of trapped air bubbles, they will be visible in the short (between 3 and 8 inches) tubing segment 118. In such a situation, the user would simply disconnect and dispose of the entire subsystem 60.

[0057] The stopcock 116 defines three ports: a first port 170 in communication with the rear fitting 158 of the bypass cannula, a second port 172 adapted to mate with a coupling 174 on the reservoir 112, and a third port 176 adapted to couple to one end of the elbow 120. The elbow 120 in turn includes a fitting on its opposite end that mates with a coupling 178 on the sample collection vessel 114. A handle 180 of the stopcock 116 may be manipulated into three positions to provide fluid communication between any two of the three ports, to the exclusion of the other. Again, the engagement of the various ports and connected elements may be through luer fittings, snap fittings, or the like. The use of standard luer connection fittings enables the users to substitute standardized components if they so choose

[0058] Figure 6 illustrates a slightly modified flowthrough bypass cannula 190 engaged with a sampling site 100, 102. The bypass probe 194 is shown piercing the elastomeric seal 140 of the sampling site to enter the chamber 136. The tapered distal end 192 of the bypass probe 194 seats against a similarly tapered internal opening (not numbered) to the proximal port 134 of the sampling site. Because of one or more side openings 196 in the bypass probe 194, an inner throughbore (not shown) of the bypass cannula 190 opens to the chamber 136 within the sampling site. Inner threads on a front fitting 198 of the bypass cannula 190 mate with external threads formed on the sampling port 138 of the sampling site.

[0059] Operation of the fluid sampling system of one embodiment of the present invention will now be described with reference to the exemplary

structures shown in Figures 5 and 6, and the schematic sequence of events shown in Figures 7A-7E.

[0060] First, the fluid sampling subsystem 60 is removed from the sterile package 122 (Figure 4) and the appropriate components are connected with the bypass cannula 110, 190 engaging the sampling port 138 of the sampling site 100, 102 (Figure 7A). As seen in Figure 6, this causes the bypass probe 154, 194 to pass through the elastomeric septum 140 into the chamber 136. The length of the probe 194 and its configuration is such that its distal tip 192 engages and occludes the opening to the proximal port 134 of the sampling site. The single step of engaging the cannula 110 to the sampling site 100, 102 places the reservoir 112 into fluid communication with the distal segment 124 of the conduit line and simultaneously blocks flow between the proximal segment 126 and the sampling site chamber 136.

[0061] The step of engaging the bypass cannula 110, 190 with the sampling site 100, 102 is desirably accomplished with the handle 180 of the stopcock 116 in a position that blocks fluid flow through the stopcock; that is, the first port 170 is closed. After secure engagement of the bypass cannula 110, 190 with the sampling site, the clinician manipulates the stopcock handle 180 into a position that permits fluid flow from the sampling site through the bypass cannula 110, 190 and to the reservoir 112; that is, the first port 170 communicates with the second port 172.

[0062] Retraction of a plunger of the reservoir 112 creates a negative pressure differential such that a fluid sample from the distal segment 124 is drawn into the chamber 136 and into the reservoir 112 (Figure 7B). The reservoir 112 has a sufficient volume, typically 5-15 ml, to draw blood from the patient P past both sampling sites 100, 102. If blood is being taken from distal sampling site 100 in the ICU/CCU, the prime volume is typically about 5 ml, whereas if blood is taken from the proximal sampling site 102 in the OR, the prime volume is typically about 12 ml. Please note that the syringe-type reservoir 112 could be used, or another manual draw type reservoir, or even mechanically-assisted fluid draw device.

[0063] Once all of the saline and mixed saline and blood has been pulled into the reservoir 112, the clinician can then take a sample of undiluted blood from the site 100, 102. To do so, he/she manipulates the stopcock handle 180 into a position that blocks flow to the reservoir 112 and permits flow between the bypass cannula 110 and the third port 176 leading to the elbow 120 and sample collection vessel 114. As indicated in Figure 7C, a sample of blood is then drawn into the collection vessel 114 through action of a plunger, or as soon as the stopcock handle 180 opens the flow, if the collection vessel is an evacuated container (e.g., Vacutainer®). The sample collection vessel 114 is designed to be detached from the elbow 120 or directly from the stopcock 116 for remote analysis of the blood therein. It should be understood that in one use of the disposable blood sampling subsystem 60 more than one sample may be taken by simply engaging more than one collection vessel 114 in sequence.

[0064] After the desired sample is taken, the stopcock handle 180 is again manipulated into a position that closes off the third port 176 and opens flow between the first and second ports 170, 172 (i.e., between the sampling site 100, 102 and reservoir 112). Subsequently, the blood and other fluids drawn into the reservoir 112 during the sample priming operation are re-infused by depressing the reservoir plunger (Figure 7D) into the distal segment 124, and ultimately back to the patient. It should be noted that during this re-infusion step the bypass probe 154, 194 remains occluding the proximal port 134 of the sampling site so that fluid from the reservoir 112 does not travel into the proximal segment 126 toward the pressure transducer.

[0065] It is important to understand that the sampling system 96 provides a closed reservoir 112 since the priming volume that ensures a pure sample of blood reaches the sampling site 100, 102 remains within the system 96 and is re-infused into the patient without removal of the reservoir. That is, because the reservoir 112 as a part of the sampling subsystem 60 remains connected to the sampling site 100, 102 during the entire process until re-infusion, the conduit line is not "broken," meaning the reservoir is not detached between drawing the prime volume and re-infusing it. Of course, as mentioned

above, if the clinician notices bubbles have formed within the reservoir 112 or adjacent tubing, the subsystem 60 can be removed from the sampling site 100, 102 without re-infusing the prime volume, which is then also discarded. This is a significant advantage over earlier "dedicated" reservoirs which could not be removed and had to be operated with great care to prevent formation of bubbles.

[0066] Finally, as indicated in Figure 7E, after obtaining a blood sample the clinician detaches the fluid sampling subsystem 60 from the sampling site 100, 102 and discards it. Again, this is preferred over dedicated reservoirs which can get tangled with sheets and such.

[0067] The reader will now appreciate certain benefits of the improved fluid sampling system as follows:

- The pull back reservoir 112 desirably comprises a simple inexpensive syringe. Because this is a single use device no contamination shield is required.
- Elimination of the pull back reservoir from the pressure monitoring system eliminates the chances of air bubbles, residual blood, and makes priming and initial set-up much easier.
- By eliminating the reservoir from the pressure monitoring system there is no impact to the pressure wave form fidelity.
- The pull back reservoir is no longer integrated into the tubing system. This eliminates the tangling or snagging with the patients bedding or other equipment. Elimination of the reservoir makes for a much cleaner, or less cluttered, system.
- Blood pressure monitoring kits can be configured with two Z-sites so that both ICU and OR clinicians can have easy access to blood samples. A single "universal" blood pressure monitoring kit can serve both the ICU and the OR user.
- Products that are currently available require the user to first manipulate the reservoir, and valve. They then have to reposition their hands to take a sample from the Z-site. Then they have to reposition their hands back to the reservoir and

valve. This sequence requires the user to reposition three times. The advantage of the present system is that all sampling activities happen with one single user positioning.

- Because the reservoir is only used once there is no need for a complex design, nor is there a need for a contamination shield. A standard syringe can be incorporated into the kit configuration thereby providing a low cost sampling system.

[0068] The bypass function (i.e., excluding the proximal segment) of the sampling system of the present invention can be achieved in a number of ways. Figures 8A-8C and 9A-9E illustrate in great detail an alternative exemplary sampling site 200 and bypass cannula 202. The sampling site 200 is shown exploded in Figure 8C and features a main body 204 adapted to project upward from a base plate 206. The base plate 206 includes slots for securing it with tape, for example, to a base surface. The main body 204 is desirably rigid molded plastic having a central column 208 with a closed bottom and a sampling port 210 opening upward. A proximal port 212 projects horizontally from one side of the column 208, while a distal port 214 projects horizontally in the opposite direction but offset vertically. The main body 204 mounts on top of a tubular flange 216 on the base plate 206 via an intermediate O-ring 218. As seen in the sectional views of Figures 9B and 9C, a plug member 220 extends upward into a countersunk bore in the base plate 206 to contact the underside of the main body 204. Desirably, the main body 204 and the plug member 220 are attached via adhesive, or other similar expedient.

[0069] The bypass cannula 202 is similar to those described above and includes a front fitting 230 bifurcated into a pair of fingers or skirts 232. The front fitting 230 positively engages the sampling port 210 of the sampling site 200, while a rear fitting 234 projects upward. The vertical gaps between the bifurcated skirts 232 receive the outwardly projecting proximal and distal ports 212, 214.

[0070] With reference to Figures 9B and 9C, the bypass cannula 202 further includes a bypass probe 240 aligned along a central axis defining a throughbore 242 therein and terminating in an open and tapered distal tip 244. When the bypass cannula 202 couples to the sampling site 200, the bypass probe 240 projects through an elastomeric septum 246 provided at the opening of the sampling port 210. The length of the bypass probe 240 is sufficient so that the tapered tip 244 extends into a central chamber of the sampling site main body 204 and into engagement with a similarly tapered opening (not numbered) that communicates with a passageway opening leading to the distal port 214. Upon engagement between the bypass cannula 202 and sampling site 200, the throughbore in the bypass probe 240 and rear fitting 234 is placed in fluid communication with the passageway through the distal port 214, to the exclusion of the proximal port 212. That is, instead of forming the bypass probe 240 with a solid distal end and side openings as before, it is a continuous tubular member open only at its distal end, so that engagement of the passageway opening with the distal port 214 excludes communication between the proximal port 212 and the throughbore 242.

[0071] The bifurcated skirts 232 of the bypass cannula 202 extend axially farther than the length of the bypass probe 240. The bypass cannula 202 therefore includes the safety feature of a blunt-tipped probe 240 which is also protected from undesirable contact or damage by the generally parallel and laterally adjacent skirts 232. The skirts 232 each have on their lowermost ends small internal depressions that receive similarly-shaped teeth 250 on the tubular flange 216 of the sampling site 200. Furthermore, the external shape of the central column 208 of the sampling site main body 204 is slightly conical, though the skirts 232 are not and they are slightly outwardly biased upon engagement with the main body 204. Engaging the bypass cannula 202 onto the sampling site 200 involves pressing the cannula downward such that the probe 240 extends through the elastomeric septum 246 and the bifurcated skirts 232 flex outward until the lower depressions are engaged with the teeth 250. Desirably, the engagement provides an audible "snap," and the coupling is

made more secure by the frictional contact of the skirts 232 against the intermediate O-ring 218. Once the bypass cannula 202 and sampling site 200 are fully engaged, the tapered tip 244 of the bypass probe 240 accurately seats within the tapered opening in the sampling site main body 204. The procedure for taking a fluid sample using the combined bypass cannula 202 and sampling site 200 is similar to that described above.

[0072] Figure 10 illustrates an alternative bypass cannula 260 and sampling site 262 combination of one embodiment of the present invention which is very similar to that shown in Figures 8-9. As before, the sampling site 262 includes a main body 264 defining an internal chamber opening at a distal port 266, a proximal port 268, and a sampling port 270. An elastomeric seal or septum 272 occludes the sampling port 270 until the bypass cannula 260 engages the sampling site 262 and a bypass probe 274 projects therethrough. As above, the bypass probe 274 has a tapered tip, but instead of fitting into a tapered seat within the main body 264, it expands within and contacts the bore of a tubular sealing member 276. The sealing member 276 is made of a compressible material such as silicone rubber which provides good sealing contact against the bypass probe 274. It will thus be apparent that engagement of the bypass cannula 260 over the sampling site 262 enables a fluid flow between the bypass cannula throughbore and the distal port 266, thus bypassing the proximal port 268.

[0073] Figure 11 illustrates another alternative bypass cannula 280 and sampling site 282 combination of one embodiment of the present invention which is similar to that shown in Figure 5. As before, the sampling site 282 includes a main body 284 defining an internal chamber opening at a distal port 286, a proximal port 288, and a sampling port 290. An elastomeric seal or septum 292 occludes the sampling port 290 until the bypass cannula 280 engages the sampling site 282 and a bypass probe 294 projects therethrough. As with the embodiment of Figure 5, the bypass probe 294 terminates in an enlarged and tapered tip 296. The tip 296 acts as a plug to contact and occlude a passageway leading to the proximal port 288. One or more side openings 298

provided in the bypass probe 294 enable fluid communication between the internal chamber of the main body 284 and the throughbore of the bypass cannula 280. It will thus be apparent that engagement of the bypass cannula 280 over the sampling site 282 enables a fluid flow between the bypass cannula throughbore and the distal port 286, to the exclusion of the proximal port 288. To further enhance the ability of the bypass probe 294 to plug the opening to the proximal port 288, the tapered tip 296 may be supplemented with an elastomeric head or other compressible coating.

[0074] Figures 12A and 12B illustrate a still further alternative bypass cannula 300 and sampling site 302 combination, as well as an exemplary bubble trap 304 that may be used therewith. The bypass cannula 300 has a threaded front fitting 306 adapted to mate with a threaded sampling port 308 of the sampling site 302. As before, the bypass cannula 300 includes a bypass probe 310 sized to extend through an elastomeric seal or septum 312 into engagement with a passage leading to a distal port 314 of the sampling site 302. The bypass probe 310 is similar to the bypass probe 240 of Figures 8 and 9 in that it is a continuous tube having a central throughbore 316. The engagement of bypass cannula 300 with the sampling site 302 therefore connects the throughbore of the cannula with the distal port 314 and a distal segment 318 of a conduit line leading to a patient, and excludes a proximal port 320 and a proximal segment 322 from the flow path.

[0075] The bypass cannula 300 connects through the bubble trap 304 to a 3-way stopcock 330, and from there to a reservoir 332 and elbow conduit 334. Although not shown, a sampling collection vessel may be connected to the opposite end of the elbow conduit 334. Indeed, the system functions in a similar manner to those described above, with the exception of the interposition of the bubble trap 304.

[0076] With reference to Figure 12B, the bubble trap 304 includes a generally tubular outer body 340 having a conical lower end 342 and defining a float chamber 344 therewith. The lower end 342 opens into the central throughbore 316 of the bypass probe 310. A ball valve 346 floats on any fluid

within the chamber 344, and nests within a similarly shaped inner surface at the bottom of the float chamber 344. A flow separator 348 projects downward from an upper cap 350 of the bubble trap 304. Passages around the flow separator 348 leading to an upper throughbore 352 within the cap 350. The upper cap 350 receives the optional flexible tubing 354 leading to the 3-way stopcock 330.

[0077] In use, fluid drawn into the reservoir 332 passes upward through the bubble trap 304 without hindrance. Bubbles that may form from the suction created by the reservoir 332 rise to the fluid surface layer within the chamber 344 and pop. Upon re-infusion from the reservoir 332, the fluid passes downward through the bubble trap 304, bypass cannula 300, and into the distal port 314 and distal segment 318 of the conduit line. Once the fluid level within the chamber 344 lowers enough, the ball valve 346 contacts the shaped inner surface of the float chamber 344 to prevent any air or bubbles being passed into the conduit line.

[0078] Figure 13 is an alternative disposable fluid sampling system 360 of one embodiment of the present invention that again permits fluid to be drawn into and expelled from a removable reservoir 362 to and from a distal segment 364 of a conduit line while occluding a proximal segment 366. Although not shown, the distal and proximal segments 364, 366 desirably formed a part of a pressure monitoring conduit line where the distal segment 364 communicates with a fluid system of the patient and proximal segment 366 connects to a disposable pressure transducer (DPT) and an intravenous (I.V.) drip. The fluid sampling system 360 resembles somewhat that shown in Figure 5, wherein a disposable subsystem comprises the reservoir 362, a 3-way stopcock 370, an optional length of flexible tubing 372, a flowthrough bypass cannula 374, an optional elbow conduit 376, and a sample collection vessel 378. The bypass cannula 374 engages a sampling port 380 of the sampling site 382 positioned in the conduit line between the distal segment 364 and proximal segment 366.

[0079] In contrast to the earlier-described embodiments, a hollow probe 390 on the bypass cannula 374 has a length sufficient to extend through a slit septum 392 within the sampling port 382 into an inner chamber 394 of the

sampling site 382, but not long enough to engage any passageway openings therein. Instead, the probe 390 extends just passed the septum 392 into the inner chamber 394 and remains in fluid communication with both the distal segment 364 and proximal segment 366. In other words, the probe 390 does not in itself provide the bypass function described above.

[0080] The fluid sampling system 360 further includes a 2-way stopcock 400 positioned adjacent to the sampling site 382 in the proximal segment 366 of the conduit line. Alternatively, the 2-way stopcock 400 could be incorporated into the sampling site 382, although such a design is relatively more expensive to manufacture. The stopcock 400 provides the bypass function of the fluid sampling system.

[0081] In use, the clinician manipulates the stopcock 400 to disconnect the proximal segment 366 of the conduit line from the sampling site 32. The disposable subsystem is removed from its sterile package (e.g., the sterile package 122 of Figure 4) and the appropriate components are connected with the bypass cannula 374 engaging the sampling port 380 of the sampling site 382. The probe 390 passes through the elastomeric septum 392 into the chamber 394.

[0082] The step of engaging the bypass cannula 374 with the sampling site 382 occurs while the stopcock 370 blocks fluid flow therethrough. After secure engagement of the bypass cannula 374 with the sampling site 382, the clinician manipulates the stopcock 370 into a position that permits fluid flow from the distal segment 364 and sampling site 382 through the bypass cannula 374 and to the reservoir 362. Retraction of a plunger (not shown) of the reservoir 362 creates a negative pressure differential such that a fluid sample from the distal segment 364 is drawn into the chamber 394 and into the reservoir 362.

[0083] Once all of the saline and mixed saline and blood has been pulled into the reservoir 362, the clinician can then take a sample of undiluted blood from the site 382. To do so, he/she manipulates the stopcock 370 into a position

that blocks flow to the reservoir 362 and permits flow between the bypass cannula 374 and the elbow conduit 376 and sample collection vessel 378.

[0084] After the desired sample is taken, the clinician again manipulates the stopcock 370 into a position that closes off the elbow conduit 376 and opens flow between the reservoir 362 and sampling site 382. Blood and other fluids drawn into the reservoir 362 during the sample priming operation are re-infused by depressing the reservoir plunger into the distal segment 364, and ultimately back to the patient. It should be noted that during this re-infusion step the stopcock 400 remains closed so that fluid re-infused from the reservoir 362 does not travel into the proximal segment 366 toward the DPT. After re-infusion of the prime volume the clinician manipulates the stopcock 370 to close off the communication between the sampling port 380 and reservoir 362 and removes and discards the disposable subsystem by disconnecting the bypass cannula 374 from the sampling site 382. The clinician opens the stopcock 400 and the "normal" operation of the conduit line resumes, such as a flushing drip and pressure monitoring.

[0085] Again, the sampling system 360 provides a closed reservoir 362 since the priming volume that ensures a pure sample of blood reaches the sampling site 382 remains within the system and is re-infused into the patient without removal of the reservoir. That is, because the reservoir 362 as a part of the disposable subsystem remains connected to the sampling site 382 during the entire process until re-infusion, the conduit line is not "broken," meaning the reservoir is not detached between drawing the prime volume and re-infusing it. Of course, as mentioned above, if the clinician notices bubbles have formed within the reservoir 362 or adjacent tubing, the disposable subsystem can be removed from the sampling site 382 without re-infusing the prime volume, which is then also discarded.

[0086] The system 360 of Figure 13 functions in a similar manner as the earlier-described embodiments, in that the sampling subsystem including the fluid draw reservoir is removable and disposable. Moreover, the reservoir is closed because it remains in place during the fluid draw and re-infusion.

However, if bubbles are detected in the reservoir or intermediate tubing the fluid draw can be discarded which is not possible with a dedicated reservoir. All of the systems of the present invention provide a removable/disposable closed reservoir that can be isolated from the proximal or upstream segment of the conduit line.

[0087] In contrast to the earlier-described embodiments of the present invention, the bypass feature of the fluid sampling system 360 is enabled by the proximal stopcock 400 rather than by simple engagement of a bypass cannula with the sampling site. One advantage with such a system is the elimination of the need for special components such as the bypass probes described above, and therefore there is an attendant reduction in manufacturing costs. A potential drawback, however, is the possibility of including some saline in the blood sample taken because of the spacing between the stopcock 400 and the sampling site 382. That is, the reservoir 362 draws most of the saline and mixed saline and blood therein, though some saline or diluted blood may remain in the passages that are not in the direct line of reservoir flow. Also, because a second stopcock 400 is included, the system 360 is less elegant and not as simple to use.

[0088] While the invention has been described in its preferred embodiments, it is to be understood that the words which have been used are words of description and not of limitation. Therefore, changes may be made within the appended claims without departing from the true scope of the invention.

WHAT IS CLAIMED IS:

1. A medical system for sampling of a fluid system of a patient for use with a conduit line with a proximal segment adapted to be supplied with a physiological fluid and a distal segment adapted to be in communication with the fluid system of a patient, and a fluid sampling site in the conduit line, the sampling site including a housing having a distal port connected to the distal segment and a proximal port connected to the proximal segment, wherein fluid may flow freely through a chamber in the housing between the proximal and distal ports, the sampling site further defining a sampling port open to the chamber and closed from the exterior by an elastomeric seal, the medical system comprising:

a flowthrough bypass cannula having a body shaped to engage the sampling port and a bypass probe having a throughbore and being sized to pierce the elastomeric seal, project into the chamber and place the throughbore into fluid communication with the distal port of the sampling site while occluding the proximal port from the throughbore, wherein a fluid sample may be drawn into the bypass cannula from the distal segment of the conduit line to the exclusion of the proximal segment.

2. The system of claim 1, wherein the bypass probe terminates in a tip that contacts a passageway opening in the fluid sampling site housing leading to one of the distal or proximal ports when the bypass cannula engages the sampling site, and the tip is tapered and matches the passageway opening.

3. The system of claim 1, wherein the bypass probe terminates in a closed tip that contacts and occludes a passageway opening in the fluid sampling site housing leading to the proximal port when the bypass cannula engages the sampling site, and the bypass probe includes at least one side opening open to the chamber in the sampling site housing.

4. The system of claim 3, wherein the bypass probe tip is at least partly compressible.

5. The system of claim 1, wherein the bypass probe defines a continuous tubular member and terminates in an open tip that contacts a passageway opening in the fluid sampling site housing leading to the distal port when the bypass cannula engages the sampling site.

6. The system of claim 5, further including a sealing member positioned in the passageway opening that contacts and seals against the open tip of the bypass probe.

7. The system of claim 1, wherein the bypass cannula and sampling site include mating structure such that they engage with a positive snap fit.

8. A system for sampling fluid from a medical conduit line including a disposable subsystem, comprising:

a conduit line with a proximal segment adapted to be supplied with a physiological fluid and a distal segment adapted to be in communication with a fluid system of a patient;

a fluid sampling site in the conduit line having an internal chamber in communication with all of: a proximal port connected to the proximal segment, a distal port connected to the distal segment, and a sampling port closed by an elastomeric seal;

a disposable sampling subsystem for engaging the fluid sampling site including:

a bypass cannula adapted to engage the sampling port of the sampling site and simultaneously occlude the proximal port therein;

a stopcock having three ports, a first port in communication with the bypass cannula;

a fluid reservoir connected to a second port of the stopcock;

a fluid sampling vessel in fluid communication with the third port of the stopcock;

wherein in a first position the stopcock enables fluid communication between the first and second ports so that fluid may be drawn into the reservoir from the distal segment, and in a second position the stopcock enables fluid communication between the first and third ports so that fluid may be drawn into the fluid sampling vessel from the distal segment.

9. The system of claim 8, further including:

a pressure transducer connected to the proximal segment of the conduit line for sensing the pressure of the fluid system of a patient through the fluid in the conduit line.

10. The system of claim 8, wherein the bypass cannula includes a bypass probe terminating in a closed tip that contacts and occludes a passageway opening in the fluid sampling site housing leading to the proximal port when the bypass cannula engages the sampling site, and the bypass probe includes at least one side opening open to the chamber in the sampling site housing.

11. The system of claim 8, wherein the bypass cannula includes a continuous tubular bypass probe terminating in an open tip that contacts a passageway opening in the fluid sampling site housing leading to the distal port when the bypass cannula engages the sampling site.

12. The system of claim 8, wherein the system further includes a stopcock positioned adjacent the proximal port of the sampling site for occluding the proximal port when fluid is drawn into and expelled from the reservoir and drawn into the fluid sampling container.

13. The system of claim 8, further including:

a bubble trap connected to the bypass cannula between the sampling site and reservoir that prevents bubbles from entering the sampling site from the bypass cannula.

14. A method for sampling blood from a medical fluid conduit line using a disposable subsystem, the conduit line having a proximal segment supplied with a physiological fluid and a distal segment in communication with the blood system of a patient, the conduit line also having a fluid sampling site defining an internal chamber in communication with all of: a proximal port connected to the proximal segment, a distal port connected to the distal segment, and a sampling port closed by an elastomeric seal, the method comprising:

providing a disposable sampling subsystem for engaging the fluid sampling site including a flowthrough bypass cannula having a probe, a fluid reservoir, and a fluid sampling container;

engaging the bypass cannula with the sampling site so that the probe passes through the elastomeric seal;

opening fluid communication between the bypass cannula and reservoir while closing fluid communication between the bypass cannula and fluid sampling container;

closing fluid communication between the bypass cannula and proximal segment of the conduit line and drawing fluid into the reservoir from the distal segment through the bypass cannula until blood enters the sampling site;

opening fluid communication between the bypass cannula and fluid sampling vessel while closing fluid communication between the bypass cannula and reservoir;

drawing blood into the fluid sampling vessel from the distal segment;

maintaining the bypass cannula engaged with the sampling site until a sample of blood is drawn into the fluid sampling container; and

detaching the bypass cannula from the sampling site and disposing of the sampling subsystem.

15. The method of claim 14, wherein the disposable sampling subsystem further includes a stopcock having three ports, a first port in communication with the bypass cannula, a second ports in communication with the fluid reservoir, and a third port in communication with the fluid sampling container, wherein following steps of the method are enabled by manipulating the stopcock:

opening fluid communication between the bypass cannula and reservoir while closing fluid communication between the bypass cannula and fluid sampling container; and

opening fluid communication between the bypass cannula and fluid sampling vessel while closing fluid communication between the bypass cannula and reservoir.

16. The method of claim 14, further including:

providing a pressure transducer connected to the proximal segment of the conduit line and sensing the pressure of the fluid system of a patient through the fluid in the conduit line.

17. The method of claim 14, wherein the step of opening fluid communication between the bypass cannula and reservoir while closing fluid

communication between the bypass cannula and fluid sampling vessel is accomplished by the step of engaging the bypass cannula with the sampling site.

18. The method of claim 17, wherein the probe of the bypass cannula has a size sufficient to contact and occlude a passageway opening leading to the proximal port of the sampling site.

19. The method of claim 17, wherein the probe of the bypass cannula has a size sufficient to contact a passageway opening leading to the distal port of the sampling site and exclude fluid communication between the proximal port and the distal port.

20. The method of claim 14, wherein the method further includes providing a stopcock adjacent the proximal port of the sampling site for occluding the proximal port when fluid is drawn into and expelled from the reservoir and drawn into the fluid sampling container.

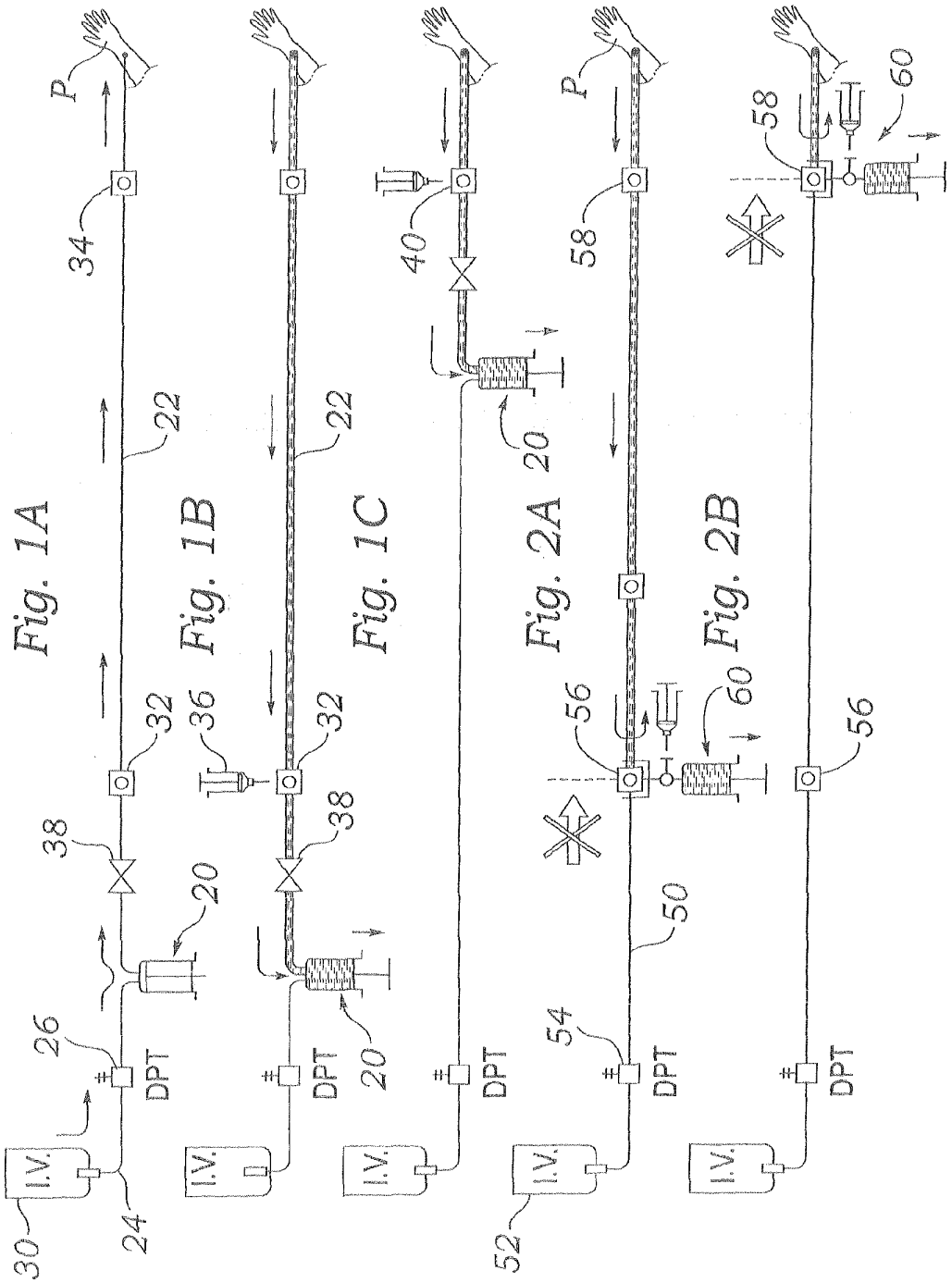
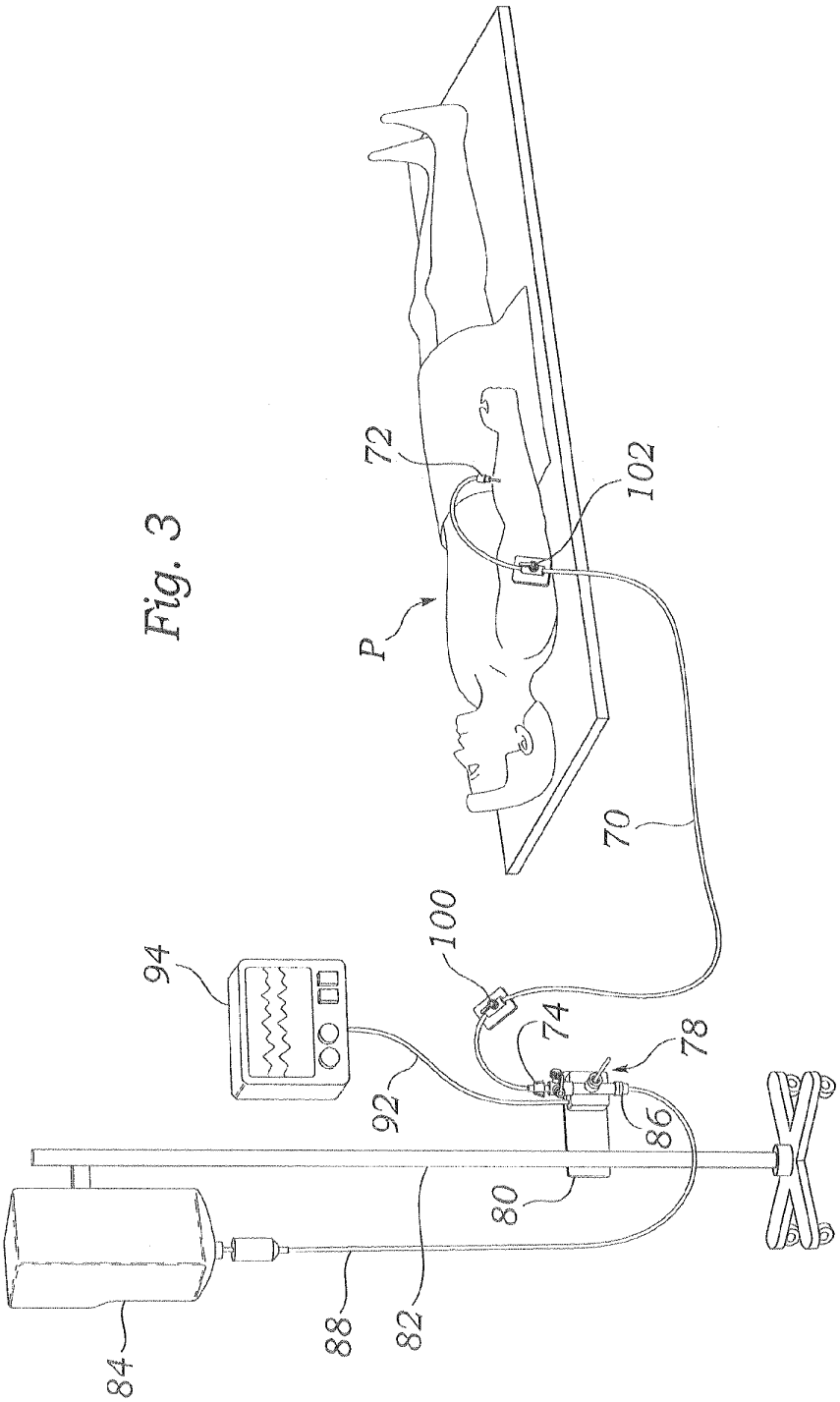

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Fig. 2B

Fig. 3



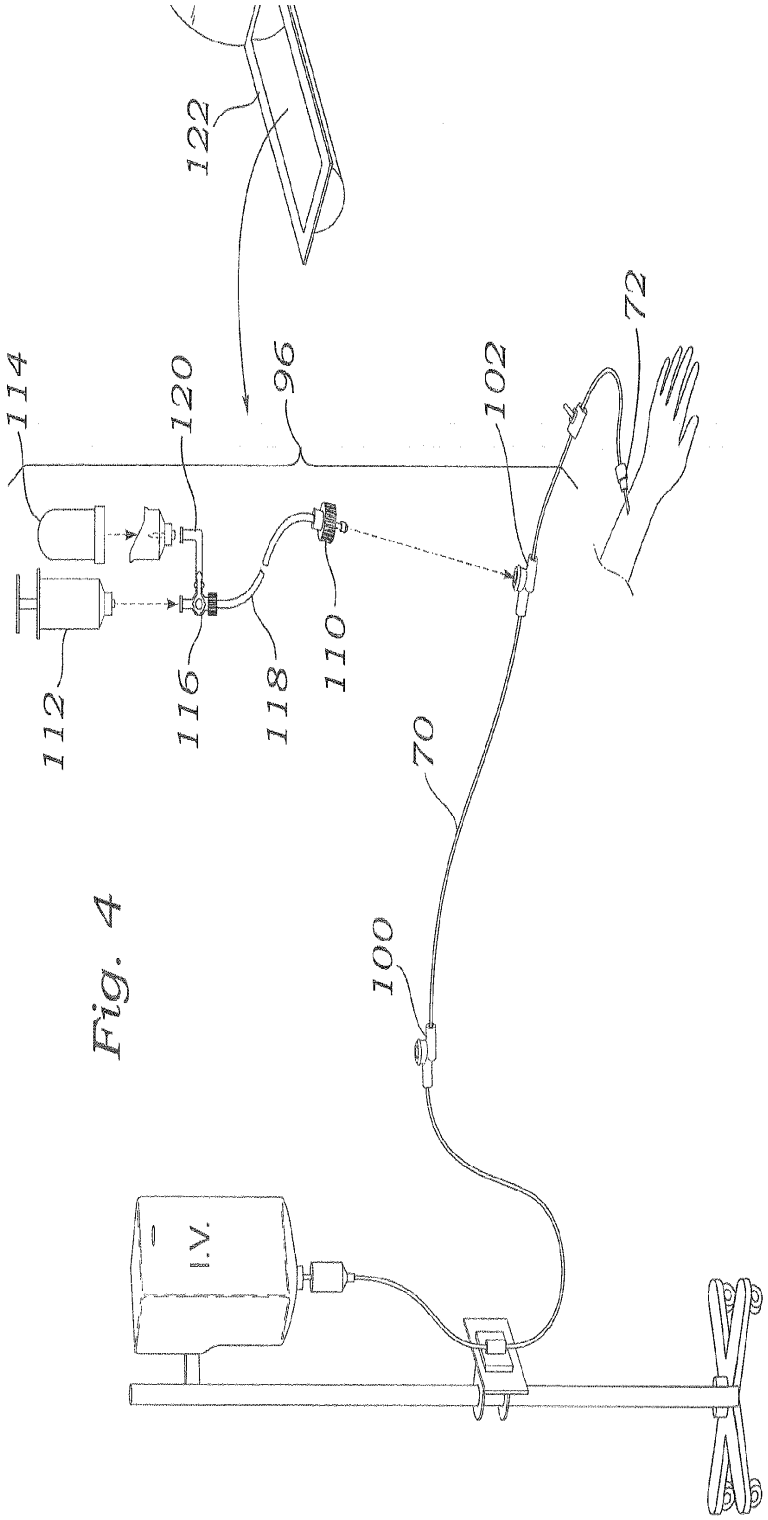


Fig. 4

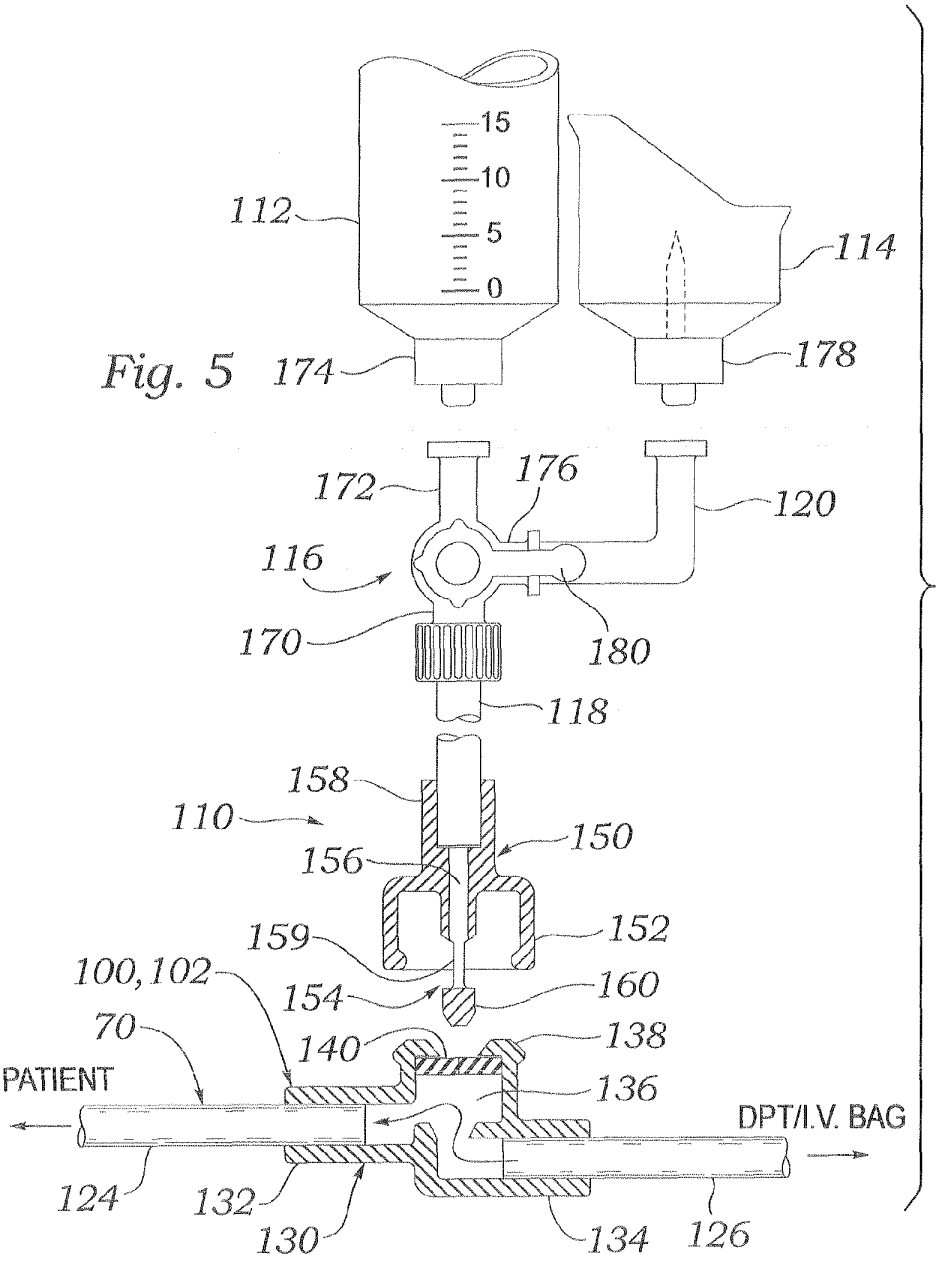

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Fig. 5

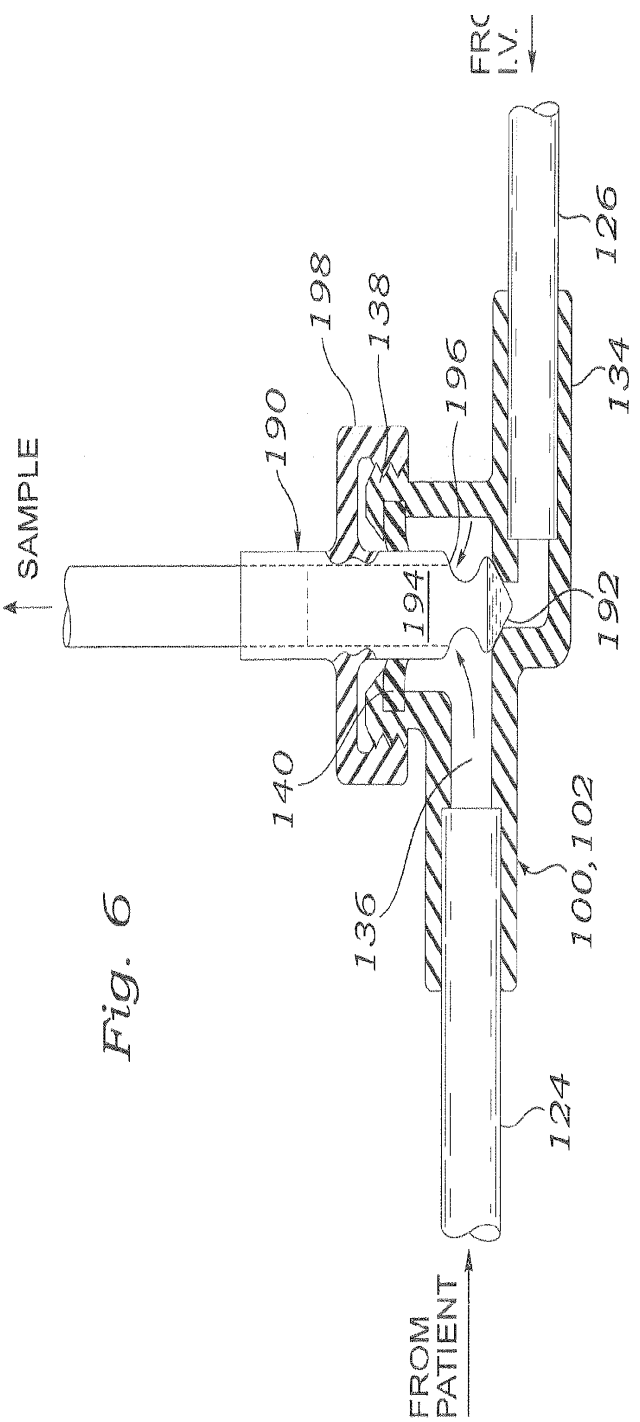

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Fig. 6

Fig. 7A

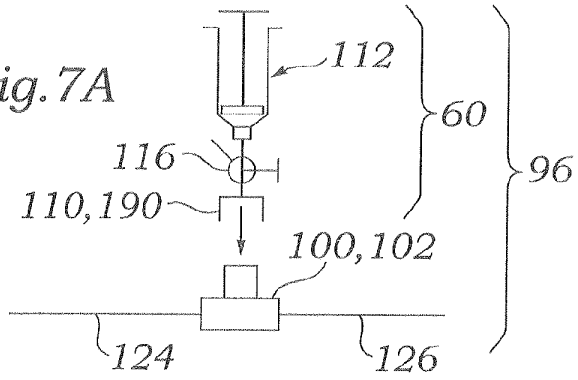


Fig. 7B

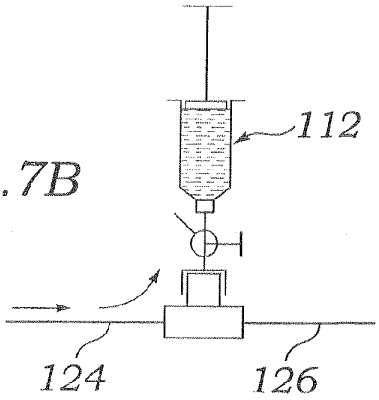


Fig. 7C

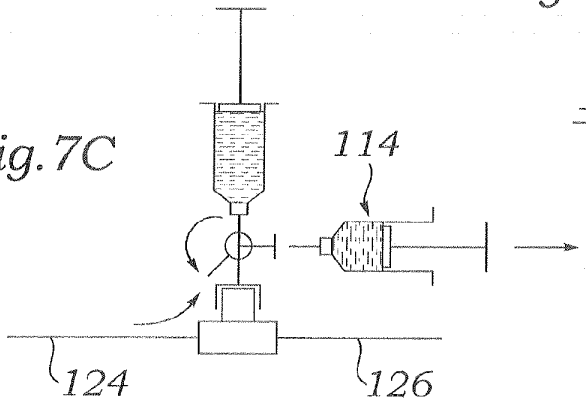


Fig. 7D

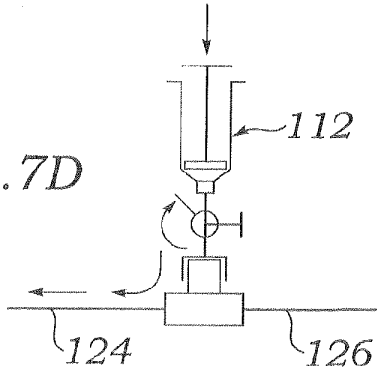
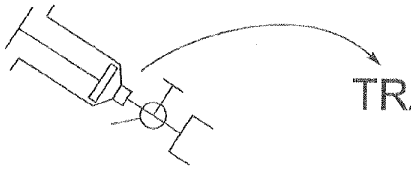


Fig. 7E



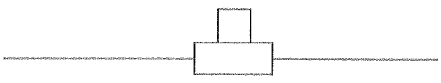


Fig.9A

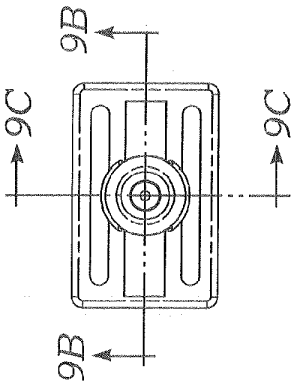


Fig.8B

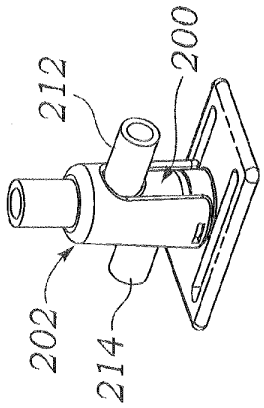


Fig.8A

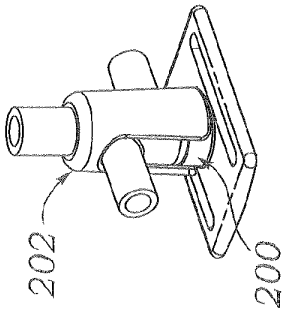


Fig.9C

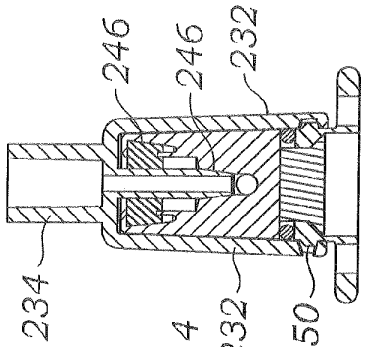


Fig.9B

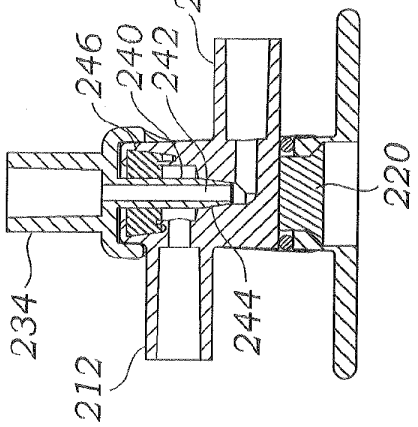


Fig.8C

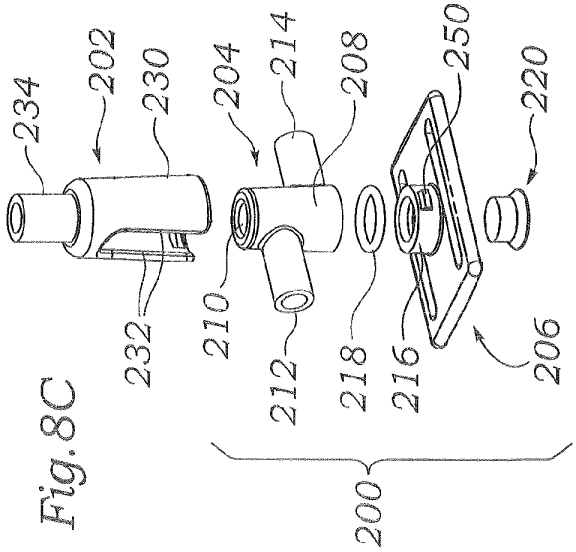


Fig. 10

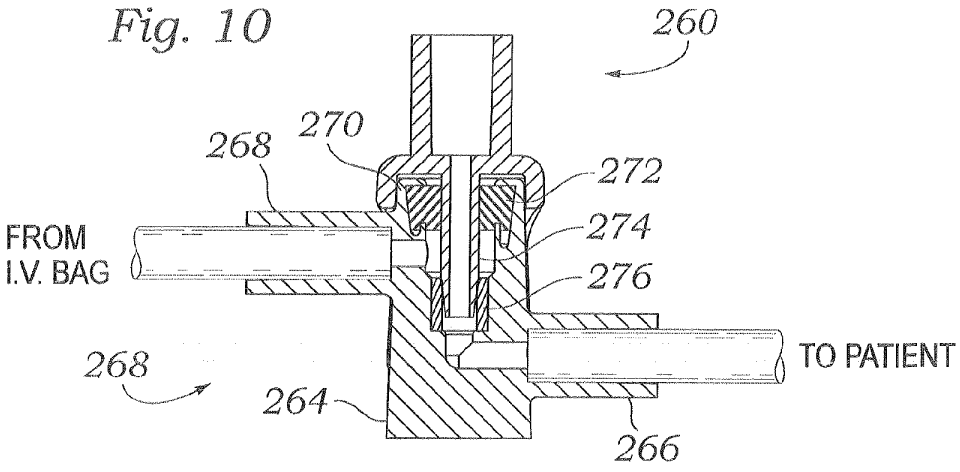

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Fig. 11

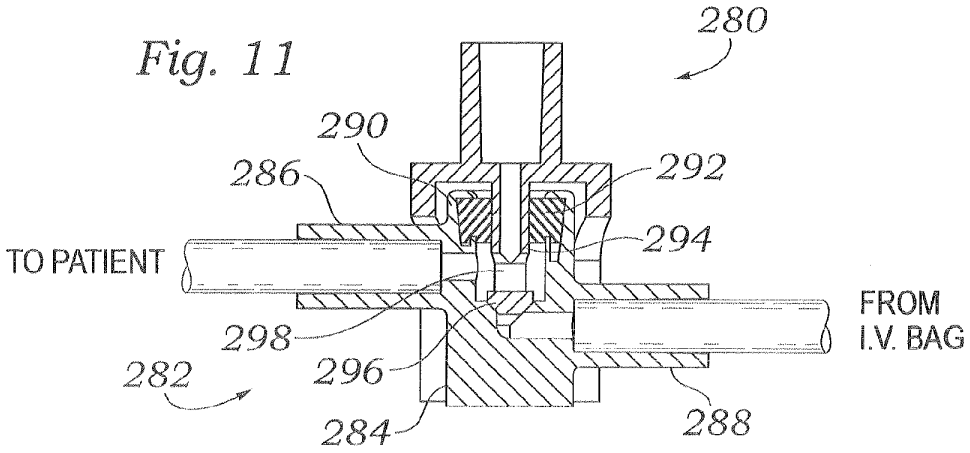

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Fig. 12A

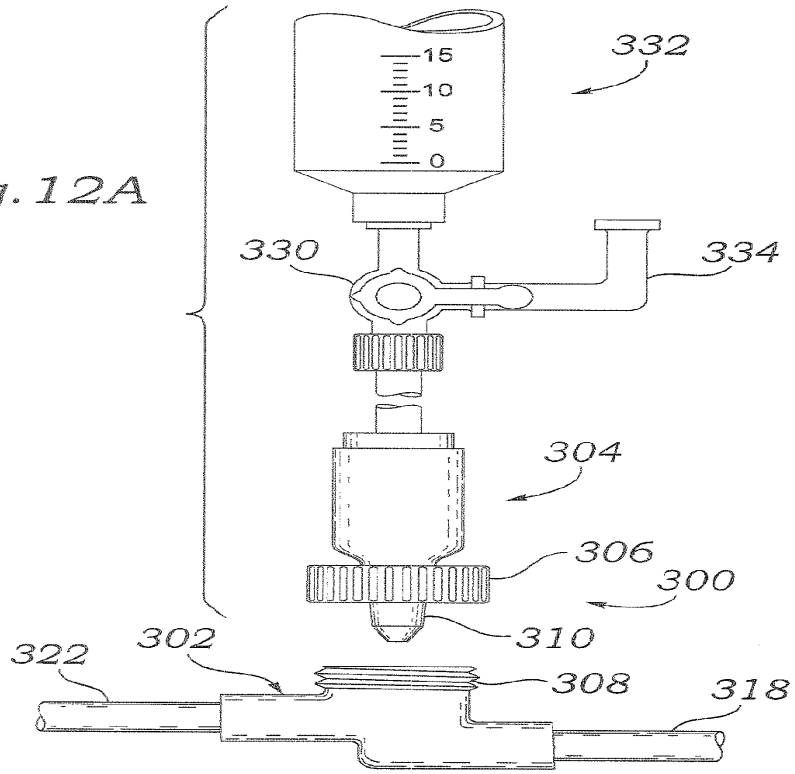
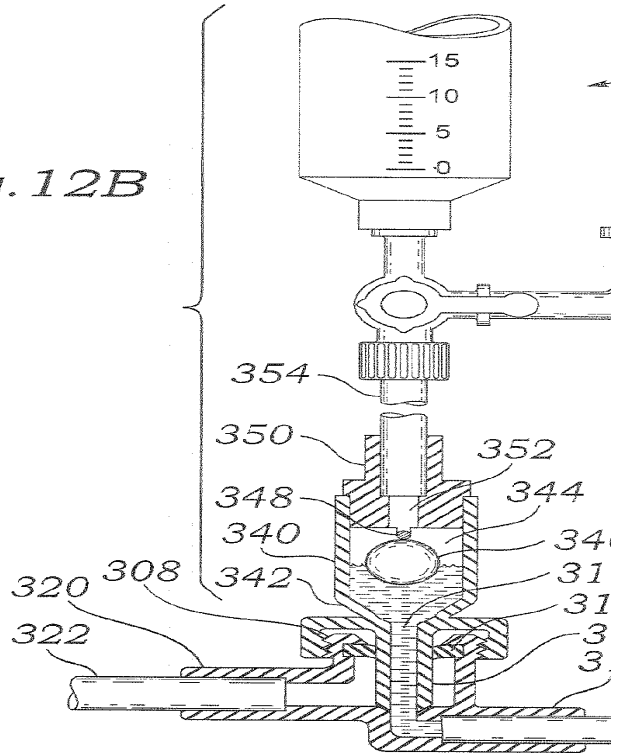


Fig. 12B



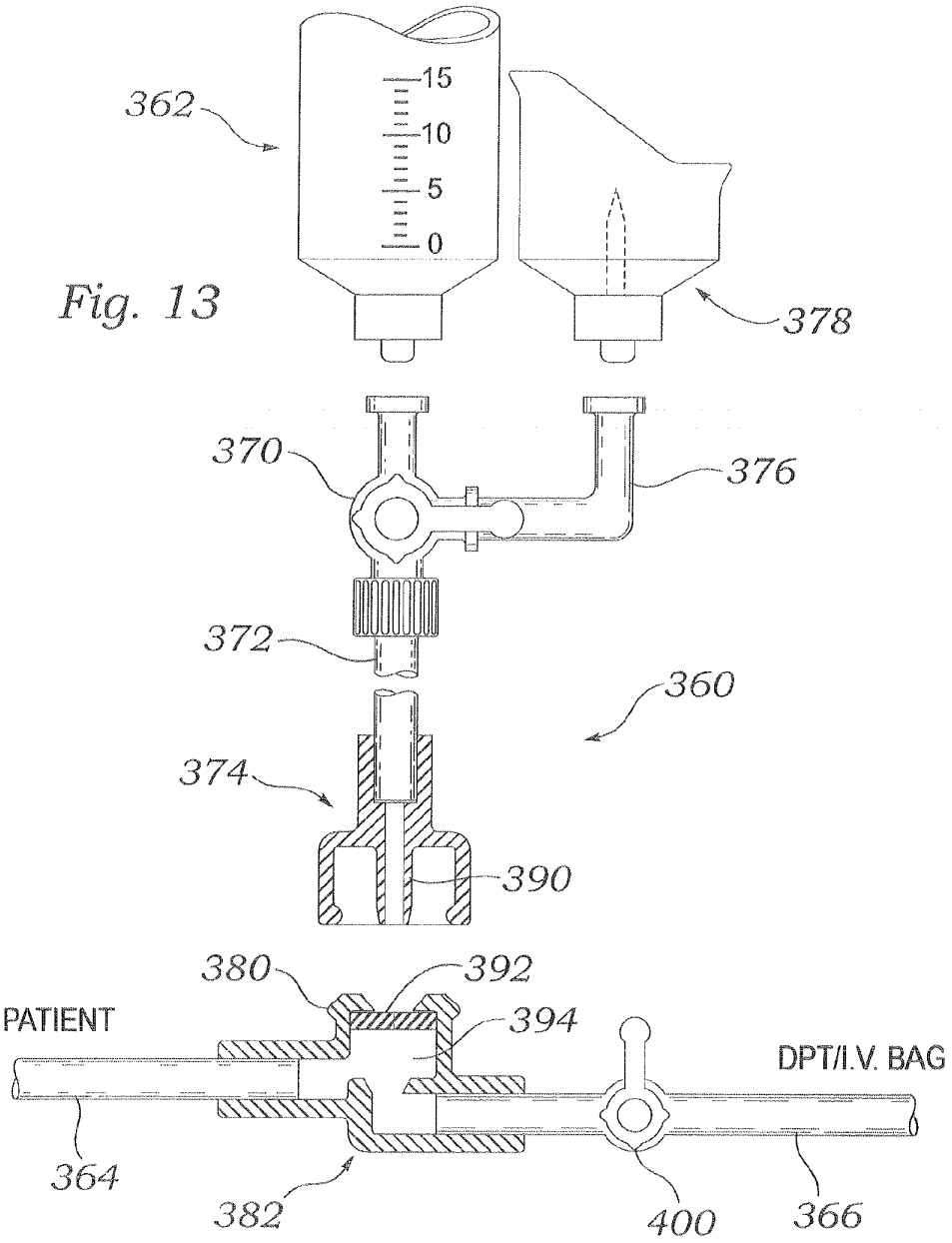

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Fig. 13

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2008/053871

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61B5/15 A61M39/04 A61M39/02
ADD. A61M1/02

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 A61M

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 practical, search terms used)
EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X Y	EP 0 637 455 A (SIEMENS ELEMA AB [SE]) 8 February 1995 (1995-02-08) column 1, lines 21,22 column 3, line 56 - column 4, line 4 column 4, line 47 - column 5, line 18; figures 1,3,12	1-7 8-13
X	EP 0 240 590 A (INTERMEDICAT GMBH [CH]) 14 October 1987 (1987-10-14) column 7, lines 11-32; figure 4	1
X	US 5 348 542 A (ELLIS DAVID W [US]) 20 September 1994 (1994-09-20) column 2, line 57 - column 3, line 9; figure 1	1
	-/--	

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

[X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document 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
4 July 2008	14/07/2008

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, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Böttcher, Stephanie

Form PCT/ISA/210 (second sheet) (April 2005)

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2008/053871

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 6 287 265 B1 (GLEASON CINDY L [US]) 11 September 2001 (2001-09-11) column 6, line 16 - column 7, line 32; figure 7	8-13

Form PCT/ISA/210 (continuation of second sheet) (April 2005)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2008/053871

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. [X] Claims Nos.: 14-20
because they relate to subject matter not required to be searched by this Authority, namely:

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by surgeryThe sampling of blood requires a surgical step, namely the withdrawal of blood from a patient's blood vessel.

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 additional search fees were timely paid by the applicant, this international search report covers allsearchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an 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 reportcovers 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/US2008/053871

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 0637455 A	08-02-1995	JP 7051386 A	28-02-1995
		US 5549582 A	27-08-1996
EP 0240590 A	14-10-1987	AT 66622 T	15-09-1991
		DE 3681158 D1	02-10-1991
		JP 1708152 C	11-11-1992
		JP 3062113 B	24-09-1991
		JP 62243563 A	24-10-1987
		US 4819684 A	11-04-1989
US 5348542 A	20-09-1994	NONE	
US 6287265 B1	11-09-2001	NONE	

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

BD

BD Saf-T-Intima™ closed IV cat



BD Saf-T-Intima™ closed IV catheter system

The BD Saf-T-Intima™ closed IV catheter system incorporates preattached extension tubing to help support reduction in blood exposure.

About

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A removable PRN adapter allows the use of an ISO-compliant needleless connector.

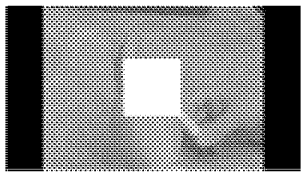
Closed system

Preattached extension tubing offers a closed system to minimize blood exposure during catheter insertion.

BD Vialon™ biomaterial

The system is constructed with BD Vialon biomaterial, a proprietary catheter material that softens in the vein.

Related Videos



BD Saf-T-Intima™ Closed IV Catheter...

Related Products



BD Nexiva™ closed IV catheter system



BD Nexiva™ Diffusics™ closed IV catheter system

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BD Saf-T-Intima™ points to practice in-service material

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Infusion Resource Library

Notes

* Compared to a nontapered tip

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT		
	Application Number	18/783,088
	Filing Date	07/24/2024
	First Named Inventor	Bobby E. ROGERS
	Art Unit	OPAP
	Client Number	069366
Page 1 of 1	**Matter Number**	0580418_KUR2C06US

GENERAL

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

Although the information submitted herewith may be "material" to the Examiner's consideration of the subject application, this submission is not intended to constitute an admission that such information is "prior art" as to the claimed invention, nor is it intended to constitute an admission that such information is "analogous prior art".

In accordance with 37 C.F.R. 1.97(g), the filing of this Information Disclosure Statement shall not be construed to mean that a search has been made.

TIMING

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

CERTIFICATION STATEMENT

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

FEE

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

ADDITIONAL COMMENTS

SIGNATURE

Signature	/Benjamin F. Hudson/	**Date**	2024-08-26
Name	Benjamin F. Hudson	**Registration Number**	71,474

SyncIDS.com

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 5736-PCT	**FOR FURTHER ACTION**	see Form PCT/ISA/220 as well as, where applicable, item 5 below.
International application No. PCT/US 2015/035870	International filing date *(day/month/year)* 15 June 2015 (15.06.2015)	(Earliest) Priority Date *(day/month/year)* 13 June 2014 (13.06.2014)
Applicant GARRET, Chad et al.		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 2 sheets.

☐ It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

a. With regard to the **language**, the international search was carried out on the basis of:

☒ the international application in the language in which it was filed.

☐ a translation of the international application into _____, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b)).

b. ☐ This international search report has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43.6*bis*(a)).

c. ☐ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. ☐ **Certain claims were found unsearchable** (see Box No. II).

3. ☐ **Unity of invention is lacking** (see Box No. III).

4. With regard to the **title,**

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract,**

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2, by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regard to the **drawings,**

a. the figure of the drawings to be published with the abstract is Figure No. 1

☒ as suggested by the applicant.

☐ as selected by this Authority, because the applicant failed to suggest a figure.

☐ as selected by this Authority, because this figure better characterizes the invention.

b. ☐ none of the figures is to be published with the abstract.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 2015/035870

A. CLASSIFICATION OF SUBJECT MATTER

A61B 5/15 *(2006.01)*
A61M 25/01 *(2006.01)*
G01N 33/48 *(2006.01)*

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 5/15, A61M 5/19, 25/01 G01N 33/48

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)

PatSearch, Espacenet, USPTO, Google

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X Y	WO 2013/082301 A1 (TELEFLEX MEDICAL, INC.) 06.06.2013 claims, [0006]-[0008], [0037], [0041], [0044]-[0054], fig. 1-5	1-9 10-13, 15-16, 18-19
Y	JP 2009131273 A (CSL BEHRING GMBH) 18.06.2009 abstract	10-13
X Y	EP 2593169 A1 (BECTON DICKINSON CO) 22.05.2013 abstract, [0006]-[0013]	14, 17 15-16, 18-19

☐ 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 document 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
19 October 2015 (19.10.2015)	05 November 2015 (05.11.2015)
Name and mailing address of the ISA/RU: Federal Institute of Industrial Property, Berezhkovskaya nab., 30-1, Moscow, G-59, GSP-3, Russia, 125993 Facsimile No: (8-495) 531-63-18, (8-499) 243-33-37	Authorized officer E. Kazak Telephone No. 8 (495) 531 64 81

Form PCT/ISA/210 (second sheet) (January 2015)

PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

To:
HARMS, Donn K.
12702 Via Cortina, Suite 100
Del Mar, CA 92014
United States of America

Date of mailing *(day/month/year)* 05 November 2015 (05.11.2015)	
Applicant's or agent's file reference 5736-PCT	**FOR FURTHER ACTION** See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US 2015/035870	15 June 2015 (15.06.2015)	13 June 2014 (13.06.2014)

International Patent Classification (IPC) or both national classification and IPC
A61B 5/15 *(2006.01)*
A61M 25/01 *(2006.01)*
G01N 33/48 *(2006.01)*

Applicant
GARRET, Chad et al.

1. This opinion contains indications relating to the following items:

- [X] Box No. I Basis of the opinion
- [ ] Box No. II Priority
- [ ] Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- [ ] Box No. IV Lack of unity of invention
- [X] Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement
- [ ] Box No. VI Certain documents cited
- [ ] Box No. VII Certain defects in the international application
- [ ] Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

Name and mailing address of the ISA/RU:	Date of completion of this opinion	Authorized officer
Federal Institute of Industrial Property, Berezhkovskaya nab., 30-1, Moscow, G-59, GSP-3, Russia, 125993 Facsimile No: (8-495) 531-63-18, (8-499) 243-33-37	19 October 2015 (19.10.2015)	E. Kazak Telephone No. 8 (495) 531 64 81

Form PCT/ISA/237 (cover sheet) (January 2015)

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US 2015/035870

Box No. I Basis of this opinion

1. With regard to the **language**, this opinion has been established on the basis of:

   [X] the international application in the language in which it was filed.

   [ ] a translation of the international application into _____ which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b)).

2. [ ] This opinion has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43*bis*.1(a))

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, this opinion has been established on the basis of a sequence listing filed or furnished:

   a. [ ] forming part of the international application as filed:

      [ ] in the form of an Annex C/ST.25 text file.

      [ ] on paper or in the form of an image file.

   b. [ ] furnished together with the international application under PCT Rule 13*ter*.1(a) for the purposes of international search only in the form of an Annex C/ST.25 text file.

   c. [ ] furnished subsequent to the international filing date for the purposes of international search only:

      [ ] in the form of an Annex C/ST.25 text file (Rule 13*ter*.1(a)).

      [ ] on paper or in the form of an image file (Rule 13*ter*.1(b) and Administrative Instructions, Section 713).

4. [ ] In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

5. Additional comments:

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US 2015/035870

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	10-13, 15-16, 18-19	YES
	Claims	1-9, 14, 17	NO
Inventive step (IS)	Claims		YES
	Claims	10-13, 15-16, 18-19	NO
Industrial applicability (IA)	Claims	1-19	YES
	Claims		NO

2. Citations and explanations:

D1 - WO 2013/082301 A1
D2 - JP 2009131273 A
D3 - EP 2593169 A1

D1 can be regarded as the closest prior art of test component for blood according to claim 1.

D1 (claims, [0006] - [0008]) discloses a substrate configured to generate a visually discernable reaction to the presence or a threshold level of a substance in said blood; said substrate adapted for positioning in a fluid communication pathway carrying blood from a flash chamber defined by a surrounding sidewall of a housing of an introducer; and said substrate generating said visually discernable reaction viewable by a user of said introducer, subsequent to a fluid communication of said blood from said flash chamber to said substrate.

Thus, the invention according to claim 1 does not meet the criterion of novelty.

D3 can be regarded as the closest prior art of the inventions according to independent claims 14, 17.

D3 (abstract, [0006] - [0013]) discloses an introducer for the introduction of a catheter into the vein or artery of a patient: said introducer having a needle in axial communication between a distal end and a flash chamber with a housing of said introducer; a testing substrate within a substrate housing, said substrate housing in a fluid communication with said flash chamber through a passage in a sidewall of said flash chamber; said testing substrate configured to generate a visually discernable result, to a substance contained within blood communicated through said needle to said flash chamber; and said testing substrate viewable through a cover of said substrate housing, whereby said user can concurrently introduce a catheter to a patient and view test results for the presence of said substance with said blood from said patient communicated to said flash chamber.

D3 (abstract, [0006] - [0013]) discloses a method of testing a patient's blood for a substance comprising the steps of: placing a substrate having a visually discernable reaction area thereon to a said substance, in a fluid communication with a flash chamber of an introducer employed for the insertion of a catheter into the vein or artery of a patient; puncturing the vein or artery of said patient with a needle engaged to said introducer; allowing blood from said vein or artery to communicate axially through said needle to a flash chamber in said introducer; allowing a portion of said blood to fluidly communicate with said substrate; and viewing said substrate to ascertain said visually discernable reaction.

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.
Continuation of V:

Thus, the inventions according to independent claims 14, 17 do not meet the criterion of novelty.

The features of dependent claims 2-4, describing the fluid communication being through the microporous membrane disposed within the flash chamber, are disclosed in D1 ([0037], [0041], [0044], [0054]).

The features of dependent claims 5-6, indicating that positioned within a chamber of a substrate housing, said housing being engageable with an exterior of said sidewall of said substrate housing; and said fluid communication to said substrate communicating through an aperture in said sidewall , are disclosed in D1 ([0054]).

The features of dependent claims 7-9, indicating that substrate housing having a transparent cover in an engagement with a base having a passage aligned with said aperture in said sidewall; and providing for visually discernable reaction are disclosed in D1 ([0054], fig.1-5).

Thus, the invention according to dependent claims 2-9 does not meet the criterion of novelty.

The features of dependent claims 10-13, indicating that a clotting factor on or adjacent to said separation membrane generating a cessation of said fluid communication through said separation membrane subsequent to a duration of time sufficient to clot said blood at said separation membrane are disclosed in D2 (abstract).

The features of dependent claim 15 indicating that a separation membrane interposed between said flash chamber and said substrate: and said separation membrane allowing only blood plasma from said portion of blood therethrough to a said fluid communication with said substrate are disclosed in D1 ([0044], [0054]).

The features of dependent claim 16, indicating a plurality of said testing substrates, each located within separate said substrate housing, each said substrate housing in a fluid communication with said flash chamber through a passage in a sidewall of said flash chamber are also disclosed inD1 ([0044], [0054]).

The features of dependent claims 18, 19, indicating a visually discernable reaction area of substrate positioned in substrate housing are disclosed in D1 ([0044]).

Thus, the invention according to dependent claims 10-13, 15, 16, 18, 19 does not meet the criterion of inventive step.

The inventions according to claims 1-19 meet the criterion of industrial applicability.

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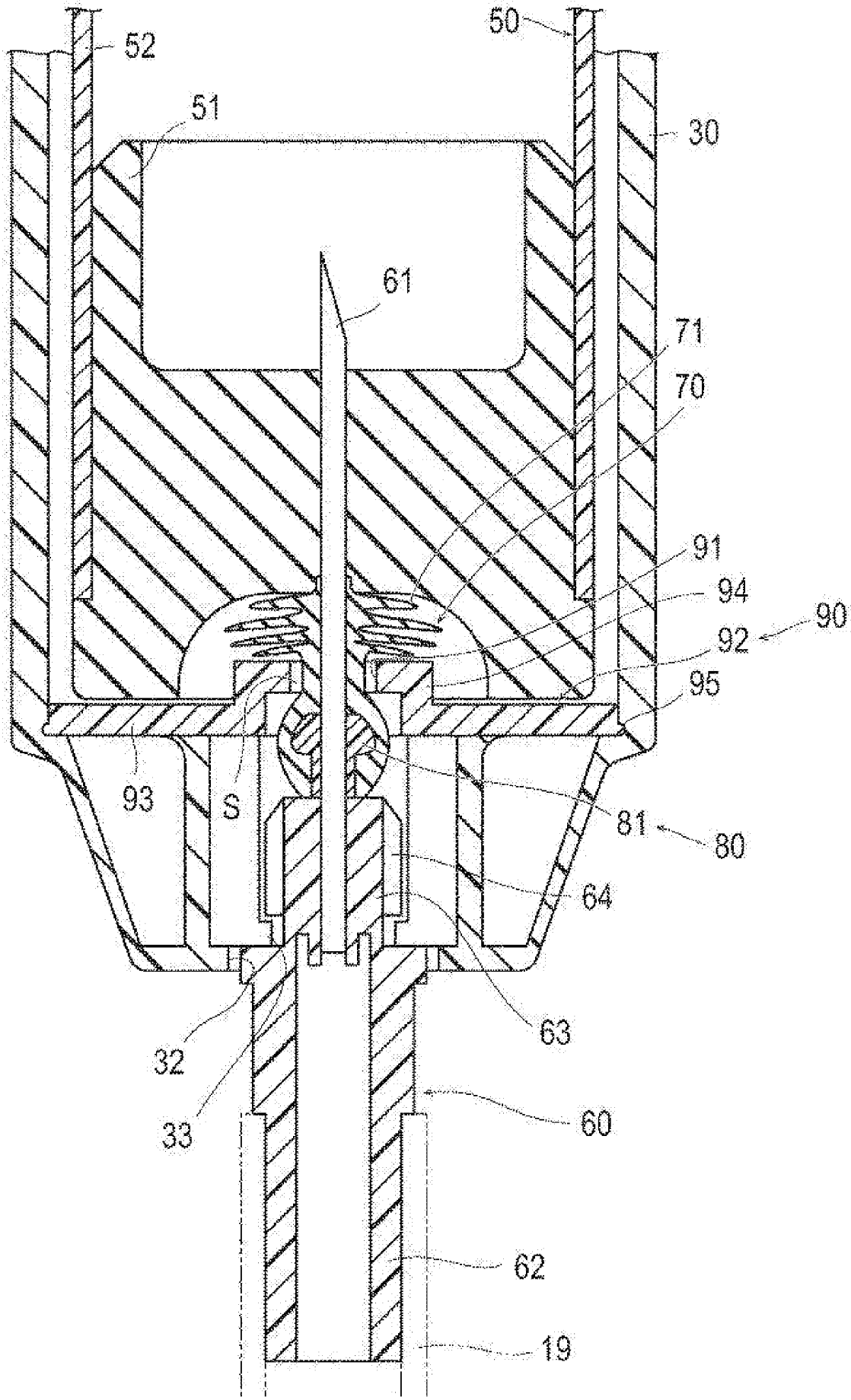
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wrap up close

(57) [Summary]
[Problem] To hold a rubber cap on a needle assembly even when the rubber cap is elastically contracted and wrinkled as a hollow needle is passed through a rubber plug of a blood collecti on tube. To provide a sampling port capable of maintaining force and sufficiently preventing le akage of blood.

A sampling port (20) includes a main body (30) formed with an opening (31) for inserting a bl ood collection tube (50) having a rubber plug (51), a hollow needle (61) that can be freely ins erted into the rubber plug of the blood collection tube, and a hollow needle. a needle assembl y 60 attached to the main body, comprising a hub 64 supporting the proximal end of the need le, an elastic rubber cap 70 covering the hollow needle, and a holding portion 80 holding the r ubber cap; A through hole 91 through which a hollow needle covered with a rubber cap penetr ates is provided, and wrinkles 71 generated by elastic contraction of the rubber cap accompan ying insertion of the hollow needle into the rubber stopper are suppressed from reaching the holding portion. and a plate 92 as a suppressing member 90 .

[Selection drawing] Fig. 4


50
52
51
30
61
71
70
91
94
90
92
95
93
S
81
80
64
63
32
33
60
62
19



The scope of the claims open

What is claimed is

: 1.

A main body having an opening for inserting a blood collection tube having a rubber stopper, a hollow

needle that can be inserted through the rubber stopper of the blood collection tube, and the hollow needle. a hub for supporting the proximal end of the hollow needle; an elastic rubber c ap placed on the hollow needle; and a holding portion for holding the rubber cap

. A through hole is provided through which the hollow needle covered with a rubber cap pen etrates, and wrinkles generated by elastic contraction of the rubber cap as the hollow needle i s inserted into the rubber plug reach the holding portion. and a suppression member that sup presses the sampling port.

2.

The main body is rotatably attached to the needle assembly,

the suppressing member is fixed to the main body, and between the through hole and the ru bber cap, 2. The sampling port of claim 1, having clearance to allow rotation of said body porti on.

3.

The main body has a cylindrical shape, and

the suppressing member has a disk shape and includes a projection projecting toward the op ening of the main body. 3. The sampling port of claim 2.

4.

The sampling port according to any one of claims 1 to 3, wherein a ring-shaped projection pr otruding radially outward is provided on the outer peripheral edge of said suppressing membe r.

[Claim 5]

The main body portion is made of a resin material that shrinks more than the resin material forming the suppressing member when heat is applied, and the suppressing member is shrun k to the main body portion by applying heat for sterilization. A sampling port according to any one of claims 1 to 4, fixed with respect to

detailed description open

Description: BACKGROUND OF THE INVENTION 1.

Field of the Invention The present invention relates to sampling ports for holding blood collec tion tubes. 2. Description of the Related Art When blood is collected using a blood collection tube with a rubber stopper, a sampling port for holding the blood collection tube is used (see Patent Document 1). The sampling port has a main body with an opening for inserting a blood collection tube, and a needle assembly having a hollow needle that can be freely inserted into the rubber stopper of the blood collection tube is attached to the main body. there is The hollo w needle is covered with an elastic rubber cap to prevent leakage of blood. [0003] As the bl ood collection tube is inserted into the body of the sampling port and the hollow needle is pas sed through the rubber plug, the rubber cap is elastically contracted and wrinkled to expose t he hollow needle. The exposed hollow needle is used to collect blood into a collection tube. W hen the blood collection tube is pulled out after blood collection, the rubber cap elastically stre tches from the contracted state as if smoothing the wrinkles, and restores to the state where i t covers the hollow needle again. This prevents leakage of blood from the hollow needle. The r ubber cap is held on the needle assembly by, for example, fitting the root portion to the needl e assembly. [Prior Art Document] [Patent Document] [Patent Document 1] Japanese Patent A pplication Laid-Open No. 2002-291724 [Summary of the Invention]

[0005] However, when the hollow needle is passed

through the rubber plug of the blood collection tube, the wrinkles caused by the elastic contr action of the rubber cap may reach the base of the rubber cap. There is In such a case, the ro ot portion of the rubber cap swells, weakening the holding force for holding the rubber cap to the needle assembly. For this reason, if the tip of the rubber cap is biting into the small inserti on hole of the rubber stopper of the blood collection tube, the rubber cap will be pulled togeth er when the blood collection tube is pulled out, and the position of the rubber cap will be affec ted. There is a risk that the blood will not be sufficiently prevented from leaking.

[0006]

The present invention was made in order to solve the above-mentioned problems associated with the prior art. When a hollow needle is passed through a rubber plug of a blood collection tube, the rubber cap is elastically contracted and wrinkled. It is an object of the present inven tion to provide a sampling port capable of maintaining a holding force for holding a rubber cap to a needle assembly even when the needle assembly is closed, thereby sufficiently preventin g leakage of blood. [0007] A sampling port of the present invention for achieving the above objects comprises a main body having an opening for inser ting a blood collection tube having a rubber stopper, and the blood collection tube . a hollow needle that can be freely inserted into the rubber plug of the above, a hub that supports the b ase end of the hollow needle, an elastic rubber cap that covers the hollow needle, and a holdi ng portion that holds the rubber cap a needle assembly attached to the main body, and a thro ugh hole through which the hollow needle covered with the rubber cap passes, wherein the r ubber cap is elastic as the hollow needle is inserted into the rubber plug and a suppressing m ember that suppresses wrinkles generated by the contraction from reaching the holding portio n.

[0008] The suppressing member suppresses wrinkles generated by elastic contraction of the rubber cap as the hollo w needle is passed through the rubber stopper of the blood collection tube from reaching the holding portion. , the rubber cap does not swell at the holding part, and the holding force for holding the rubber cap to the needle assembly does not weaken. Therefore, even if the rubber cap is pulled together when the blood collection tube is pulled out after blood collection, the p osition of the rubber cap will not be displaced, and blood leakage can be sufficiently prevente d. Thus, even if the rubber cap is elastically contracted and wrinkled as the hollow needle is p assed through the rubber plug of the blood collection tube, the holding force for holding the ru bber cap to the needle assembly can be maintained, Thus, a sampling port that can sufficientl y prevent blood leakage can be provided.

BRIEF DESCRIPTION OF THE DRAWINGS

[0009]

FIG. 1 is a block diagram showing a blood bag system incorporating a sampling port;

2 is a perspective view showing the initial blood bag shown in FIG. 1 and a sampling port; FI G.

FIG. 3 is a cross-sectional view showing essential parts of a sampling port before a blood colle ction tube is inserted;

FIG. 4 is a cross-sectional view showing the essential parts of the sampling port after the bloo d collection tube has been inserted;

5(A) is a perspective view showing a plate as a suppressing member, FIG. 5(B) is a cross-sect ional view along line 5B-5B in FIG. 5(A), and FIG. It is sectional drawing which expands and s hows 5C part of FIG.5(B).

6A and 6B are cross-sectional views showing how a plate as a suppressing member is fixed to the main body; FIG.

FIG. 7A is a conceptual diagram for explaining the action of the present embodiment, and FI G. 7B is a conceptual diagram for explaining the action in the case of contrast without a plate;

8A to 8D are cross-sectional views showing modified examples of the plate; FIG.

9A and 9B are plan views showing further modifications of the plate; FIG.

DETAILED DESCRIPTION OF THE INVENTION Embodiments of the present invention will now

be described with reference to the accompanying drawings. In the description of the drawing s, the same elements are denoted by the same reference numerals, and overlapping descripti ons are omitted. Also, the dimensional ratios in the drawings are exaggerated for convenience of explanation, and may differ from the actual ratios.

Referring to FIG .

1, the illustrated blood bag system 10 removes the initial flow (initial blood flow) of the colle cted blood when collecting blood, and uses the initial blood flow as test blood. It is a blood coll ection device. Bacteria present on and under the skin enter along with the skin fragments at t he time of puncture, so the initial blood flow is removed. A blood bag system 10 includes a b lood collecting needle 11, a blood bag 12 containing blood collected through the blood collecti ng needle 11, a blood collecting tube 13 connecting the blood collecting needle 11 and the blo od bag 12, and a blood collecting tube

.

13, an initial blood flow bag 16 communicating with the blood collection tube 13 via a branch t ube 15 connected to the branch connector 14, and a sampling port 20 connected to the end of the initial blood flow bag 16. ,have. The branch connector 14 is provided with a sealing memb er 17 that seals communication with the blood bag 12 . The sealing member 17 seals the com munication with the blood bag 12 until the collection of the initial blood flow into the initial blo od bag 16 is completed. The branch tube 15 is provided with a clamp member 18 that blocks blood flow to the initial blood bag 16 . After collecting the initial blood flow, the clamp membe r 18 clamps the branch tube 15 to block the blood flow to the initial blood bag 16 . After that, the sealing member 17 is opened to start collecting blood into the blood bag 12 .

[0013]

FIG. 2 shows a state in which the initial blood contained in the initial blood bag 16 is collecte d as test blood. A sampling port 20 is connected to a blood extraction tube 19 connected to a n initial blood bag 16 . A lid member 40 that opens and closes the opening 31 is rotatably con

nected to the sampling port 20 via a hinge 41 . When collecting the initial blood contained in t he initial blood bag 16 as test blood, a reduced-pressure blood collection tube 50 (correspondi ng to a blood collection tube) having a rubber plug 51 is inserted into the sampling port 20 thr ough the opening 31 .

A reduced

-pressure blood collection tube 50 is an instrument for collecting the initial blood that is stor ed in the initial blood bag 16 . The vacuum blood collection tube 50 has a blood collection tub e body 52 and a rubber plug 51 fitted into the opening of the blood collection tube body 52 . T he vacuum blood collection tube 50 is in a vacuum or a reduced pressure state. When the vac uum blood collection tube 50 is connected to the sampling port 20 , the rubber stopper 51 is p ierced by the hollow needle 61 . As a result, the inside of the vacuum blood collection tube 50 and the blood extraction tube 19 are communicated, and the initial blood flow from the blood extraction tube 19 is collected in the vacuum blood collection tube 50 .

[0015]

With reference to FIGS. 3 and 4, the sampling port 20 according to the embodiment is gener ally composed of a body portion 30 formed with an opening 31 for inserting a blood collection tube 50 having a rubber stopper 51, a blood collection tube A hollow needle 61 that can be fre ely inserted into the rubber plug 51 of 50, a hub 64 that supports the base end of the hollow needle 61, an elastic rubber cap 70 that covers the hollow needle 61, and a holder that holds the rubber cap 70. and a needle assembly 60 attached to the body portion 30 with a portion 8 0 . The sampling port 20 further suppresses wrinkles 71 (see FIG. 4) caused by elastic contra ction of the rubber cap 70 as the hollow needle 61 is inserted into the rubber plug 51 from rea ching the holding portion 80. It has a member 90 . The suppressing member 90 has a throug h hole 91 through which the hollow needle 61 covered with the rubber cap 70 passes. 3 and 4, the upper side in the drawings is defined as the "upper side" of each member, and the lowe r side in the drawings is defined as the "lower side" of each member. Details are given below.

The body portion 30 has a cylindrical shape and has a tapered shape on the lower side

.

The main body 30 has

, an insertion port 32 for inserting the needle assembly 60, and an engaging portion 33 for pr eventing the inserted needle assembly 60 from coming off.

Body

portion 30 is rotatably attached to needle assembly 60 . By making it rotatable, the body po rtion 30 can be rotated with respect to the needle assembly 60 to easily finely adjust the posit ion of the lid member 40 with respect to the initial blood flow bag 16 . A needle assembly 60 includes a hollow needle 61 having a sharp tip at its tip, a connecting portion 62 connected to the blood extraction tube 19, a boss portion 63 holding the proximal end portion of the hollow needle 61

,

have. The hub 64 is provided so as to protrude radially outward from the boss portion 63 . Th e needle assembly 60 is attached to the body portion 30 with the hub 64 overcoming the locki ng portion 33 when it is inserted into the insertion port 32 of the body portion 30 . The upper end of the hub 64 in the figure is formed into an inclined surface so that it can easily get over the engaging portion 33 when it is inserted. In order to pivotally attach the body portion 30 t o the needle assembly 60, the clearance between the connecting portion 62 of the needle ass embly 60 and the receptacle 32 of the body portion 30 and the outer circumference of the hu b 64

are

and the body portion 30 are adjusted. As the blood collection tube 50 is inserted into the ma in body 30 and the hollow needle 61 is passed through the rubber stopper 51, the rubber cap 70 is elastically contracted to form wrinkles 71, thereby exposing the hollow needle 61

.

Let When the blood collection tube 50 is pulled out, the rubber cap 70 is elastically stretched f rom the shrunk state so as to smooth out the wrinkles 71, and restores to the state where it c overs the hollow needle 61 again. This prevents blood from leaking from the hollow needle 61

.

[0021]

The holding portion 80 includes a lock member 81 through which the hollow needle 61 is ins erted and which is attached to the boss portion 63 of the needle assembly 60 . The locking m ember 81 has an undercut shape in which the base end side of the hollow needle 61 has a sm aller diameter than the tip end side. The undercut shape of the locking member 81 holds the r ubber cap 70 .

5(A) and 5(B), restraining member 90 includes a disk -

shaped flat plate portion 93 fitted in main body portion 30 and a center portion of flat plate portion 93 protruding upward. It consists of a plate 92 with a projection 94 . A through-hole 9 1 through which the hollow needle 61 with the rubber cap 70 is attached is formed in the conv ex portion 94 . As shown in FIG. 5C , a ring-shaped projection 95 projecting radially outward i s provided integrally with the flat plate portion 93 on the outer peripheral edge of the flat plat e portion 93 . 3 and 4, the plate 92 is mounted inside the main body 30 at a position above t he lock member 81 forming the holding portion 80. As shown in FIG

.

As the blood collection tube 50 is inserted into the main body 30 and the hollow needle 61 is passed through the rubber stopper 51, the rubber cap 70 is elastically contracted to form wrin kles 71, thereby exposing the hollow needle 61. . A clearance S between the through hole 91 of the plate 92 and the rubber cap 70 is relatively small. Therefore, the plate 92 prevents the wrinkles 71 generated by the elastic contraction of the rubber cap 70 from reaching the holdin g portion 80 (FIG. 4).

[0024]

As described above, the body portion 30 is rotatably attached to the needle assembly 60 . A clearance S is provided between the through hole 91 of the plate 92 fixed to the main body 30 and the rubber cap 70 to allow the main body 30 to rotate. By setting the clearance S to a di mension that does not hinder the rotation of the main body 30, the rotational position of the main body 30 with respect to the needle assembly 60, the position of the lid member 40 with respect to the initial blood bag 16, and the like can be easily finely adjusted. becomes possibl e.

By providing the plate 92 with the protrusions 94, it is possible to increase the area of the ru bber cap 70 in the longitudinal direction that is not affected by the wrinkles 71. As shown in F IG . As a result, a decrease in holding force for holding the rubber cap 70 to the needle assem bly 60 can be further suppressed. Even if the arrangement position of the plate 92 is shifted u pward from the position shown in FIG. 4, the area in the longitudinal direction of the rubber c ap 70 that is not affected by the wrinkles 71 can be increased. However, in this case, since th e position of the blood collection tube 50 is also shifted upward, it may be necessary to slightl y increase the longitudinal dimension of the main body 30 . Therefore, by providing the plate 92 with the convex portion 94 projecting toward the opening 31 side of the body portion 30, while maintaining the length of the body portion 30 in the longitudinal direction, It is possible to secure a sufficient holding force for holding the rubber cap 70 to the needle assembly 60 b y increasing the area not affected by the wrinkles 71 .

[0026]

The material of the main body 30, the cover member 40, the needle assembly 60 excluding t he hollow needle 61, the holding part 80, and the plate 92 is not particularly limited, but exa mples thereof include polycarbonate, polyethylene, polypropylene, ethylene- Examples include polyolefins such as vinyl acetate copolymers and modified polyolefins. The material of the ho llow needle 61 is not particularly limited, but examples include various metal materials such a s stainless steel, aluminum or aluminum alloys, titanium or titanium alloys, superelastic alloys such as Ni--Ti alloys, polyphenylene sulfide, and the like

.

and various hard resin materials.

[0028]

The material constituting the rubber cap 70 is not particularly limited, but examples include natural rubber, isoprene rubber, butadiene rubber, styrene-butadiene rubber, nitrile rubber, chl oroprene rubber, butyl rubber, acrylic rubber, ethylene-propylene rubber, hydrin rubber, Variou s rubber materials such as urethane rubber, silicone rubber, and fluororubber can be used.

FIGS.

6A and 6B show how the plate 92 is fixed to the body portion 30. FIG. In this embodiment, t he body portion 30 is made of a resin material that shrinks more than the resin material formi ng the plate 92 when heat is applied. This is because the plate 92 can be fixed to the body po

rtion 30 by applying heat for sterilization. More specifically, as shown in FIG. 6A, before heat is applied, the inner diameter of the main body 30 is relatively large, and the ring-shaped proj ection 95 of the plate 92 bites into the main body 30 by a small amount

.

I'm in. Since the plate 92 can be inserted into the main body 30 relatively easily, the assembl y work of the plate 92 can be easily performed.

Then ,

as shown in FIG. 6(B), when heat is applied for sterilization, for example, in a high-pressure steam sterilization method (autoclave), the main body 30 shrinks more than the plate 92 doe s. As a result, the ring-shaped protrusion 95 of the plate 92 further bites into the body portion 30 , and the plate 92 can be easily fixed to the body portion 30 . As an example of a combin ation of resin materials as described above, for example, polypropylene can be used as the m olding material for the main body 30 and polycarbonate can be used as the molding material f or the plate 92

. [0033]

The operation of this embodiment will be described. When collecting blood, the blood collec tion tube 50 is inserted into the body portion 30 of the sampling port 20, and is hollow

.

A needle 61 is passed through the rubber stopper 51 . As the hollow needle 61 is inserted thr ough the rubber stopper 51, the rubber cap 70 is elastically contracted to form wrinkles 71, th ereby exposing the hollow needle 61. As shown in FIG. Referring to FIG. 7B, in the case of c ontrast without plate 92, rubber cap 170 is elastically closed as hollow needle 161 is inserted i nto rubber plug 51 of blood collection tube 50

.

Wrinkles 171 caused by shrinking may reach the base of the rubber cap 170 . In such a case, the base portion of rubber cap 170 swells, and the holding force for holding rubber cap 170 to needle assembly 160 is weakened. Therefore, when the blood collection tube 50 is pulled out, the rubber cap 170 may be pulled together, and the position of the rubber cap 170 may be dis placed, resulting in insufficient prevention of blood leakage. On the other hand, referring to FIGS. 4 and 7A, in the present embodiment, the plate 92 is positioned above the locking mem ber 81 forming the holding portion 80, and the main

body

It is installed inside the part 30 . This plate 92 prevents wrinkles 71 generated by elastic contr action of the rubber cap 70 as the hollow needle 61 is inserted into the rubber plug 51 of the blood collection tube 50 from reaching the locking member 81 . Since the rubber cap 70 does not swell at the portion of the lock member 81, the holding force for holding the rubber cap 7

0 to the needle assembly 60 is not weakened.

[0037]

The exposed hollow needle 61 is inserted through the rubber stopper 51 and blood is collected into the blood collection tube 50 . When the blood collection tube 50 is pulled out after blood collection, the rubber cap 70 elastically expands from the shrunk state so as to smooth out the wrinkles 71 and restores to the state where it covers the hollow needle 61 again. This prevents blood from leaking from the hollow needle 61 . The rubber cap 70 is held by the needle assembly 60 at the locking member 81 .

When the tip of the rubber cap 70 bites into the

minute insertion hole of the rubber stopper 51 of the blood collection tube 50 and the blood collection tube 50 is pulled out, the rubber cap 70 is pulled together. However, since the portion of the locking member 81 is not affected by the wrinkles 71, the holding force remains set at the initial stage. Therefore, the rubber cap 70 does not come off from the hollow needle 61 and the blood collection tube 50 is released from biting into the rubber plug 51 . As a result, the position of the rubber cap 70 is not displaced, and blood leakage can be sufficiently prevented.

As described

above, even if the rubber cap 70 is elastically contracted as the hollow needle 61 is inserted into the rubber stopper 51 of the blood collection tube 50 and wrinkles 71 are generated, the rubber cap 70 is attached to the needle assembly 60. It is possible to provide the sampling port 20 which can maintain a holding force for holding and thereby sufficiently prevent leakage of blood. Main body 30 is rotatably attached to needle assembly 60 , plate 92 is fixed to main body 30 , and main body 30 is positioned between through hole 91 and rubber cap 70

.

Since there is a clearance S that allows rotation, it is possible to easily finely adjust the rotation position of the main body 30 with respect to the needle assembly 60 .

[0041]

In addition, since the plate 92 has a convex portion 94 that protrudes toward the opening 31 side of the body portion 30, the longitudinal length of the rubber cap 70 is increased while maintaining the length of the body portion 30 in the longitudinal direction. It is possible to secure a sufficient holding force for holding the rubber cap 70 to the needle assembly 60 by enlarging the area that is not affected by the wrinkles 71 . In addition, since the ring-shaped projection 95 projecting radially outward is provided on the outer peripheral edge of the plate 92, the plate 92 is attached to the body portion 30 so that the ring-shaped projection 95 bites into the body portion 30 by a small amount

.

It can be inserted into the plate 30, and the assembly work of the plate 92 can be easily performed.

becomes possible. The main body 30 is made of a resin material that shrinks more than the

resin material forming the plate 92 when heat is applied

.

Since it is fixed to the body portion 30, the plate 92 can be relatively easily inserted into the b ody portion 30 before heat is applied, and the plate 92 can be easily assembled. On the other hand, when heat is applied for sterilization, the body portion 30 contracts more than the plate 92 . This makes it possible to easily fix the plate 92 to the body portion 30 .

(

Modified Example of Plate)

The plate has a through hole 91 through which the hollow needle 61 with the rubber cap 70 attached passes. As long as wrinkles 71 generated by elastic contraction of 70 are prevented f rom reaching holding portion 80, the shape can be modified as appropriate.

For example, referring to FIG. 8, a plate 92a (FIG. 8A) in which

a projection 94 smoothly protrudes from a flat plate portion 93, a plate 92b with a thicker ov erall thickness and a flat upper surface, 92c (FIGS. 8B and 8C), and a cap-shaped plate 92d (FIG. 8D) that covers the holding portion 80 without covering the entire bottom surface of the main body portion 30 can be exemplified. Further, referring to FIG. 9, a plate 92e (FIG. 9A) i n which the flat plate portion 93 is not formed with the through portion, and a plate 92f (FIG. 9A) in which the flat plate portion 93 is formed with the through portion 96 are provided

.

(B)).

(

Other modifications)

Although the lock member 81 having an undercut shape has been exemplified as the holding portion 80 that holds the rubber cap 70, the holding portion 80 is not limited to this case. The holding part 80 can be appropriately modified as long as it has a function of preventing the ru bber cap 70 from coming off and holding it in the needle assembly 60 . For example, the holdi ng part 80 uses a form in which the rubber cap 70 is adhered to the hollow needle 61 with an adhesive to hold it, a form in which the rubber cap 70 is held by being fused to the hollow nee dle 61 by ultrasonic fusion, or a clip. For example, a configuration in which the rubber cap 70 i s held on the hollow needle 61 by fitting is exemplified. These holding portions 80 may be use d alone, or may be a holding portion 80 in which two or more types are combined.

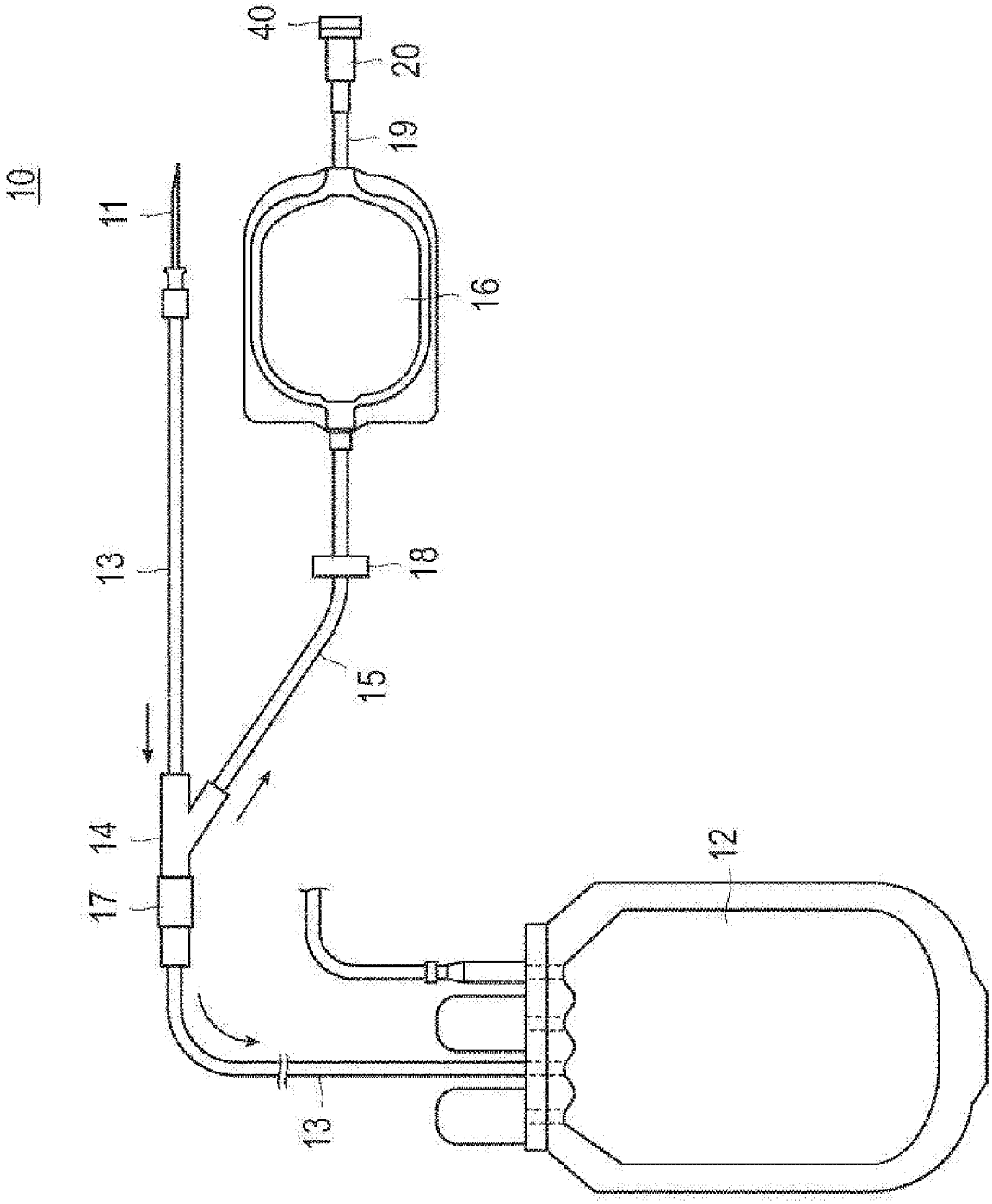
20 sampling port 30 main body 31 opening 50 vacuum

blood collection tube (collection tube) 51 rubber plug 60 needle assembly 61 hollow needle 64 hub 70 rubber cap 71 wrinkles 80 holding part 81 locking member 90 suppressing member 91 through hole 92 plate (suppressing member);

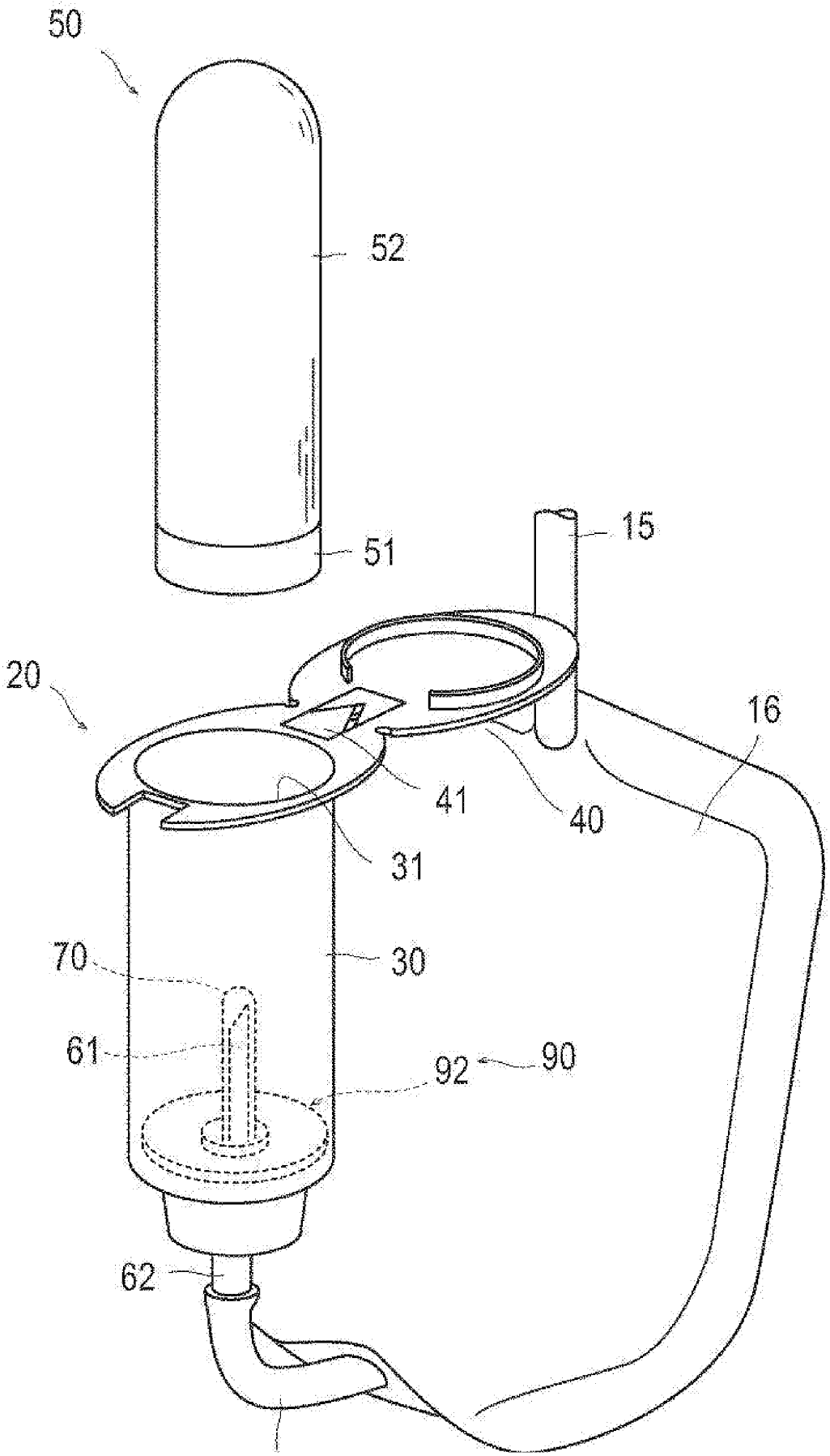
93 flat plate portion,
94 convex portion,
95 ring-shaped projection,
S clearance.

drawing open —

[Fig. 1]

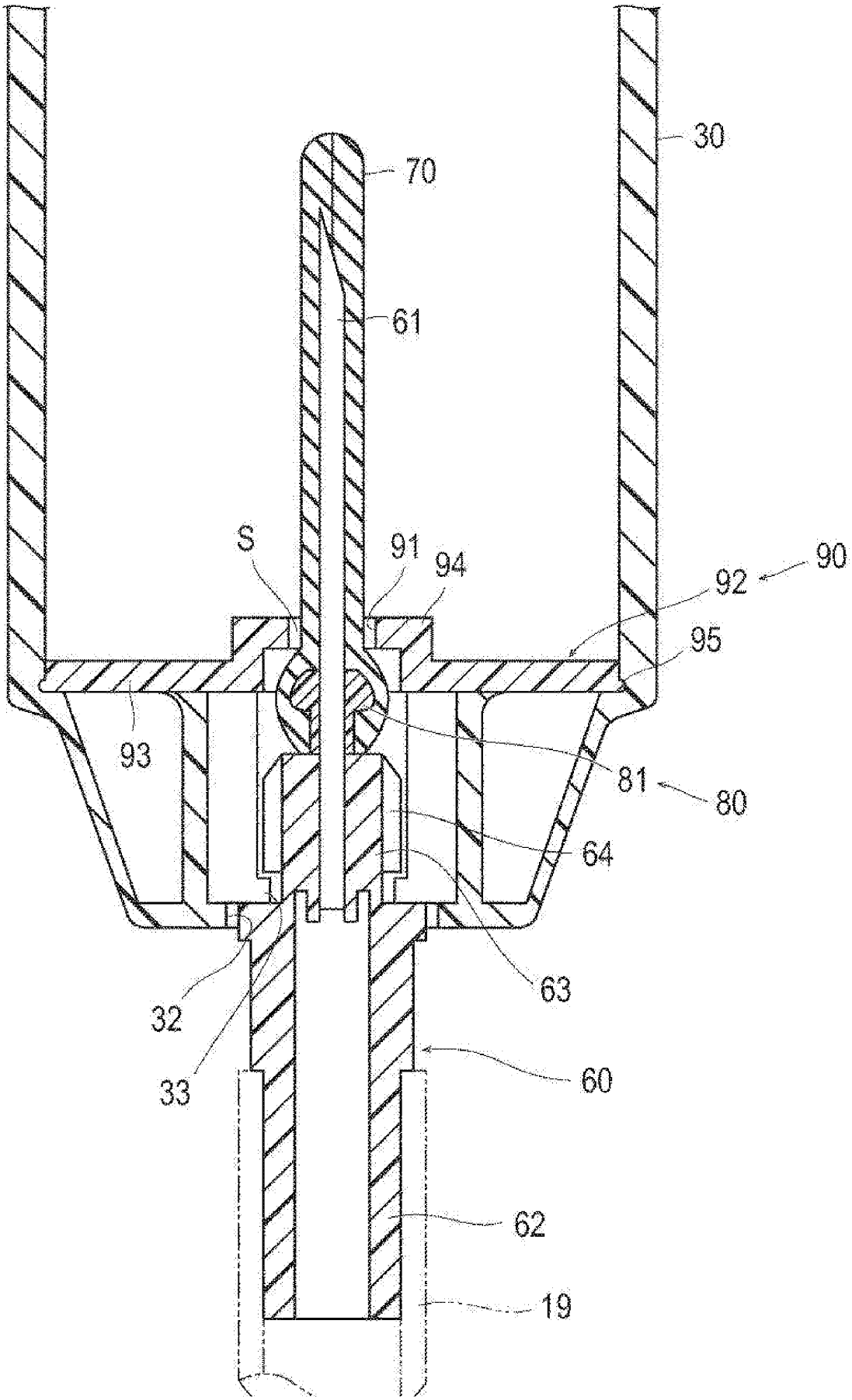


[Figure 2]

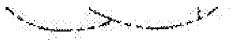

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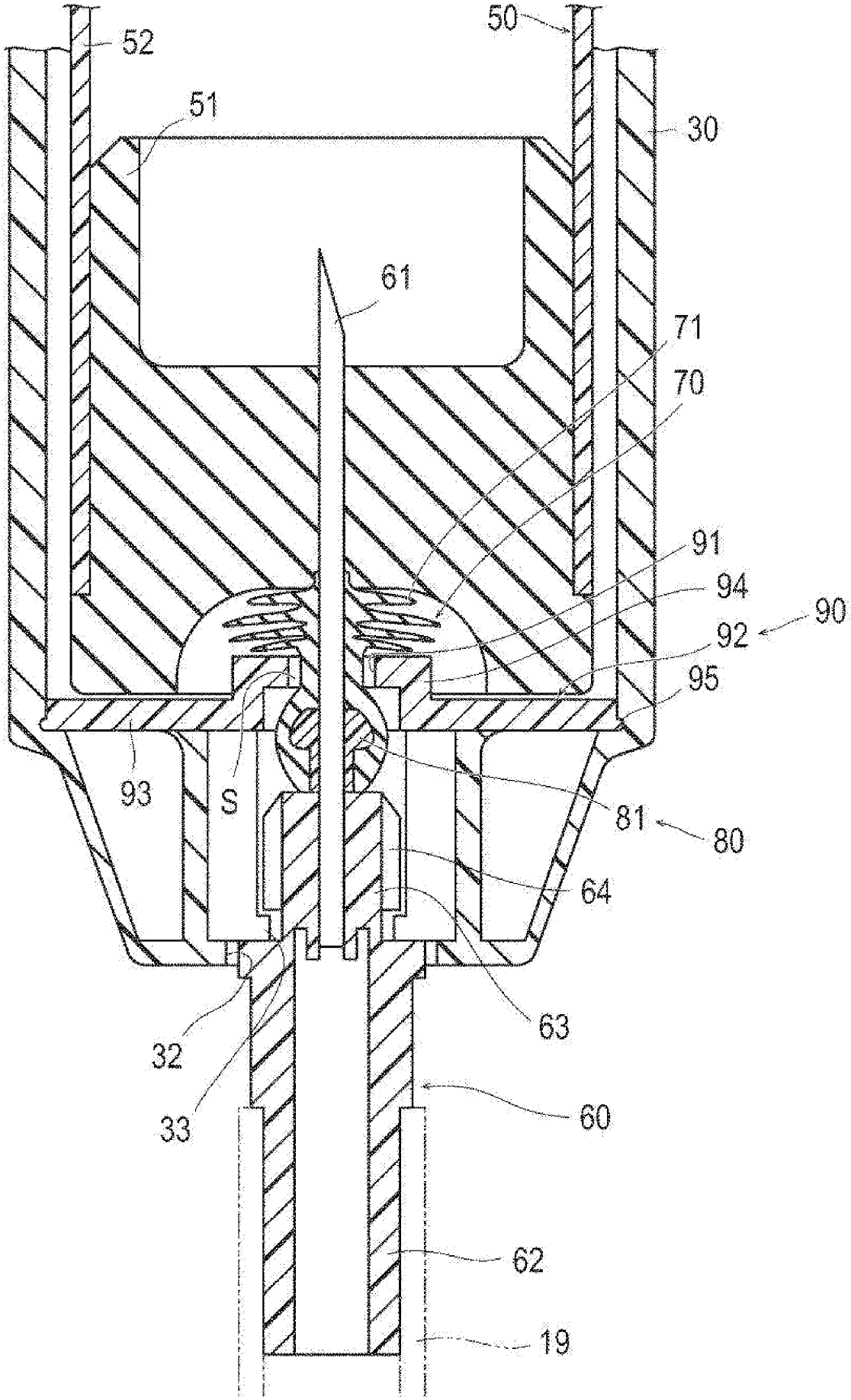
[Figure 3]




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[Figure 4]

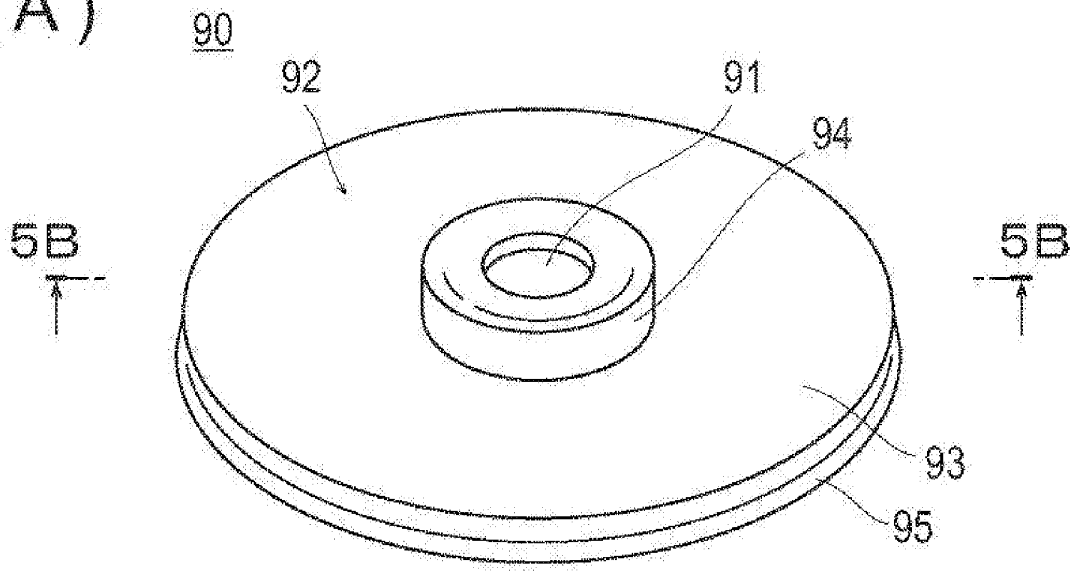



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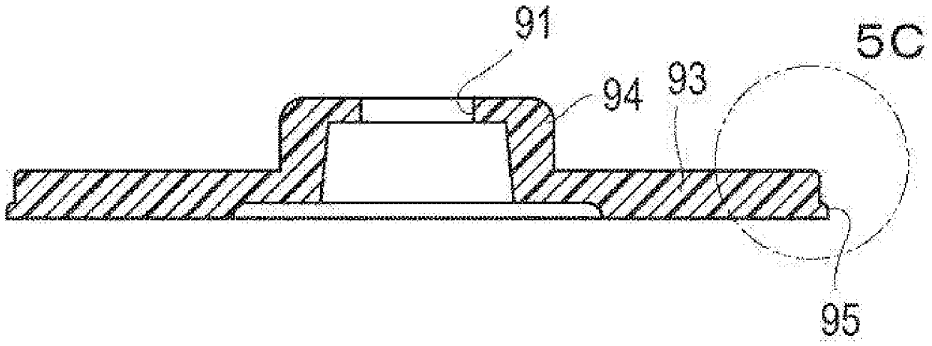
[Figure 5]



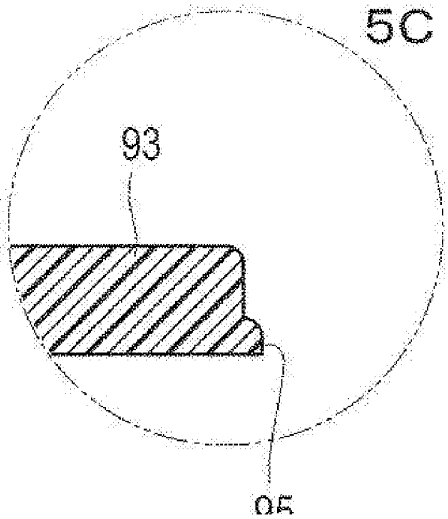
(A)



(B)

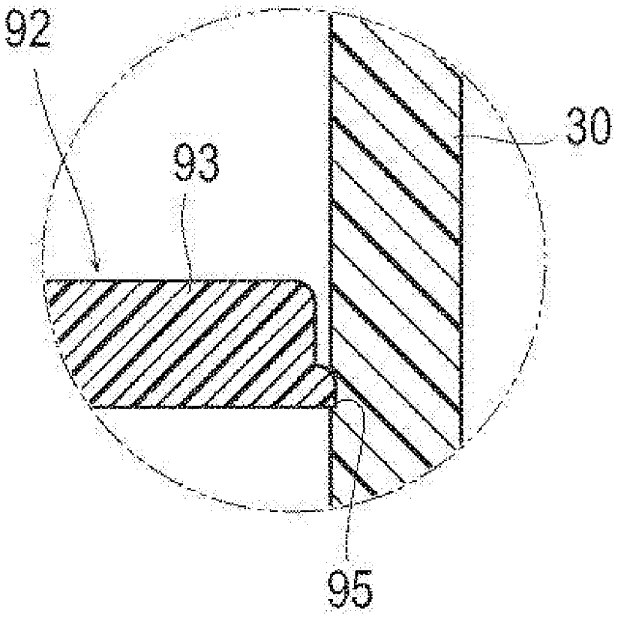


(C)

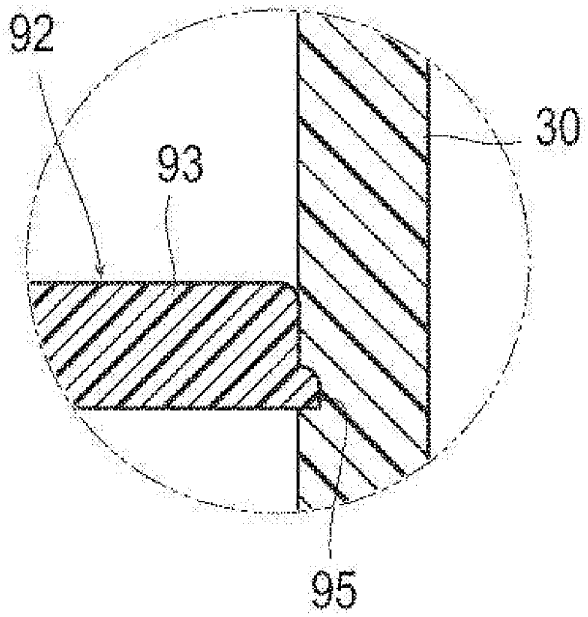


[Fig. 6]

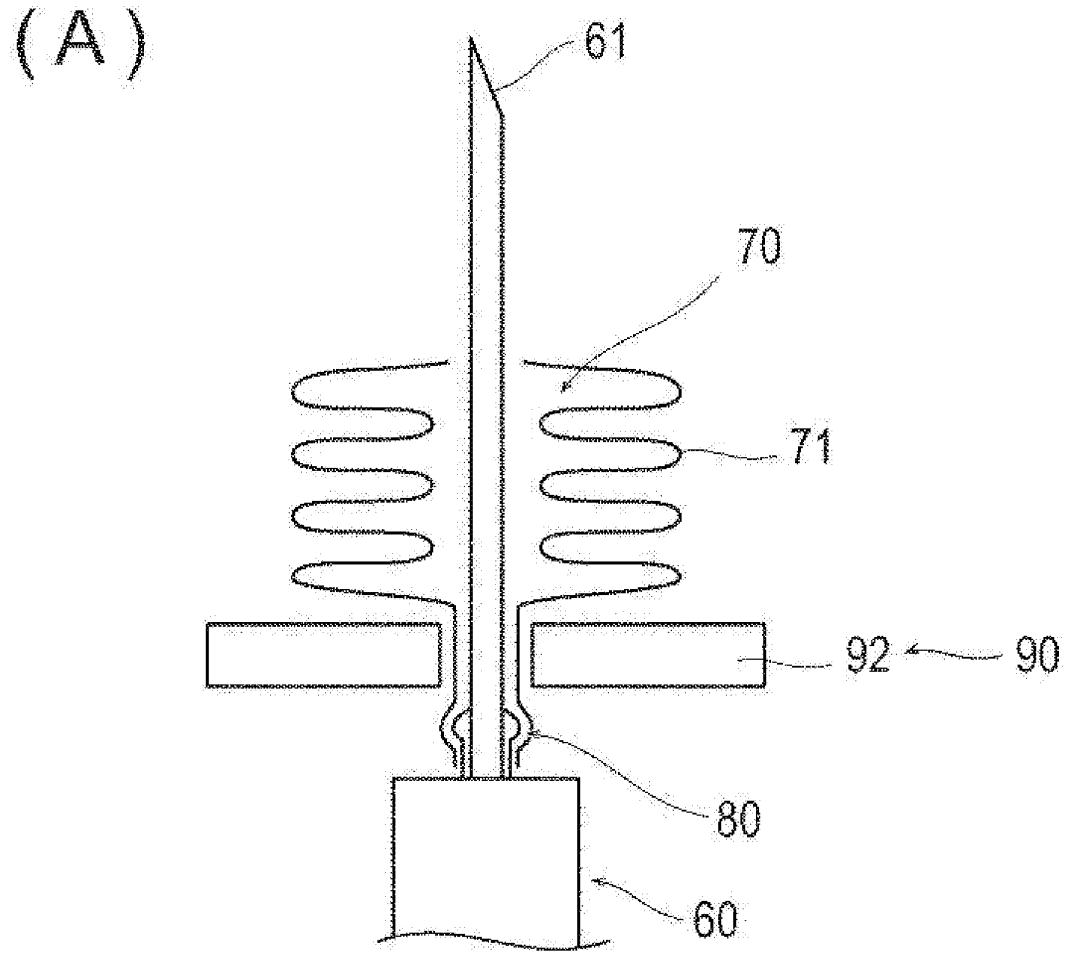
(A)

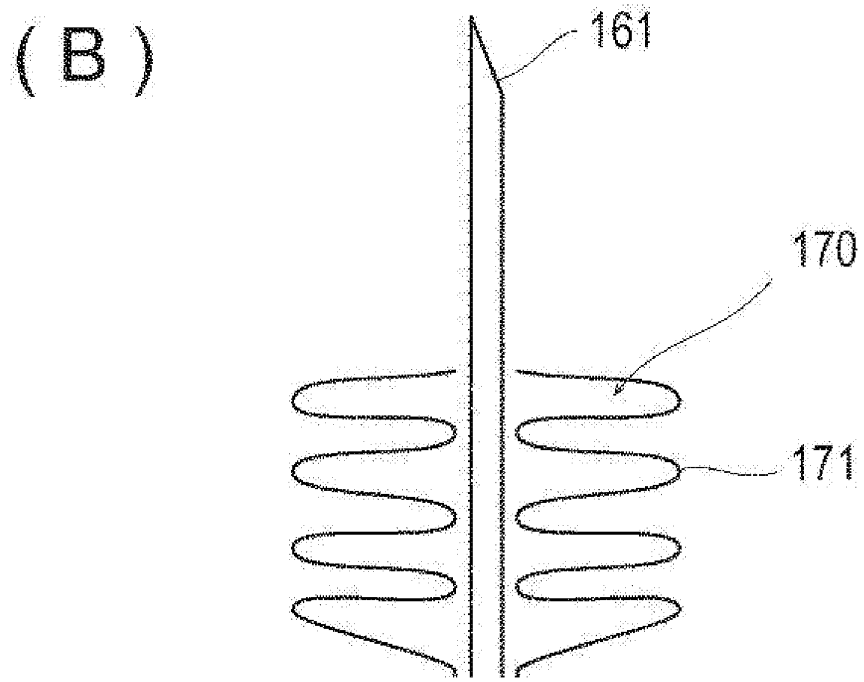


(B)

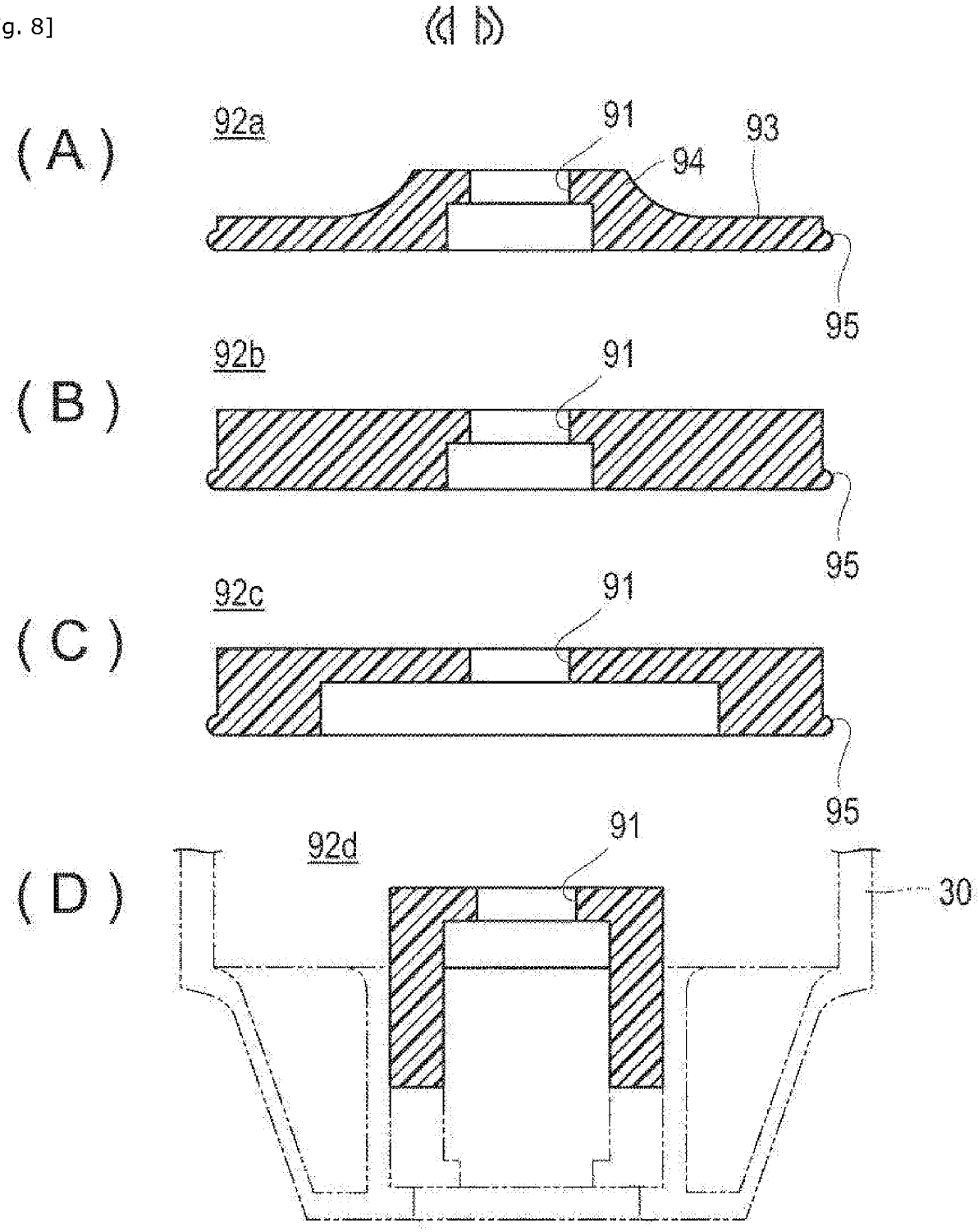


[Fig. 7]

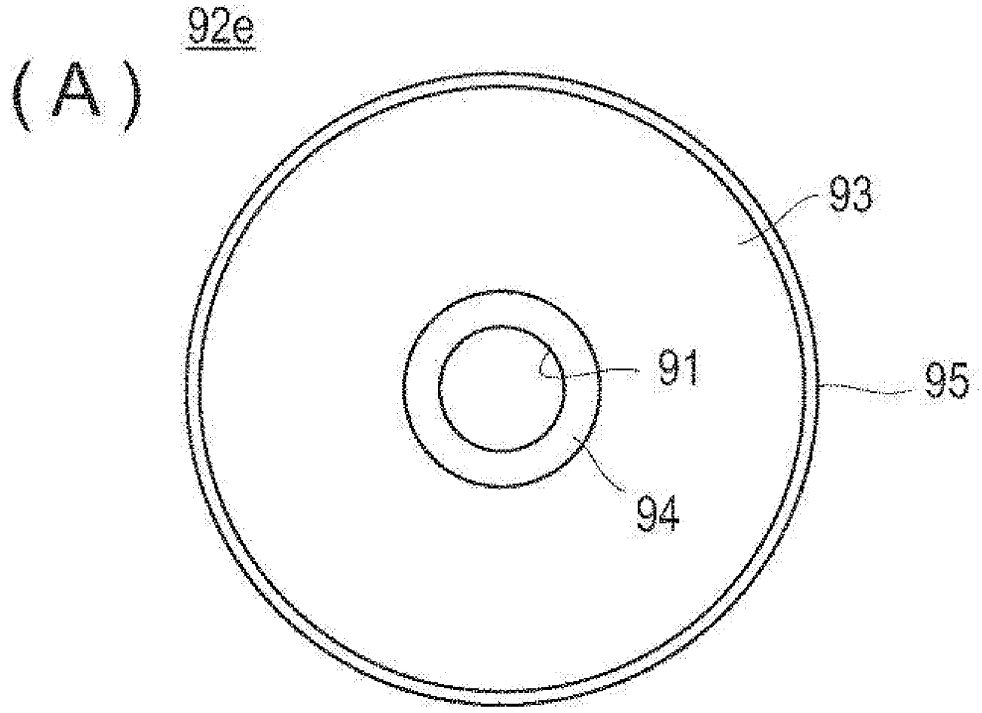

(A)
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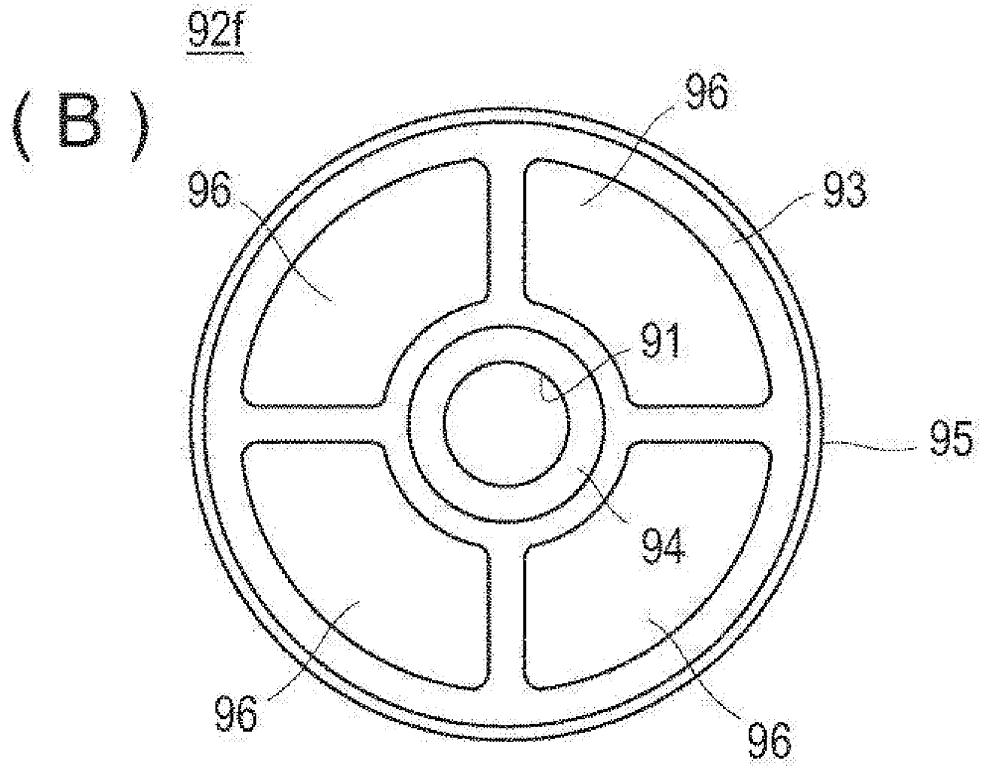

(B)
161
170
171

[Fig. 8]



[Fig. 9]

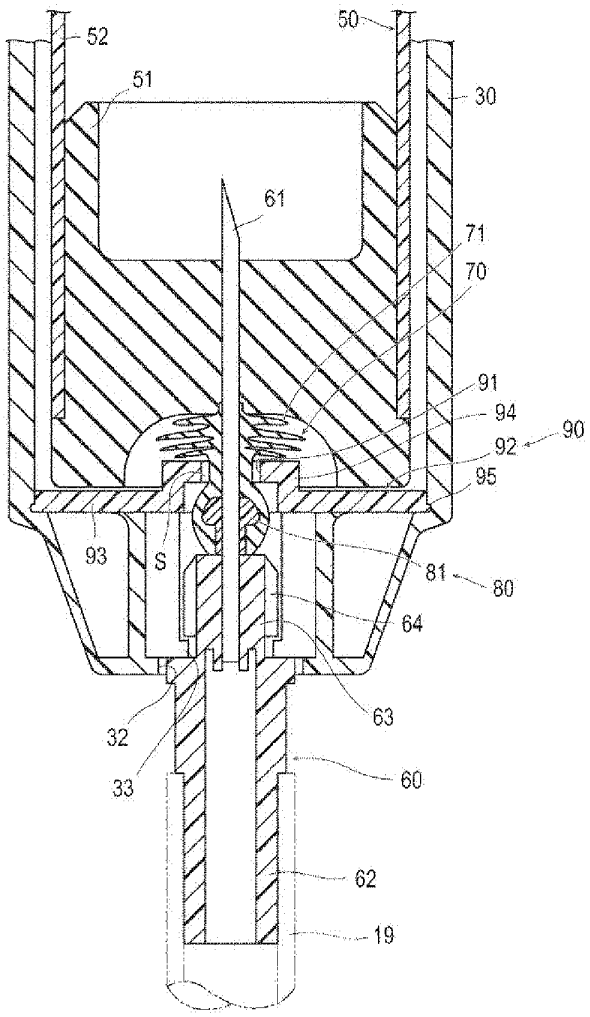

92e
(A)
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92f
(B)
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96

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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A61B 5/154	***(2006.01)***	A61B	5/14	300E	4C066
A61M 39/02	*(2006.01)*	A61M	5/14	459P	

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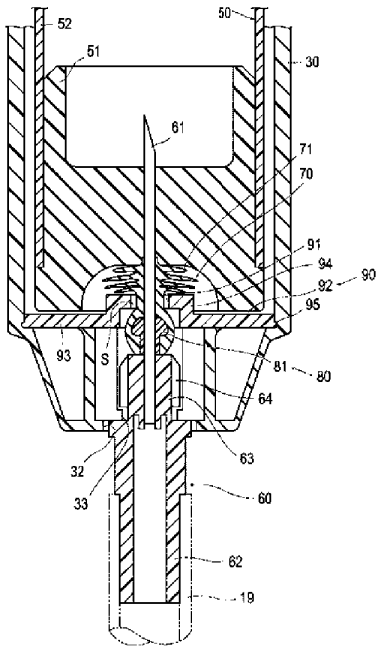
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最終頁に続く

(54)【発明の名称】サンプリングポート

(57)【要約】
【課題】採血管のゴム栓への中空針の挿通に伴ってゴムキャップが弾性的に縮められて皺が生じても、ゴムキャップを針組立体に保持するための保持力を維持でき、もって、血液の漏洩を十分に防止し得るサンプリングポートを提供する。
【解決手段】サンプリングポート２０は、ゴム栓５１を備える採血管５０を挿入するための開口部３１が形成された本体部３０と、採血管のゴム栓に挿通自在な中空針６１と、中空針の基端部を支持するハブ６４と、中空針に被せられた弾性を有するゴムキャップ７０と、ゴムキャップを保持する保持部８０と、を備え、本体部に取り付けられた針組立体６０と、ゴムキャップが被せられた中空針が貫通する貫通孔９１を備え、ゴム栓への中空針の挿通に伴ってゴムキャップが弾性的に縮められることによって生じる皺７１が保持部に達することを抑制する抑制部材９０としてのプレート９２と、を有している。
【選択図】図４



【特許請求の範囲】
【請求項１】
ゴム栓を備える採血管を挿入するための開口部が形成された本体部と、
前記採血管の前記ゴム栓に挿通自在な中空針と、前記中空針の基端部を支持するハブと、前記中空針に被せられた弾性を有するゴムキャップと、前記ゴムキャップを保持する保持部と、を備え、前記本体部に取り付けられた針組立体と、
前記ゴムキャップが被せられた前記中空針が貫通する貫通孔を備え、前記ゴム栓への前記中空針の挿通に伴って前記ゴムキャップが弾性的に縮められることによって生じる皺が前記保持部に達することを抑制する抑制部材と、を有することを特徴とするサンプリングポート。
【請求項２】
前記本体部は、前記針組立体に対して回動自在に取り付けられ、
前記抑制部材は、前記本体部に固定されており、前記貫通孔と前記ゴムキャップとの間に、前記本体部の回動を許容するクリアランスを有する、請求項１に記載のサンプリングポート。
【請求項３】
前記本体部は、円筒形状であり、
前記抑制部材は、円盤形状であり、前記本体部の前記開口部の側に向けて突出する凸部を備えている、請求項１または請求項２に記載のサンプリングポート。
【請求項４】
前記抑制部材の外周縁には、径方向外方に突出するリング状突起が設けられている、請求項１～３のいずれか１つに記載のサンプリングポート。
【請求項５】
前記本体部は、熱を印加したときに前記抑制部材を形成する樹脂材料よりも大きく収縮する樹脂材料から形成されており、滅菌のための熱を印加することによって、前記抑制部材を前記本体部に対して固定する、請求項１～４のいずれか１つに記載のサンプリングポート。
【発明の詳細な説明】
【技術分野】
【０００１】
本発明は、採血管を保持するサンプリングポートに関する。
【背景技術】
【０００２】
ゴム栓を備える採血管を用いて採血するときには、採血管を保持するサンプリングポートが使用される（特許文献１を参照）。サンプリングポートは、採血管を挿入するための開口部が形成された本体部を有し、この本体部には、採血管のゴム栓に挿通自在な中空針を備えた針組立体が取り付けられている。中空針には、血液の漏洩を防止するために、弾性を有するゴムキャップが被せられている。
【０００３】
サンプリングポートの本体部に採血管を挿入し、中空針をゴム栓に挿通させるのに伴って、ゴムキャップは、弾性的に縮められて皺を生じながら中空針を露出させる。露出した中空針は、採血管に採血する。採血後に採血管を引き抜くと、ゴムキャップは、縮んだ状態から、皺を伸ばすように弾性的に伸び、中空針に再び被せられる状態まで復元する。これによって、中空針からの血液の漏洩を防止する。ゴムキャップは、例えば根元部分を針組立体に密着させることによって、針組立体に保持されている。
【先行技術文献】
【特許文献】
【０００４】
【特許文献１】特開２００２－２９１７２４
【発明の概要】

【発明が解決しようとする課題】
【０００５】
しかしながら、採血管のゴム栓への中空針の挿通に伴ってゴムキャップが弾性的に縮められることによって生じる皺が、ゴムキャップの根元部に達することがある。このような場合には、ゴムキャップの根元部が膨らんでしまい、ゴムキャップを針組立体に保持するための保持力が弱くなる。このため、採血管のゴム栓の微小な挿通孔にゴムキャップの先端部が食い込んでいるような場合においては、採血管を引き抜くときにゴムキャップが一緒に引っ張られてしまい、ゴムキャップの位置などがずれてしまい、血液の漏洩の防止が不十分になる虞がある。
【０００６】
本発明は、上記従来技術に伴う課題を解決するためになされたものであり、採血管のゴム栓への中空針の挿通に伴ってゴムキャップが弾性的に縮められて皺が生じても、ゴムキャップを針組立体に保持するための保持力を維持でき、もって、血液の漏洩を十分に防止し得るサンプリングポートを提供することを目的とする。
【課題を解決するための手段】
【０００７】
上記目的を達成するための本発明のサンプリングポートは、ゴム栓を備える採血管を挿入するための開口部が形成された本体部と、
前記採血管の前記ゴム栓に挿通自在な中空針と、前記中空針の基端部を支持するハブと、前記中空針に被せられた弾性を有するゴムキャップと、前記ゴムキャップを保持する保持部と、を備え、前記本体部に取り付けられた針組立体と、
前記ゴムキャップが被せられた前記中空針が貫通する貫通孔を備え、前記ゴム栓への前記中空針の挿通に伴って前記ゴムキャップが弾性的に縮められることによって生じる皺が前記保持部に達することを抑制する抑制部材と、を有している。
【発明の効果】
【０００８】
抑制部材によって、採血管のゴム栓への中空針の挿通に伴ってゴムキャップが弾性的に縮められることによって生じる皺が保持部に達することが抑制されているので、保持部の部分でゴムキャップが膨らむことがなく、ゴムキャップを針組立体に保持するための保持力が弱くならない。このため、採血後に採血管を引き抜くときにゴムキャップが一緒に引っ張られてしまっても、ゴムキャップの位置などがずれることがなく、血液の漏洩を十分に防止することが可能となる。このように、採血管のゴム栓への中空針の挿通に伴ってゴムキャップが弾性的に縮められて皺が生じても、ゴムキャップを針組立体に保持するための保持力を維持でき、もって、血液の漏洩を十分に防止し得るサンプリングポートを提供できる。
【図面の簡単な説明】
【０００９】
【図１】サンプリングポートが組み込まれた血液バッグシステムを示す構成図である。
【図２】図１に示される初流血バッグと、サンプリングポートとを示す斜視図である。
【図３】採血管を挿入する前のサンプリングポートの要部を示す断面図である。
【図４】採血管を挿入した後のサンプリングポートの要部を示す断面図である。
【図５】図５（Ａ）は、抑制部材としてのプレートを示す斜視図、図５（Ｂ）は、図５（Ａ）の５Ｂ－５Ｂ線に沿う断面図、図５（Ｃ）は、図５（Ｂ）の５Ｃ部分を拡大して示す断面図である。
【図６】図６（Ａ）（Ｂ）は、抑制部材としてのプレートを本体部に対して固定する様子を示す断面図である。
【図７】図７（Ａ）は、本実施形態の作用の説明に供する概念図、図７（Ｂ）は、プレートを設けていない対比例の場合の作用の説明に供する概念図である。
【図８】図８（Ａ）～（Ｄ）は、プレートの改変例を示す断面図である。
【図９】図９（Ａ）（Ｂ）は、プレートのさらなる改変例を示す平面図である。

【発明を実施するための形態】
【００１０】
以下、添付した図面を参照しながら、本発明の実施形態を説明する。なお、図面の説明において同一の要素には同一の符号を付し、重複する説明を省略する。また、図面の寸法比率は、説明の都合上誇張されており、実際の比率とは異なる場合がある。
【００１１】
図１を参照して、図示する血液バッグシステム１０は、血液を採取する際に、採取された血液の初流（初流血）を除去し、その初流血を検査用血液として利用する採血器具である。皮膚上や皮下に存在する細菌が穿刺時の皮膚のかけらとともに侵入するため、初流血を除去している。
【００１２】
血液バッグシステム１０は、採血針１１と、採血針１１を介して採取された血液を収納する血液バッグ１２と、採血針１１と血液バッグ１２とを連通する採血チューブ１３と、採血チューブ１３の途中に配置した分岐コネクタ１４と、分岐コネクタ１４に接続した分岐チューブ１５を介して採血チューブ１３に連通する初流血バッグ１６と、初流血バッグ１６の端部に接続されたサンプリングポート２０と、を有している。分岐コネクタ１４には血液バッグ１２への連通を封止する封止部材１７が設けられている。初流血バッグ１６への初流血の採血が終わるまで、封止部材１７は血液バッグ１２への連通を封止している。分岐チューブ１５には、初流血バッグ１６への血流を遮断するクランプ部材１８が設けられている。初流血の採血が終わると、クランプ部材１８によって分岐チューブ１５をクランプし、初流血バッグ１６への血流が遮断される。その後、封止部材１７を開放し、血液バッグ１２への採血を開始する。
【００１３】
図２には、初流血バッグ１６に収納した初流血を検査用血液として回収するときの状態が示されている。初流血バッグ１６に接続された血液取出チューブ１９にサンプリングポート２０が接続されている。サンプリングポート２０には、開口部３１を開閉する蓋部材４０がヒンジ４１を介して回動自在に接続されている。初流血バッグ１６に収納した初流血を検査用血液として回収するときには、ゴム栓５１を備える減圧採血管５０（採血管に相当する）が開口部３１からサンプリングポート２０内に挿入される。
【００１４】
減圧採血管５０は、初流血バッグ１６内に貯留された初流血を採取するための器具である。この減圧採血管５０は、採血管本体５２と、この採血管本体５２の開口に嵌め込まれているゴム栓５１と、を有している。減圧採血管５０内は、真空または減圧状態になっている。減圧採血管５０は、サンプリングポート２０に接続されたとき、ゴム栓５１が中空針６１によって刺通される。これによって、減圧採血管５０内と血液取出チューブ１９とが連通し、当該血液取出チューブ１９からの初流血が減圧採血管５０に回収される。
【００１５】
図３および図４を参照して、実施形態に係るサンプリングポート２０は、概説すれば、ゴム栓５１を備える採血管５０を挿入するための開口部３１が形成された本体部３０と、採血管５０のゴム栓５１に挿通自在な中空針６１と、中空針６１の基端部を支持するハブ６４と、中空針６１に被せられた弾性を有するゴムキャップ７０と、ゴムキャップ７０を保持する保持部８０と、を備え、本体部３０に取り付けられた針組立体６０と、を有している。サンプリングポート２０はさらに、ゴム栓５１への中空針６１の挿通に伴ってゴムキャップ７０が弾性的に縮められることによって生じる皺７１（図４を参照）が保持部８０に達することを抑制する抑制部材９０を有している。抑制部材９０は、ゴムキャップ７０が被せられた中空針６１が貫通する貫通孔９１を備えている。なお、図３および図４において図中上側を各部材における「上部側」とし、図中下側を各部材における「下部側」とする。以下詳述する。
【００１６】
本体部３０は、円筒形状を有し、下部側は先細りの形状を有している。本体部３０には

、針組立体６０を差し込むための差込口３２と、差し込まれた針組立体６０の抜けを防止する係止部３３とが設けられている。

【００１７】

本体部３０は、針組立体６０に対して回動自在に取り付けられている。回動自在にすることによって、本体部３０を針組立体６０に対して回動させて、初流血バッグ１６に対する蓋部材４０の位置などを簡単に微調整することができる。

【００１８】

針組立体６０は、先端に鋭利な針先を有する中空針６１と、血液取出チューブ１９に接続される接続部６２と、中空針６１の基端部を保持するボス部６３と、を有している。ハブ６４は、ボス部６３の径方向外方へ突出するように設けている。針組立体６０は、本体部３０の差込口３２に差し込むときにハブ６４が係止部３３を乗り越えて、本体部３０に取り付けられる。ハブ６４の図中上端は、差し込むときに係止部３３を乗り越え易いように傾斜面に形成されている。

【００１９】

本体部３０を針組立体６０に対して回動自在に取り付けるために、針組立体６０の接続部６２と本体部３０の差込口３２との間のクリアランス、およびハブ６４の外周と本体部３０との間のクリアランスの寸法が調整されている。

【００２０】

ゴムキャップ７０は、本体部３０に採血管５０を挿入させ、中空針６１をゴム栓５１に挿通させるのに伴って、弾性的に縮められて皺７１を生じながら中空針６１を露出させる。採血管５０を引き抜くと、ゴムキャップ７０は、縮んだ状態から、皺７１を伸ばすように弾性的に伸び、中空針６１に再び被せられる状態まで復元する。これによって、中空針６１からの血液の漏洩を防止する。

【００２１】

保持部８０は、中空針６１が挿通されるとともに針組立体６０のボス部６３に取り付けられたロック部材８１から構成されている。ロック部材８１は、中空針６１の基端部側が先端側よりも小径部となったアンダーカット形状を有している。ロック部材８１におけるアンダーカット形状によって、ゴムキャップ７０を保持している。

【００２２】

図５（Ａ）（Ｂ）を参照して、抑制部材９０は、本体部３０内に嵌り込む円盤形状の平板部９３と、平板部９３の中央部分において上部側に向けて突出する凸部９４とを有するプレート９２から構成されている。凸部９４に、ゴムキャップ７０が取り付けられた中空針６１が貫通する貫通孔９１が形成されている。図５（Ｃ）に示すように、平板部９３の外周縁には、径方向外方に突出するリング状突起９５が、平板部９３と一体的に設けられている。

【００２３】

図３および図４を再び参照して、プレート９２は、保持部８０をなすロック部材８１よりも上部側の位置において、本体部３０内に取り付けられている。本体部３０に採血管５０を挿入し、中空針６１をゴム栓５１に挿通させるのに伴って、ゴムキャップ７０は、弾性的に縮められて皺７１を生じながら中空針６１を露出させている。プレート９２の貫通孔９１とゴムキャップ７０との間のクリアランスＳは比較的小さい。したがって、プレート９２によって、ゴムキャップ７０が弾性的に縮められることによって生じる皺７１が保持部８０に達することが抑制される（図４）。

【００２４】

前述のように本体部３０は、針組立体６０に対して回動自在に取り付けられている。そして、本体部３０に固定されたプレート９２の貫通孔９１とゴムキャップ７０との間に、本体部３０の回動を許容するクリアランスＳを設定してある。クリアランスＳを本体部３０の回動を阻害しない寸法に設定することによって、針組立体６０に対する本体部３０の回動位置や、初流血バッグ１６に対する蓋部材４０の位置などを簡単に微調整することが可能となる。

【００２５】
プレート９２に凸部９４を備えさせることによって、ゴムキャップ７０の長手方向のうち皺７１の影響を受けない範囲を大きくすることができる。その結果、ゴムキャップ７０を針組立体６０に保持するための保持力の低下をより一層抑えることができる。プレート９２の配置位置を図４に示される位置から上部側にずらしても、ゴムキャップ７０の長手方向のうち皺７１の影響を受けない範囲を大きくすることができる。但し、この場合には、採血管５０の位置も上部側にずれるため、本体部３０の長手方向の長さ寸法を若干大きくする必要が生じる場合がある。したがって、プレート９２に本体部３０の開口部３１の側に向けて突出する凸部９４を備えさせることによって、本体部３０の長手方向の長さを維持したまま、ゴムキャップ７０の長手方向のうち皺７１の影響を受けない範囲を大きくして、ゴムキャップ７０を針組立体６０に保持するための十分な保持力を確保することが可能となる。

【００２６】
本体部３０、蓋部材４０、中空針６１を除いた針組立体６０、保持部８０、およびプレート９２の構成材料としては、特に限定されないが、例えば、ポリカーボネート、ポリエチレン、ポリプロピレン、エチレン－酢酸ビニル共重合体等のポリオレフィン、変性ポリオレフィンが挙げられる。

【００２７】
中空針６１の構成材料としては、特に限定されないが、例えば、ステンレス鋼、アルミニウムまたはアルミニウム合金、チタンまたはチタン合金、Ｎｉ－Ｔｉ合金等の超弾性合金等の各種金属材料、ポリフェニレンサルファイド等の各種硬質樹脂材料等が挙げられる。

【００２８】
また、ゴムキャップ７０の構成材料としては、特に限定されないが、例えば、天然ゴム、イソプレンゴム、ブタジエンゴム、スチレン－ブタジエンゴム、ニトリルゴム、クロロプレンゴム、ブチルゴム、アクリルゴム、エチレン－プロピレンゴム、ヒドリンゴム、ウレタンゴム、シリコーンゴム、フッ素ゴムのような各種ゴム材料が挙げられる。

【００２９】
図６（Ａ）（Ｂ）に、プレート９２を本体部３０に対して固定する様子が示される。本実施形態においては、本体部３０は、熱を印加したときにプレート９２を形成する樹脂材料よりも大きく収縮する樹脂材料から形成してある。滅菌のための熱を印加することによって、プレート９２を本体部３０に対して固定することができるからである。

【００３０】
さらに詳しくは、図６（Ａ）に示すように、熱を印加する前では、本体部３０の内径が比較的大きく、プレート９２のリング状突起９５が若干寸法だけ本体部３０に食い込んでいる。プレート９２を比較的簡単に本体部３０内に挿入できることから、プレート９２の組み込み作業を行いやすい。

【００３１】
そして、図６（Ｂ）に示すように、滅菌のために行われる例えば高圧蒸気滅菌法（オートクレーブ）における熱を印加すると、本体部３０がプレート９２よりも大きく収縮する。これによって、プレート９２のリング状突起９５が本体部３０にさらに食い込み、プレート９２を本体部３０に対して簡単に固定することができる。

【００３２】
上記のような樹脂材料の組み合わせ例として、例えば、本体部３０の成形材料としてポリプロピレンを適用し、プレート９２の成形材料としてポリカーボネートを適用することができる。

【００３３】
本実施形態の作用を説明する。

【００３４】
採血するときには、サンプリングポート２０の本体部３０に採血管５０を挿入し、中空

針６１をゴム栓５１に挿通させる。ゴム栓５１に中空針６１が挿通するのに伴って、ゴムキャップ７０は、弾性的に縮められて皺７１を生じながら中空針６１を露出させる。

【００３５】

図７（Ｂ）を参照して、プレート９２を設けていない対比例の場合には、採血管５０のゴム栓５１への中空針１６１の挿通に伴ってゴムキャップ１７０が弾性的に縮められることによって生じる皺１７１が、ゴムキャップ１７０の根元部に達することがある。このような場合には、ゴムキャップ１７０の根元部が膨らんでしまい、ゴムキャップ１７０を針組立体１６０に保持するための保持力が弱くなる。このため、採血管５０を引き抜くときにゴムキャップ１７０が一緒に引っ張られてしまい、ゴムキャップ１７０の位置などがずれてしまい、血液の漏洩の防止が不十分になる虞がある。

【００３６】

これに対して、図４および図７（Ａ）を参照して、本実施形態にあっては、プレート９２を、保持部８０をなすロック部材８１よりも上部側の位置において、本体部３０内に取り付けている。このプレート９２によって、採血管５０のゴム栓５１への中空針６１の挿通に伴ってゴムキャップ７０が弾性的に縮められることによって生じる皺７１がロック部材８１に達することが抑制される。ロック部材８１の部分でゴムキャップ７０が膨らむことがないので、ゴムキャップ７０を針組立体６０に保持するための保持力が弱くならない。

【００３７】

露出した中空針６１は、ゴム栓５１に挿通されて、採血管５０に採血する。採血後に採血管５０を引き抜くと、ゴムキャップ７０は、縮んだ状態から、皺７１を伸ばすように弾性的に伸び、中空針６１に再び被せられる状態まで復元する。これによって、中空針６１からの血液の漏洩を防止する。ゴムキャップ７０は、ロック部材８１の部分で針組立体６０に保持されている。

【００３８】

採血管５０のゴム栓５１の微小な挿通孔にゴムキャップ７０の先端部が食い込んだ状態で採血管５０を引き抜くと、ゴムキャップ７０が一緒に引っ張られる。しかし、ロック部材８１の部分は皺７１の影響を受けていないので、保持力は初期に設定したままである。このため、ゴムキャップ７０は、中空針６１から抜けずに、採血管５０のゴム栓５１への食い込みが解除される。これによって、ゴムキャップ７０の位置などがずれることがなく、血液の漏洩を十分に防止することが可能となる。

【００３９】

このように、採血管５０のゴム栓５１への中空針６１の挿通に伴ってゴムキャップ７０が弾性的に縮められて皺７１が生じても、ゴムキャップ７０を針組立体６０に保持するための保持力を維持でき、もって、血液の漏洩を十分に防止し得るサンプリングポート２０を提供できる。

【００４０】

また、本体部３０は針組立体６０に対して回動自在に取り付けられ、プレート９２は本体部３０に固定されており、貫通孔９１とゴムキャップ７０との間に本体部３０の回動を許容するクリアランスＳを有するため、針組立体６０に対する本体部３０の回動位置などを簡単に微調整することが可能となる。

【００４１】

また、プレート９２は、本体部３０の開口部３１の側に向けて突出する凸部９４を備えているため、本体部３０の長手方向の長さを維持したまま、ゴムキャップ７０の長手方向のうち皺７１の影響を受けない範囲を大きくして、ゴムキャップ７０を針組立体６０に保持するための十分な保持力を確保することが可能となる。

【００４２】

また、プレート９２の外周縁に径方向外方に突出するリング状突起９５を設けているため、リング状突起９５を若干寸法だけ本体部３０に食い込ませるようにしてプレート９２を本体部３０内に挿入させることができ、簡単にプレート９２の組み込み作業を行うこと

が可能となる。

【００４３】

また、本体部３０は、熱を印加したときにプレート９２を形成する樹脂材料よりも大きく収縮する樹脂材料から形成されており、滅菌のための熱を印加することによって、プレート９２を本体部３０に対して固定するため、熱を印加する前ではプレート９２を比較的簡単に本体部３０内に挿入でき、プレート９２の組み込み作業を行いやすい。一方、滅菌のための熱を印加すると、本体部３０がプレート９２よりも大きく収縮する。これによって、プレート９２を本体部３０に対して簡単に固定することができる。

【００４４】

（プレートの改変例）

プレートは、ゴムキャップ７０が取り付けられた中空針６１が貫通する貫通孔９１を備え、採血管５０のゴム栓５１への中空針６１の挿通に伴ってゴムキャップ７０が弾性的に縮められることによって生じる皺７１が保持部８０に達することを抑制する限りにおいて適宜の形状に改変することができる。

【００４５】

例えば、図８を参照して、凸部９４を平板部９３から滑らかに突出させたプレート９２ａ（図８（Ａ））、全体の厚みを厚くし上面を平坦面としたプレート９２ｂ、９２ｃ（図８（Ｂ）（Ｃ））、本体部３０の底面全体を覆わずに保持部８０に被せるようなキャップ形状を有するプレート９２ｄ（図８（Ｄ））などを例示することができる。

【００４６】

また、図９を参照して、平板部９３に貫通部を形成しないタイプのプレート９２ｅ（図９（Ａ））、平板部９３に貫通部９６を形成したタイプのプレート９２ｆ（図９（Ｂ））とすることもできる。

【００４７】

（その他の改変例）

ゴムキャップ７０を保持する保持部８０として、アンダーカット形状を有するロック部材８１を例示したが、保持部８０はこの場合に限定されるものではない。保持部８０は、針組立体６０に設けられゴムキャップ７０の抜けを防止して保持する機能を有している限りにおいて適宜改変することができる。例えば、保持部８０は、接着剤によってゴムキャップ７０を中空針６１に接着させて保持する形態、超音波融着によってゴムキャップ７０を中空針６１に融着させて保持する形態、クリップなどを用いた嵌め込みによってゴムキャップ７０を中空針６１に保持する形態などを例示することができる。これらの保持部８０を単独で用いてもよいし、２種以上を組み合わせた保持部８０であってもよい。

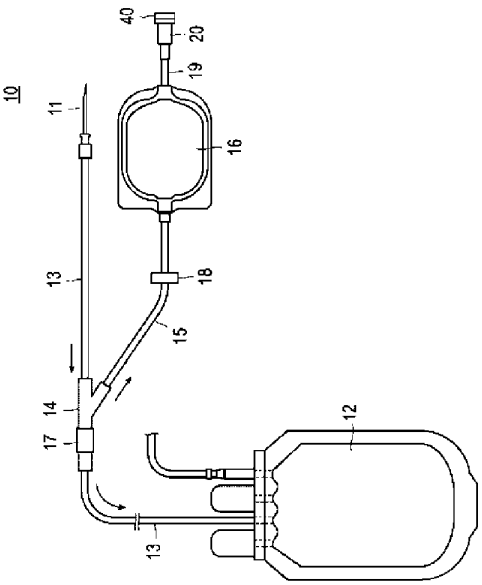
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【００４８】

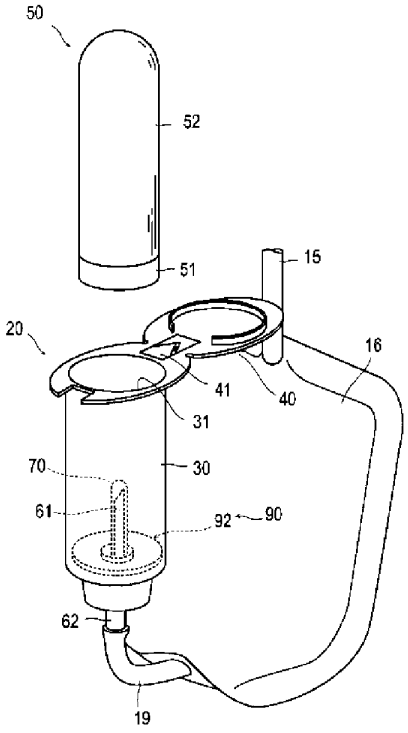
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３０　本体部、
３１　開口部、
５０　減圧採血管（採血管）、
５１　ゴム栓、
６０　針組立体、
６１　中空針、
６４　ハブ、
７０　ゴムキャップ、
７１　皺、
８０　保持部、
８１　ロック部材、
９０　抑制部材、
９１　貫通孔、
９２　プレート（抑制部材）、

９３　　平板部、
９４　　凸部、
９５　　リング状突起、
Ｓ　　クリアランス。

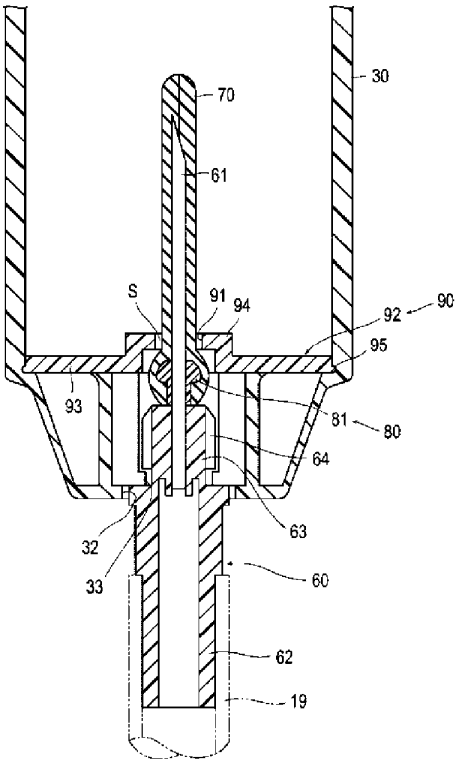
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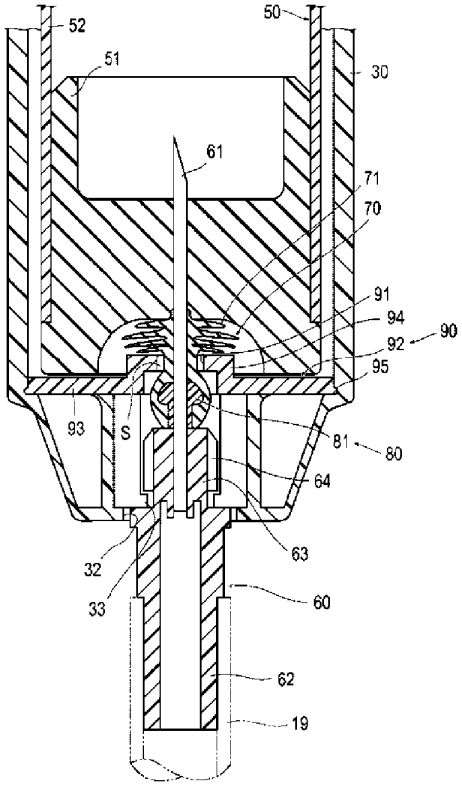
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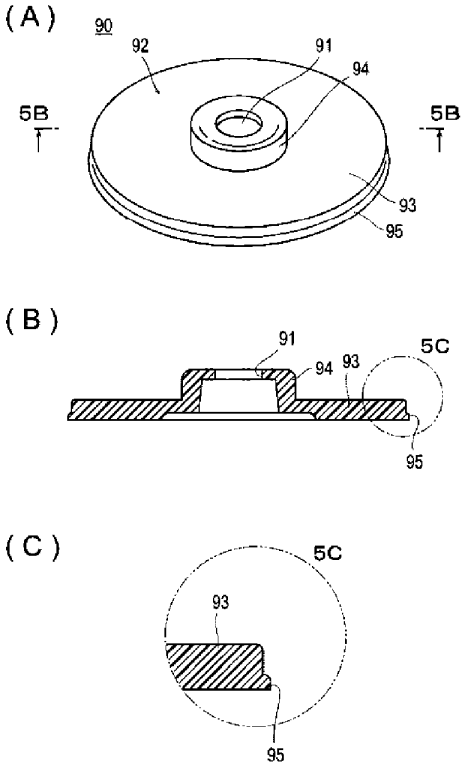
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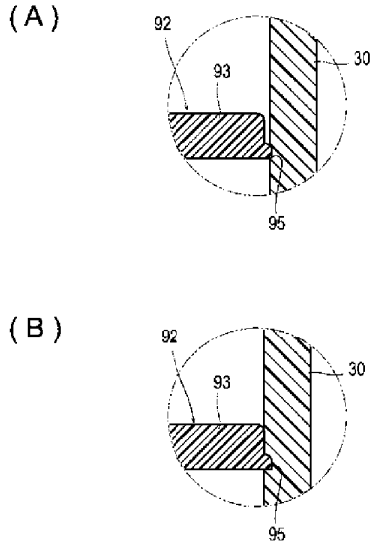
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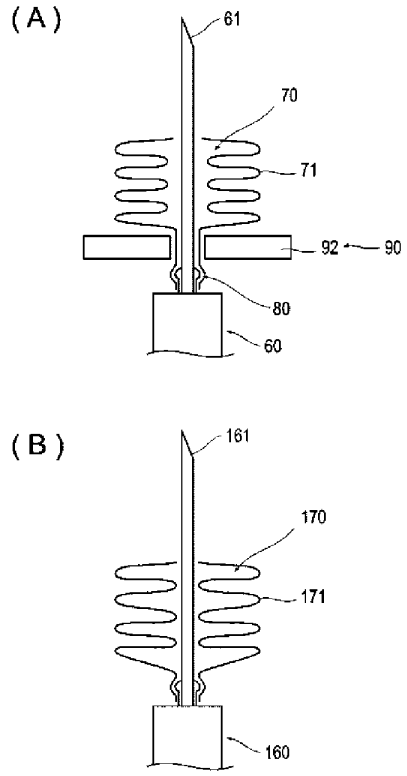
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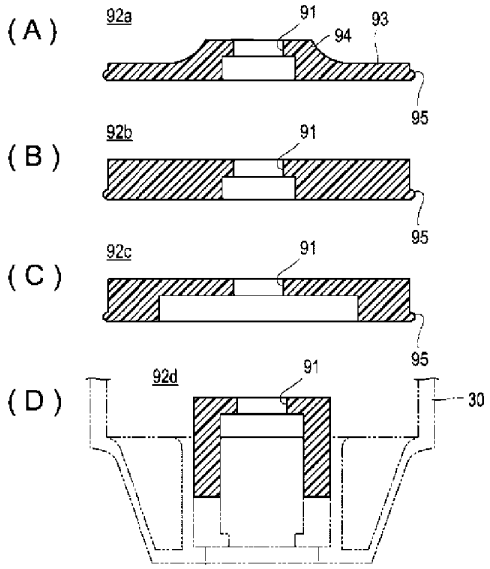
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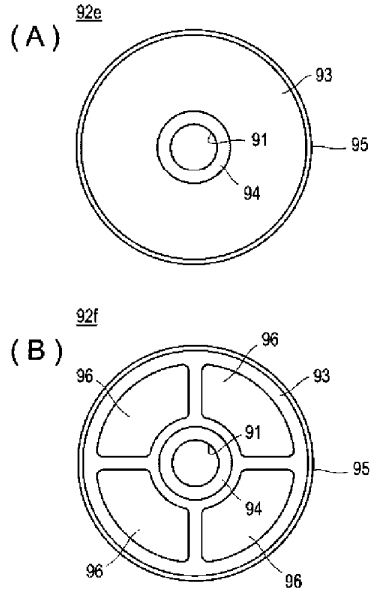
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Ｆターム(参考) 4C038 TA01 TA10 UA10 UB07 UF03 UF11 UF14
4C066 AA07 BB10 FF05 JJ08

The Clinical Significance of Positive Blood Cultures in the 1990s: A Prospective Comprehensive Evaluation of the Microbiology, Epidemiology, and Outcome of Bacteremia and Fungemia in Adults

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To assess changes since the mid-1970s, we reviewed 843 episodes of positive blood cultures in 707 patients with septicemia. The five most common pathogens were *Staphylococcus aureus, Escherichia coli,* coagulase-negative staphylococci (CNS), *Klebsiella pneumoniae,* and *Enterococcus* species. Although CNS were isolated most often, only 12.4% were clinically significant. Half of all episodes were nosocomial, and a quarter had no recognized source. Leading identifiable sources included intravenous catheters, the respiratory and genitourinary tracts, and intraabdominal foci. Septicemia-associated mortality was 17.5%. Patients who received appropriate antimicrobial therapy throughout the course of infection had the lowest mortality (13.3%). Multivariate analysis showed that age (relative risk [RR], 1.80), microorganism (RR, 2.27), source of infection (RR, 2.86), predisposing factors (RR, 1.98), blood pressure (RR, 2.29), body temperature (RR, 2.04), and therapy (RR, 2.72) independently influenced outcome. Bloodstream infections in the 1990s are notable for the increased importance of CNS as both contaminants and pathogens, the proportionate increase in fungi and decrease in anaerobes as pathogens, the emergence of *Mycobacterium avium* complex as an important cause of bacteremia in patients with advanced human immunodeficiency virus infection, and the reduction in mortality associated with infection.

The presence of living microorganisms in blood has substantial clinical importance. From the diagnostic standpoint, a positive blood culture yielding a clinically important microorganism represents either failure of host defenses to contain an infection at its primary focus or failure of the physician to effectively eradicate, drain, excise, or otherwise remove that focus of infection. The presence of bacteremia or fungemia also is an indicator of disseminated infection and, as such, generally indicates a poorer prognosis than that associated with localized disease. A positive blood culture, however, is not always clinically significant, since contamination may occur or the positive result might represent the transient and self-limited presence of microorganisms in the blood [1].

Our current understanding of the clinical significance of positive blood cultures has been enhanced by studies reported over several decades [2–21]. In recent years there have been many changes in medical practice, influenced in part by technologic advances and in part by the increased incidence of diseases not recognized previously. Just a few examples include the more frequent use of invasive or prosthetic devices; the increase in solid-organ and bone marrow transplantation as well as improvements in posttransplantation medical management; the introduction of HIV infection and AIDS as a scourge on late 20th century society; and therapeutic advances in the form of improved imaging techniques, less invasive methods of draining pus from closed spaces, and availability of broader spectrum antiinfective therapy.

We therefore undertook a comprehensive analysis of positive blood cultures in the 1990s. As a template for this project, we used an earlier review of bacteremia and fungemia [10, 11] authored by two of the current investigators (M.P.W. and L.B.R.). Although the earlier work has been widely recognized, the aforementioned changes in medicine and its practice argued for the need to reevaluate the clinical and prognostic importance of positive blood cultures. The primary goal of this study, therefore, was to determine the current microbiology, epidemiology, and prognostic importance of positive blood cultures, with special reference to similarities with and differences from the earlier reports from our group [10, 11, 22, 23].

Materials and Methods

For a 12-month period, February 1992 through January 1993, all inpatients ≥18 years of age with culture-positive blood

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were evaluated at Duke University Medical Center (DUMC), in Durham, NC; Robert Wood Johnson University Hospital (RWJUH), in New Brunswick, NJ; and the Salt Lake City Veterans Administration Medical Center (SLCVAMC), in Salt Lake City. Each patient was observed prospectively from the time the blood culture became positive, unless the patient had been discharged or had died before review of the hospital records by one of the investigators, in which case the review of the medical record was retrospective. Charts were evaluated according to the method of Feinstein et al. [24, 25], such that if the presence or absence of a particular finding was not clearly indicated, that case was excluded from analysis for that finding.

During the study period, 20 mL or more of blood was obtained for each culture and inoculated into media for processing on the BACTEC NR660 (Becton Dickinson Diagnostic Instrument Systems, Sparks, MD) or BacT/Alert (Organon Teknika, Durham, NC) blood culture system or both systems at all three centers. Blood was obtained at the bedside by house officers, medical students, or other trained health care personnel (nurses, phlebotomists, etc.) using 70% isopropyl alcohol and then 10% povidone-iodine. Although most of the blood culture specimens were obtained by peripheral venipuncture, it was not possible to determine specifically which ones were obtained in this manner and which were obtained through access devices.

Bottles were transported to the laboratory and incubated until flagged as positive or for 7 days in either BACTEC nonradiometric instruments (NR6 and NR7 bottles) or BacT/Alert continuous-monitoring instruments (BacT/Alert aerobic and anaerobic bottles). Broth from positive bottles was gram-stained and subcultured with use of standard techniques [26]. Susceptibility testing of isolates was done according to guidelines established by the National Committee on Clinical Laboratory Standards [27, 28].

All information obtained from patients' records was recorded on data worksheets and then transferred to a database software program for analysis.

Definitions

Definitions for this study for the most part were identical to those of Weinstein et al. [10, 11]. Only a few will be detailed here. New or modified definitions also will be detailed.

True septicemia vs. contamination. Each positive blood culture was assessed critically by one of the investigators, each an infectious disease physician. All isolates were categorized as true-positives, contaminants, or of unknown clinical significance. The categorical decision was made after the following factors were taken into account: the patient's clinical history, physical findings, body temperature at the time of the blood culture, leukocyte count and differential cell counts, number of positive blood cultures out of the total number performed, results of cultures of specimens from other sites, imaging results, histopathologic findings, and clinical course and response to therapy. If the clinical significance of the positive culture was not clear on the basis of the available information, the isolate was categorized as being of unknown significance.

Episode. An episode of bacteremia, fungemia, or mycobacteremia was defined by the first positive blood culture in a series or by any new positive blood culture result that occurred >48 hours after the previous positive result, unless it was clear to the investigator that the new positive culture was part of the same episode. For example, a positive blood culture for *Staphylococcus aureus* on the fifth day of antibiotic therapy for *S. aureus* endocarditis was considered part of the original bacteremic episode.

Community- vs. hospital-acquired septicemia. Each episode was classified as either community- or hospital-acquired septicemia, according to guidelines of the Centers for Disease Control and Prevention [29]. Septicemia in nursing home patients with positive blood cultures was always classified as hospital-acquired, whereas that in patients transferred from other outside facilities was classified according to their total period of hospitalization at both institutions.

Antimicrobial Therapy

Data on antimicrobial therapy were obtained at four chronologic points for each episode. These points were as follows: (1) at the time the first positive blood culture specimen was obtained, (2) after the blood culture was performed but before positive culture results were reported (i.e., empirical therapy), (3) after the blood culture was reported to be positive and gram-stained smear results were made known to the primary physician(s) but before organism identification and susceptibility test results were available, and (4) after organism identification and susceptibility test results were reported to the physicians.

Therapy was assessed critically at each time point on the basis of the clinical information available (time points 1–3) or the identification of the isolate and susceptibility test results (time point 4).

Treatment was judged to be the first choice if it was in accordance with the recommendations of a standard reference for antimicrobial therapy [30] and an alternative choice if the etiologic microorganism(s) was (were) susceptible to the agent administered but that agent was not considered the first choice. For purposes of judging the adequacy of therapy, both first-choice and alternative-choice agents were considered appropriate. Therapy was designated as the wrong choice if the causative microorganism was resistant to the antibiotic given. Superfluous therapy was defined as either the administration of unnecessary antibiotics in addition to a first- or alternative-choice agent or the administration of antibiotics for contaminant isolates. Ineffective or superfluous agents given for infections elsewhere in the body were recorded separately.

If a patient died before susceptibility results became available, that fact was recorded. When no therapy was given after the report of a positive blood culture to the physician, one of

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three assessments was made: (1) appropriate, if the isolate was a contaminant; (2) appropriate, if the episode was judged to represent true but transient bacteremia or fungemia that resolved spontaneously without adversely affecting the patient; or (3) inappropriate, if the culture represented true sepsis and the patient's status deteriorated because of the infection.

Outcome

The outcome of each episode was categorized as follows. The patient was (1) discharged alive, (2) alive but still hospitalized 30 days or longer after the onset of bacteremia or fungemia, (3) dead from causes attributable to the septicemic episode, or (4) dead from causes unrelated to septicemia. For the purposes of this study, mortality is termed associated or nonassociated in the subsequent text and tables.

Statistical Methods

For univariate analyses, statistical significance was calculated with the χ^2 test as described by O'Brien and Shampo [31]. The multivariate analysis and the resulting significance calculations were based on the logistic regression model [32], as implemented by the function "glm" in the statistical package S+ [33].

Results

During the study period, 1,585 blood culture–positive episodes occurred in 1,267 patients and yielded 1,844 microorganisms. Nine hundred forty-four microorganisms were isolated from 707 patients who had 843 episodes of true bacteremia or fungemia. There were 658 contaminant episodes and 84 episodes of unknown clinical significance.

Microbiological Features

The microorganisms isolated from positive blood cultures and the frequency with which they caused true bacteremia or fungemia are shown in table 1. The most common isolates from blood were coagulase-negative staphylococci. *S. aureus* was the microorganism most frequently causing true bacteremia; 87.2% of isolates were judged clinically significant. In contrast, only 12.4% of the coagulase-negative staphylococci were clinically significant, but they ranked as the third most frequent cause of bacteremia by virtue of their high prevalence.

Given the frequency with which coagulase-negative staphylococci were isolated from blood and the difficulty in determining their clinical significance, we analyzed *Staphylococcus epidermidis* isolates on the basis of the number of culture sets positive vs. the number of sets performed for each episode. The results are shown in table 2. When only a single culture set yielded *S. epidermidis,* the culture result almost always was judged to be of indeterminate significance or to represent contamination. When all of two or three culture sets yielded *S. epidermidis,* the isolates usually were judged clinically significant, but a substantial minority were of unknown (i.e., indeterminate) significance.

Whereas pneumococci always represented real infection, enterococcal isolates did so only 70% of the time, and viridans streptococci more often were contaminants (49%) than clinically significant isolates (38%) (table 1). Among the gram-negative aerobic and facultative bacteria, *Escherichia coli* was the most common isolate, and this microorganism was second only to *S. aureus* as a cause of septicemia. Overall, the Enterobacteriaceae and *Pseudomonas aeruginosa* represented true bacteremia >95% of the time when isolated.

Anaerobic bacteria were not common blood pathogens, accounting for only 3.9% of clinically important isolates. The isolation of a member of the *Bacteroides fragilis* group, however, almost always indicated true bacteremia (89%). *Clostridium perfringens* usually represented contamination when isolated from the blood, whereas the isolation of other *Clostridium* species usually represented true bacteremia.

Yeasts were relatively common isolates from blood cultures and almost always represented true fungemia when detected (91.7%). These organisms were present as clinically important pathogens almost twice as often as anaerobic bacteria, and *Candida albicans* ranked among the top 10 microorganisms causing septicemia. All mycobacteria and all but one *Cryptococcus neoformans* isolate were isolated from HIV-infected patients.

Of the 843 episodes of bacteremia and fungemia, 764 (90.6%) were unimicrobial and 79 (9.4%) were polymicrobial. Two microorganisms were isolated in 57 (72.2%) of the polymicrobial episodes, and ⩾3 microorganisms were isolated in 22 episodes (27.8%).

Epidemiological Features

Age and sex. Patients ranged in age from 17 to 103 years (mean, 56.2 years). Patients with HIV infection were younger (mean age, 36.9 years). Four hundred ninety of the episodes (58.1%) occurred in men. Ninety-nine percent of the episodes at the SLCVAMC, vs. 54% at both DUMC and RWJUH, were in men.

Community- vs. hospital-acquired infection. Of the 843 episodes, 404 (47.9%) were of community-acquired infection and 439 (52.1%) were of nosocomial infection. The microorganisms isolated in these episodes, categorized according to place of acquisition, are shown in table 3. Microorganisms more often associated with nosocomial acquisition were coagulase-negative staphylococci, enterococci, Enterobacteriaceae other than *E. coli, P. aeruginosa, Clostridium* species, *Bacteroides* species, and yeasts other than *C. neoformans.* A somewhat surprising finding was that nearly 40% of *P. aeruginosa* bacteremias were community-acquired.

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Table 1. Microorganisms isolated from blood of patients at Duke University Medical Center, Robert Wood Johnson University Hospital, and the Salt Lake City VA Medical Center, February 1992 through January 1993.

Microorganism (no. of isolates)	No. (%) of isolates per indicated category		
	True pathogen	Contaminant	Unknown
Aerobic and facultative bacteria			
Gram-positive			
Staphylococcus aureus (204)	178 (87.2)	13 (6.4)	13 (6.4)
Coagulase-negative staphylococci (703)	87 (12.4)	575 (81.9)	41 (5.8)
Enterococcus species (93)	65 (69.9)	15 (16.1)	13 (14.0)
Viridans streptococci (71)	27 (38.0)	35 (49.3)	9 (12.7)
Streptococcus pneumoniae (34)	34 (100)	0	0
Group A streptococci (3)	3 (100)	0	0
Group B streptococci (15)	10 (66.7)	3 (20.0)	2 (13.3)
Other streptococci (13)	8 (61.5)	3 (23.1)	2 (15.4)
Bacillus species (12)	1 (8.3)	11 (91.7)	0
Corynebacterium species (53)	1 (1.9)	51 (96.2)	1 (1.9)
Listeria monocytogenes (2)	1 (50.0)	0	1 (50.0)
Lactobacillus species (15)	6 (54.5)	2 (18.2)	3 (27.3)
Other gram-positive bacteria (15)	2 (13.3)	12 (80)	1 (6.7)
Gram-negative			
Escherichia coli (143)	142 (99.3)	0	1 (0.7)
Klebsiella pneumoniae (65)	65 (100)	0	0
Enterobacter cloacae (25)	25 (100)	0	0
Serratia marcescens (22)	22 (100)	0	0
Proteus mirabilis (16)	16 (100)	0	0
Other Enterobacteriaceae (45)	41 (91)	1 (2.2)	3 (6.7)
Pseudomonas aeruginosa (55)	53 (96.4)	1 (1.8)	1 (1.8)
Pseudomonas species (8)	6 (75)	0	2 (25)
Stenotrophomonas maltophilia (7)	5 (71.4)	0	2 (28.6)
Acinetobacter baumanii (16)	13 (81.2)	1 (6.2)	2 (12.5)
Haemophilus influenzae (3)	3 (100)	0	0
Other gram-negative bacteria (16)	10 (62.5)	3 (18.8)	3 (18.8)
Anaerobic bacteria			
Clostridium perfringens (13)	3 (23.1)	10 (76.9)	0
Clostridium species (15)	12 (80)	3 (20)	0
Propionibacterium species (48)	0	48 (100)	0
Other gram-positive anaerobic bacteria (7)	4 (57.1)	2 (28.6)	1 (14.3)
Bacteroides fragilis group (18)	16 (88.9)	0	2 (11.1)
Other gram-negative anaerobic bacteria (5)	2 (40)	2 (40)	1 (20)
Yeasts and fungi			
Candida albicans (30)	27 (90)	0	3 (10)
Other *Candida* species (15)	15 (100)	0	0
Cryptococcus neoformans (8)	8 (100)	0	0
Torulopsis glabrata (15)	14 (93.3)	0	1 (6.7)
Other yeasts and fungi (4)	2 (50)	1 (25)	1 (25)
Mycobacteria			
Mycobacterium avium complex (16)	16 (100)	0	0
M. tuberculosis (1)	1 (100)	0	0
All microorganisms (1,844)	944 (51.2)	791 (42.9)	109 (5.9)

Hospital service. Six hundred twenty of the 843 bacteremic and fungemic episodes (73.5%) occurred in patients hospitalized on the medical services of our institutions. Patients hospitalized on the nontransplantation surgical services accounted for 21.3% of total episodes, with the remaining 5.2% of episodes distributed among the transplantation surgery, obstetric and gynecologic services, and emergency and outpatient departments. Pneumococcal bacteremia, not surprisingly, was seen almost exclusively in patients on the medical service.

Proportionately, enterococcal and pseudomonas bacteremias were twofold more common on the general and transplantation surgical services than on the medical service. Indeed, *P. aeruginosa* accounted for only 4.4% of septicemias on the medical service. Fungemia was proportionately most common on the

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Table 2. Clinical significance of *Staphylococcus epidermidis* isolates (unimicrobial episodes only).

No. of culture sets		Clinical significance: no. (%) of isolates		
Positive	Performed	Significant	Contaminant	Indeterminate
1	1	0	33 (97.1)	1 (2.9)
1	2	3 (2.2)	129 (94.8)	4 (3.0)
2	2	18 (60.0)	1 (3.3)	11 (36.7)
1	3	0	2 (100)	0
2	3	3 (75.0)	0	1 (25)
3	3	4 (100)	0	0

transplantation surgical service, accounting for nearly 25% of septicemic episodes. Anaerobic bacteremia, which was uncommon in general, was seen most frequently in patients on the general surgery service (6.6% of episodes) and obstetric and gynecologic service (11.1% of episodes).

Sources of infection. The sources of bacteremia and fungemia were identifiable in 627 (74.4%) of episodes and are listed in table 4. Intravenous catheters were the most common primary foci for septicemia. Despite the availability of increasingly sophisticated imaging techniques, the sources for nearly one-fourth of episodes could not be determined.

The relationship between microorganism and sources of unimicrobial bacteremia and fungemia are presented in table 5, which also delineates those episodes confirmed by cultures of specimens other than blood or by clinical evidence. The majority of *S. aureus* and coagulase-negative staphylococcal bacteremias were associated with intravascular devices. Not surprisingly, pneumococcal bacteremia was most often associated with pneumonia, but in 7 of 34 episodes (20.6%) a primary source could not be determined. Among the Enterobacteriaceae, primary foci of infection below the diaphragm predominated (table 5), as would be expected given the normal habitat of these bacteria. In contrast, the most common focus for bacteremia due to *P. aeruginosa* was the respiratory tract, which was the focus more than twice as frequently as the next most common focus, the genitourinary tract.

Several microorganisms or microorganism groups were associated at a particularly high frequency with bacteremia or fungemia in which a primary focus for infection could not be determined. These included the viridans streptococci (44.4%), *Enterobacter cloacae* (58.3%), *Klebsiella pneumoniae* (33.3%), *Candida* species (37.5%), *Torulopsis glabrata* (41.7%), and *Mycobacterium avium* complex (100%). All of the *E. cloacae* bacteremias and many of the fungemias and *K. pneumoniae* bacteremias with unknown sources occurred in patients with underlying malignancies.

Table 3. Community-acquired and hospital-acquired microorganisms and major microorganism groups involved in episodes of bacteremia and fungemia.

	No. (%) of isolates per place of acquisition of infection	
Microorganisms	Community	Hospital
Staphylococcus aureus	90 (50.6)	88 (49.4)
Coagulase-negative staphylococci	27 (31.0)	60 (69.0)
Streptococcus pneumoniae	31 (91.2)	3 (8.8)
Other streptococci	32 (68.1)	15 (31.9)
Enterococcus species	15 (23.1)	50 (76.9)
Escherichia coli	87 (61.3)	55 (38.7)
Other Enterobacteriaceae	61 (36.1)	108 (63.9)
Pseudomonas aeruginosa	21 (39.6)	32 (60.4)
Other nonfermentative gram-negative rods	16 (51.6)	15 (49.4)
Clostridium species	5 (33.3)	10 (66.7)
Bacteroides species	7 (38.9)	11 (61.1)
Candida species	7 (16.7)	35 (83.8)
Cryptococcus neoformans	8 (100)	0
Torulopsis glabrata	2 (14.3)	12 (85.7)
Mycobacterium avium complex	16 (100)	0

Clinical Observations

In order to determine whether certain indicators might assist in assessing the clinical significance of positive blood cultures, we examined the relationship between positive cultures and the peripheral leukocyte count, absolute neutrophil count, blood pressure, and body temperature at the time the first positive blood culture specimen was obtained for a given episode. We also examined the relationship between each of these variables and the microorganisms isolated from true positive cultures. In addition, we critically assessed the antimicrobial therapy as described in the Materials and Methods section.

Leukocyte count and absolute neutrophil count. Patients with culture-positive blood and a peripheral leukocyte count of $<4{,}000/\mu L$ or $\geq 20{,}000/\mu L$ were significantly more likely

Table 4. Sources of bacteremia and fungemia.

	No. of episodes confirmed by		
Source	Culture	Clinical evidence	Total no. (%) of episodes
Intravascular catheter	29	97	161 (19.1)
Genitourinary tract	115	28	147 (17.4)
Respiratory tract	56	46	104 (12.3)
Bowel and peritoneum	22	21	45 (5.3)
Biliary tract	9	21	33 (3.9)
Intraabdominal abscess	9	15	24 (2.8)
Skin	11	29	42 (5.0)
Bone and joint	11	5	16 (2.0)
Surgical wound	7	2	11 (1.3)
Other	25	18	44 (5.2)
Unknown	0	0	216 (25.6)

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Table 5. Sources and confirmatory evidence for episodes of unimicrobial bacteremia and fungemia, according to microorganism.

Microorganism(s) (no. of episodes)	No. of sources confirmed by		Common source(s) (no. of episodes)*
	Culture	Clinical evidence	
Staphylococcus aureus (159)	56	74	IV (56), skin (19), respiratory (18), bone/joint (10)
Coagulase-negative staphylococci (73)	16	45	IV (59), skin (5)
Streptococcus pneumoniae (34)	5	22	Respiratory (26)
Group B streptococci (8)	4	3	Skin (3), GU (3)
Viridans group streptococci (24)	3	10	Respiratory (3), skin (2)
Enterococcus species (38)	13	9	GU (15), IV (3)
Escherichia coli (116)	70	30	GU (67), biliary (11), peritoneal (10)
Klebsiella pneumoniae (48)	15	15	Biliary (10), GU (8), peritoneal (5)
Enterobacter cloacae (12)	3	2	Biliary (2), respiratory (2)
Serratia marcescens (20)	11	6	GU (4), respiratory (4), IV (3)
Proteus mirabilis (13)	10	2	GU (9)
Pseudomonas aeruginosa (48)	25	12	Respiratory (19), GU (9)
Acinetobacter baumanii (12)	4	0	Respiratory (3)
Bacteroides fragilis group (9)	3	4	Abscess (6)
Candida albicans (21)	7	2	IV (5), peritoneal (2)
Candida tropicalis (7)	1	4	IV (1), GU (1), peritoneal (1)
Torulopsis glabrata (12)	1	4	GU (4)
Mycobacterium avium (15)	0	0	No sources identified

NOTE. The list of microorganisms includes all those isolated ≥5 times as causes of unimicrobial bacteremia or fungemia.

* Abscess = intraabdominal abscess; GU = genitourinary tract; IV = intravascular device; respiratory = respiratory tract.

($P < .001$) to have true bacteremia or fungemia episodes (62.5% and 60.3%, respectively) than contaminant episodes when compared with patients who had peripheral leukocyte counts between 4,000 and 19,999/μL (proportion of true bacteremias, 49.2%). Similarly, patients with absolute neutropenia were significantly more likely ($P < .001$) than nonneutropenic patients to have a positive blood culture represent true bacteremia or fungemia (70.2% vs. 51.4% of positive cultures, respectively).

The distribution of microorganisms causing septicemia in neutropenic and nonneutropenic patients is shown in table 6. Neutropenic patients were significantly less likely to have bacteremia due to *S. aureus* ($P < .0001$; RR, 0.33) but were significantly more likely to have fungemia ($P < .01$; RR, 1.81) and polymicrobial bacteremia ($P < .0001$; RR, 2.63) than were nonneutropenic individuals.

Blood pressure. Approximately 14% of patients were hypotensive at the time the first positive blood culture specimen was obtained. The positive blood cultures of these patients were more likely to represent true bacteremia than were positive blood cultures of patients with normal blood pressure at the time cultures were performed (72.7% vs. 51.1% of positive cultures, respectively; $P < .0001$). The distribution of microorganisms causing bacteremia and fungemia in these patients is shown in table 7. There were no statistically significant differences in microorganisms or microorganism groups in hypotensive vs. normotensive patients. However, polymicrobial episodes occurred significantly more often in hypotensive patients than in patients whose blood pressure was normal at the time of blood culture ($P < .05$; RR, 1.58).

Temperature. Cultures of patients who were hypothermic (temperature, <36°C) or who had marked fever (temperature, ≥40°C) were more likely to be true-positives (67.7% and 69.6% of positive cultures, respectively) than were those of patients whose temperatures were normal (39.2% of positive cultures) or moderately elevated (55.9% of positive cultures) at the time the positive blood culture specimen was obtained.

Endocarditis. Of 31 episodes (in 31 patients) of endocarditis, 11 were due to *S. aureus,* 10 to viridans streptococci, and 3 to enterococci. All episodes were unimicrobial; 30 of the 31 were due to gram-positive bacteria, and one was caused by *K. pneumoniae.* Twenty-one patients presented following <1 week of symptoms, 8 following 1–3 weeks of symptoms, and 2 following >3 weeks of symptoms. Seven of 11 patients with endocarditis due to *S. aureus* and 7 of 10 patients with endocarditis caused by viridans streptococci presented following <1 week of symptoms.

Antibiotic therapy. Of the 1,585 episodes of positive blood cultures, 454 (28.6%) involved patients receiving antimicrobial agents at the time the first positive blood culture specimen was obtained. The proportion of patients who were receiving antibiotics was the same regardless of whether growth repre-

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Table 6. Microorganisms recovered from and types of episodes in patients with bacteremia and fungemia, according to absolute neutrophil count.

Variable	No. (%) of isolates from patients with indicated neutrophil count	
	<1,000/μL	≥1,000/μL
Microorganisms		
Staphylococcus aureus	9 (6.0)*	169 (21.1)*
Coagulase-negative staphylococci	12 (8.1)	75 (9.4)
Streptococci	9 (6.0)	78 (9.7)
Enterococcus species	13 (8.7)	52 (6.5)
Enterobacteriaceae	58 (38.9)	253 (31.6)
Pseudomonas aeruginosa	11 (7.4)	42 (5.2)
Other nonfermentative gram-negative rods	2 (1.3)	29 (3.6)
Anaerobic bacteria	9 (6.1)	29 (3.6)
Yeasts and fungi	17 (12.1)†	48 (6.0)†
Type of episode: total no. (%)		
Unimicrobial	96 (69.6)	668 (87.4)
Polymicrobial	24 (30.4)*	55 (12.6)*

* $P < .0001$.
† $P < .01$.

sented true bacteremia or contamination. Of the 843 episodes of true bacteremia or fungemia, 71 (8.4%) occurred in patients who were receiving therapy that was effective against the microorganism(s) that grew in the blood culture. This proportion was the same at all three hospitals (range, 8.0%–9.1%).

Appropriate antimicrobial therapy was administered to a substantial majority of patients at all of the time points assessed. Excluding the 48 patients who died prior to the availability of susceptibility test results, 620 of 795 patients (78%) received appropriate therapy at all time points. In addition, 111 patients (14%) were given appropriate therapy after susceptibility test results were available, regardless of whether they had received inappropriate empirical therapy at an earlier time point.

Patients with unimicrobial septicemia were more likely than those with polymicrobial septicemia to be treated with appropriate therapy, especially after susceptibility test results were available (92.7% vs. 83.6%, respectively). At all time points assessed, medical patients were somewhat more likely than surgical patients to receive appropriate therapy. Among medical patients, the proportion who received appropriate therapy at the different time points ranged from 89.4% to 91.0%, versus a range of 83.0% to 87.1% among surgical patients.

After susceptibility test results were available, approximately one-quarter of all patients were receiving antimicrobial agents judged to be superfluous for the infecting microorganism(s) and clinical setting. Twenty-six patients (3.3%) were receiving agents to which their infecting organisms were resistant in vitro, and nine patients (1.1%) received no antimicrobials despite a clinical setting that should have mandated therapeutic intervention.

Outcome and Factors Influencing Prognosis

One hundred forty-eight patients (17.5%) died of causes directly or indirectly attributable to an episode of septicemia (associated mortality). Five hundred thirty-five patients (63.5%) were discharged alive, 118 (14.0%) were alive but remained hospitalized 30 days after onset of the septicemic episode, and 42 (5.0%) died from causes that were judged by the investigators not to be associated with the bacteremia or fungemia. There were no significant differences in mortality at the three collaborating hospitals.

Univariate Analyses

Age and sex. The effect of age on outcome of bacteremia and fungemia was assessed according to the decade of life of the infected patients. As shown in figure 1, septicemia-associated mortality gradually increased with age and was especially notable after the age of 70 years. The infection-associated mortality for septicemic patients over 70 years of age was 24.2% compared with 15.2% for patients 70 years of age or less. In comparison with other patients, the relative risks of death from bacteremia and fungemia for patients between 71 and 80 years of age and >80 years of age were 2.58 and 3.4, respectively. There were no significant differences in infection-associated mortality between septicemic men and women.

Hospital service. The septicemia-associated mortality rates ranged from zero among obstetric and gynecologic patients to 19% and 23% among medical and cardiovascular surgery patients, respectively. However, none of the differences in mortality, when sorted according to hospital service, were statistically significant.

Table 7. Microorganisms recovered from and types of episodes in hypotensive and normotensive patients with bacteremia and fungemia.

Variable	No. (%) of isolates from patients with indicated blood pressure status	
	Hypotensive	Normotensive
Microorganism		
Staphylococcus aureus	21 (16.0)	157 (19.3)
Coagulase-negative staphylococci	6 (4.6)	81 (10.0)
Streptococcus pneumoniae	8 (6.1)	26 (3.2)
Other streptococci	6 (4.6)	41 (5.0)
Enterococcus species	13 (10.0)	52 (6.4)
Enterobacteriaceae	46 (35.1)	265 (32.6)
Pseudomonas aeruginosa	7 (5.3)	46 (5.7)
Other nonfermentative gram-negative rods	1 (0.8)	30 (3.7)
Anaerobic bacteria	5 (3.8)	33 (4.1)
Yeasts and fungi	12 (9.2)	54 (6.6)
Type of episode: total no. (%)		
Unimicrobial	96 (85.7)	668 (91.4)
Polymicrobial	16 (14.3)*	63 (8.6)*

* $P < .05$.

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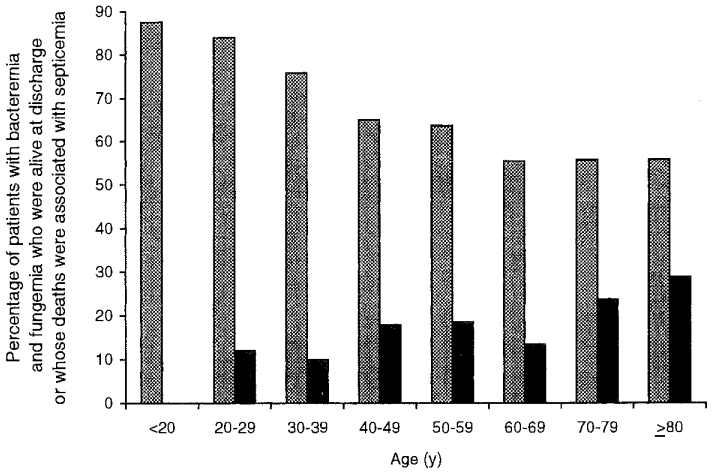


Figure 1. Outcome of bacteremia or fungemia, according to age group of patients (▩ = alive at discharge; ■ = death, associated with septicemia).

Place of acquisition of bacteremia and fungemia. Patients who developed bacteremia or fungemia during the course of hospitalization had an infection-associated mortality rate of 20.3%, vs. 14.6% for patients with community-acquired disease. The relative risk of death associated with nosocomial septicemia was 1.39 ($P < .05$).

Table 8. Associated mortality in episodes of bacteremia and fungemia and relative risk of death, as related to etiologic microorganisms in unimicrobial episodes and to the type of episode.

Variable	Associated mortality: no. (%) of deaths per no. of episodes	Relative risk of death
Microorganisms		
Staphylococcus aureus	19/159 (11.9)	2.18
Coagulase-negative staphylococci	4/73 (5.5)*	1.0
Streptococcus pneumoniae	6/34 (17.6)	3.22
Other streptococci	5/38 (13.1)	2.40
Enterococcus species	5/38 (13.1)	2.40
Other gram-positive aerobic bacteria	1/9 (11.1)	2.03
Escherichia coli	14/116 (12.1)	2.20
Other Enterobacteriaceae	31/125 (24.8)†	4.53
Pseudomonas aeruginosa	8/48 (16.7)	3.04
Other nonfermentative gram-negative rods	3/25 (12.0)	2.19
Other gram-negative aerobic bacteria	0/6	0.04
Gram-negative anaerobic bacteria	2/14 (14.3)	2.61
Gram-positive anaerobic bacteria	2/8 (25.0)	3.65
Yeasts and fungi	19/53 (35.8)‡	6.54
Mycobacteria	2/16 (12.5)	2.28
Type of episode		
Unimicrobial	120/764 (15.7)	1.0
Polymicrobial	27/79 (34.2)‡	2.16

* $P < .05$.
† $P < .01$.
‡ $P < .001$.

Microorganism. The microorganism isolated and type of bacteremia or fungemia (i.e., unimicrobial or polymicrobial) influenced outcome (table 8). Among the common etiologic agents of bacteremia and fungemia, the lowest associated mortality occurred with coagulase-negative staphylococci (5.5%) and the highest with yeasts and fungi (35.8%). Infection-associated mortality was lower with gram-positive unimicrobial bacteremia (11.1%) than with gram-negative bacteremia (17.6%), anaerobic bacteremia (18.2%), or fungemia (35.8%).

The mortality associated with pneumococcal bacteremia was greater than that associated with enterococcal or *S. aureus* bacteremia (table 8). Also noteworthy was the mortality rate with *P. aeruginosa* bacteremia, which was less than that with bacteremia due to enteric gram-negative rods other than *E. coli* (table 8). The mortality associated with polymicrobial bacteremia was more than twice that associated with unimicrobial episodes.

Table 9. Associated mortality in episodes of bacteremia and fungemia, according to source of infection.

Source of infection	Associated mortality: no. (%) of deaths per no. of episodes	Relative risk of death
Intravascular catheter	12/161 (7.4)*	1.0
Genitourinary tract	16/147 (10.8)†	1.46
Respiratory tract	26/104 (25.0)†	3.35
Bowel and peritoneum	23/45 (51.1)‡	6.86
Biliary tract	4/33 (12.1)	1.63
Intraabdominal abscess	3/24 (12.5)	1.68
Skin	6/42 (14.3)	1.92
Bone and joint	1/16 (6.25)	0.84
Surgical wound	0/11	0.01
Other	3/44 (6.8)	0.91
Unknown	54/216 (25.0)*	3.35

* $P < .01$.
† $P < .05$.
‡ $P < .001$.

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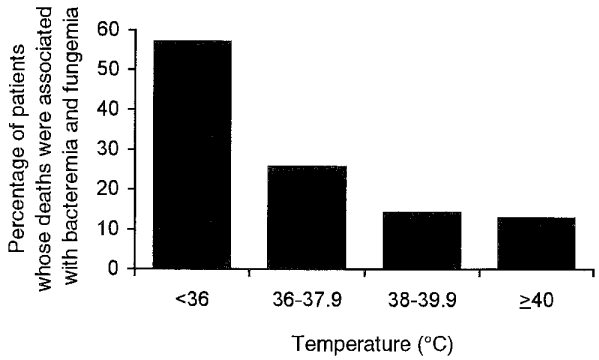


Figure 2. Septicemia-associated mortality as related to temperature of patients at the time the first positive blood culture specimen was obtained.

Source of infection. The outcome of bacteremia and fungemia was affected by the primary source of infection (table 9). For risk factor analysis, we assigned a risk of 1.0 to septicemia associated with iv catheters in order to maintain consistency with our earlier work [11]. Significantly increased septicemia-associated mortality and relative risk of death occurred with respiratory tract sources ($P < .05$), with bowel and peritoneal sources ($P < .01$), and when a primary focus of infection could not be found ($P < .05$).

Body temperature. The mortality associated with bacteremia and fungemia was inversely related to the body temperature of patients at the time the first positive blood culture specimen was obtained (figure 2). Risk factor analysis showed significantly increased mortality ($P < .05$) among the patients who were hypothermic at the onset of septicemia.

Blood pressure. Septic shock, as evidenced by the presence of hypotension at the time the first positive blood culture specimen was obtained, was associated with increased mortality. Table 10 reveals that this relationship was a virtually uniform finding, regardless of the etiologic microorganism or the type of septic episode.

Leukocyte count and absolute neutrophil count. The relationship between septicemia-associated mortality and total leukocyte count or absolute neutrophil count is shown in table 11. Patients who had leukocyte counts of <4,000/μL or ≥20,000/μL had a twofold increase in relative risk of death from septicemia. Patients with absolute neutropenia had a significantly increased relative risk of death in comparison with that for nonneutropenic patients.

Predisposing factors. The influence of predisposing factors on the outcome of septicemia was analyzed both when individual factors were present alone and when multiple factors were present (table 12). Nearly one-quarter of the patients had no predisposing factors, and these patients had the lowest septicemia-associated mortality (8.2%; RR, 1.0). The greatest mortality was associated with moderate renal failure (61.5%; RR, 7.54).

Table 10. Associated mortality in episodes of bacteremia and fungemia, as related to etiologic microorganism in unimicrobial episodes, type of episode, and blood pressure status at the time of onset of septicemia.

Variable	Associated mortality: no. (%) of deaths per no. of episodes in indicated group	
	Hypotensive	Normotensive
Microorganisms		
Staphylococcus aureus	5/18 (27.8)*	14/141 (9.9)*
Coagulase-negative staphylococci	1/4 (25)	3/69 (4.3)
Streptococcus pneumoniae	1/8 (12.5)	5/26 (19.2)
Other streptococci	1/3 (33.3)	3/35 (8.6)
Enterococcus species	1/5 (20)	4/33 (12.1)
Escherichia coli	4/13 (30.8)*	10/103 (9.7)*
Other Enterobacteriaceae	12/23 (52.2)†	19/104 (18.3)†
Pseudomonas aeruginosa	3/6 (50)*	5/42 (11.9)*
Other nonfermentative gram-negative rods	0/1	3/28 (10.7)
Anaerobic bacteria	1/2 (50)	3/24 (12.5)
Yeasts and fungi	5/7 (71.4)*	14/46 (30.4)*
Type of episode		
Unimicrobial	35/96 (36.4)‡	85/668 (12.7)
Polymicrobial	10/16 (62.5)†	17/63 (27.0)

* $P < .05$.
† $P < .01$.
‡ $P < .001$.

Although the relative risk of death was high in the presence of severe renal failure and biopsy-proven cirrhosis, statistical significance was not achieved because of the relative infrequency of each of these predisposing factors as the sole underlying problem. Not surprisingly, there was a direct relationship between septicemia-associated mortality and the number of predisposing factors present. Thus, mortality was greater among the patients with multiple predisposing factors than among patients with only a single factor.

Table 11. Associated mortality in episodes of bacteremia and fungemia, as related to leukocyte count and absolute neutrophil count.

Variable	Associated mortality: no. (%) of deaths per no. of episodes	Relative risk of death
Total leukocyte count (per μL)		
<4,000	42/177 (23.7)	2.11*
4,000–10,999	28/249 (11.2)	1.0
11,000–19,999	48/293 (16.4)	1.46
20,000–49,999	27/115 (23.5)	2.09*
≥50,000	2/8 (25)	2.22
Absolute neutrophil count (per μL)		
<1,000	31/120 (25.8)	1.58*
≥1,000	115/702 (16.4)	1.0

* $P < .05$.

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Table 12. Influence of predisposing factors on associated mortality in episodes of bacteremia and fungemia.

Factor(s)	Associated mortality: no. (%) of deaths* per no. of episodes	Relative risk of death
None	16/196 (8.2)	1.0
Hematologic malignancy	14/70 (20.0)	2.45†
Other neoplasm	27/150 (18.0)	2.20†
Corticosteroids	3/28 (10.7)	1.31
AIDS	11/51 (21.6)	2.64†
Trauma	1/11 (9.1)	1.11
Recent surgery	7/49 (14.3)	1.75
Diabetes mellitus	6/59 (10.2)	1.25
Creatinine level, 2–5 mg/dL	16/26 (61.5)	7.54‡
Creatinine level, >5 mg/dL	4/16 (25)	3.06
Cirrhosis	2/6 (33.3)	4.08
One factor	91/477 (19.1)	2.34†
Two or more factors	41/168 (24.4)	2.99†

* No. of deaths among patients in whom listed predisposing factor was the only one present.
† $P < .05$.
‡ $P < .01$.

Antibiotic and other therapy. The mortality associated with bacteremia and fungemia clearly was affected by the type of antimicrobial therapy administered (table 13). The great majority (78%) of patients received appropriate therapy at all three time points at which assessments were made, and this group of patients had the lowest septicemia-associated mortality. Patients who received inappropriate empirical therapy but whose physicians administered appropriate therapy once the blood culture was reported to be positive also had low mortality. By contrast, among the small group of patients who received inappropriate therapy at all three time points, three of nine (33%) died of causes attributable to sepsis.

Indeed, the data shown in table 13 clearly indicate that septicemia-associated mortality increased in proportion to the duration of inappropriate antimicrobial therapy. Since our definition of appropriate empirical therapy allowed for the possibility that the organism(s) grown in blood culture might not be susceptible to the agents given, we also assessed outcome in terms of whether the infecting organisms were susceptible to therapy being administered at each time point. The results of this analysis were very similar; that is, associated mortality was lowest (9.8%) when the organism was susceptible at all three time points and also was low (12.6%) when patients received effective antimicrobial therapy after blood cultures were reported to be positive.

When mortality following the availability of susceptibility test results was analyzed alone, the mortality rates when first-choice or alternative-choice agents were given were identical (8.3%), but the rate was 24% when superfluous therapy was given. Since superfluous therapy included at least one agent with in vitro activity against the infecting microorganism, other factors that may have influenced outcome were assessed. Patients receiving superfluous therapy were twofold to threefold more likely to have absolute granulocytopenia, fungemia, or polymicrobial episodes than were patients who received first-choice or alternative-choice agents.

The removal, excision, or drainage of a primary focus of infection, if feasible, often has a salutary effect on the outcome of septicemia. Therefore, we assessed outcome when such therapeutic maneuvers were undertaken. The results confirmed the beneficial effect of these interventions. Among patients who survived until susceptibility test results were available, associated mortality was 6.2% (14 of 224) when an infected focus was excised, drained, or removed, vs. 15.6% (87 of 557) when no additional interventions were (or could be) undertaken ($P < .001$). Among patients with catheter-associated bacteremia or fungemia, removal of the catheter was associated with death due to septicemia in only 3.9%.

Table 13. Associated mortality in episodes of bacteremia and fungemia, as related to appropriateness of antimicrobial therapy at different time points during septicemia.

Assessment of therapy at indicated time point*				
Initial empirical therapy	After culture reported positive	After susceptibility results available	Associated mortality: no. (%) of deaths per no. of patients	RR
A	A	A	65/620 (10.5)	1.0
I	A	A	6/45 (13.3)	1.27
A	I	A	7/35 (20.0)	1.91
A	A	I	7/35 (20.0)	1.91
I	I	A	8/31 (25.8)	2.46
A	I	I	4/14 (28.6)	2.73
I	A	I	0/2	0.05
I	I	I	3/9 (33.3)	3.18

* A = appropriate; I = inappropriate. Therapy was considered appropriate after susceptibility test results became available if the microorganism(s) were susceptible (on the basis of in vitro testing) to at least one agent administered, whereas therapy was considered appropriate at the earlier time points it if was appropriate for the clinical situation.

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Multivariate Analysis

Based on the results of univariate analysis, high- and low-risk categories were established for each variable assessed. When there was more than one high-risk component for a variable (e.g., microorganism, source, or predisposing factor), these components were grouped and assigned a univariate relative risk for the purpose of multivariate analysis. Then, with use of logistic regression, the relative risk of death was determined for each variable in the presence of all others.

The results of this analysis are shown in table 14. Those variables associated with a significantly increased risk of death in multivariate analysis were advanced age (>70 years); isolation of fungi or Enterobacteriaceae other than *E. coli;* a primary source of infection in the respiratory tract, bowel, or peritoneum or that was unknown; underlying malignancy, AIDS, or renal failure; shock, as manifested by hypotension; inability to mount a febrile response to sepsis; and inappropriate antibiotic therapy at two or more of the time points assessed.

Discussion

It was our hypothesis that the many changes in medicine since the mid-1970s, when two of us and other investigators [10, 11] comprehensively reviewed a large series of patients with bacteremia and fungemia, would lead to substantive changes in the microbiology, epidemiology, and clinical and prognostic significance of positive blood cultures in the 1990s. Indeed, the more aggressive and widespread use of prosthetic materials and intravascular devices, the occurrence of syndromes such as AIDS not known 2 decades ago, and therapeutic advances in imaging, interventional radiology, and antimicrobial therapy virtually ensured the presence of important differences and underscored the need for this update.

In order to best compare the differences and similarities of bacteremia and fungemia in the 1990s versus the mid-1970s, we used definitions, including clinical and diagnostic criteria, that were similar to those in our earlier work [10, 11]. However, we performed this study prospectively, gathering data concurrently on patients with culture-positive blood, to better assess the ways in which physicians used laboratory results for therapeutic decisions.

Laboratory Observations

True septicemia vs. contamination. The observations from this study suggest that contaminants in blood cultures are more frequent in the 1990s than they were 2 decades ago. Of 1,582 positive blood culture episodes in the current study, 655 (41.5%) were judged to represent contamination and another 84 (5.3%) were of indeterminate significance. Thus, only about half of all positive blood cultures represented true bloodstream infection. These findings contrast markedly with the observations in our earlier study, in which approximately one-third of all positive blood cultures represented contamination [10].

There are several possible explanations for these findings. One is the increasing use of central, long-term intravascular catheters (e.g., Hickman and Broviac) and the utilization of these access devices for the purpose of obtaining blood for culture. Access ports from intravascular devices may be more difficult to sterilize than skin at venipuncture sites, thereby resulting in increased contamination rates; at least one study has documented increased contamination rates when blood culture specimens are obtained from central lines [34].

Although physicians may believe they are benefiting their patients by obtaining blood culture specimens from catheters (i.e., saving patients from needlesticks), they actually may be doing a disservice, since culture contaminants (false-positives)

Table 14. Comparison of univariate and multivariate analysis of factors affecting risk of death in patients with bacteremia and fungemia.

Variable	Univariate high risk	Univariate RR	Multivariate RR
Age	>70 y	1.88	1.80*
Place of acquisition	Hospital	1.39	1.12
Microorganisms	Fungi and Enterobacteriaceae other than *E. coli*	5.13	2.27†
Type of episode	Polymicrobial	2.16	1.55
Source of infection	Respiratory tract, bowel, peritoneum, or unknown	2.56	2.86†
Predisposing factor	Malignancy, AIDS, or renal failure	1.92	1.98†
Blood pressure	Hypotension	2.85	2.29†
Leukocyte count	<4,000/μL or >20,000/μL	1.67	1.24
Absolute neutrophil count	<1,000/μL	1.58	0.65
Body temperature	Absence of fever (<37.9°C)	2.06	2.04†
Antibiotic therapy	Inappropriate at ≥2 time points	2.32	2.72†

* $P < .05$.
† $P < .01$.

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cultures) have been shown to result in longer hospitalizations and increased costs to patients and institutions [35].

A second possible reason for the increased incidence of contaminants is blood culture technique. Although several recent studies have indicated that the current single-needle technique for obtaining blood and inoculating cultures is not associated with increased rates of contamination [14, 36, 37], Spitalnic et al. [38], in a meta-analysis, have suggested otherwise. Alternatively, it may be that in institutions such as ours, in which house officers and medical students obtain the majority of blood culture specimens, failure to apply antiseptic solutions (usually iodophors and alcohol) properly and to let them exert their antimicrobial effect over 1–2 minutes as recommended results in increased contamination.

Possible remedies include use of blood culture teams from the laboratory's phlebotomy service, which seems unlikely in the managed care era, or the development and use of potentially more effective antiseptic skin preparation materials (e.g., 2% iodine tincture) before blood sampling. A final possible explanation for increased rates of contamination of blood cultures could be that newer blood culture systems and media are more sensitive and capable of detecting the few viable skin bacteria that might remain after appropriate antiseptic preparation.

Of the 843 septicemias, a source was confirmed by culture in 294 (34.9%) and by clinical evidence in 282 (33.4%). Of the remaining 267 episodes, at least two blood cultures were positive for the same microorganism in 181 (67.8%; 21.5% of total septicemias). Thus, there was objective evidence of true infection in 757 of the 843 episodes (89.8%), an observation that is remarkably similar to that in our earlier study [10]. This finding is important clinically, since it suggests that, despite increased rates of contamination of blood cultures, in the great majority of instances physicians should be able to determine with some confidence whether a positive blood culture represents significant infection.

Nevertheless, positive blood cultures yielding coagulase-negative staphylococci may present great interpretative difficulties, even when more than one culture set is positive. For example, Zaidi et al. [39] have found that coagulase-negative staphylococci with identical species designations, serotypes, and antibiograms recovered from the blood of infants sometimes represented different strains when the isolates were analyzed by molecular typing techniques. Similarly, even when both of two blood cultures yielded *S. epidermidis* of the same biotype in the current study, we were frequently not certain of the isolates' clinical significance (table 2).

Patterns of positive blood cultures. In our earlier study [10], we noted different patterns of blood culture positivity in patients with endocarditis, those with true septicemia that was not due to endocarditis, and those with contaminant isolates. Similar observations were made in this study. Thus, in patients with endocarditis, a disease characterized by continuous seeding of blood from the infected heart valve, all blood cultures obtained in a series were positive.

By contrast, for patients with septicemia not due to endocarditis, most but not all blood cultures obtained in a series were positive, a finding consistent with the understanding that bloodstream infection in such patients may be short-lived or intermittent (abscesses). For patients whose blood cultures were contaminated, an initial positive culture in a series virtually always was followed by negative cultures. When a subsequent culture was positive, it usually was positive with a different microorganism (e.g., *S. epidermidis* followed by a diphtheroid).

The proportion of patients with polymicrobial septicemia in this study (79 of 843; 9.4%) is consistent with findings in earlier studies, in which frequencies of polymicrobial bacteremia ranged from 6% to 18% [10, 17, 40–43].

Epidemiological Observations

Place of acquisition of septicemia. At our institutions the proportions of episodes that were of community-acquired septicemia and hospital-acquired septicemia were nearly equal (48% vs. 52%). This observation contrasts with the results of our earlier study at the University of Colorado hospitals, in which nearly two-thirds of episodes were nosocomial [10]. The difference may relate not only to patient-population variability [44, 45] but also to changes in health care, particularly shorter lengths of stay in the 1990s than those of 2 decades ago, as well as outpatient surgery and chemotherapy.

In contrast to the relative equivalence of community- and hospital-acquired septicemic episodes overall, there were important differences with regard to individual microorganisms. For example, 91% of pneumococcal bacteremias and all mycobacteremias and cryptococcemias were community-acquired. These observations are consistent with prior reports (on pneumococci) and with our understanding of the epidemiology of infections due to these microorganisms [10, 44, 46]. However, nosocomial pneumococcal bacteremia can occur and may be relatively common in institutions with longer patient stays [47, 48].

Fungemia, enterococcal bacteremia, and coagulase-negative staphylococcal bacteremia disproportionately were nosocomial in origin (table 3). The observations for fungi and enterococci were virtually identical to those in our earlier studies of bacteremia [10] and probably relate to the fact that infection with these microorganisms tend to occur in more debilitated patients. The predominance of hospital-acquired coagulase-negative staphylococcal bacteremia is explained by the current use of long-term indwelling central and peripheral catheters as well as other prosthetic devices, the ubiquity of these bacteria as normal skin flora, and the ability of these relatively avirulent microorganisms to adhere to the surfaces of biomaterials.

P. aeruginosa bacteremia usually occurs as a nosocomial infection. In the current study, *P. aeruginosa* bacteremia was community-acquired in 39.6% of episodes, compared with 17% in our earlier study. The explanation for this difference in the epidemiology of *P. aeruginosa* bacteremia may be related in

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part to the prevalence of HIV infection. In bacteremic patients known to be infected with HIV, *P. aeruginosa* was the third most frequently isolated pathogen, and in seven of 11 episodes in these patients, bacteremia was community-acquired. Several recent reports have documented similar findings in patients with HIV infections [49–51].

Hospital service. The overwhelming majority of bloodstream infections in this series occurred in patients hospitalized on either the medical services (73.6%) or nontransplantation surgical services (21.3%), an observation similar to that in our previous report [10] in which 54.6% of episodes occurred in medical patients and 27.2% of episodes occurred in surgical patients.

The current study also confirmed the rarity of *P. aeruginosa* bacteremia in medical patients (4.4% of episodes), the absence of enterococcal bacteremias in obstetrical and gynecologic patients, the high proportion of fungemias in transplantation patients (23.1% of episodes), and the proportionately increased frequency of anaerobic bacteremia in patients hospitalized on the surgical and gynecologic services (6.6% and 11.1% of episodes, respectively).

Sources of septicemia. Onc of the striking findings in the currcnt scries in comparison with our earlier work [10] was the ascendancy of intravascular catheters as an important source of bloodstream infections. Whereas only 3% of episodes were catheter-related in the previous study, iv catheters were the source of 19% of the episodes in the current series. The increasing importance of intravascular catheters also was noted by Mylotte et al. [47], who examined nosocomial bacteremia between 1979 and 1987; in that study, the proportion of episodes associated with intravascular devices increased from 6% (1979) to 19% (1987). During a similar time period, the proportion of bloodstream infections due to intravascular devices at a university hospital in Berlin was consistently ~16% [19].

The inability to determine the focus of bacteremia and fungemia remains a vexing problem. Despite substantial advances in diagnostic imaging over the past 2 decades, 26% of the septicemic episodes in this series, compared with 31% in our earlier study [10], had no discernible focus. Leibovici and colleagues [20] noted similar results; 23% of episodes during 1988 and 1989 at their university hospital in Israel were of unknown origin.

Since episodes with unknown foci are associated with increased mortality ([11, 20] and present study), improved methods for determining the primary site of infection in septicemic patients clearly are needed. Microorganisms from unknown foci commonly are assumed to have a gut mucosal source. The organisms associated highly with an unknown source in this study (e.g., *E. cloacae, K. pneumoniae, Candida* species, *T. glabrata,* viridans streptococci, and *M. avium* complex) support this hypothesis.

When we examined the sources of septicemia according to each microorganism or microorganism group (table 5), there were several noteworthy observations. For example, in the years since our previous study, the proportion of *S. aureus* bacteremias associated with intravascular catheters has nearly doubled, from 20% to 35%. Respiratory and skin sources remained important primary foci for staphylococcal bacteremia. The recent report by Roberts and colleagues [18] confirmed the importance of intravascular and pulmonary foci for staphylococcal bacteremia. In addition, in the current study and in the report by Roberts et al. [18], respiratory foci for klebsiella bacteremia were considerably less prominent than we observed previously [10]; intraabdominal and genitourinary sources now predominate. In contrast to the findings of Roberts et al., who found enterococcal bacteremia most commonly to have wound sources [18], our patients most often had genitourinary tract foci.

Epidemiology of septicemia in neutropenic patients. The differences in the microbiology of bacteremia and fungemia in neutropenic patients compared with nonneutropenic patients (table 6) stand in contrast with the observations in our earlier report [10]. In the present series bacteremia due to *S. aureus* was significantly less common and fungemia significantly more common in neutropenic than nonneutropenic patients, whereas there were no such differences noted in the previous study. However, in both series, polymicrobial episodes were more frequent in granulocytopenic patients.

A study of bacteremia and fungemia in granulocytopenic patients during 1985 and 1986 at the University of Colorado Health Sciences Center [52], which was the site of our earlier study, showed both similarities to and differences from the distributions of microorganisms in the 1975–1977 review [10] and the current one. For example, in the study by Ehni et al. [52], fungemias were proportionately less common (2%, vs. 11% [10] and 12% [current study]) and *P. aeruginosa* bacteremias were more common (27%, vs. 9% [10] and 7% [current study]). However, the proportionate frequency of bacteremias due to Enterobacteriaceae was similar in all three studies.

In the study by Ehni and colleagues [52] and the present report, bacteremia due to *S. aureus* accounted for ~5% of episodes in neutropenic patients, whereas in the 1975–1977 review [10], 13% of episodes in neutropenic patients were caused by *S. aureus.* Finally, the increasing importance of bacteremia due to coagulase-negative staphylococci in neutropenic patients was evident in the study of Ehni et al. [52] and in the current one (14% and 8% of episodes in neutropenic patients, respectively). In our earlier review, coagulase-negative staphylococcal bacteremia was sufficiently uncommon in granulocytopenic patients that it did not merit mention [10].

A possible explanation for the higher rates of fungemia currently includes the extensive use of more effective antipseudomonal β-lactam drugs such as piperacillin, ceftazidime, and imipenem. Although their early and empirical use may decrease mortality owing to *P. aeruginosa* infection, their prolonged pressure on normal gut flora is associated with overgrowth of yeasts and increased risk of subsequent fungemia [53]. The relative importance of coagulase-negative staphylococci presently probably relates to the common and prolonged use of

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central iv catheters and the resistance of this group of organisms to commonly used antimicrobial agents.

Epidemiology of septicemia in hypotensive patients. Septic shock most frequently has been associated with gram-negative bacteremia. Indeed, in our earlier review [10], aerobic or facultative gram-negative rods accounted for 53% of the isolates from hypotensive patients. In the current series, however, whereas we observed that aerobic or facultative gram-negative rods continued to be common etiologic agents of septic shock, they were isolated less frequently than in the past (43% of isolates). *S. aureus* was detected twice as frequently in hypotensive patients in the current series (16%, vs. 7% in the earlier series), and anaerobic bacteria were detected substantially less often in hypotensive patients (4%, vs. 11% in the earlier series). In both series, hypotensive patients were twice as likely as normotensive patients to have polymicrobial bacteremia ([10] and table 7).

Clinical and Prognostic Observations

Our observations suggest that the mortality associated with bacteremia and fungemia appears to have decreased during the past 2 decades. However, this conclusion may not be applicable widely and should be interpreted with caution. Indeed, the differences in patient population as well as the prospective nature of the current study vs. our retrospective earlier review [11] limited the ability to make direct comparisons with the previous work. Nonetheless, mortality attributable to septicemia in this study was markedly less than in the 1975–1977 study (17.5% vs. 31%, respectively). Moreover, Geerdes et al. [19] recently reported that between 1979 and 1989, mortality from septicemia at a university hospital in Berlin decreased from 34% to 21%.

Crude mortality has varied substantially in recent reports of bacteremic patients, ranging from 16% at a Swedish university hospital from 1973 to 1980 [54] to >40% among patients with nosocomial bacteremia from 1981 to 1983 at a university hospital in the United States [55] and with gram-negative bacteremia at a Turkish university hospital from 1983–1989 [21]. By comparison, crude mortality among septicemic patients at the University of Colorado during 1975–1977 was 42% [11], vs. 22.5% in this study (patients were followed for a maximum of 30 days after detection of bacteremia). Most comparable to our data are the observations of Roberts and colleagues, who recently reported a 30-day mortality of 27% among bacteremic patients studied during 1984–1987 in western Canada [18].

Age and sex. Numerous reports have emphasized the importance of advanced age as an unfavorable prognostic factor in septicemic patients [11, 15, 18, 21, 54, 55]. In contrast to our earlier data, which showed a statistically significant increase in mortality due to septicemia after age 40 years [11], in this series significantly increased mortality occurred after age 70 years. No differences in mortality according to sex were evident in this study or in a recent report from a Swedish university hospital [54].

Place of acquisition of bacteremia and fungemia. Nosocomial septicemias historically have been associated with substantially higher mortality than community-acquired septicemias [9, 11, 44]. In the current series and in another recent report [21], however, the evidence suggests that the increase in mortality associated with hospital-acquired bacteremia and fungemia may be less dramatic than reported in the past. Uzun et al. [21] noted crude mortality of 46% in episodes of nosocomial bacteremia vs. 37% in those of community-acquired bacteremia. In this series, associated mortality due to nosocomial septicemia was 20.3%, vs. 14.6% due to community-acquired septicemia.

Microorganisms. Many studies have looked at the mortality rates with bloodstream infections due to individual microorganisms; some have focused only on certain patient populations. Unfortunately, definitions of mortality in the various reports have not been uniform: some have evaluated total (or crude) mortality, others have evaluated only septic deaths (those judged to be directly related to septicemia), and still others have addressed mortality judged directly or indirectly attributable to septicemia. Furthermore, not all studies have indicated clearly whether mortality rates have been calculated on the basis of unimicrobial episodes, thereby excluding the confounding variable of concomitant bacteremia with other microorganisms. These differences make direct comparisons of mortality in other reports problematic, and the comments that follow should be interpreted accordingly.

The lower mortality overall from bacteremia in this series compared with that noted in our earlier work [11] was reflected in the mortality rates associated with individual microorganisms or groups thereof (table 8). Several comparisons and contrasts with regard to etiologic microorganisms deserve emphasis.

Fungemia, which was associated with more than a sixfold increased risk of death in the earlier series [11], also carried a sixfold increased relative risk of death in the present study (table 8). Overall mortality associated with fungemia, however, was lower in the current series than in our earlier report [11], and the associated mortality in this series was somewhat less (36%) than that due to candida and torulopsis fungemias (44%) in Detroit in the mid-1980s [56].

Among episodes of polymicrobial septicemia, for which the directly related mortality was 35% in the earlier series [11], the associated mortality in this series was 34% and the risk of death was significantly increased compared with that in unimicrobial episodes. The mortality associated with polymicrobial bacteremia in the recent report by Cooper et al. [17] was remarkably similar to the observations in our earlier and current series.

In our earlier review, the mortality directly related to pneumococcal bacteremia was 15% (crude mortality, 22%), vs. 17.6% associated mortality in this series. Data from other recent reports are consistent with these findings [57, 58]. These data

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provide impressive evidence that there has been little change in the outcome of *Streptococcus pneumoniae* bacteremia since the classic studies of Austrian and Gold >3 decades ago [59].

By contrast, the dramatically increased risk of death from bacteremia due to *P. aeruginosa* in our earlier report (RR, 6.84) was moderated in this study (RR, 3.04). The mortality associated with pseudomonas bacteremia was 16.7%, compared with 36% for deaths directly due to bacteremia in the earlier review [11]. Two studies examining pseudomonas bacteremia during the early 1980s revealed case fatality rates attributable to sepsis of 41% and 48% [60, 61]. Thus, our data suggest the possibility that the outcome of bacteremia due to *P. aeruginosa* may have improved over the past decade.

Mortality from bacteremia due to gram-positive organisms also was lower in the current study than in the prior review [11]. In the case of *S. aureus,* septicemia-associated mortality in the current series was 11.9%, compared with crude mortality of 33% and directly related mortality of 9% in the earlier series. By comparison, in the recent report from Lautenschlager et al. [62] encompassing the years 1980–1986 in Basel, Switzerland, total mortality was 34% and directly related mortality was 20%.

Coagulase-negative staphylococcal bacteremia had the lowest attributable mortality of all microorganism groups in the current study (5.5%); case-fatality rates were somewhat higher during the mid-1980s: 13.6% at the University of Iowa Hospital [63] and 18% at a large hospital in Spain [64]. The mortality associated with enterococcal bacteremia was 13% in this series, considerably lower than the crude or directly related mortality (45% and 27%, respectively) in our earlier series [11], despite the presence of vancomycin-resistant enterococci at both RWJUH and DUMC during the current study period. By comparison, reports based on data from the 1980s have described case fatality rates associated with enterococcal bacteremia varying from 12% to 51% [65–67].

Several studies have recently provided data on the outcome of bacteremia due to members of the family Enterobacteriaceae. Mortality due to *E. coli* bacteremia appears to be lower now than 2 decades ago. In our earlier report [11], 41% of patients died of causes directly related to bacteremia, compared with an associated mortality of 10.3% in this study.

Grandsen et al. [68] prospectively evaluated *E. coli* bacteremia in London from 1969 through 1987 and noted a case-fatality rate of 20.7%; approximately half the deaths were judged to be directly related to sepsis. Similarly, the recent review by Roberts and colleagues [18] noted that the 30-day mortality due to *E. coli* bacteremia was 21.5%. Mortality associated with *K. pneumoniae* bacteremia has ranged from 14.6% in the current study to 37% (crude mortality) in another recent report [69]. Korvick et al. [70] reported 19% mortality at 14 days in a recent multicenter study of 230 patients with klebsiella bacteremia.

Mortality associated with serratia bacteremia was 30% among our patients; by contrast, Saito and colleagues [71] reported a mortality rate of 23% in cancer patients between 1982 and 1987. In the present series, associated mortality among 12 patients with *E. cloacae* bacteremia was 8.3%, compared with crude mortality of 24% in a recent multicenter study of 129 patients with enterobacter (all species) bacteremia [72]. The attributable mortality between 1980 and 1992 among patients with *Proteus mirabilis* bacteremia was 25.6% in a recent report [73], remarkably similar to the bacteremia-associated mortality of 23.1% in this series.

Source of infection. As in our earlier study [11], the mortality associated with bacteremia was increased when the primary focus of infection was either unknown or at a site that was difficult to treat, such as the respiratory tract or the bowel and peritoneum. Similarly, when the primary focus of infection could be removed or drained easily (e.g., the genitourinary tract), the mortality was reduced (table 9). The higher mortality in septicemia with an unknown primary focus of infection also has been noted by others [19–21].

Body temperature. The current study confirmed the observations made in our earlier report [11], namely, that the inability of a patient to mount a febrile response to septicemia is a poor prognostic sign (figure 2). This relationship has been noted by others [9, 74, 75] but could not be confirmed in a study designed to examine independent predictors of mortality associated with bloodstream infections [55]. Kluger [76] and Roberts [77] have each recently presented information to support the premise that the presence of physiologically elevated body temperature is beneficial.

Blood pressure. The well-known association between hypotension as a marker for septic shock and poor outcome was again confirmed during this study. This association was noted not only in prior studies [9, 11, 74] but also in more recent reports [18–21]. Compared with data in our earlier review [11], the incremental risk of death when hypotension was present was greater in the current series than was noted previously (RR, 2.8 vs. 2.0).

Total leukocyte count and absolute neutrophil count. Infection-associated mortality and relative risk of death from bacteremia were increased among patients with leukopenia and absolute granulocytopenia, as in our earlier study [11]. In addition, in this study mortality was increased also among patients with total leukocyte counts $\geq 20{,}000/\mu L$. Recent studies in varied patient groups have provided similar observations [17, 60].

Predisposing factors. For consistency and to enable accurate comparisons of risk associated with various underlying conditions that may affect mortality among patients with bacteremia and fungemia, we used the same criteria and definitions as in our earlier review [11] and included HIV infection and AIDS, neither of which were known at the time the earlier study was undertaken. Moreover, the risk associated with each factor was judged when that condition was the only one present (table 12).

As in the earlier study [11], increased risk of death in bacteremia was associated with the presence of malignancies and

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biopsy-proven hepatic cirrhosis. In contrast with our earlier observations, the presence of moderate renal failure (serum creatinine level, 2.0–5.0 mg/dL) but not severe renal failure (serum creatinine level, >5 mg/dL) was associated with increased mortality among bacteremic patients.

Although this observation may seem paradoxical, we interpret the results to suggest that patients with chronic renal failure probably were undergoing dialysis and therefore had stable albeit poor renal function, whereas those with moderate renal failure were more likely to have acute deterioration of function and greater metabolic instability which, in turn, was associated with a greater likelihood of a poor outcome. Finally, the presence of AIDS was associated with an increased risk of death associated with bacteremia or fungemia.

Antibiotic and other therapy. Intuitively, one would expect that administration of antimicrobial agents active in vitro against the infecting microorganism(s) would be associated with improved prognosis. Our prior study and others [11, 78, 79] have supported this assumption, and the current study again confirmed the principle (table 13). By assessing therapy at several different time points, we hoped to determine that degree to which appropriate treatment affected outcome at each stage.

One might have expected, for example, that appropriate therapy given early (empirical therapy time point) would be associated with lower attributable mortality than would appropriate therapy delayed until after susceptibility test results were available to the physician. Indeed, this was the case. As is evident in table 13, the lowest attributable mortality occurred among those patients who received appropriate therapy throughout the course of their septicemic episodes (10.4%). Prompt initiation of appropriate therapy by physicians after notification of a positive blood culture also was associated with low mortality (13.3%). If appropriate therapy was not initiated until after susceptibility test results were available, mortality was 25.8%.

Why 60 (7.6%) of 791 septicemic patients received inappropriate therapy even after the identification and antibiotic susceptibilities of infecting microorganisms were reported is uncertain (table 13). Antibiotic misuse has been studied by others. In one report [80], the most common form of misuse in bacteremic patients was the administration of superfluous agents, a finding that corroborates our observations. In another study [81], multivariate analysis showed that four clinical variables (i.e., nosocomial bacteremia, recent prior antibiotic therapy, nursing home residence, and central iv catheters) and four microorganisms (i.e., *Candida, Acinetobacter, Enterococcus,* and *Pseudomonas* species) were independently associated with inappropriate antimicrobial therapy. Our data also showed that the use of inappropriate therapy was more likely to occur on the surgical services.

A fundamental principle in the management of bloodstream infections has always been that eradication of the primary source of infection is a necessary component of the therapeutic regimen. Thus, removal, drainage, or excision of an infected focus, when possible, should result in an improved prognosis. Both the current study and our prior report [11] provide support for this principle. Indeed, in the current study, infection-associated mortality among patients who had a primary focus that was excised, drained, or removed was less than one-third that among patients who did not have these interventions (6.2% vs. 22.0%, respectively).

Multivariate Analysis of Factors Influencing Prognosis

As in the earlier review by our group [11], we subjected each of the variables that were associated with an increased risk of death in univariate analyses to multivariate analysis (table 14). In the earlier report, seven variables were independently associated with an increased risk of death; all but one were confirmed in the current study. These included advanced age, microorganism, source of infection, predisposing factors, hypotension, and absence of fever. Nosocomial acquisition of bacteremia was not an independent predictor of death in the current study, in contrast to the observations in the earlier report.

In our earlier report we were unable to include antimicrobial therapy in the multivariate analysis. Inclusion of therapy was possible in this study and confirmed the importance of administering appropriate antimicrobial agents.

Although advanced age again was an independent predictor of poor prognosis, the increased risk statistically was greatest after age 70 years in the current study, compared with age >40 years in the earlier series. Septicemia caused by a high-risk microorganism also was again an independent risk factor in multivariate analysis, but there were some changes in the individual microorganisms associated with a high risk of death. In the earlier report there was increased risk with gram-negative rods generally, whereas in the current study increased risk was observed only with Enterobacteriaceae other than *E. coli.*

The reasons for this difference are not readily apparent. Speculation might focus on greater resistance to antimicrobial agents among these strains than among *E. coli.* In contrast to the results of the earlier series, enterococcal bacteremia was not associated with increased risk in the current study. However, fungemia was confirmed to be associated with poor prognosis, in concordance with our earlier observations.

Primary foci of infection in the respiratory tract, bowel, or peritoneum and septicemia from an unknown source again were shown to be independent predictors of poor prognosis. However, primary foci in abscesses, skin, and surgical wounds, each of which was associated with an increased risk of death in the earlier series, were not associated independently with increased risk in the present study.

As in the earlier study, the presence of underlying diseases associated with high risk in univariate analysis was an independent predictor of increased mortality in the multivariate analysis. The underlying diseases associated with high risk were somewhat different from those in the earlier report and included AIDS, a syndrome that was unknown at the time of the earlier

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review; renal failure, which was not a high-risk factor in the prior study; and malignancies, which were high-risk factors in the earlier study.

Comparative Features of Bacteremia and Fungemia in the 1970s and 1990s

During the past 20 years, numerous changes have occurred in medicine and health care. Nevertheless, several fundamental aspects of bloodstream infections have remained constant. Major examples include the continued frequency with which *S. aureus* and *E. coli* are causative agents of bacteremia; the importance of the respiratory tract, genitourinary tract, and bowel as primary foci; the association between gram-negative or polymicrobial bacteremia and septic shock; and the importance of advanced age, difficult-to-eradicate or unknown sources, malignancies and renal failure, hypotension, and absence of fever as independent predictors of a poor outcome (table 15).

The differences noted in the 1990s provide cause for concern but perhaps also for optimism (table 15). The increased proportion of blood isolates representing contamination is of concern, especially in an environment that mandates cost-effective care. The frequency of coagulase-negative staphylococcal isolation particularly is problematic, since it often is difficult for clinicians to determine the clinical significance of these bacteria. The decrease in anaerobic bacteremia and proportionate increase in fungemia have prompted some authorities to recommend changes in routine blood culture techniques [82].

Table 15. Major similarities and differences in positive blood cultures, 1975–1977 [10, 11] and 1992–1993.

Similarities	• *Staphylococcus aureus* and *Escherichia coli* most frequent etiologic agents
	• Importance of respiratory tract, genitourinary tract, and bowel as primary foci
	• Association of gram-negative and polymicrobial bacteremia with septic shock
	• Importance of age, source of infection, predisposing factors, hypotension, and absence of fever as independent predictors of poor outcome
Differences	• Increased importance of iv catheters as source of septicemia
	• Increased proportion of isolates representing contamination
	• Increased isolation of coagulase-negative staphylococci, both as contaminants and as pathogens
	• Increased frequency of *Pseudomonas aeruginosa* as a community-acquired pathogen
	• Emergence of *M. avium* complex as cause of bloodstream infection in HIV-infected patients
	• Proportionate increase in fungemia and decrease in anaerobic bacteremia
	• Decreased mortality

The most frequent source of bloodstream infections has become the intravenous catheter, and it may be expected that prosthetic materials and devices will continue to be important sources of infection. HIV infection and AIDS have allowed *M. avium* complex to become a bloodstream pathogen, and the increased frequency of community-acquired *P. aeruginosa* bacteremia also seems to be associated with HIV-infected patients [49–51].

The most optimistic finding with regard to bacteremia and fungemia in the 1990s is that mortality associated with these serious infections has decreased. The reasons for this improved outcome are not fully explained but could be related to earlier detection with use of modern blood culture systems; more sophisticated imaging methods that better elucidate primary foci of infection; the frequency of infections emanating from easily removed (iv catheters) or drained (genitourinary tract) foci; and improved antimicrobial agents and use thereof by clinicians.

Although we have shown that mortality is lower than it was 2 decades ago, bacteremia and fungemia remain serious syndromes with substantial risk. Moreover, the combination of an aging population, improved survival among immunocompromised patients and those with organ transplants, and the emergence of β-lactam-drug-resistant gram-positive and gram-negative bacteria as well as vancomycin-resistant enterococci (and possibly staphylococci in the future) [83], will continue to challenge all who care for patients with bloodstream infections.

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DEVICE AND METHOD FOR PREPARING BLOOD

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The invention relates to a preparation device (100) for treating suspension samples, especially for preparing blood cryobanks. Said device comprises an arrangement of at least two containers for receiving suspension samples, sample parts and/or additives. Said containers are formed as chambers (13 to 15, 90) having fixed walls and are arranged in a fixed manner in relation to each other. A transfer device comprising at least one connecting line (22) is provided, by which means the chambers (13 to 15) can be interconnected.

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DESCRIPTION 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.

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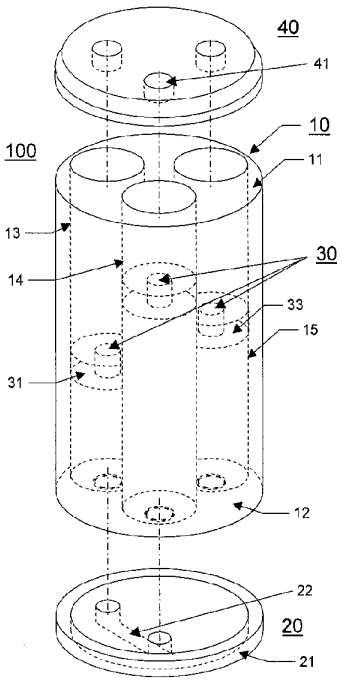
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DE 298 05 538 U1
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(54) Vorrichtung und Verfahren zur Blutpräparation

(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

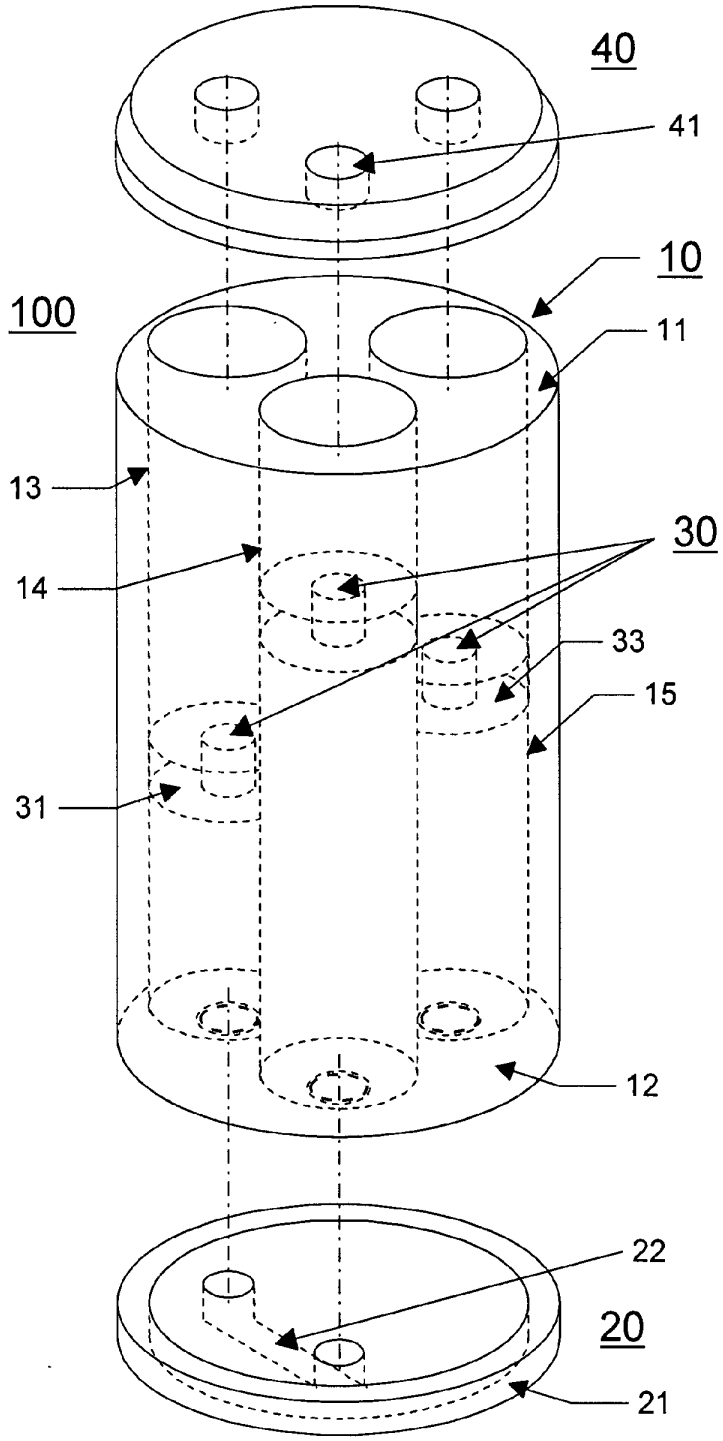


Fig. 1

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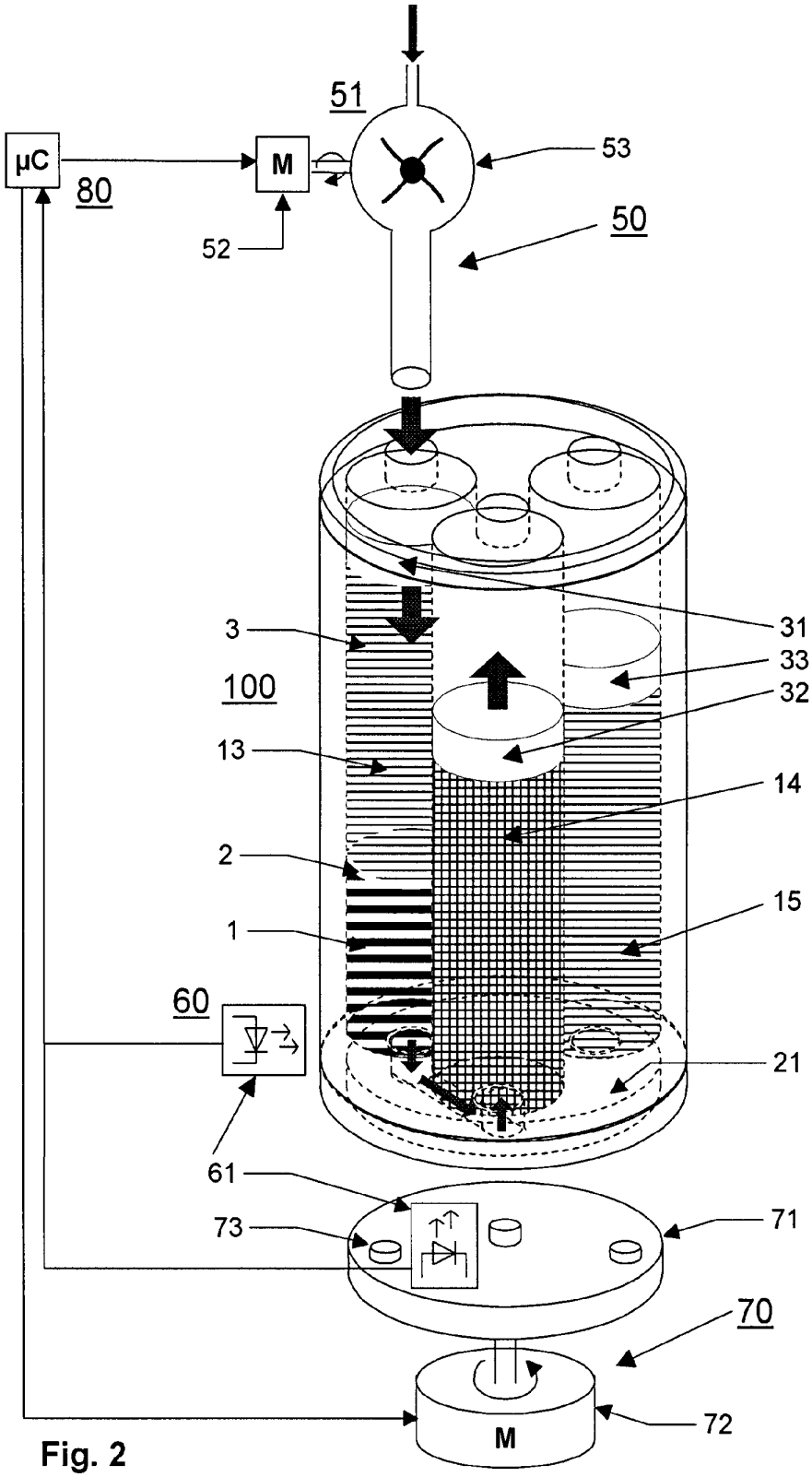


Fig. 2

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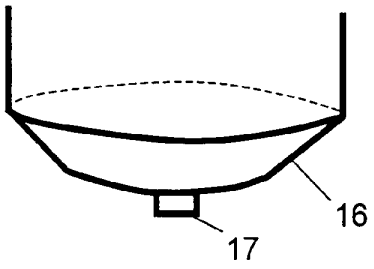


Fig. 3

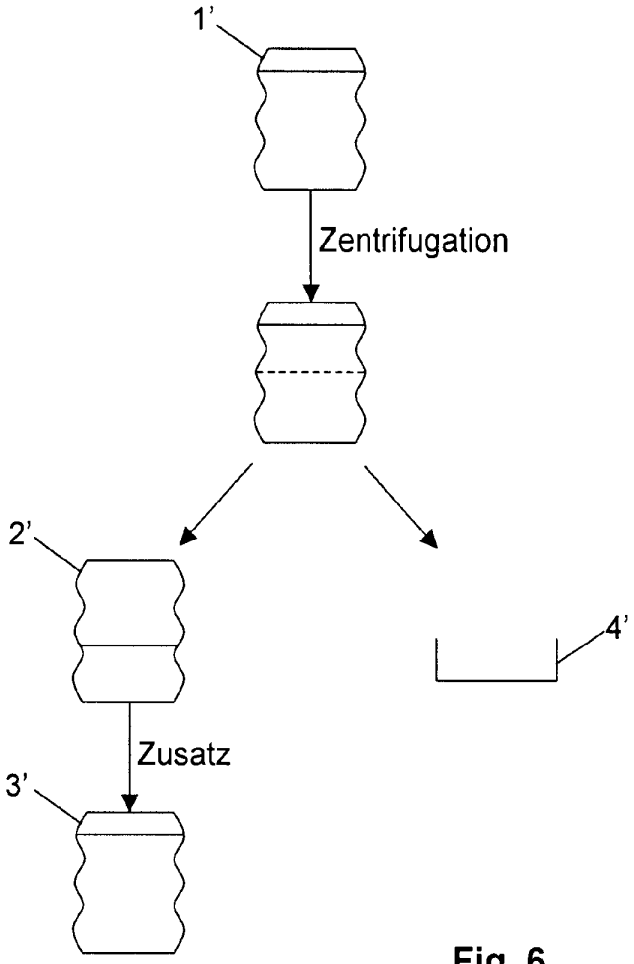
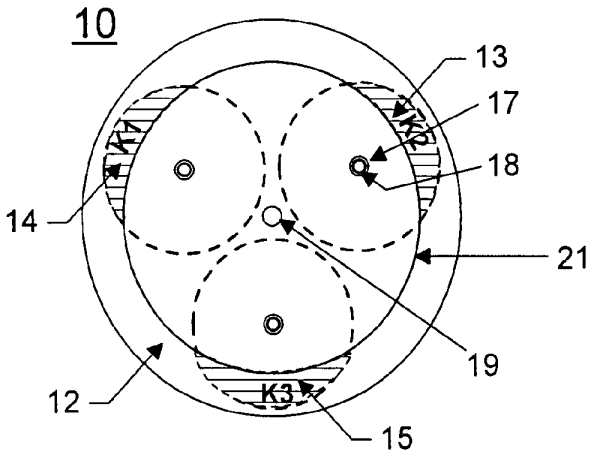
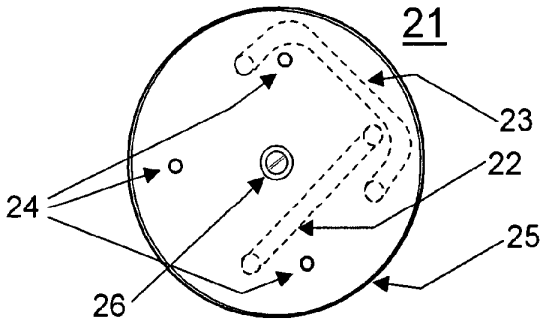


Fig. 6
(Stand der Technik)

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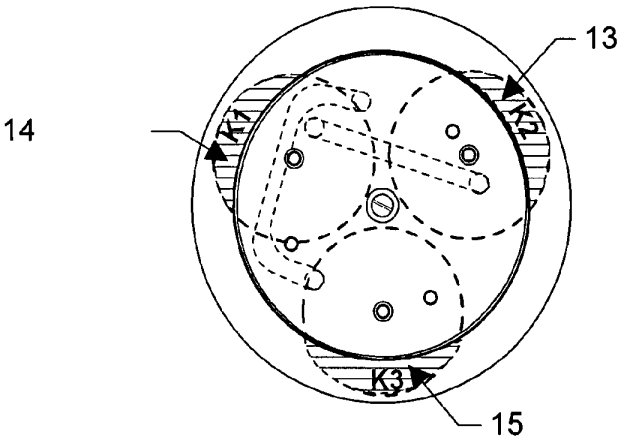


Fig. 4

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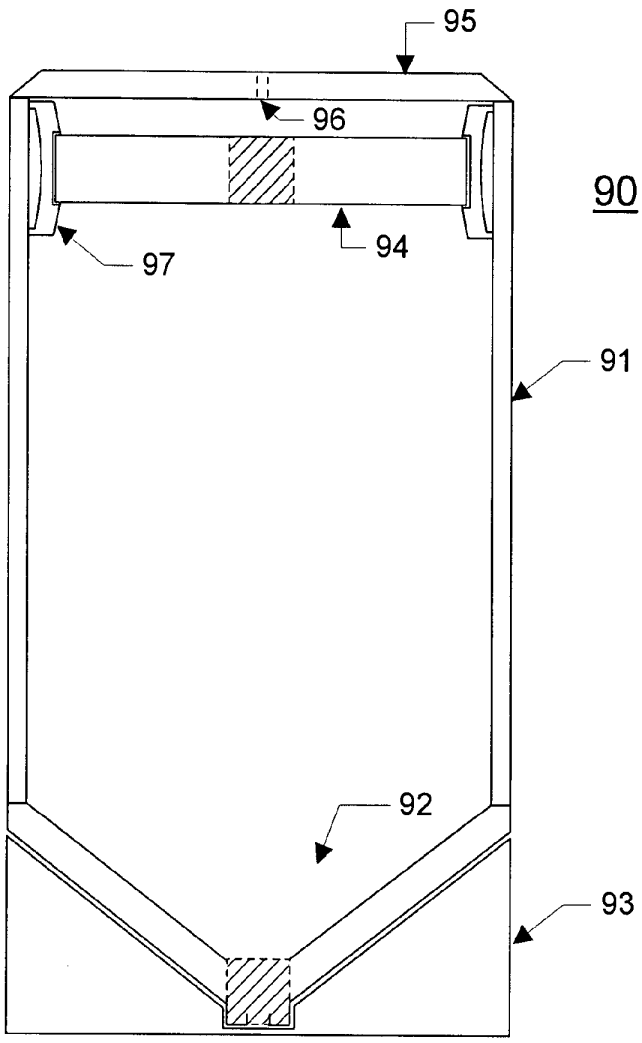


Fig. 5

Espacenet

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Compartmental body fluid collection tube.

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Abstract of EP0448795 (A2)

A compartmented body fluid specimen collection tube (10) is provided which allows the user to select a size compartment (14,16) depending upon the quantity of specimen required. Thus, the tube of the invention may be of the standard size which is much easier for the user to handle than very small tubes when taking a blood sample, but a selected size compartment (14,16) is available. The manufacturer of the tube itself may use a single moid for making tubes accommodating differing required specimen quantities, and, thereafter the vendor may select either size compartment (14,16) for imparting a vacuum and the other processing required into a final product. The invention allows the use of a single standard size laboratory equipment array for processing collected specimens of varying quantities, as well as a single standard stopper (28). Finally, reduced vacuum application or "partial draw" tubes are avoided, thus eliminating the problem of unpredictable specimen draw response because of varying atmospheric pressures at different locations of use.

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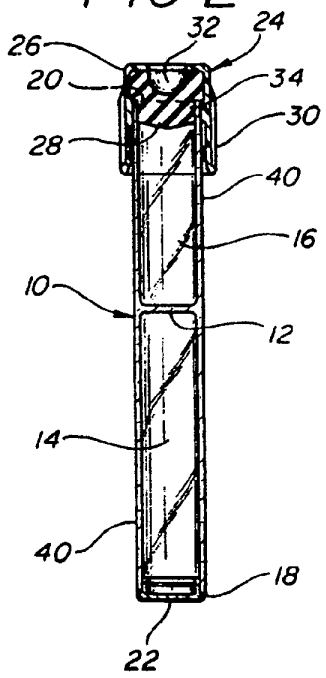
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(54) Compartmental body fluid collection tube.

(57) A compartmented body fluid specimen collection tube is provided which allows the user to select a size compartment depending upon the quantity of specimen required. Thus, the tube of the invention may be of the standard size which is much easier for the user to handle than very small tubes when taking a blood sample, but a selected size compartment is available. The manufacturer of the tube itself may use a single mold for making tubes accommodating differing required specimen quantities, and, thereafter the vendor may select either size compartment for imparting a vacuum and the other processing required into a final product. The invention allows the use of a single standard size laboratory equipment array for processing collected specimens of varying quantities, as well as a single standard stopper. Finally, reduced vacuum application or "partial draw" tubes are avoided, thus eliminating the problem of unpredictable specimen draw response because of varying atmospheric pressures at different locations of use.

FIG-2



EP 0 448 795 A2

BACKGROUND AND STATEMENT OF THE INVENTION

This invention relates to body fluid collection tubes for collecting a body fluid specimen from a patient for subsequent examination in a laboratory. More particularly, this invention relates to a blood collection tube for taking such specimens in which the tube has imparted thereto an internal vacuum with the vacuum being utilized for drawing the blood specimen from the vein of a patient.

Attempts have been made to overcome the problem of proliferation of a number of tubes for taking a plurality of specimens from a single venous entry into a patient. For example, Japanese Patent Application No. 62-51238, filed March 6, 1987 teaches a device in which a tube is divided axially into two chambers for taking two blood specimens simultaneously. However, there is no recognition for arranging different size compartments for taking different separate specimens of different size to accommodate subsequent laboratory testing of those specimens.

Other prior art arrangements, such as that taught in U.S. Patent 3,894,951, for example, provide for compartmentalized blood collection tubes in which the compartments have fluid connections for subsequent separation of a single blood sample into separate components.

In taking such specimens, differing quantities or volumes of specimens are required for certain applications. For this reason, larger and smaller tubes are manufactured for this purpose. As an alternative to making larger and smaller tubes, so-called "partial draw" tubes are provided in which the vacuum imparted to the tube is varied in order to accommodate differing quantities of specimen as required. All of these variations increase the cost of collecting blood specimens, and when it is understood that literally billions of such tubes are used and discarded after a single use each year the costs become substantial for medical applications.

This invention overcomes this problem by using a conventionally sized tube of, for example, 6cc in volume and incorporates an integral divider substantially centrally of the length of the tube to provide two compartments of differing size. Such compartments may be, for example, 2cc and 3cc. Thus, the manufacturer, rather than having to use two separate molds and two separate production lines, may manufacture a single tube having a selection of a 2cc and a 3cc compartment or chamber. Thereafter, the user or vendor may utilize or select one of the sizes of compartment and impart a vacuum thereto and place a stopper in the open end of the compartment size selected. The remaining compartment or chamber not being utilized for this particular series of tubes has a plug for closing the open end of the non-utilized chamber or compartment.

Conventional blood collection tubes have only one chamber, and volume in those conventional tubes is varied by using either larger or smaller diameter tubes, taller or shorter length tubes or varying the degree of vacuum imparted. As will be understood by practitioners-in-the-art, larger and smaller diameter tubes require specific dimensioned stoppers for accommodating those various sizes. Moreover, taller and shorter tubes require different packaging to accommodate tube length. If an accommodation is made to utilizing only a single size tube and imparting a partial vacuum for subsequent use in which only a small quantity of specimen is required in relatively large tubes, there is inconsistent draw over different areas of use because of differing atmospheric pressure gradients.

Finally, the users of tubes of different length and diameter must have varying size equipment, such as centrifuges, tube racks and like supporting arrangements to accommodate the varying sizes of tubes being utilized for collecting differing quantities of body fluid specimens for different applications.

With this invention, by contrast, a single size tube, as noted above is utilized. For this reason, the user, in the sometimes tense environment of taking a blood specimen from an individual, has a relatively large tube for handling during the collection activity Nevertheless the tube has a smaller compartment; for accommodating the actual size specimen required. Moreover, because only a single size tube relative to diameter is being utilized with the invention here, a single stopper size is required rather than a plurality of stopper sizes of differing diameters to accommodate differing diametered tubes. This reduces manufacturing requirements as well as storage requirements for such a variety of stopper sizes.

Moreover, because of the large size tubes having small compartmentalized areas, no "partial draw" vacuum applications are required. This eliminates the problem of inconsistency depending upon the atmospheric pressure gradients over many areas of use of such tubes. Finally, because of the uniformity of size of the tube, the hospital or clinical laboratory only needs to have one size equipment necessary for handling the tubes of a standard size.

A further feature of the invention may be the use of both compartments of a single tube by the phlebotomist. That is, the vendor or manufacturer of the tubes may, for example, impart vacuum to both a 3cc and a 2cc compartment or chamber in a single tube and place stoppers for sealing and

maintaining the vacuum. Thereafter, the phlebotomist, in requiring two separate blood sample volumes for different tests subsequently can first draw blood into one chamber followed by inversion of the tube and collection of blood into the second chamber. Two blood samples would then be contained in a single tube for subsequent examination in the clinical laboratory, and with only one venous entry.

Other objects and advantages of this invention will be apparent from the following description, the accompanying drawings and the appended claims.

DESCRIPTION OF THE DRAWINGS

Fig. 1 is longitudinal sectional view of the compartmentalized blood collection tube of the invention;

Fig. 2 is a longitudinal sectional view of one embodiment of the invention wherein a vacuum has been imparted to the smaller chamber or compartment of the tube of the invention and showing the sealing stopper arrangement for such a tube, together with a plug for the unused chamber;

Fig. 3 is a longitudinal sectional view of the tube of the invention reversed in its application from that shown in Fig. 2;

Fig. 4 is an enlarged partial cross-sectional view of one open end of the tube of the invention showing the mating configuration of a sealing plug applied to the open end for closing off the non-utilized chamber or compartment of the tube of the invention;

Fig. 5 is a longitudinal sectional view of a blood sample tube holder for taking a blood sample from a vein of a patient with the tube of the invention inserted therein; and

Fig. 6 is a longitudinal sectional view of a tube similar to that shown in Fig. 1, but both chambers being closed with a stopper closure for use in evacuating two chambers for collecting two specimens sequentially.

DETAILED DESCRIPTION OF THE INVENTION

Referring to the drawings in which like reference characters refer to like parts throughout the several views thereof, Fig. 1 illustrates the invention in the form of a conventionally sized blood collection tube compartmentalized in its formation to provide two chambers or compartments of differing size to accommodate differing blood sample requirements.

In Fig. 1, the device 10 is an elongated tube with walls 40 and having open ends 18, 20 at each end thereof. As can be seen in Fig. 1, tube 10 is divided by a wall 12 into compartments or chambers 14 and 16. Also, as will be seen in Fig. 1, chamber 14 is larger than chamber 16. For example, in a 6cc tube, chamber 14 may be, for example, 3cc in volume while chamber 16 may be 2cc in volume.

It will be understood that the volume amounts may be varied as use requirements dictate. Tube 10 may be comprised of a thermoplastic resin material, for example, formed in a mold to provide wall 12 integrally joined to wall 40 of tube 10.

Referring now to Fig. 2, tube 10 is shown in a prepared form for use by a vendor. In this case, the smaller dimensioned chamber 16 has had, for example, a vacuum applied thereto with a subsequent insertion of a stopper assembly 24 for maintaining the vacuum in chamber 16. The assembly 24 includes a rubber stopper for closing the open end, 20 of the tube, assembly 10. That is, the outer surface of lower portion of stopper 28 seals against the internal surface of walls 40 of the upper end of tube 10. The assembly 24 includes a plastic cap 26 connected to and surrounding elastomer stopper 28. This serves to accommodate removal of stopper 28 in a simple fashion, when required, to obtain access to the collected sample in chamber 16.

Stopper 28 includes a well 32 formed in the top surface thereof which has the purpose of reducing the vertical extent of stopper 28 in the center portion thereof to provide a diaphragm 34 of vertically smaller dimension through stopper 28 for receiving a needle such as needle 52 and the point 54 thereof, as shown in Fig. 5. The plastic portion 26 of stopper 24 assembly includes outer ridges 34 to provide an easier grip of the assembly 24 for removal thereof from the evacuated chamber 16, when required.

Referring to Fig. 4, the open end 18 of chamber 14, which in this case is not being utilized for fluid collection includes a plug 22 for stabilizing the open end 18 of the tube assembly 10 for subsequent use of the tube or for storing the tube prior to use.

In Fig. 4, an enlarged view of the open end 18 or 20 is shown to accommodate the snap-fit arrangement of plug 22 in the open end 18 or 20 of chamber 14 or 16, as the case may be, when they are not being utilized in a particular tube 10 assembly. That is, the lower end of wall 40 may include an annular indentation 36 for receiving in snap-fit engagement an annular abutment, 38 on plug 22.

Referring now to Fig. 3, a tube 10 is shown reversed from the Fig. 2 showing for accommodating use of the 3cc and/or larger compartment 14 as desired by the user. In this case, stopper assembly 24 closes the open end 18 rather than 20, while the open end 20 is closed with a plug 22. It will be understood by practitioners-in-the-art that both compartments or chambers 14, 16 may be utilized in a single tube 10 by imparting a vacuum to both chambers and using a stopper closure assembly

24 for closing both open ends 18 and 20. In such cases, a plug 22 is not utilized.

Such an arrangement is shown in Fig. 6 wherein a tube 60 similar to tube 10 is shown with chambers 64, 66 divided by wall 62. Tube 60 includes two open ends 68 and 70. In this case, a stopper assembly 24 is applied to both open ends after application of vacuum to chambers 64, 68, respectively. As discussed above, in such an application, the user collects two different volumes of specimen from a patient as required for subsequent testing purposes.

In use, the assembly 10 of the invention is inserted into a blood collection needle holder such as 42 shown in Fig. 5. Holders 42, for example, include at the closed end thereof a hub 46 with internal screw threads 48 for accommodating the screw threads of a needle holder hub 50. Thus, a plurality of needle holder hubs 50 may be, sequentially, screwed into hub 46 of needle holder 42 for repeated use. The needle 52 includes a sharpened end 56 which is inserted into the vein of a patient for collecting a blood Specimen.

Subsequent to insertion of the needle 56 into the vein of a patient, the laboratory technician, doctor or nurse inserts the tube assembly 10 into the blood collection holder 42 at the open end 43 thereof. In doing so, the technician holds onto the holder 42 utilizing the flange 44. Subsequently, the tube 10 is moved forward toward the closed end of the holder 42 until such time as the negative pressure needle point 54 passes through stopper 28. When this happens, access to the vacuum in chamber 16 takes place and the vacuum draws blood from the patient's vein through the needle 52 into chamber 16.

As will be understood by practitioners-in-the-art, the smaller chamber 16 may be, for example, of a volume of 2ccs which is all that is required for certain subsequent examinations of the specimen in the lab. A tube such as tube 60 shown in Fig. 6 may be used in holder 42 instead of tube 10. With such an arrangement, the double-ended needle assembly would include a sealing valve sleeve well known in the art so that the tube 60 may be pulled off needle point 54, and reversed for inserting the needle point 54 into the subsequent stopper 28 without blood loss, for collecting a second blood sample in chamber 66, for example.

Alternatively, the technician may use a standard size blood collection container and collect a subsequent larger blood sample, as required from the single insertion of point 56 of needle 52 in the patient's vein all as will be understood by the practitioner-in-the-art.

The blood collection tube of the invention may be comprised, preferably, from a clear molded thermoplastic material such as polyethylene, for example, or glass. Other materials which may be used, as will be appreciated by practitioners-in-the-art include various other thermoplastics such as polypropylene, polyethylene terephthalate, and polyvinyl chloride.

The evacuated chambers utilized for collection in the device of the invention here may have incorporated therein materials for reaction with the specimen being collected for providing a proper response to the collected specimen for subsequent examination in the clinical laboratory. The stopper may be comprised of an elastomer appropriate for providing the sealing required to maintain the imparted vacuum in the chamber selected for subsequent use by the laboratory technician. The plastic cover portion 26 of stopper assembly 24 may be comprised of polyethylene or other thermoplastic which may be molded into the proper shape for the assembly of the invention.

Whereas, as discussed above, specific embodiments of associated stoppers and caps have been shown, it should be understood that it is within the purview of this invention to provide other forms of closures for blood collection tubes of the kind discussed herein.

It will be understood that the invention here is most appropriate for medical applications because of the substantial reduced cost in accommodating a variety of different requirements for a body fluid specimen collection, and for reducing the number of molds required for providing an assembly which is nevertheless, much easier to handle than the miniaturized collection tubes presently being utilized for small volume specimen collection. Moreover, the arrangement herein eliminates the need for the application of "partial draw" tubes and the inconsistency apparent with the use of such partial draw tubes.

While the forms of apparatus herein described constitute preferred embodiments of the invention, it is to be understood that the invention is not limited to these precise forms of apparatus and that changes may be made therein without departing from the scope of the invention which is defined in the appended claims.

Claims

1. A blood collection tube; comprising
   (a) a tube body;
   (b) said tube body comprised of walls formed as a cylinder to define a tube body chamber;
   (c) said tube body chamber having a first open end at one end of said tube body chamber and a second open end at the end of said tube body chamber opposite said first open end;

(d) a divider wall positioned between said first and second open ends;
(e) said divider wall dividing said tube body chamber into a first and a second compartment; and
(f) said divider wall being formed integrally as one piece with said cylindrical tube body walls.

2. The blood collection tube of Claim 1, further comprising
(a) said first and second compartments being of different volume capacity.

3. The blood collection tube of Claim 1 further comprising
(a) a stopper closing one of said first and second open ends; and
(b) a plug closing the other of said open ends not closed by said stopper.

4. The blood collection tube of Claim 3, further comprising
(a) said compartment with the open end closed by said stopper being evacuated.

5. The blood collection tube of Claim 3, further comprising said stopper being comprised of
(a) a first elastomeric portion inserted into said open end in sealing engagement therewith;
(b) a plastic portion fitted over and surrounding said elastomeric portion;
(c) said plastic portion encompassing said tubular walls adjacent said open end into which said stopper is inserted;
(d) the top of said plastic portion having an opening adjacent the axis thereof for providing needle access to said elastomeric portion; and
(e) cooperating abutment means on said elastomeric portion and said plastic portion for holding said elastomeric portion and said plastic portion together.

6. The blood collection tube of Claim 3, further comprising
(a) said tube walls and said divider wall are comprised of a material selected from the group consisting of polyethylene, polypropylene, polyethylene terephthalate, polyvinyl chloride and glass.

7. A blood collection tube; comprising
(a) a tube body;
(b) said tube body comprised of walls formed as a cylinder to define a tube body chamber;
(c) said tube body chamber having a first open end at one end of said tube body chamber and a second open end at the end of said tube body chamber opposite said first open end;
(d) a divider wall positioned between said first and second open ends;
(e) said divider wall dividing said tube body chamber into a first and a second compartment;
(f) said divider wall being formed integrally as one piece with said cylindrical tube body walls;
(g) said first and second compartments being of different volume capacity;
(h) a first stopper closing said first open end; and
(i) a second stopper closing said second open end.

8. The blood collection tube of Claim 7, further comprising
(a) both said first and said second compartments being evacuated.

9. The blood collection tube of Claim 7, further comprising each of said first and second stoppers comprised of
(a) a first elastomeric portion inserted into said open end in sealing engagement therewith;
(b) a plastic portion fitted over and surrounding said elastomeric portion;
(c) said plastic portion encompassing said tubular walls adjacent said open end into which said stopper is inserted;
(d) the top of said plastic portion having an opening adjacent the axis thereof for providing needle access to said elastomeric portion; and
(e) cooperating abutment means on said elastomeric portion and said plastic portion for holding said elastomeric portion and said plastic portion together.

10. The blood collection tube of Claim 7, further comprising
(a) said tube walls and said divider wall are comprised of a material selected from the group consisting of polyethylene, polypropylene, polyethylene terephthalate, polyvinyl chloride and glass..

FIG-1

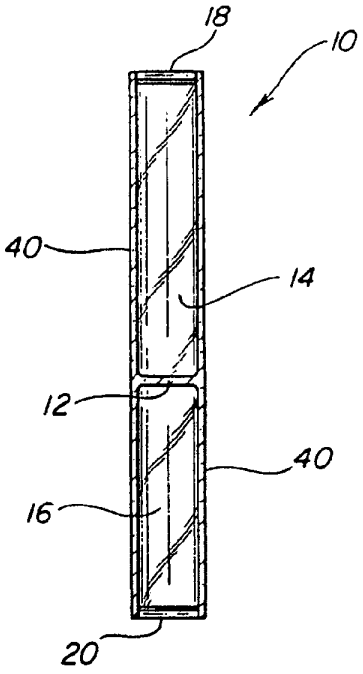


FIG-2

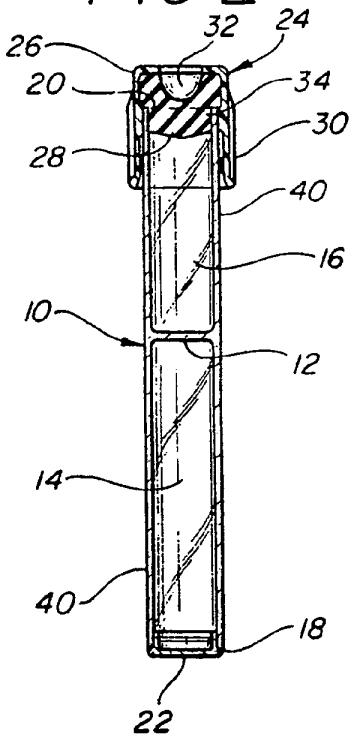


FIG-3

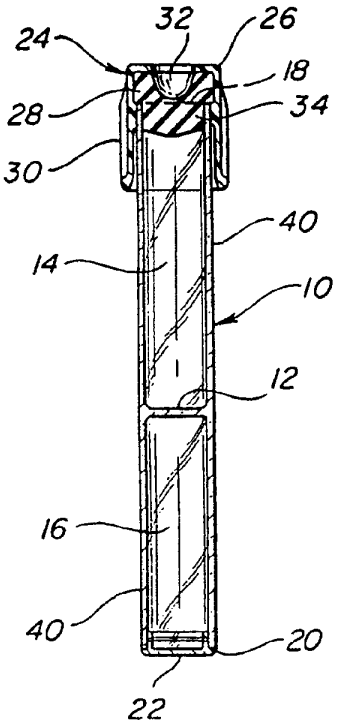


FIG-4

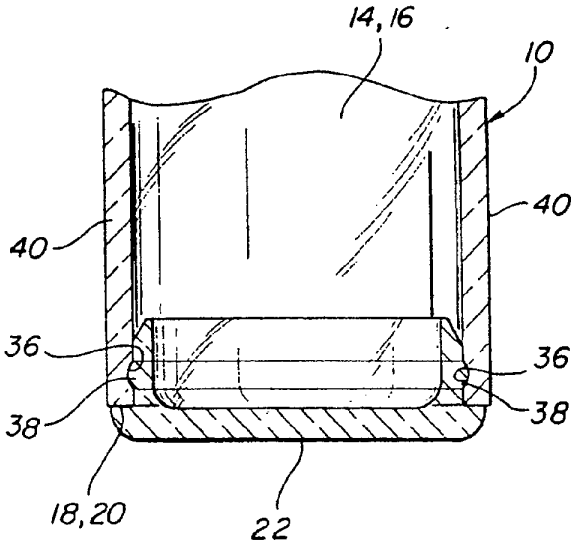


FIG-5

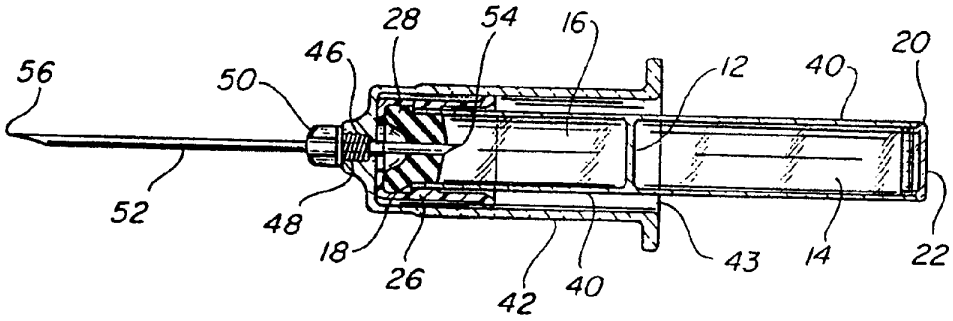
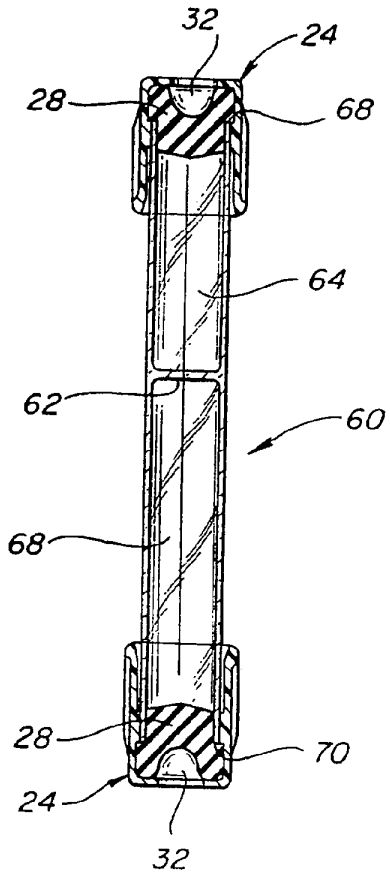

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FIG-6


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Literature display help

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[Examiner] Hirokatsu Shimizu

(56) [Reference]
[Reference] Japanese Patent Application Laid-Open No. 58-025146 (JP, A) [Reference] Japanese Patent Application Laid-Open No. 58-067238 (JP, A) [Reference] Japanese Patent Application Laid- Open No. 2012-016496 (JP, A) [Reference] JP-A-57-089869 (JP, A) [Reference] National Publication of International Patent Application No. 09-504726 (JP, A) [Reference] JP-A-02-224742 (JP, A) [Reference] United States Patent No. 04207870 (US, A)

(58) [Investigated field] (Int.Cl., DB name)
A61B 5/153-5/154

The scope of the claims open ----

(57) [Claims]
[Claim 1]
A blood sample optimization system, a blood
collection system,
a patient configured for venipuncture of a patient to allow withdrawal of a patient blood sample. a needle,
a blood collection path connected to said patient needle and configured to carry said blood sample, and a
sample configured to receive an evacuated blood collection tube for collecting and contain

g a subsequent portion of said blood sample. a blood isolation
device
connected along the blood collection path between the patient needle and the sample needl e, the inlet port
configured to receive the blood sample
; An isolation chamber connected to the inlet port and having a vent including an air perme able blood barrier for receiving said initial volume of blood sample and isolating at least a first portion of said initial volume of blood sample. a configured isolation chamber and a samplin g flow path having a proximal end connected to the inlet port and configured to receive a s ubsequent portion of the blood sample; the passageway and the inlet port are connected to th e blood sample

bypassing the isolation chamber and a first portion of the blood sample isolated in the isolatio n chamber and connecting the subsequent portion of the blood sample to the distal end of the sampling channel. an outlet port configured to direct a subsequent portion of the blood sampl e into the evacuated blood collection tube, the inlet port, the outlet port, the isolation chambe r and
the
blood sample optimization system, further comprising a housing containing and defining a sa mpling flow path; and a blood isolation device .
2.
The isolation chamber of the blood isolation device is at ambient air pressure, and wherein t he isolation chamber receives a first portion of the blood sample by patient blood pressure ov ercoming the ambient air pressure within the isolation chamber. 2. The blood sample optimiza tion system of claim 1. 3. The blood of claim 2, wherein said sample needle includes a seal p ierced by said evacuated blood collection tube to open access to said patient needle via said bl ood collection path and said sampling flow path
.
Sample optimization system.
4. The
blood isolation device of claim 3, wherein said sampling channel of said blood isolation devic e permits a subsequent portion of said blood sample to enter said inlet port under vacuum pre ssure by said evacuated blood collection tube opening said sample needle. blood sample opti mization system.
5.
The blood sample optimization system of claim 1, wherein said air permeable blood barrier o f said blood isolation device comprises an air permeable material that seals upon contact wit

blood.

[Claim 6]

3. The blood sample optimization system of Claim 1, wherein the blood collection path of the blood collection system comprises a tube.

7. A

patient needle configured to enable removal of a blood sample from a patient and a sealed s ample needle, wherein the sample needle is unsealed and the blood sample adapted to be re moved from the patient. a blood isolation device connected to a blood collection system comp rising a sample needle adapted to receive an evacuated blood collection tube

for receiving a blood sample from a patient connected to said patient needle; an isolation ch amber having a configured inlet port,

an outlet port connected to the inlet port, and

a vent connected to the inlet port and including an air permeable blood barrier, wherein the sample needle is connected to the vacuum an isolation chamber configured to receive and isol ate a first portion of the blood sample before it is opened by a blood vessel; and a proximal e nd connected to the inlet port for receiving subsequent portions of the blood sample

. a sampling channel configured to receive said isolation chamber

,

said sampling channel and said inlet port are adapted to receive said blood sample with subs equent portions of said blood sample isolated within said isolation chamber and said isolation chamber. and to direct subsequent portions of the blood sample to the outlet port connected t o the distal end of the sampling channel, said inlet port, said outlet

port , a blood isolation device, further comprising a housing containing and defining said isol ation chamber and said sampling channel.

[Claim 8]

8. The blood isolation device of claim 7, wherein the isolation chamber is at ambient air pres sure and the isolation chamber receives an initial portion of the blood sample by patient blood pressure overcoming the ambient air pressure within the isolation chamber.

[Claim 9]

8. The blood isolation device of Claim 7, wherein the air permeable blood barrier comprises a n air permeable material that seals upon contact with blood.

10.

The blood isolation device of claim 7, wherein said isolation chamber includes an isolation ch annel defined within said housing.

11.

A blood sample optimization system, a blood

collection system, comprising:

a patient needle configured for venipuncture of a patient to enable withdrawal of a patient blood sample; and a patient

needle connected to the patient needle. a blood collection system comprising: a blood colle ction path configured to carry said blood sample; and a sample needle

configured to receive an evacuated blood collection tube for withdrawing and containing a s ubsequent portion of said blood sample; A blood isolation device connected along the blood co llection path between a patient needle and the sample needle, the inlet port configured to rec eive the blood sample, and a sample needle of the inlet port and the blood collection syste m . and an isolation chamber having a vent connected to the inlet port and including an air permeable blood barrier for receiving the initial volume of the blood sample and for removi ng the initial volume of the blood sample. an isolation chamber configured to isolate at least a first portion ;

a sampling channel having a proximal end connected to said inlet port and configured to re ceive a subsequent portion of said blood sample, said isolation chamber, said sampling channe l and said inlet port being connected to said blood
sample

; allowing a subsequent portion of the blood sample to bypass the isolation chamber and a first portion of the blood sample isolated within the isolation chamber and directing the subse quent portion of the blood sample to a distal end of the sampling channel; and a blood isolatio n device configured to direct the outlet port connected to a

blood vessel and further comprising a housing containing and defining the inlet port, the ou tlet port, the isolation chamber and the sampling flow path.
Sample optimization system.
12.
The isolation chamber of the blood isolation device is at ambient air pressure, and wherein t he isolation chamber receives a first portion of the blood sample by patient blood pressure ov ercoming the ambient air pressure within the isolation chamber. 12. The blood sample optimiz ation system according to 11.
13.
The blood sample optimization system of claim 11, wherein said sample needle includes a se al pierced by said evacuated blood collection tube to open access to said patient needle via sai d blood collection pathway.
14.
The blood sample optimization system of claim 11, wherein said air permeable blood barrier of said blood isolation device comprises an air permeable material that seals upon contact wit h blood.

15.

The blood sample optimization system of claim 11, wherein said isolation chamber includes a n isolation flow path defined within said housing.

[Claim 16]

12. The blood sample optimization system of Claim 11, wherein the blood collection path of t he blood collection system includes a tube.

detailed description open —

[Detailed description of the invention]

[Background art]

CROSS

-REFERENCE TO RELATED APPLICATIONS

This application is based on US Nonprovisional Application Serial No. 15/140,443, entitled "B lood Sample Optimization System and Blood Contaminant Isolation Apparatus and Method," fil ed April 27, 2016. and U.S. nonprovisional application Ser. and both of these U.S. nonprovisio nal applications are U.S. Provisional Patent Application Serial No. 62/196,797, entitled "Blood Culture Improvement Systems and Methods," filed on Jul. 24, 2015, dated Oct. 7, 2015; U.S. Provisional Application No. 62/238,636, entitled "Blood Isolation System for Clean Blood Colle ction," filed on April 4, 2016, and "Blood Sample Optimization System and Blood Contaminant Isolation Device and No. 62/318,194 entitled "Methods", the disclosure of which is hereby inc orporated by reference in its entirety.

Bacteremia

is the presence of microorganisms in the blood. Sepsis, on the other hand, is bacteremia wit h clinical symptoms and signs such as fever, tachycardia, tachypnea and hypotension. Bactere mia and sepsis are associated with high mortality, hospitalization incidence and length of stay and associated costs. Many bacteremia, sepsis, fungemia, and other pathogens do occur withi n hospitals or other medical facilities, and catheters and venipunctures are sources of contami nation as potential carriers of these pathogens.

[0003]

Blood cultures are the standard test used to detect microbial pathogens associated with bact eremia and sepsis in the blood of patients. The term blood culture refers to a single venipunct ure from a peripheral site or central or arterial line in which blood is inoculated into one or mo re blood culture bottles or vessels. One bottle is considered one blood culture and two or mor e are considered a set. Multiple sets are obtained from multiple venipunctures and are associa ted with different sites in the patient.

[0004]

Although these methods enable microbial identification and susceptibility testing, which are important factors in the management of sepsis, their lack of rapid results and low sensitivity to nasty pathogens pose challenges for improvement. This has led to the development of refined systems and adjunctive molecular or proteomics tests.

[0005]

The collection of blood samples for blood culture is an important component of modern patient care, both positively impacting patient outcome by providing an accurate diagnosis and eliminating unnecessary antimicrobial therapy. It can also adversely affect outcomes by prolonging morbidity, lengthening hospital stays, and increasing costs.

One

consequence of blood culture collection is contamination. Contamination of blood cultures can lead to false positive culture results and/or significantly increased healthcare-related costs. Sources of blood culture contamination include inadequate skin disinfection, inadequate collection tube disinfection, and contamination of the initial blood draw, which can skew results.

[0007]

Blood culture collection kits generally include "butterfly" sets, infusion sets, or other types of venipuncture devices provided by companies such as BD, Smith, and B.Brown, as well as aerobic and anaerobic blood culture bottles. Consists of a bottle and A variety of different bottles are also available depending on inspection requirements. These bottles are specially designed to optimize the collection of both aerobic and anaerobic organisms. In conventional kits, the bottle used is commonly known as a "vacutainer", which is used to create a vacuum inside the tube to facilitate the collection of a predetermined amount of liquid, such as blood. A blood collection tube formed from a sterile glass or plastic tube with a lid that is evacuated to a vacuum.

[0008]

False positive blood cultures are generally the result of poor sampling techniques. They cause antibiotics to be used when they are not needed, increasing hospital costs and patient anxiety. Blood cultures are taken from a needle prick into the skin, after which a Vacutainer® is attached to take a sample of blood. Contamination can result from improper or incomplete disinfection of the puncture site and the surrounding skin area. It can also result from the piercing of the skin by the needle during insertion, which draws pierced skin cells and associated contaminants into the sample.

[0009]

Blood flow through a hypodermic needle is laminar, which causes a flow velocity gradient across the flow tube when a pressure drop is applied across the hypodermic needle. Strong aspiration of blood or use of a very small hypodermic needle can cause lysis and release of potassium from red blood cells, thereby making the blood sample abnormal.

[0010]

In another example, some patients have delicate veins that are subject to pressure drops or vacuums, such as those exerted by the plunger of a syringe that is withdrawn too rapidly, esp ecially for the patient's condition. can collapse under Such venous collapse is dangerous and v ery difficult to control because such a condition cannot be known in advance. Various strateg ies have been implemented to reduce the contamination rate of blood cultures, such as staff t raining in sterile collection techniques, feedback on contamination rates, and the introduction of blood culture collection kits

.

Skin antisepsis can reduce contamination concerns, but more than 20% of skin microbes are l ocated deep in the dermis and are not affected by antisepsis. Changing needles prior to bottle inoculation is not recommended as it increases the risk of needlestick injuries without reducin g contamination rates.

[0012]

Some conventional systems and techniques for reducing contamination of blood cultures inv olve discarding the initial aliquot of blood drawn from central venous catheters, venous punctu res and other vascular access systems. However, these systems either require the user to me chanically manipulate the intravascular device or require a complex series of steps that are dif ficult to ensure.

SUMMARY OF THE INVENTION

[

0013]

The present specification presents systems and methods for reducing blood culture contamin ation, cell lysis, and venous collapse. In some implementations, the systems and methods can eliminate variability in user disinfection and also eliminate the risk of skin cells entering blood culture samples. The systems and methods disclosed herein potentially indicate when to attac h a Vacutainer® or other blood collection device (i.e., a syringe) to obtain a contaminant-free blood sample. , does not require changes to existing clinical processes. In some implementat ions of the systems and methods disclosed herein, blood sampling is accomplished passively t hrough the use of the patient's own blood pressure, thereby reducing the risk of venous collap se and reducing current practice

.

eliminates further user steps beyond The system and method can be adapted to suit short-pat h direct puncture or butterfly venipuncture systems. It can also be used with samples taken t hrough a catheter. Means

for Solving the Problems

In one aspect, a blood isolation device is presented. A blood isolation device includes an inlet port and an outlet port. The blood isolation device further includes an isolation chamber conne cted to the inlet port, the isolation chamber having a vent including an air permeable blood b

rrier. The blood isolation device has a proximal end connected with the inlet port and a distal e nd connected with the outlet port, a sampling channel
further includes

[0016]

In another aspect, a blood isolation device is described that is connected to a blood collectio n path. The blood collection path has a patient needle and a sample collection device. The blo od isolation device includes an entry port connected to the patient needle and an isolation cha mber connected to the entry port, the isolation chamber having a vent including an air perme able blood barrier. The blood isolation device further includes a sampling channel having a pro ximal end connected to the inlet port, and an outlet port connected to the distal end of the sa mpling channel and the sample collection device.

[0017]

In yet another aspect, a blood isolation device is described that interfaces with a blood collec tion system. The blood collection system includes a patient needle for allowing a blood sample to be drawn from a patient and a sample needle that is sealed and adapted to receive an evac uated blood collection tube. A blood isolation device includes an inlet port connected to a patie nt needle for receiving a blood sample from a patient. A blood isolation device is an isolation c hamber connected to an inlet port and having a vent containing an air permeable blood barrie r for receiving and receiving an initial portion of a blood sample before the sample needle is o pened by an evacuated blood collection tube. Further includes an isolating isolation chamber. The blood isolation device further includes a sampling channel having a proximal end connect ed to the inlet port for carrying a subsequent portion of the blood sample when the sample ne edle is opened by the evacuated blood collection tube. The blood isolation device further inclu des an exit port connected with the distal end of the sampling channel for carrying subsequen t portions of the blood sample to the sample needle.

[0018]

In yet another aspect, a blood sample optimization system is disclosed and described. The bl ood sample optimization system includes a blood collection system for enabling and obtaining one or more samples of a patient's blood and false positive identification of pathogens in the p atient's blood that may have been contaminated by the venipuncture process. a blood isolatio n device for receiving and isolating an initial portion of one or more samples of the patient's bl ood that may result in

A

blood collection system includes a patient needle configured for venipuncture of a patient to enable withdrawal of a sample of the patient's blood, a blood collection channel connected to t he patient needle for carrying the blood sample, and a blood sample. and a sample needle co nfigured to receive an evacuated blood collection container for collecting and containing a sub sequent portion of the blood sample.

[0020]

In yet another aspect, a blood isolation device is disclosed and described. In some implementations, a blood isolation device can include an inlet port, an outlet port connected to the inlet port, and an isolation chamber connected to the inlet port. The isolation chamber can have a vent containing an air permeable blood barrier.

[0021]

A blood isolation device is connected along the blood collection path between the patient needle and the sample needle and includes an entry port for receiving the blood sample. A blood isolation device is an isolation chamber connected with an inlet port for receiving an initial volume of blood sample and includes an air permeable blood barrier to isolate at least a first portion of the initial volume of blood sample. Further includes an isolation chamber having a vent. The blood isolation device is a sampling channel having a proximal end connected with the inlet port, the isolation chamber isolating at least a first portion of a first volume of blood sample and a subsequent volume of blood sample into the evacuated blood collection container. It further includes a sampling channel that carries to. The blood isolation device further includes an outlet port connected to the distal end of the sampling channel for outputting a subsequent volume of the blood sample. 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 specification and drawings, and from the claims.

[Brief description of the drawing]

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

1 shows a blood sample optimization system; FIG.

FIG. 2 shows a blood sample optimization system according to an alternative implementation;

FIG. 3 shows a blood sample optimization system according to another alternative implementation;

FIG. 4 shows a blood sample optimization system according to another alternative implementation;

FIG. 5 shows a blood sample optimization system according to another alternative implementation;

FIG. 6 shows a blood sample optimization system according to an alternative implementation;

FIG. 7 is a flowchart of a method for optimizing blood culture quality;

FIG. 8A illustrates a blood isolation system for non-contaminated blood collection, according to some implementations;

FIG. 8B illustrates a blood isolation system for clean blood collection, according to some implementations.

FIG. 8C illustrates a blood isolation system for clean blood collection, according to some imp

mentations;

FIG. 8D illustrates a blood isolation system for clean blood collection, according to some implementations.

FIG. 8E illustrates a blood isolation system for clean blood collection, according to some implementations.

FIG. 9 shows a path splitter for use in a blood sequestration system;

FIG. 10A shows a blood isolation system for non-contaminated blood collection according to an alternative implementation;

FIG. 10B shows a blood isolation system for non-contaminated blood collection according to an alternative implementation;

FIG. 10C shows a blood isolation system for non-contaminated blood collection according to an alternative implementation;

FIG. 10D shows a blood isolation system for non-contaminated blood collection according to an alternative implementation;

FIG. 11A shows a blood isolation system for non-contaminated blood collection according to another alternative implementation;

FIG. 11B shows a blood isolation system for non-contaminated blood collection according to another alternative implementation;

FIG. 11C shows a blood isolation system for non-contaminated blood collection according to another alternative implementation;

FIG. 11D shows a blood isolation system for non-contaminated blood collection according to another alternative implementation;

FIG. 11E shows a blood isolation system for non-contaminated blood collection according to another alternative implementation;

FIG. 12A shows a blood sample optimization system including a blood isolation device according to yet another alternative implementation;

12B shows a blood sample optimization system including a blood isolation device according to yet another alternative implementation; FIG.

FIG. 12C shows a blood sample optimization system including a blood isolation device according to yet another alternative implementation;

FIG. 12D shows a blood sample optimization system including a blood isolation device according to yet another alternative implementation;

FIG. 13A shows blood sample optimization system 1300 according to yet another alternative implementation.

FIG. 13B shows blood sample optimization system 1300 according to yet another alternative implementation.

FIG. 13C shows blood sample optimization system 1300 according to yet another alternative implementation.

FIG. 13D shows blood sample optimization system 1300 according to yet another alternative

mplementation.

FIG. 14A illustrates yet another implementation of a blood collection system that isolates cont aminants in the initial aliquot or sample to reduce false positives in blood cultures or tests per formed on patient blood samples.

FIG. 14B illustrates yet another implementation of a blood collection system that isolates cont aminants in the initial aliquot or sample to reduce false positives in blood cultures or tests per formed on patient blood samples.

FIG. 14C shows yet another implementation of a blood collection system that isolates contami nants in the initial aliquot or sample to reduce false positives in blood cultures or tests perfor med on patient blood samples.

FIG. 14D illustrates yet another implementation of a blood collection system that isolates cont aminants in the initial aliquot or sample to reduce false positives in blood cultures or tests per formed on patient blood samples.

FIG. 14E further illustrates a blood collection system that isolates contaminants of an initial ali quot or sample to reduce false positives in blood cultures or tests performed on patient blood samples.

Show another implementation.

15A-B illustrate a blood isolation device and method of using the same according to yet anoth er implementation.

15B illustrates a blood isolation device and method of using the same according to yet anothe r implementation; FIG.

FIG. 15C illustrates a blood isolation device and method of using the same according to yet an other implementation;

FIG. 15D illustrates a blood isolation device and method of using the same according to yet an other implementation;

FIG. 15E illustrates a blood isolation device and method of using the same according to yet an other implementation;

Figure 15F illustrates a blood isolation device and method of using the same according to yet another implementation;

FIG. 15G shows a blood isolation device and method of using the same according to yet anoth er implementation;

FIG. 16A shows a blood isolation device according to yet another implementation;

16B shows a blood isolation device according to yet another implementation; FIG.

16C shows a blood isolation device according to yet another implementation; FIG.

16D shows a blood isolation device according to yet another implementation; FIG.

Figure 17A shows a lower member of a housing for a blood isolation device;

Figure 17B shows a lower member of a housing for a blood isolation device;

Figure 17C shows a lower member of a housing for a blood isolation device;

Figure 17D shows a lower member of a housing for a blood isolation device;

Figure 17E shows a lower member of a housing for a blood isolation device;
Figure 18A shows a top member of a housing for a blood isolation device;
Figure 18B shows a top member of a housing for a blood isolation device;
Figure 18C shows a top member of a housing for a blood isolation device;
Figure 18D shows a top member of a housing for a blood isolation device;
Figure 18E shows a top member of a housing for a blood isolation device;
Figure 18F shows a top member of a housing for a blood isolation device;
Figure 19A shows a blood isolation device having an upper member that mates with a lower member.
Figure 19B shows a blood isolation device having an upper member that mates with a lower member.
FIG. 20 shows a blood sample optimization system including a blood sequestration device;
Figure 21 shows a non-vented blood isolation device using a wicking material chamber.
Figure 22A shows the material composition of a filter for isolating blood in an isolation chamb er of a blood isolation device;
Figure 22B shows the material composition of a filter for isolating blood in an isolation chamb er of a blood isolation device;
FIG. 23A shows another implementation of a blood isolation device using vacuum force from a blood collection device;
Figure 23B shows another implementation of a blood isolation device using vacuum force from a blood collection device. Like numbers in the various drawings indicate like elements.
DETAILED DESCRIPTION OF THE INVENTION
[0024]
The present specification provides a blood sample optimization system that reduces or elimin ates contaminants in a blood sample taken, thereby reducing or eliminating false positive read ings in blood cultures or other tests of the blood sample taken. and methods. In some implem entations, the blood sample optimization system includes a patient needle for vascular access to the patient's bloodstream and a blood collection container such as a vacutainer or evacuate d blood collection tube or other and a blood isolation device positioned between the patient ne edle and the sample needle. The blood isolation device includes an isolation chamber for isolat ing a first aliquot of blood that may be contaminated, and after the first aliquot of blood is isol ated in the isolation chamber, the blood is isolated between the patient needle and the sample needle. A sampling flow path bypassing the isolation chamber for carrying potentially unconta minated blood may also be included.
FIG .
1 shows a blood sample optimization system according to some implementations. The syste m includes a patient needle 1 for puncturing the patient's skin to access the patient's vein and intravenous blood therein. The system may include a resealable boot 10, a luer actuated valv e, or another sampling interface.

or with a sample needle (i.e., a Vacutainer®, etc.) that can be housed within the device and i nitially sealed by a resealable boot 10, a luer-actuated valve, or another collection interface or device. It further includes a resealably sealed needle) 5 for. The resealable boot 10 can be pus hed by or around the sample needle 5 by using a Vacutainer® bottle (not shown) for collectin g the patient's blood. The system can further include a low volume chamber 30 leading to the sample needle 5, but also includes a hole or one or more channels 45 leading to the isolation chamber 55 formed by the housing 50. FIG. Isolation chamber 55 includes chambers, chann els, passages for receiving and holding an initial aliquot of patient blood, which can be of a pr edetermined or measured volume, depending on the volume of isolation chamber 55

.

, locks, or other structures. Initial blood draws generally contain or are more susceptible to co ntain microorganisms or other pathogens that cause bacteremia and sepsis than subsequent blood draws. The isolation chamber 55 can be contained within a rigid housing, can be a conta iner formed in or defined by the housing itself, or can be realized as a tube or lumen. Isolation chamber 55 can have a predetermined volume, regardless of how it is formed and implement ed. In some implementations, the predetermined volume is based on the volume of the patien t needle, i.e., ranges from a volume less than the volume of the patient needle to any volume to a volume greater than 20 times the volume of the patient needle. can be done. The predet ermined volume of isolation chamber 55 can also be set to conserve or minimize the amount of blood that is isolated and disposed of.

[0027]

Isolation chamber 55 may be formed, contained, or housed within chamber housing 50 and may be made of plastic, rubber, steel, aluminum, or other suitable material. For example, isol ation chamber 55 can be formed from flexible tubing or other elastomeric material. The isolati on chamber 55 further includes an air permeable blood barrier 20 that allows air to exit the is olation chamber 55 . As used herein, the term "air permeable blood barrier" means an air per meable but substantially blood impermeable substance, material or structure. Representative examples are hydrophobic membranes and hydrophobic coatings, hydrophilic membranes or h ydrophilic coatings in combination with hydrophobic membranes or coatings, meshes, filters, mechanical valves, antimicrobial materials, or isolation chamber 55 is blood. Any other means capable of expelling air from the isolation chamber 55 when filled with air may be included. In various exemplary embodiments, the air permeable blood barrier can be formed by one or mo re materials that allow air to pass through until it contacts liquid, such materials being air per meable. and/or completely or partially sealed to prevent or block the passage of liquids. In ot her words, the material forms an air permeable barrier prior to contact with the liquid. After c ontact with liquid, the material substantially or completely prevents further passage of air an d/or liquid.

[0028]

Holes or channels 45 can be of any desired length, cross-sectional shape or size and/or can

be formed away from low volume chamber 30 at any desired angle or orientation. The hole or channel 45 may also include a one-way flap or valve 60 that retains the first aliquot of blood sample within the isolation chamber 55 . In some particular implementations, hole or channel 45 may include a "duckbill" valve or flapper valve 60 or the like for unidirectional blood flow from low volume chamber 30 to isolation chamber 55 . Air permeable blood barrier 20 may also be constructed of a material that allows air to escape but seals upon contact with blood, thereby not allowing outside air to enter isolation chamber 55 . This seal eliminates the need for valves.

Valve 60

can be any type of valve or opening/closing mechanism. The chamber 30 is designed to retain substantially no residual blood and retains a specific volume or percentage of blood in the isolation chamber.

It can be configured to hold or pass through the member 55 . Similarly, the isolation chamber 55 may also include any type of coating, such as an antimicrobial coating, or a coating that assists in identifying and/or diagnosing components of the isolated primary blood draw. Housings 50 and 40 may be formed from any suitable material, including plastics such as acrylonitrile butadiene styrene (ABS) or other thermoplastic or polymeric materials, rubber, steel, or aluminum

.

The air permeable blood barrier 20 is activated upon contact with blood from the first draw or when the expulsion of air is stopped, or upon any combination of events and blood in the isolation chamber 55, color A donator or other signaling mechanism may be included. The air permeable barrier can also include an outer layer such as a hydrophobic membrane or cover that inhibits or prevents inadvertent or premature sealing of the filter by external fluid sources, splashes, and the like. The isolation chamber 55 can also be translucent or transparent to allow the user to visually confirm that the chamber has been filled.

[0031]

FIG. 2 shows a blood sample optimization system according to some alternative implementations. In the implementation shown in FIG. 2, an isolation chamber 55 or waste chamber surrounds the patient needle 1 and an open-ended cuff or housing is connected to the waste chamber and surrounds the sample needle housing base and housing. The patient needle 1 and the sample needle 5 are connected to each other by a boot 56 which forms a continuous blood collection flow path therethrough. Boot 56 includes a single hole or channel leading from the blood collection channel to isolation chamber 55 . The device can include multiple holes or channels in other implementations. Each hole or channel can include a one-way valve and can be sized and adapted for a predetermined amount of blood flow.

Isolation

chamber 55 contains an air permeable blood barrier. The filter may further include sensors or indicators, respectively, for sensing and/or indicating when a predetermined volume of bloc

has been collected in the isolation chamber 55 . The instructions alert the user to attach an ev acuated blood collection tube or bottle, such as a Vacutainer®, to the sample needle 5 . The h ousing for isolation chamber 55 can be of any size or shape and can include any type of mater ial to define an interior space or volume within the housing. The interior space is initially filled with air only, but can also be coated with agents or substances such as decontamination agen ts, coagulants, and the like. When the evacuated blood collection tube is attached to the samp le needle 5, blood automatically flows into the patient needle 1, through the blood collection c hannel and the sample needle 5 into the bottle. The sample needle 5 is covered by a resealabl e boot, coating or membrane that seals the sample needle when no blood collection bottle is a ttached to the sample needle.

[0033]

FIG. 3 shows a blood sample optimization system according to some alternative implementa tions. In the illustrated implementation, sample needle 5 is surrounded by a resealable boot o r membrane and is also connected to patient needle 1 . A blood flow path is formed through t he sample needle and the patient needle. The connection between the sample needle and the patient needle includes a 'T' or 'Y' connector 102 that includes a flow path, port or opening lea ding from the main blood flow path to the isolation chamber 104 .

The T or Y connector 102 includes a

flap or one-way valve and has holes sized and adapted for a predetermined flow rate of bloo d. The isolation chamber 104 can be formed from a tube or formed by a rigid housing and is i nitially filled with air. The isolation chamber 104 receives blood flowing out of the patient auto matically, ie, under pressure due to the patient's own blood pressure. The isolation chamber 1 04 preferably includes an air permeable blood barrier 106 at the distal end of the tube formin g the isolation chamber 104 and connected at the proximal end to the T or Y connector 102 . The T or Y connector 102 can branch at any desired angle for most efficient blood flow and to minimize or eliminate mixing of the initial aliquot of blood with the main blood sample. Minimi ze the interface between the openings and channels and the main blood channel

can be configured to In some alternative implementations, the sample needle can be attache d to any length of tubing whose opposite end is connected to a T or Y connector 102, as show n in FIG

.

can be done. The isolation chamber 104 can be of any shape or volume so long as the initial a liquot contains a predetermined amount of blood sample. The T or Y connector 102 can also in clude openings or channels parallel to the main blood flow channel. The air permeable blood b arrier may further include an indicator 107 or other mechanism to indicate when a predetermi ned amount of blood has been collected in the isolation chamber or when the released air has reached a certain threshold, i.e. zero. . The tube can also include a clip 109 that can be used t o pinch and prevent fluid flow through the tube. Once the air permeable blood barrier and pr imary chamber are sealed, the first aliquot of blood is confined to the isolation chamber 104

nd a vacuum blood collection tube, such as a Vacutainer® bottle, is attached to the sample ne edle to obtain a sample

.

5 is attached. The blood collection tube can be removed and the sample needle 5 resealed. An y number of subsequent blood collection tubes can be attached for additional blood draws or s amples. When all blood draws are completed, the system is discarded, leaving the first aliquot of blood trapped in isolation chamber 104 .

FIG.

5 shows a blood sample optimization system according to some alternative implementations. In the illustrated implementation, the sample needle 5 is connected by tubing to the patient n eedle. A "T" or "Y" connector 120 is added at any desired location along the tube to include an opening, port or flow path leading to isolation chamber 204, substantially as described above.

[0038]

FIG. 6 illustrates a blood sample optimization system according to some alternative impleme ntations in which an isolation chamber 304 configured as the primary collection flow path rece ives the first aliquot of blood and is provided adjacent to the blood collection flow path. show. The isolation chamber 304 can surround the blood collection channel, patient needle 1 and/or sample needle 5 . The primary collection channel may include T or Y connectors 120, or other types of openings or channels. The isolation chamber 304 includes an air permeable blood bar rier and, as described above, may also include an indicator of contact with fluid such as blood.

In some implementations, either or both of the patient needle 1 or the sample needle 5 can be replaced with luer lock male or luer lock female connectors

.

However, in various implementations, the connector at the sample needle end of the blood sa mple optimization system is first sealed and the first aliquot is transferred to an isolation cha mber pressurized with ambient air pressure and containing the air outlet of the air permeable blood barrier. Allows blood to be diverted. In this way, the system passively and automatically uses the patient's own blood pressure to overcome the ambient air pressure in the isolation c hamber, force air through the air permeable blood barrier, and replace the air in the isolation c hamber with blood.

[0040]

FIG. 7 is a flowchart of an exemplary method for optimizing blood culture quality. At 702, a c linician inserts a needle into a patient's vein. At 704, blood flows into the isolation chamber, fo rcing air within the isolation chamber out of the isolation chamber through the air permeable blood barrier. In some implementations, the volume of the isolation chamber is from less than 0.1 cubic centimeters (cc) to 5 cubic centimeters (cc) or more. The isolation chamber is sized and adapted to collect a second portion of the blood sample and other subsequent portions or a first portion of the blood sample that is more susceptible to contamination than subsequent collections. The isolation chamber has an air permeable blood barrier through which air can

e expelled by the blood expelled from the patient's veins so that such blood can be placed in a vacutainer for receiving and storing blood samples. ® or other bottle, it necessarily and auto matically flows into the isolation chamber before being drawn into or otherwise entering the b ottle.

As the isolation chamber fills, blood collects or otherwise contacts an air permeable blood ba rrier that blocks or prevents blood from passing through . At 706, once the blood contacts the entire internal surface area of the air permeable blood barrier, the air permeable blood barrier is closed and air no longer flows out or in. At 708, the clinician is provided an indication or can view the full chamber indicating that an evacuated blood collection tube, such as a Vacutainer ®, can be attached. The indicator may include visibility of the primary chamber to see if the p rimary chamber is full, eg, a blood barrier that changes color, or other indicator. Since the fill t ime of the isolation chamber may be substantially instantaneous, such an indication, if presen t, may simply be that the isolation chamber is filled. Before the evacuated blood collection tu be is attached, communication between the needle, the sampling channel, and the isolation c hamber is restricted by the sealing of the isolation chamber's blood barrier, thus allowing air t o re-enter the system through isolation

.

do not. Sealing of the communication path is accomplished by mechanical twisting or other ac tion, small hole or tortuous path, obviating the need for a separate valve or mechanical action or manipulation by the clinician. At 710, the evacuated blood collection tube is removed, a self -sealing membrane seals the sample needle, and at 712, a further subsequent evacuated bloo d collection tube can be attached. At 714, once the sample has been taken, the device is rem oved from the patient and discarded.

[0043]

Figures 8A-8E show an exemplary blood sample optimization system 800 for non-contaminat ed blood collection, according to some implementations. Blood sample optimization system 80 0 includes an entry port 802 that can be connected to tubing, a patient needle (or both), or ot her vascular or venous access device, and a first exit to isolation chamber tubing 806 and sa mple collection tubing. a path splitter 804 with a second exit to 808; One or both of isolation c hamber tube 806 and sample collection tube 808 can be formed from tubing. In some implem entations, isolation chamber tube 806 is sized to accommodate a specific amount of initial blo od sample. A sample collection tube 808 receives a blood sample once the isolation chamber t ube 806 is filled. The sample collection tube 808 can be connected to a Vacutainer® base or h ousing 810, or other blood sample collection device. Blood isolation system 800 further inclu des blood isolation device 812, which includes housing 818, shown in more detail in FIGS

.

or connected at either end to a non-contaminated sample collection tube 808 . The sampling f low path 820 can be curved through the housing 818 to better secure and stabilize the hous

g 818 in position along the clean sample collection tube 808 .

[0045]

Blood isolation device 812 further includes an isolation chamber 822 or other chamber conne cted with isolation chamber tube 806 . Isolation chamber 822 terminates in air permeable blo od barrier 824 . The air permeable blood barrier 824 can also include a coloring agent that ch anges to a different color upon full contact with blood as an indicator that a blood sample (i. e., non-contaminated blood sample) can be properly taken. . Other indicators such as small li ghts, sound generating mechanisms, etc. can be used. In some implementations, the air per meable blood barrier is positioned perpendicular to the orientation of isolation chamber 822, b ut may be positioned at any distance or orientation to conserve space and materials used for housing 818. be able to. Housing 818 and its contents can be formed from any rigid or semi-ri gid material or range of materials.

FIG.

9 illustrates a path splitter for use in, for example, blood sequestration systems such as thos e shown in FIGS. 8A-8E.

900 is shown. Path splitter 900 includes inlet port 902 , main conduit outlet port 904 and isola tion channel outlet port 906 . The entry port 902 can be connected to a main tube that is also connected to the patient needle system or directly to the patient needle. The main line outlet port 904 can be connected to a main line tube to a blood collection system, such as a Vacutai ner® base or housing, or directly to such a blood collection system. The isolation channel outl et port 906 can be connected to an isolation tube for receiving and isolating the first sample o f blood up to a measured volume or predetermined threshold. Alternatively, the isolation flow path outlet port 906 can connect to the isolation chamber. The isolation channel outlet port 90 6 is preferably angled from 20 to 70 degrees from the main conduit outlet port 904 while the main conduit outlet port 904 is preferably in line with the inlet port 902 . Once an initial blood sample of predetermined volume has been isolated in an isolation tube or isolation chamber a ccording to the mechanisms and techniques described herein, subsequent blood samples can f low into inlet port 902 and pass unobstructed. It flows out directly from the main conduit outl et port 904 . 10A-10D show blood isolation device 1000 according to another implementatio n

.

Blood isolation device 1000 includes inlet port 1002 , main outlet port 1004 , and isolation flo w port 1006 . Entry port 1002 can be connected with a patient needle or associated tubing. T he main exit port 1004 can be connected to a blood sampling device such as a Vacutainer®, a ssociated tubing, or a luer-actuated valve. An isolation flow port 1006 separates from the mai n exit port 1004 into an isolation chamber 1008 . In some implementations, isolation chamber 1008 is formed as a spiral channel within housing or other container 1001 .

[0048]

Isolation chamber 1008 is connected at its distal end to air permeable blood barrier 1010, s

bstantially as described above. Air within the isolation chamber 1008 is expelled by the first al iquot of blood directed into the isolation flow path port 1006 through the air permeable blood barrier 1010 . Once the isolation chamber 1008 is filled, further blood draws through the main exit port 1004 are accomplished and these samples are clean.

11A -

11E show blood isolation device 1100 according to another alternative implementation. Bloo d isolation device 1100 includes an inlet port 1102 similar to the inlet ports described above, a main outlet port 1104 and an isolation flow port 1106 separate from main outlet port 1104 and inlet port 1102 . The isolation flow port is connected to isolation chamber 1108 . In the i mplementation shown in FIGS. 11A-11E, the blood isolation device includes a base member 1 101 having a flow path therein that functions as an isolation chamber 1108 . The flow path ca n be formed as a tortuous path through the base member 1101 while the base member 1101 is shaped and shaped to rest on the patient's limb. A portion of isolation chamber 1108 may protrude from or near the top surface of the base member just prior to exiting air permeable blood barrier 1110 to serve as blood isolation indicator 1109

.

Indicator 1109 can be made of a transparent material or a material that changes color when i n contact with blood.

[0051]

In some implementations, the blood isolation device 1100 can include a blood collection devi ce 1120, such as a normally closed needle, Vacutainer® shield, or other collection device. Blo od collection device 1120 may be manufactured and sold with blood isolation device 1100 for efficiency and convenience so that the initial aliquot of blood that may be contaminated by the patient needle insertion process can be isolated. can. Accordingly, the blood collection device 1120 can collect and ensure a clean blood sample so as to reduce the risk of false positive tes ts.

[0052]

Figures 12A-12D show a blood sample optimization system 1200 according to yet another al ternative implementation. System 1200 includes a blood isolation device 1202 for attachment to a blood collection device 1204, such as a Vacutainer® or other collection and sampling devi ce. Blood isolation device 1202 receives an initial aliquot or volume of blood before a Vacutain er® container or vial is attached to the collection needle of blood collection device 1204 and t ransfers that initial aliquot or volume to blood isolation device 1202 . Constructed and arrange d to isolate within the isolation channel.

[0053]

In some implementations, the blood isolation device 1202 can include an inlet port 1212, a main outlet port, and an isolation flow path port. Entry port 1212 can be connected to a patie nt needle or associated tubing. The main exit port 1214 is a normally closed needle or needle to allow connection with other collection devices such as evacuated blood collection containe

or vacutainers, associated tubing, luer connectors, syringes, luer actuated valves. It can be co nnected to a device. The isolation flow port separates the isolation chamber 1218 from the ma in exit port.

[0054]

In some implementations, isolation chamber 1218 is formed as a channel within the body of isolation device 1202 . The isolation chamber 1218 can be a tortuous channel, such as a U-sh aped channel, an S-shaped channel, a spiral channel, or any other tortuous channel. Isolation device 1202 can include a housing or other enclosure and one or more channels formed therei n. As shown in FIGS. 12A and 12B, isolation device 1202 includes body 1206 and cap 1208 . One or more cavities or channels are formed in the body 1206, and the cavities or channels ar e further formed with one or more arms 1210 extending from the cap 1208, the one or more arms 1210 extending from the cavities or channels of the body 1206. A primary collection por t and a main outlet port are formed against the flow path.

[0055]

Figures 13A-13D illustrate a blood sample optimization system 1300 according to yet anothe r alternative implementation. System 1300 includes a blood isolation device 1302 for attachm ent to a blood collection device 1304, such as a Vacutainer® or other body fluid collection and sampling device. Blood isolation device 1302 receives an initial aliquot or volume of blood and receives that initial aliquot or volume of blood or other bodily fluid before a Vacutainer® conta iner or vial is attached to the collection needle of blood collection device 1304 . within the isol ation channel of the blood isolation device 1302 .

[0056]

Blood isolation device 1302 includes housing 1301 having inlet port 1314 , main outlet port 1312 , and isolation flow path port 1316 . Entry port 1314 can be connected to a patient need le or associated tubing. The main exit port 1312 is a normally closed needle or needle to allow connection with other collection devices such as evacuated blood collection containers or vacu tainers, associated tubing, luer connectors, syringes, luer actuated valves. It can be connecte d to a device. An isolation flow port 1316 separates from the main inlet port 1314 into an isol ation chamber 1318 . In the embodiment shown in FIGS. 13A-13D, isolation chamber 1318 i s formed as a cavity or chamber within housing 1301 or is formed by walls defining housing 1 301

.

The isolation chamber 1318 is a tortuous flow path such as a U-shaped flow path, an S-shape d flow path, a spiral flow path, or any other tortuous flow path defined by the cooperation and connection of the housing 1301 and the cap 1307. There can be and the cap 1307 can include protrusions 1305 that provide one or more walls or directors for the tortuous flow path within the isolation chamber 1318 . Projections 1305 from cap 1307 can be straight or curved, can b e embedded with various channels, openings or grooves, and can extend from cap 1307 at an y angle or orientation. can be done. isolation chamber 13

When the cap 1307 is connected with the housing 1301 to complete the formation of 18 , the protrusions 1305 form at least a portion of the tortuous flow path and the isolation flow forme d by the tortuous flow path within the isolation chamber 1318 . Isolate the first aliquot or volu me of blood or other bodily fluid in the tract.

Isolation chamber 1318

includes air permeable blood barrier 1310 substantially as described above. Air within the iso lation chamber 1318 is expelled through the air permeable blood barrier 1310 by the first aliq uot of blood supplied into the isolation chamber 1318 by the patient's blood pressure. Once th e isolation chamber 1318 has been filled and the air within the isolation chamber 1318 has be en expelled, a force such as a vacuum or other pressure such as provided by a blood sampling device such as a Vacutainer® is applied to the next aliquot or Until a volume of blood or fluid has been provided to withdraw, the patient's blood pressure is insufficient to drive or provide additional blood to blood isolation device 1302 , particularly outlet port 1312 . Further blood d raws can be taken through the main exit port 1312 and these samples are not contaminated a s any contaminants are sequestered in the isolation chamber 1318 along with the first aliquot of blood.

[0059]

Figures 14A-14E illustrate yet another implementation of a blood collection system 1400 that sequesters contaminants in an initial aliquot or sample to reduce false positives in blood cultur es or tests performed on patient blood samples. Blood collection system 1400 includes a bloo d isolation 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 Vacutain er® or the like. Blood isolation device 1401 includes an entry port 1402 that can be connecte d to a patient needle that is inserted into the patient's vasculature for access to and collection of a blood sample. Inlet port 1402 may also be connected to a tube or other conduit that is al so connected to a patient needle.

Inlet port 1402

defines an opening to blood isolation device 1401, which opening can be of the same cross-s ectional dimensions as a tube or other conduit connected to the patient needle or the patient needle itself. For example, the opening can be circular with a diameter of about 0.045 inch (1. 143 mm), but may be from 0.01 inch (0.254 mm) to 0.2 inch (5.08 mm) or more. can have a diameter of Blood isolation device 1401 further includes an exit port 1404 that defines an ope ning from blood isolation device 1401 and to blood sampling device 1403 . Exit port 1404 can also be connected to a tube or other conduit that is also connected to blood isolation device 1 403 . The exit port 1404 has a connector device such as an unthreaded interference or glue jo int for attachment to a variety of devices including, but not limited to, threaded caps, luer con nectors (male or female), tubing, and the like. can further include

[0061]

Blood isolation device 1401 further includes a sampling channel 1406 between inlet port 14

2 and outlet port 1404, which functions as a blood sample path once the first aliquot of blood has been isolated. Sampling channel 1406 can be a channel or conduit of any size, shape or c onfiguration. In some implementations, sampling channel 1406 has a cross-sectional area sub stantially similar to the opening of inlet port 1402 . In other implementations, sampling chann el 1406 can gradually widen from inlet port 1402 to outlet port 1404 .

Blood isolation device 1401 further includes isolation chamber 1408 , which

is connected to and separated from sampling channel 1406 at any location between inlet por t 1402 and outlet port 1404 . redirected, but preferably connected to the proximal end of sam pling channel 1406 near inlet port 1402 and from the proximal end.

separated or diverted from the The isolation chamber 1408 is initially maintained at atmosphe ric pressure and includes an air outlet 1412 at or near the distal end of the isolation chamber 1408 opposite the turning point from the sampling channel 1406 . Air outlet 1412 includes air permeable blood barrier 1412 . The air permeable blood barrier 1412 can be covered with a p rotective cover 1416, as shown in FIG. 14B. The protective cover 1416 can be sized and confi gured to prevent a user from touching the air permeable blood barrier 1412 with their fingers or other external instruments while still allowing the patient's own blood pressure to pressure the isolation chamber 1408. Allowing air to exit the air permeable blood barrier 1412 as the ai r is forced out of the isolation chamber by forcing blood into it. Protective cover 1416 can also be configured to block or prevent accidental exposure of the air permeable blood barrier to su rrounding fluids or droplets. This can be done in a variety of mechanical ways including, but n ot limited to, adding a hydrophobic membrane to the protective cover. As shown in FIGS. 14 C and 14D, the sampling channel 1406 may be cylindrical or frusto-conical in shape from a sm aller diameter to a larger diameter to minimize the possibility of lysing red blood cells

.

can. Similarly, the sampling channel 1406 is formed with a minimal amount or no sharp bends or sharp angles that could lyse red blood cells. Sampling channel 1406 splits near inlet port 1 402 through diverting path 1409 into isolation chamber 1408 . Diversion pathway 1409 can h ave any cross-sectional shape or size, but is preferably similar to the cross-sectional shape of at least a portion of inlet port 1402 .

[0064]

In some implementations, sampling channel 1406 and isolation chamber 1408 are formed b y grooves, channels, locks or other pathways formed in housing 1414 . Housing 1414 can be made of plastic, metal or other rigid or semi-rigid material. The housing 1414 can have a lowe r member that sealably mates with the upper member. One or both of the lower and upper m embers can include a sampling channel 1406 and an isolation chamber 1408 as well as a dive rting passageway 1409 , an inlet port 1402 and an outlet port 1404 . In some other implemen tations, one or more of diverting path 1409 , inlet port 1402 , and/or outlet port 1404 are at l east partially closed by a cap member connected to either end of housing 1414 . can be forme d in In some implementations, the upper and lower members and the cap member can be co

nected together by laser welding, heat sealing, gluing, snapping, screwing, bolting, or the lik e. In other implementations, some or all of the interior surfaces of the diversion pathway 140 9 and/or the isolation chamber 1408 can be coated or filled with agents or substances such as decontamination agents, coagulants, and the like. For example, when the sequestration cham ber 1408 fills and the first aliquot of blood returns to the diverting path 1409, the final volume of sequestered blood clots, creating a barrier between the sequestration chamber 1408 and th e sampling channel 1406. As such, turning path 1409 may be provided with a coagulant. 15 A-15G show a blood isolation device 1500. FIG

.

The blood isolation device 1500 includes a needle or needle that is normally closed to allow co nnection with other collection devices such as evacuated blood collection containers or vacutai ners, associated tubing, luer connectors, syringes, luer actuated valves, and the like. It can b e connected to a device.

[0066]

Blood isolation device 1500 includes an entry port 1502 that can be connected to a patient n eedle that is inserted into the patient's vasculature for access to and collection of a blood sam ple. Entry port 1502 can also be connected to a tube or other conduit that is also connected t o a patient needle. Entry port 1502 defines an opening to blood isolation device 1500, which o pening can be of the same cross-sectional dimensions as a tube or other conduit connected to the patient needle or the patient needle itself. For example, the opening has a diameter of ap proximately 0.045 inches (1.143 mm).

It can be circular, but can have a diameter of 0.01 inch (0.254 mm) to 0.2 inch (5.08 mm) or more. Inlet port 1502 may also include a sealed or fluid tight connector or connection such a s a threaded or luer fitting or the like

.

In some implementations, a tube or other conduit that is coupled to the patient needle can be integrated with the entry port 1502, such as by co-molding, gluing, laser welding, or heat bon ding the parts together. This allows the blood isolation device 1500 to be manufactured and s old as a single unit with the patient needle, eliminating the need to connect the patient needle to the blood isolation device 1500 during blood draw or sampling.

Blood isolation device 1500 further includes an exit port 1504 that

defines an opening from blood isolation device 1500 and to the blood sampling device. Exit p ort 1504 may also be connected to a tube or other conduit that is also connected to a blood is olation device and may include a sealed or fluid tight connector or connection such as a threa ded or luer fitting. Thus, as noted above, the blood isolation device 1500 is manufactured and sold as a single unit with the patient needle and/or tubing and blood sample collection device such that the patient needle and blood sample collection device are connected to blood isolati on during blood collection or sampling. The need to connect to device 1500 can be eliminated.

[0069]

Blood isolation device 1500 further includes a sampling channel 1506 between inlet port 150 2 and outlet port 1504, which functions as a blood sample path once the first aliquot of blood has been isolated. Sampling channel 1506 can be a channel or conduit of any size, shape, or c onfiguration. In some implementations, sampling channel 1506 has a cross-sectional area sub stantially similar to the opening of inlet port 1502 . In other implementations, sampling chann el 1506 can gradually diverge from inlet port 1502 to outlet port 1504 .

Blood isolation device 1500 further includes isolation chamber 1508 , which

is connected to and separated from sampling channel 1506 at any location between inlet por t 1502 and outlet port 1504 . Although diverted, it is preferably connected to and disconnecte d or diverted from the proximal end of sampling channel 1506 near inlet port 1502 . In some i mplementations, the diversion channel includes a Y-junction. The isolation chamber 1508 is pr eferably maintained at atmospheric pressure and includes a vent 1510 at or near the distal en d of the isolation chamber 1508 . Vent 1510 includes air permeable blood barrier 1512 . FIG. 15C shows blood isolation device 1500 with isolation chamber 1508 filled with an initial aliquo t or sample of blood from a patient.

[0071]

Air permeable blood barrier 1512 can be covered with protective cover 1516 . The protective cover 1516 can be sized and configured to prevent a user from touching the air permeable blo od barrier 1512 with their fingers or other external instruments while still allowing the patien t's own blood pressure to pressure the isolation chamber 1508. Allowing air to exit the air per meable blood barrier 1512 as the air is forced out of the isolation chamber by forcing blood int o it. The protective cover 1516 can be configured to block or prevent accidental exposure of t he filter to ambient fluids or splashes. This can be done in a variety of mechanical ways, inclu ding but not limited to adding a hydrophobic membrane to the protective cover.

FIG.

15B is a perspective view of blood isolation device 1500 from the top of housing 1501 includi ng outlet port 1504 and vent 1510 of blood isolation device 1500 and sampling channel 1506 before the sample collection device is activated. The first aliquot of blood is separated while th e is empty.

Filling the separation chamber 1508 is shown. Figure 15G is a perspective view of the blood is olation device 1500 from the bottom of the housing 1501 and the exit port 1504 of the blood i solation device 1500, showing the initial flow while the sampling channel 1506 is empty befor e the sample collection device is activated. An aliquot of blood is shown filling the isolation ch amber 1508 . FIG. 15C is another perspective view of blood isolation device 1500 from the to p of housing 1501, including inlet port 1502 and vent 1510 of blood isolation device 1500, wit h the isolated blood substantially remaining within isolation chamber 1508. FIG. Blood is draw n through sampling channel 1506 during the period of time.

FIG .

15D is a cross-sectional view of blood isolation device 1500 according to some implementat

ons, showing housing 1501 defining sampling channel 1506 and isolation chamber 1508 . 15E and 15F illustrate various form factors of housings for blood isolation devices according to one or more implementations described herein. Isolation chamber 1508 can have a larger cross-sectional area than sampling channel 1506, and the cross-sectional area or length can be conf igured such that a predetermined or specific blood volume is isolated or locked

.

can. The sampling channel 1506 can be sized to fit tubing for either or both the patient needle tubing or the blood collection device tubing.

[0075]

Housing 1501 can be formed from multiple pieces or a single unitary piece. In some implem entations, as shown in FIG. 15D, housing 1501 includes an upper member 1520 and a lower member 1522 that mate with each other, one or both of which may be formed by, for exampl e, an injection molding process or by etching, cutting, cutting, or molding. It has grooves, cha nnels, locks, conduits or other pathways pre-formed by perforations or the like. The upper me mber 1520 may be attached by any mating or connecting mechanism, such as using laser wel ding, thermal bonding, ultrasonic welding, adhesives, screws, rivets, bolts, etc., or latches, gr ooves, tongues, pins, flanges. Other mating mechanisms, such as, can connect with lower me mber 1522 . In some implementations, the upper member 1520 can include grooves, chann els, locks, conduits or other pathways, while the lower member 1522 is the upper member 15 20, as shown in FIG. 15D

.

A protrusion 1524 sized and adapted to fit into at least one of a groove, channel, lock or other pathway may be included. Protrusions 1524 can provide surface features such as partial groov es or partial channels, for example, to complete the formation of either sampling channel 150 6 and/or isolation chamber 1508 . In some implementations, the protrusions 1524 can be for med with one or more slanted sides or faces to fit more snugly within corresponding grooves, channels, locks or other pathways. In still other implementations, both the upper member 15 20 and the lower member can include grooves, channels, locks or other pathways, as well as one or more protrusions 1524 .

[0077]

In some implementations, sampling channel 1506 and isolation chamber 1508 are formed b y grooves, channels, locks or other pathways formed in housing 1501 . Housing 1501 can be made of any suitable material including rubber, plastic, metal or other material. Housing 1501 can be formed from a transparent or translucent material, or from an opaque or non-transluce nt material. In other implementations, the housing 1501 can be largely opaque or non-transp arent, but the housing surfaces immediately adjacent the sampling channel 1506 and/or the i solation chamber 1508 are transparent or translucent and initially A visual cue or sign that the sequestration chamber 1508 is filled to the required or desired degree and/or the sequestered blood is then released while a clean blood sample is drawn through the sampling channel 15

6. Provide visual cues or signs to remain isolated.

give to the artist. Other visual cues or signs of isolation include, but are not limited to, contact, penetration, or partial penetration of blood, the air permeable blood barrier 1512 turning a different color; Color-coded tabs or indicators at any location along or adjacent to the isolation chamber, audible, vibratory, or other signals may be included. After venipuncture with a patient needle (not shown), which can collect many pathogens from the patient's skin, the patient's own blood pressure overcomes the atmospheric pressure in isolation chamber 1508 to form air permeable blood barrier 1512

.

As the air in the isolation chamber 1508 is expelled through, the initial volume of the patient's blood with these pathogens enters the blood isolation device 1500 inlet port 1502 and flows into the isolation chamber 1508 by following the path of least resistance. . The patient's blood pressure is not sufficient to overcome the rising air pressure within the sealed sampling channel 1506 . Ultimately, an isolation chamber 1508 of predetermined volume is filled with blood that drives air out through an air permeable blood barrier 1512 . When blood impinges on the air permeable blood barrier, the blood interacts with the material of air permeable blood barrier 1512 to completely or partially seal vent 1510 . A signal or indication can be provided that the practitioner can now utilize the VACUTAINER® capsule or other blood sampling device to obtain the next volume of the patient's blood for sampling. The blood in the isolation chamber 1508 is now effectively isolated within the isolation chamber.

[0079]

Upon filling the blood isolation channel 1508, and prior to use of a Vacutainer® or other blood sampling device, the patient's blood pressure causes compression of the air in the sampling channel 1506 and possibly a small amount of blood. It moves past the turning point into the isolation chamber 1508 into the sampling channel 1506 and queues clean blood to be drawn through the sampling channel 1506 .

Figures 16-19

show yet another implementation of a blood isolation device. 16A-16D are connected between a blood sample collection device such as an evacuated blood collection container such as a Vacutainer® (not shown) and a patient needle (not shown) and/or associated tubing. 16 shows a blood isolation device 1600 that can be used. Figure 17 shows the lower member of the blood isolation device and Figure 18 shows the upper member of the blood isolation device, the upper and lower members interfitting to provide an inlet port as described in more detail below. Ports, exit ports, isolation chambers and sampling channels can be formed. Figures 19A and 19B show the upper and lower members mating together. It should be appreciated that FIGS. 16-19 show one exemplary method of constructing the blood isolation devices described herein and that other forms of construction are possible.

[0081]

16A-16D, blood isolation device 1600 includes an entry port 1602 that can be connected to

patient needle that is inserted into a patient's vasculature for access and collection of a blood sample. Inlet port 1602 can also be connected to a tube or other conduit that is also connecte d to a patient needle. Entry port 1602 defines an opening to blood isolation device 1600, whic h opening can be of the same cross-sectional dimensions as a tube or other conduit connecte d to the patient needle or the patient needle itself. For example, the opening can be circular w ith a diameter of about 0.045 inch (1.143 mm), but may be from 0.01 inch (0.254 mm) to 0. 2 inch (5.08 mm) or more. can have a diameter of

Inlet port 1602

may also include a sealed or fluid tight connector or connection such as a threaded or luer fit ting or the like. In some implementations, a tube or other conduit coupled to the patient need le can be integrated with the entry port 1602, such as by co-molding, gluing, laser welding, or heat bonding the parts together. Blood isolation device 1600 is thereby manufactured and sol d as a single unit along with the patient needle and/or tubing,

The need to connect the patient needle to the blood isolation device 1600 during blood draw o r sampling can be eliminated.

Blood isolation device 1600 further includes an exit port 1604 that

defines an opening from blood isolation device 1600 and to the blood sampling device. Exit p ort 1604 may also be connected to a tube or other conduit that is also connected to a blood is olation device and may include a sealed or fluid tight connector or connection such as a threa ded or luer fitting. Thus, as noted above, the blood isolation device 1600 is manufactured and sold as a single unit along with the patient needle and/or tubing and blood sample collection d evice such that the patient needle and blood sample collection device are connected to blood i solation during blood collection or sampling. The need to connect to device 1600 can be elimin ated.

[0084]

Blood isolation device 1600 is connected to sampling channel 1606 between inlet port 1602 and outlet port 1604, and at any location between inlet port 1602 and outlet port 1604, and s ampling channel 1606. and an isolation chamber 1608 that is isolated or diverted from. Sampl ing channel 1606 functions as a blood collection path once the first aliquot of blood is sequest ered in sequestration chamber 1608 . Sampling channel 1606 can be a channel or conduit of a ny size, shape or configuration. In some implementations, sampling channel 1606 has a cross -sectional area substantially similar to the opening of inlet port 1602 . In other implementatio ns, sampling channel 1606 can gradually widen from inlet port 1602 to outlet port 1604 . The isolation chamber 1608 widens toward the path of the isolation channel so that blood first atte mpts to enter the reservoir as opposed to entering the smaller diameter of the sampling chan nel 1606, as shown in more detail in FIGS. It can have a larger cross-section to form a reserv oir. In some exemplary implementations, the diversion between sampling channel 1606 and i solation chamber 1608 is accomplished by diversion junction 1607

.

Turning junction 1607 can be substantially Y-shaped, T-shaped, or U-shaped. In some preferr ed exemplary implementations, redirection junction 1607 is configured such that flow from inl et port 1602 is preferentially directed into isolation chamber 1608, as shown in FIGS. 17A-17 B. The isolation chamber 1608 can also include or form a bend or ramp to move the initial blo od flow toward and into the isolation chamber 1608 .

[0086]

The isolation chamber 1608 is preferably maintained at atmospheric pressure and includes a vent 1610 at or near the distal end of the isolation chamber 1608 . Vent 1610 can include an air permeable blood barrier 1612 as described above. Blood isolation device 1600 can includ e a housing 1601 that can be formed from multiple pieces or a single unitary piece

.

In some implementations, as shown in FIGS. 17A-17D and 18A-18F, housing 1601 includes an upper member 1620 and a lower member 1622 that fit together. Blood isolation device 1600 i ncludes a gasket or other sealing member (not shown) such that when upper member 1620 is mechanically attached to lower member 1622, the junction therebetween is sealed by the gas ket or sealing member. can also include 17A-17D show the lower member 1622 of the housing for the blood isolation device 1600. FIG. The lower member 1622 includes pre-formed groove s, channels, locks, conduits, such as by an injection molding process or by etching, cutting, dr illing, etc., to form the sampling channels 1606, the isolation chambers 1608, and the turning junctions 1607. or other routes.

Isolation chamber 1608

prevents blood from entering the smaller diameter of sampling channel 1606 .

, can have a larger cross-section than the sampling channel 1606 so as to preferentially move into the isolation chamber first.

FIGS.

18A-18F may be attached by any mating or connecting mechanism such as using laser weldi ng, thermal bonding, gluing, screws, rivets, bolts, etc., or latches, grooves, tongues, pins, flan ges. Upper member 1620 is shown connectable with lower member 1622 by other mating me chanisms such as. Top member 1620 can include some or all of grooves, channels, locks, con duits or other pathways to form sampling channels 1606 , isolation chambers 1608 and turnin g junctions 1607 . In still other implementations, both upper member 1620 and lower membe r 1622 can include grooves, channels, locks or other pathways.

[0090]

In some implementations, sampling channel 1606 and isolation chamber 1608 are formed b y grooves, channels, locks or other pathways formed in housing 1601 . Housing 1601 can be made of rubber, plastic, metal or any other suitable material. Housing 1601 can be formed fro m a transparent or translucent material, or from an opaque or non-translucent material. In ot her implementations, housing 1601 can be largely opaque or non-translucent, but housing sur faces directly adjacent sampling channel 1606 and/or isolation chamber 1608 can be transpa

ent or translucent. There may be first a visual cue or sign that the isolation chamber 1608 is fi lled to the required or desired degree, and/or a subsequent isolation while a clean blood samp le is taken through the sampling channel 1606. Gives the practitioner a visual cue or sign that the sequestered blood remains sequestered. Other visual cues or signs of isolation include, bu t are not limited to, contact, penetration, or partial penetration of blood, causing the air perm eable blood barrier 1612 to turn a different color; Color-coded tabs or indicators at any locatio n along or adjacent to the isolation chamber, audible, vibratory, or other signals may be includ ed.

[0091]

The air permeable blood barrier 1612 can be covered or surrounded by a protective member 1616, as shown in FIGS. 18A-18F. Protective member 1616 can be sized and configured to pre vent a user from touching air permeable blood barrier 1612 with their fingers or other externa l instruments, while still allowing air to be expelled from isolation chamber 1608. Occasionally allow air to exit the air permeable blood barrier 1612 . In some implementations, protective member 1616 includes protrusions that extend from the top surface of top member 1620 up a nd around air permeable blood barrier 1612 . The protective cover 1616 can be configured to block or prevent accidental exposure of the filter to ambient fluids or splashes. This can be do ne in a variety of mechanical ways, including but not limited to adding a hydrophobic membra ne to the protective cover. In use, blood isolation device 1600 includes sampling channel 160 6 and isolation chamber 1608

.

Both pathways are initially filled with air at atmospheric pressure, but the sampling channel 1 606 is initially sealed by a Vacutainer® or other such sealed blood collection device at the outl et port 1604. , the isolation chamber 1608 terminates in a vent 1610 to the atmosphere that i ncludes an air permeable blood barrier 1612 .

[0093]

After venipuncture with a patient needle (not shown), which can collect many pathogens fro m the patient's skin, an initial volume of the patient's blood with these pathogens passes thro ugh inlet port 1602 of blood isolation device 1600 . do. This initial volume of potentially conta minated blood preferentially enters isolation chamber 1608 by finding the path of least resista nce. The patient's own blood pressure overcomes the atmospheric pressure in the vented isol ation chamber 1608 and expels the air in the isolation chamber 1608 through the air permeab le blood barrier 1612, while the air pressure builds up in the sealed sampling channel 1606. is insufficient to overcome the various exemplary

In some embodiments, isolation chamber 1608 and sampling channel 1606 can be configured such that the force generated by the patient's blood pressure is sufficient to overcome the eff ects of gravity regardless of the orientation of the blood isolation device. can.

Ultimately

, the isolation chamber 1608 fills with blood that drives air out through the air permeable b

od barrier 1612 . When blood contacts the air permeable blood barrier, the blood interacts wit h the material of air permeable blood barrier 1612 to completely or partially seal vent 1610 . A signal or indication can be provided that the practitioner can now utilize the Vacutainer® or other blood collection device. Upon filling blood isolation channel 1608 and prior to use of a Vacutainer® or other blood sampling device, the patient's blood pressure causes compression of air within sampling channel 1606, possibly a small amount

.

of blood moves past the turning point into sampling channel 1606 , queuing clean blood to be drawn through sampling channel 1506 .

FIG .

19A is a side view of blood isolation device 1600 and FIG. 19B is a cross-sectional view of bl ood isolation device 1600 showing upper member 1620 mating with lower member 1622 .

[0097]

FIG. 20 illustrates a patient needle 2002 for vascular access to a patient's bloodstream, a blo od sample collection device 2004 that facilitates the collection of one or more blood samples, and the patient needle 2002 and blood sample collection device 2004. A blood sample optimiz ation system 2000 is shown including a conduit 2006 providing a fluid connection between. In some implementations, the blood sample collection device 2004 includes a protective shield th at includes a sealed collection needle such that once a sealed vacuum container is placed on t he collection needle and the container is pierced once by the collection needle, the patient nee dle is exposed to the patient needle. A blood sample is drawn from 2002 through conduit 200 6 with vacuum pressure or force.

Blood sample optimization system 2000

further includes a blood isolation device 2008 located at any point on conduit 2006 between patient needle 2002 and blood sampling device 2004, as described herein. .

FIG.

21 shows a non-vented blood isolation device 2100 that uses wicking material chambers. Blo od isolation device 2100 includes a housing 2101 having a sampling channel 2104 at least par tially surrounded or abutted by an isolation chamber 2102 filled with wicking material. A first aliquot of blood is drawn from the patient needle into the sampling channel 2104 where it im mediately escapes into the wicking material of the isolation chamber 2102 . The wicking mate rial and/or isolation chamber 2102 is filled with a predetermined volume such that subsequent or subsequent blood draws flow past the wicking material and through the sampling channel 2 104 directly to a sampling device such as a vacutainer. Dimensioned and adapted to receive a nd retain blood. The wicking material can include substances such as solidifying agents, decon taminating agents, or other additives.

[0100]

As described herein, air permeable blood barriers can be made using a wide variety of differ ent structures and materials. As shown in Figures 22A and 22B, an air permeable blood barr

r 2202 of a blood isolation device 2200 can include a polymeric bead matrix 2204 that has be en treated to render at least some of the beads hydrophilic. Air permeable blood barrier 2202 further comprises a self-sealing material 2206 such as carboxymethylcellulose (CMC) or cellul ose gum, or other sealing material. Air permeable blood barrier 2202 may further include void s 2208 that allow air flow prior to or during partial contact with a fluid such as blood. Self-seal ing material 2206 expands upon contact with fluid, as shown in FIG. 22B.

Tightens to close void 2208, occluding air flow through void 2208, and completely or partially sealing. Figures 23A and 23B show an entry port 2302 for connection with a patient needle, an exit port 2304 for connection with a blood sampling device, an isolation chamber 2306, an isolation chamber 2306, and a contaminant to be isolated

.

23 shows yet another implementation of the blood isolation device 2300 having a sampling ch annel 2308 that bypasses the isolation chamber 2306 once the isolation chamber is filled to th e first aliquot of blood that may be present. Isolation chamber 2306 includes a hydrophobic pl ug 2312 at the distal end of isolation chamber 2306 furthest from inlet port 2302 . A vacuum or other suction force applied from outlet port 2304, such as from a Vacutainer®, draws blood into inlet port 2302 and directly into isolation chamber 2306, where the first aliquot of blood i s removed. Contacting the hydrophobic plug 2312, the first aliquot of blood is returned to the sequestration chamber 2306 where it is sequestered. A small amount of blood can enter samp ling channel 2308 which is initially closed by valve 2308 . When valve 2308 is released, a subs equent volume of blood, under additional vacuum or other force, flows into inlet port 2302, by passes isolation chamber 2306, and through sampling channel 2308 to outlet port 2304. flow towards and sent to the collection device. Sampling channel 2308 can have any suitable geo metry and can be formed from plastic tubing or any other suitable material

.

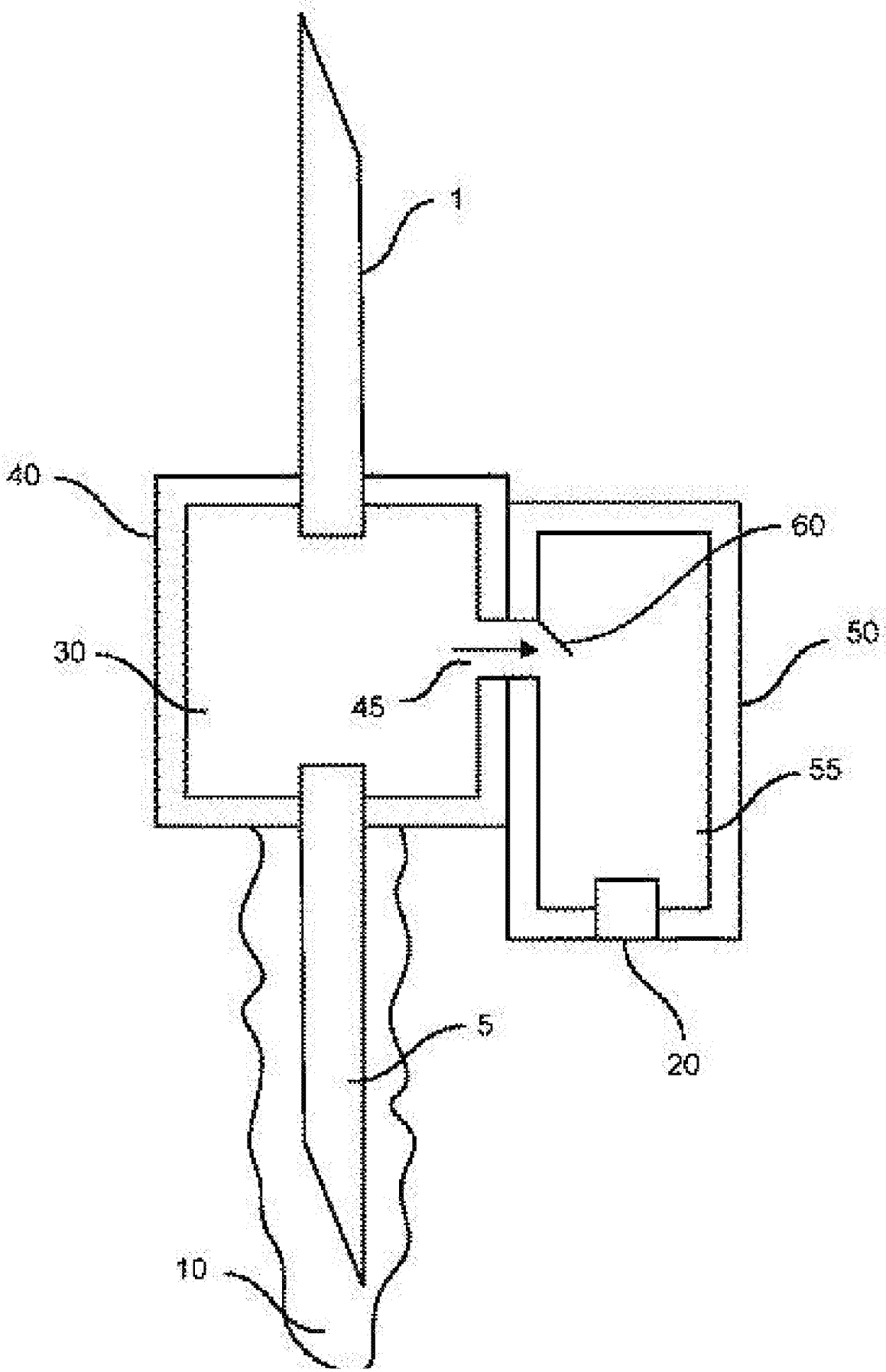
Valve 2308 can be a clip or other enclosing device to pinch, deflect, bend, or otherwise close t he sampling channel before the first aliquot of blood is sequestered in sequestration chamber 2306 . can.

[0103]

While various embodiments have been described in detail above, other modifications are pos sible. Other embodiments may be within the scope of the following claims.

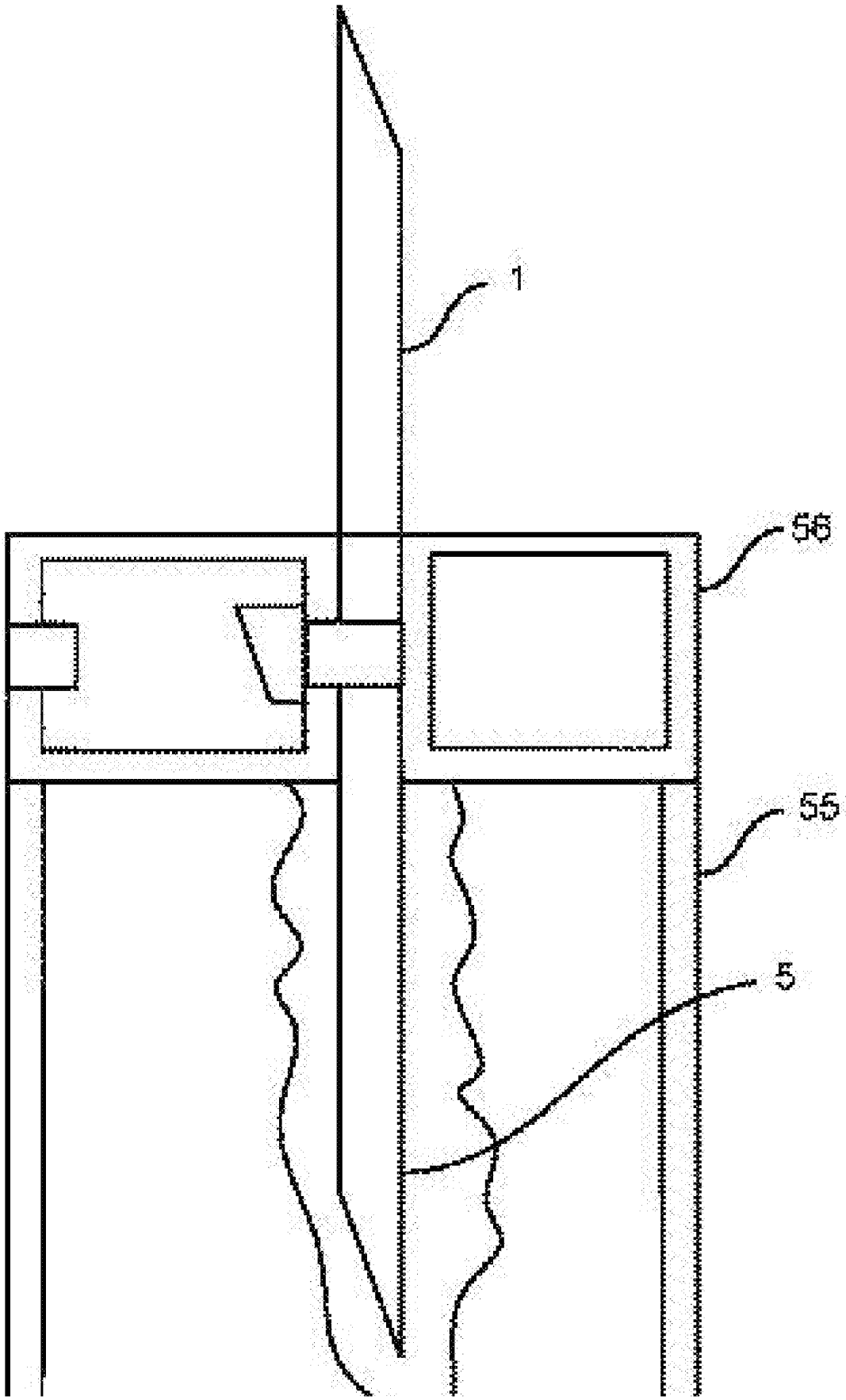
drawing open —

[Fig. 1]


1
40
60
30
50
45
55
5
20
10

[Figure 2]

FIG. 1


1
56
55
5

[Figure 3]

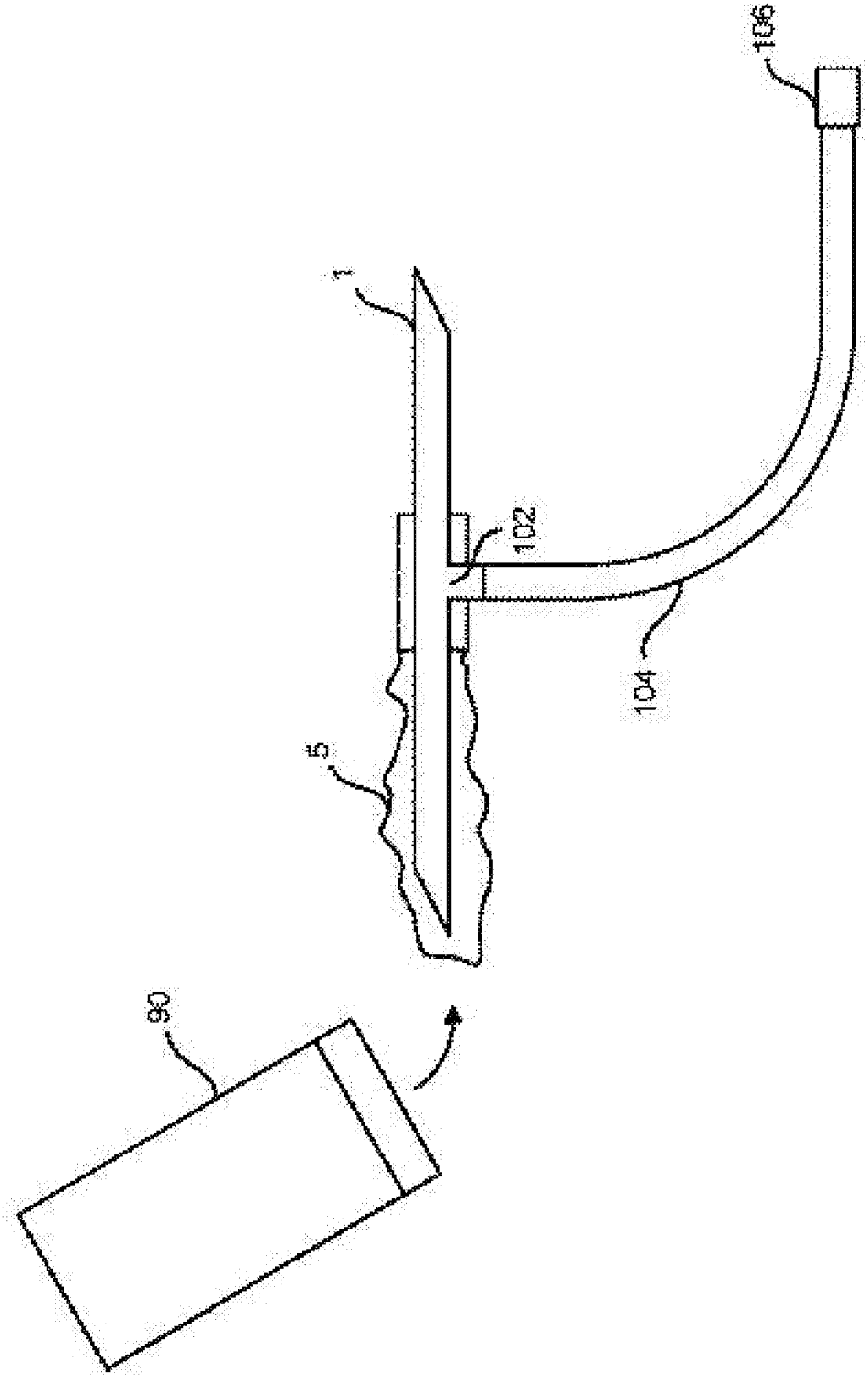


FIG. 3

[Figure 4]

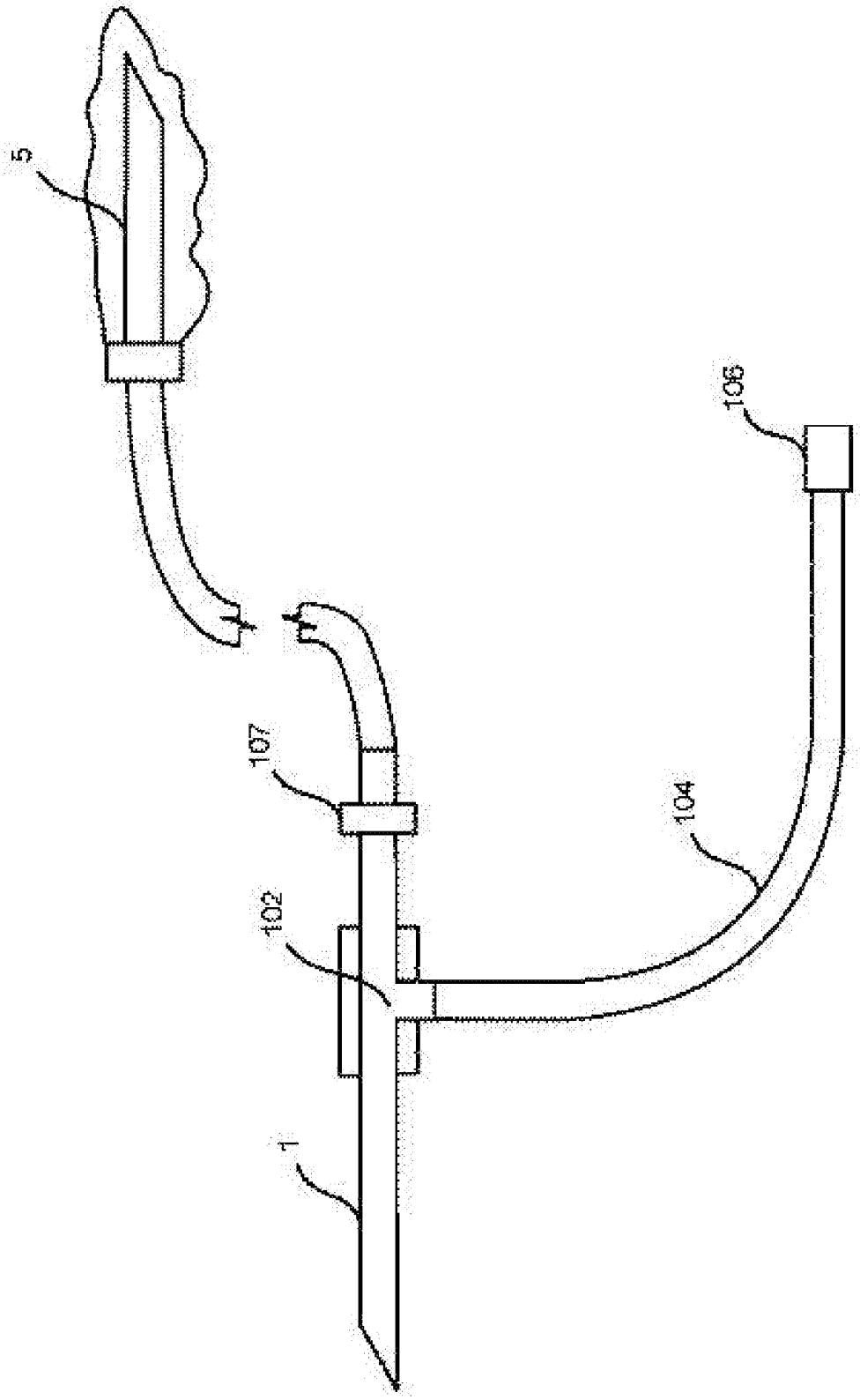


FIG. 4

[Figure 5]

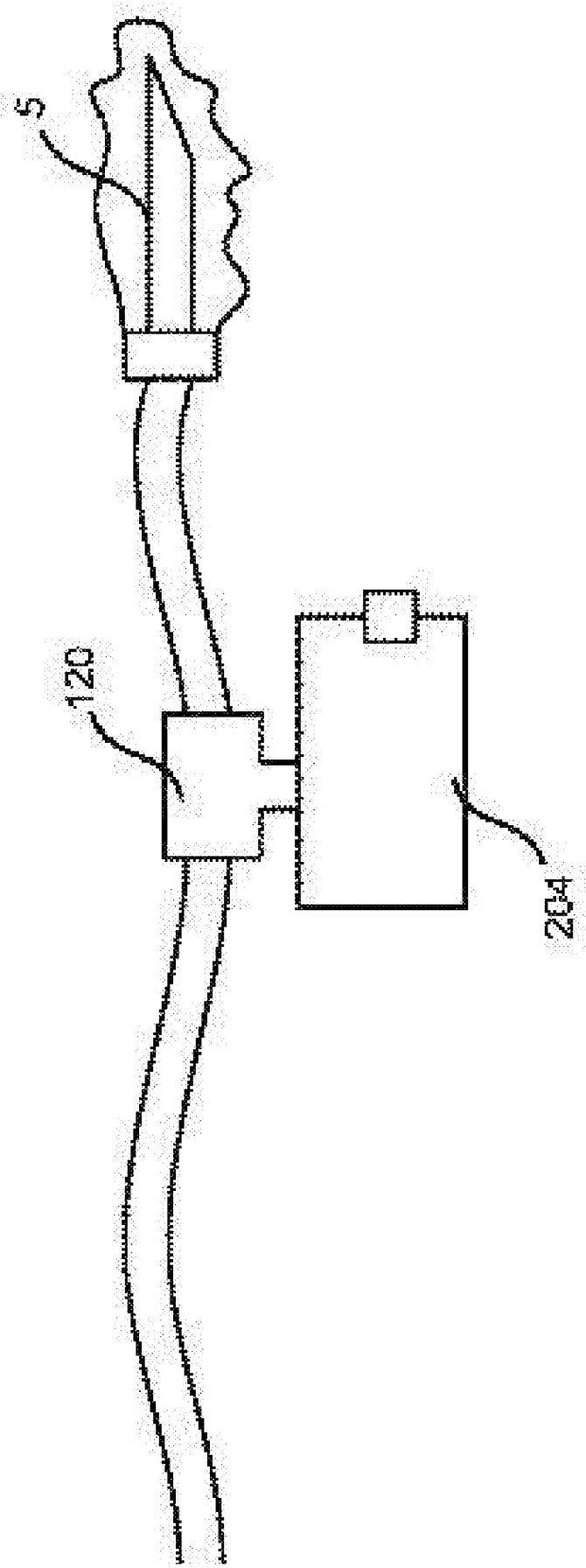
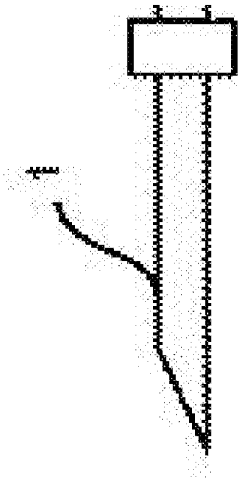


FIG. 5

[Fig. 6]



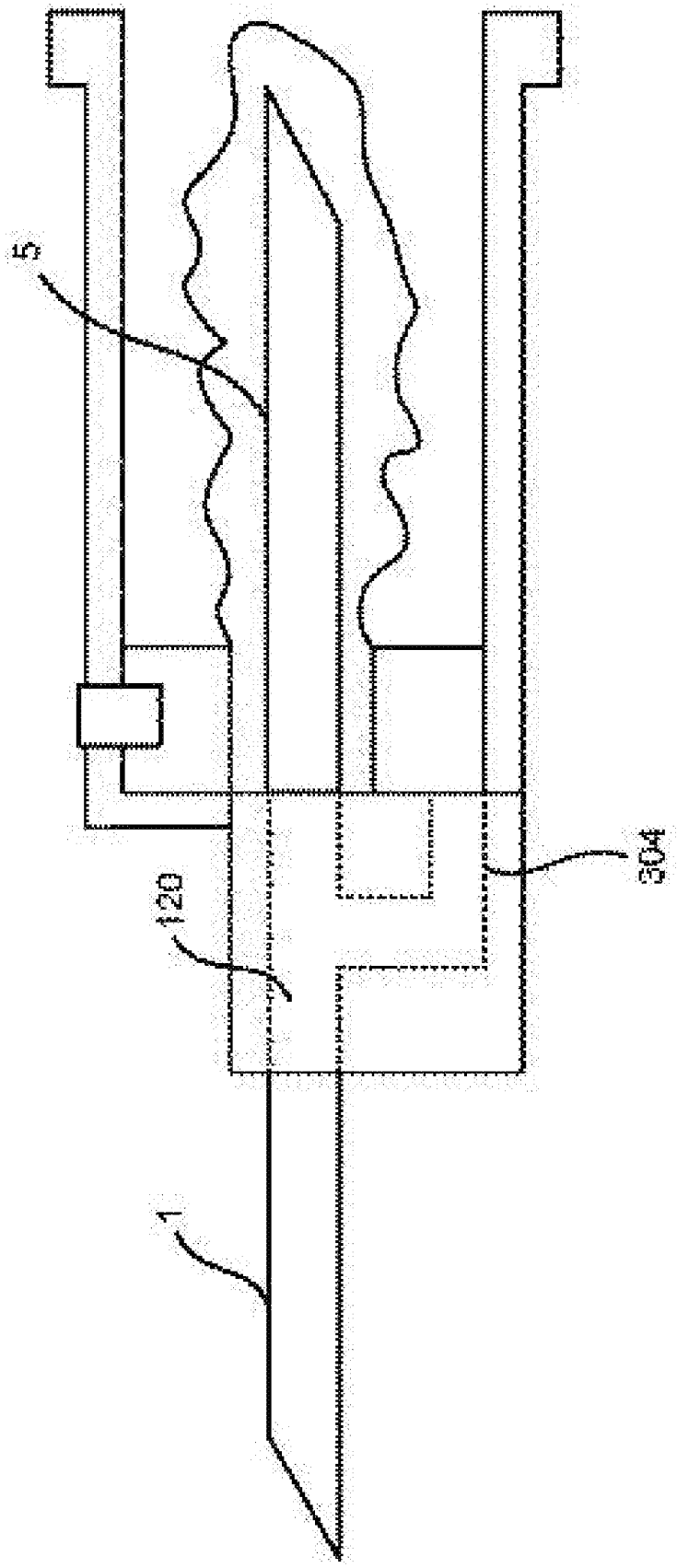


FIG. 6

[Fig. 7]

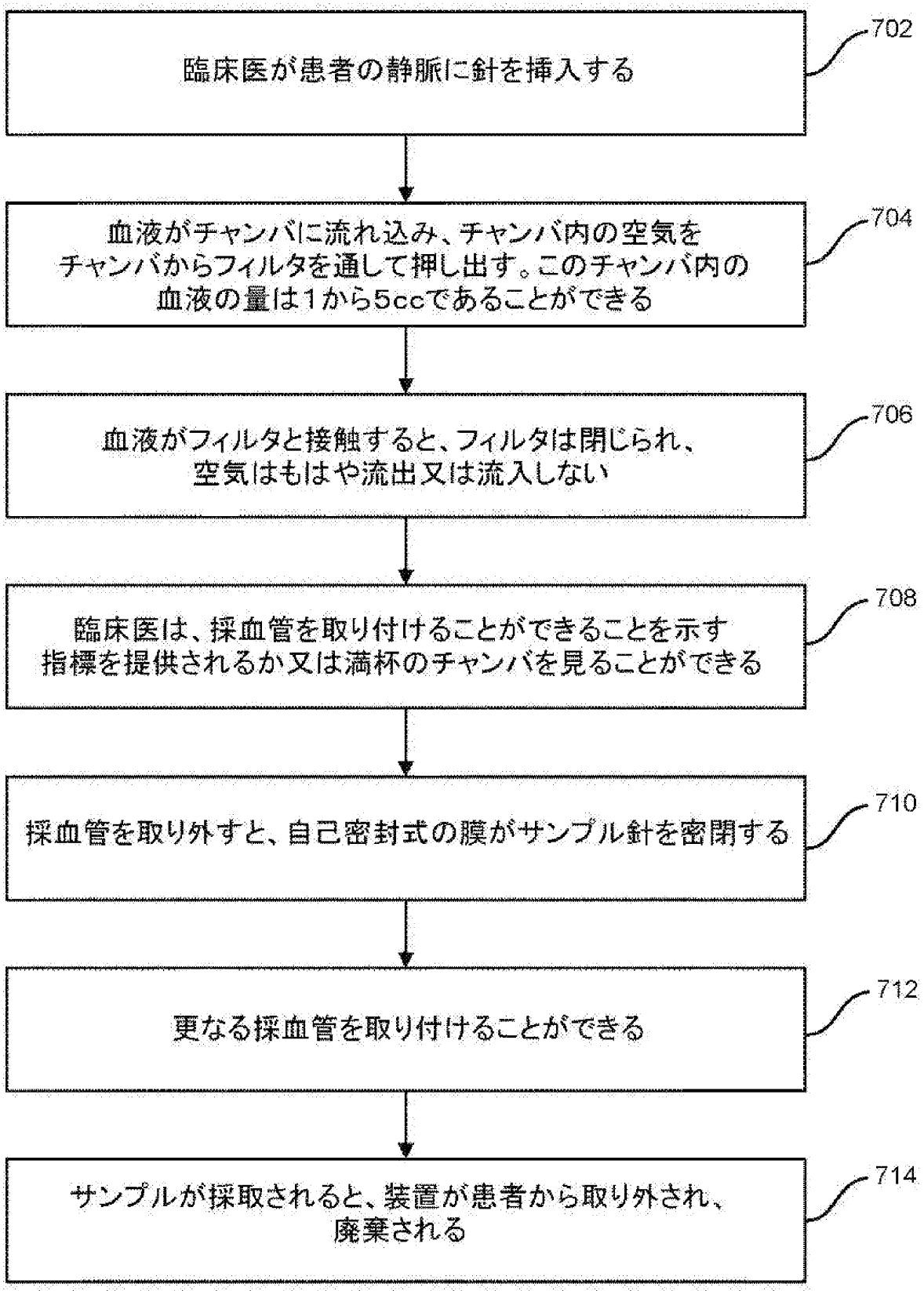
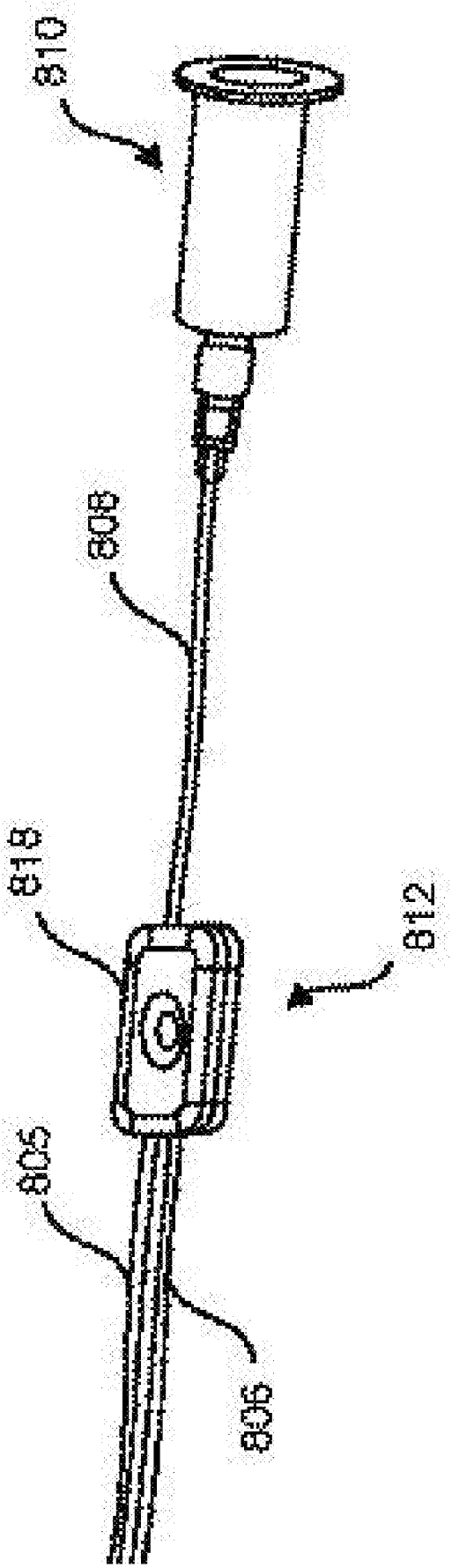

臨床医が患者の静脈に針を挿入する
702
血液がチャンバに流れ込み、チャンバ内の空気を
チャンバからフィルタを通して押し出す。このチャンバ内の
血液の量は1から5ccであることができる
704
血液がフィルタと接触すると、フィルタは閉じられ、
空気はもはや流出又は流入しない
706
臨床医は、採血管を取り付けることができることを示す
指標を提供されるか又は満杯のチャンバを見ることができる
708
採血管を取り外すと、自己密封式の膜がサンプル針を密閉する
710
更なる採血管を取り付けることができる
712
サンプルが採取されると、装置が患者から取り外され、
廃棄される
714

FIG. 7

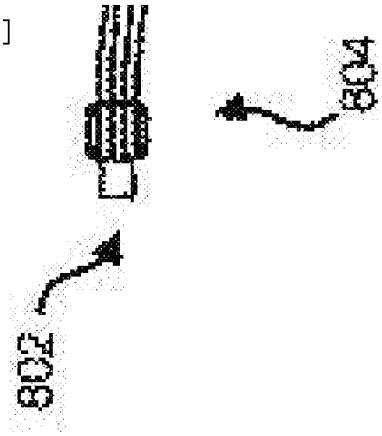
[Fig. 8A]



803

FIG. 8A

[Fig. 8B]



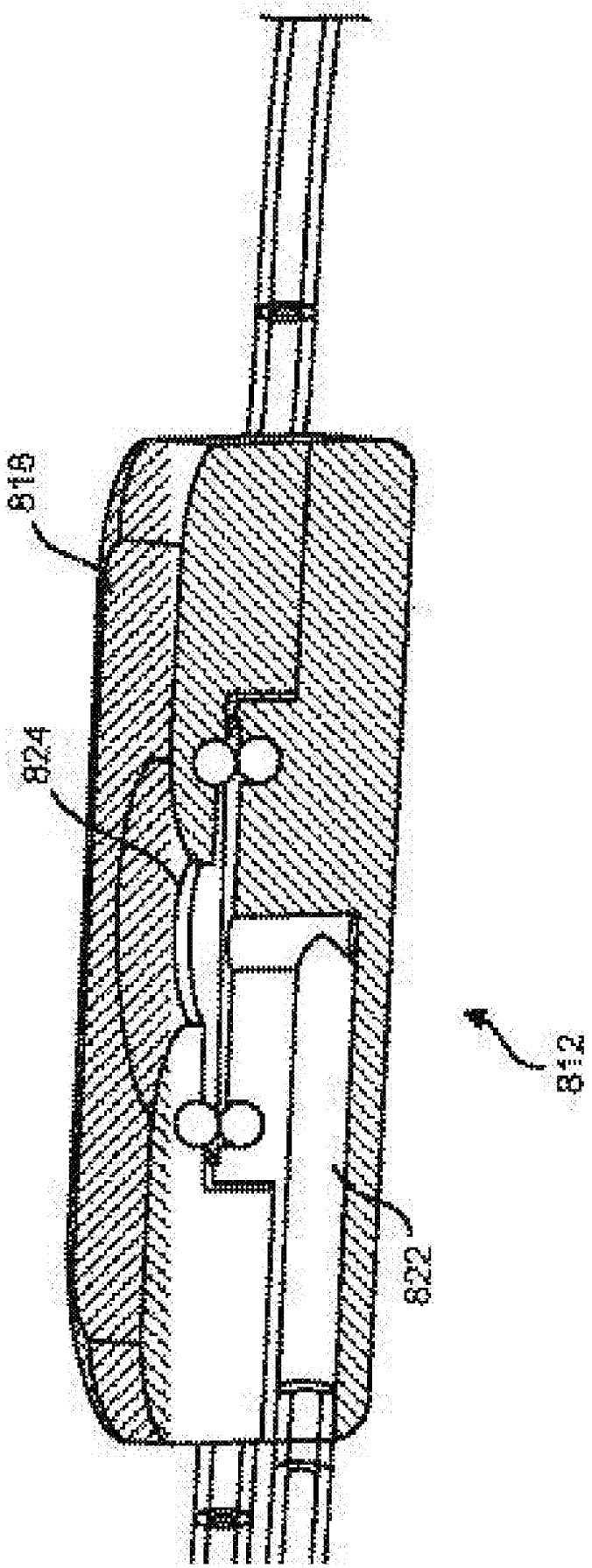
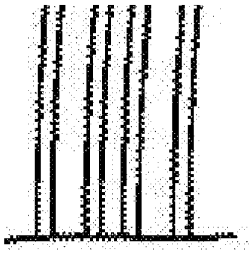


FIG. 8B

[Fig. 8C]



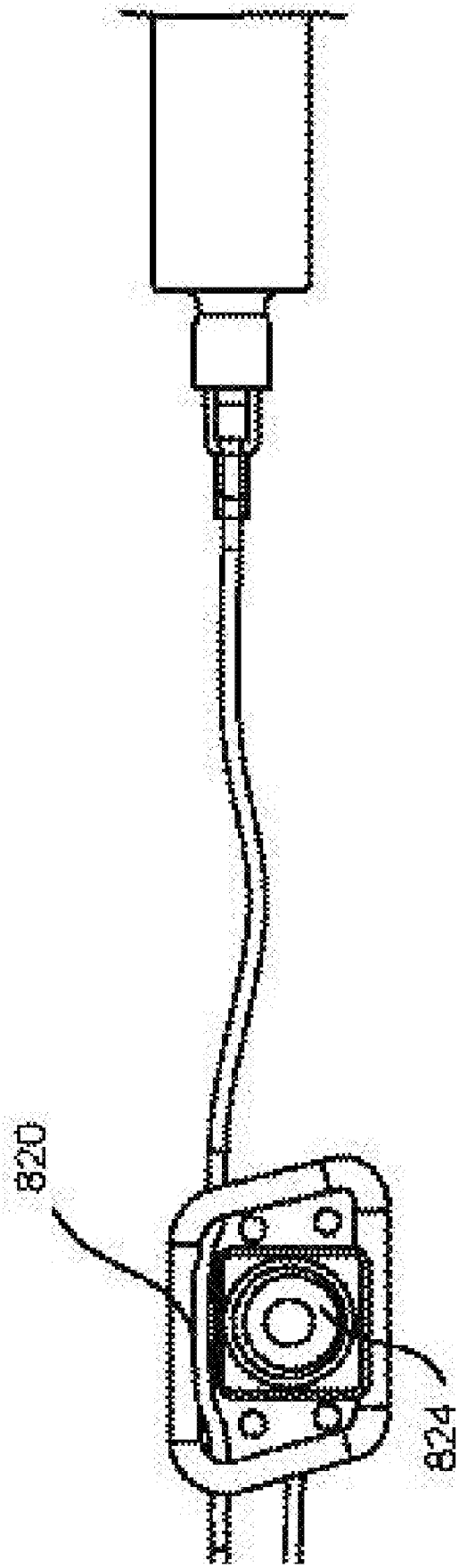
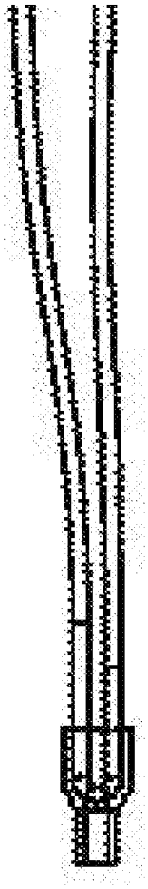


FIG. 8C

[Fig. 8D]



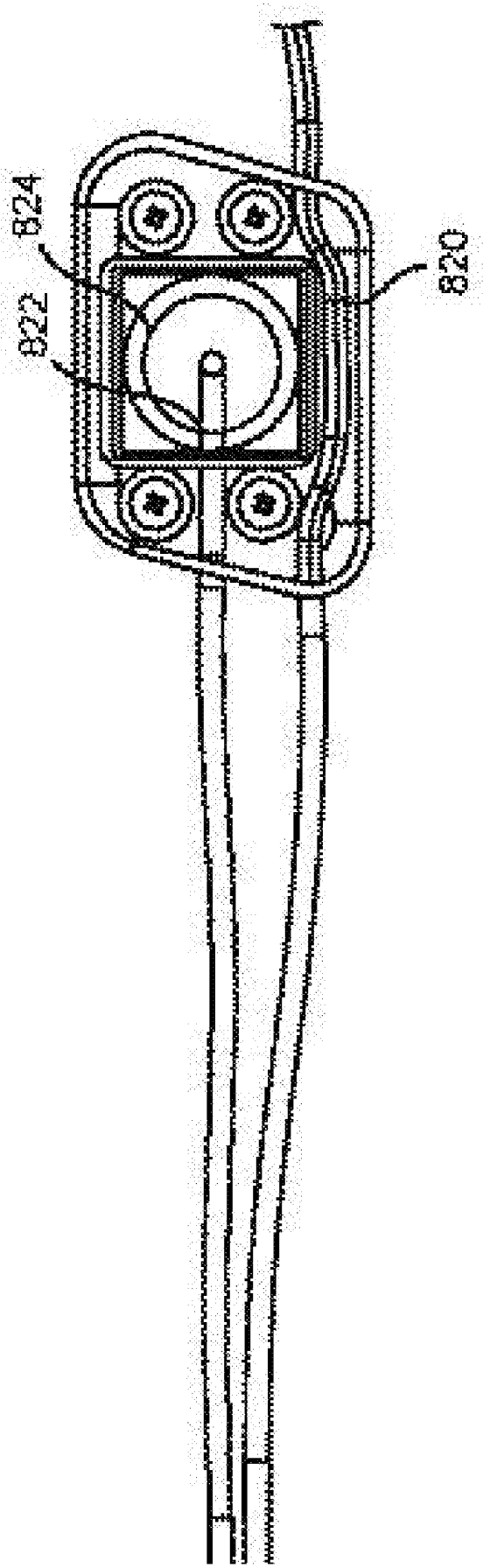
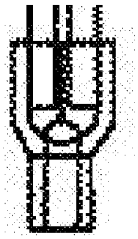


FIG. 8D

[Fig. 8E]



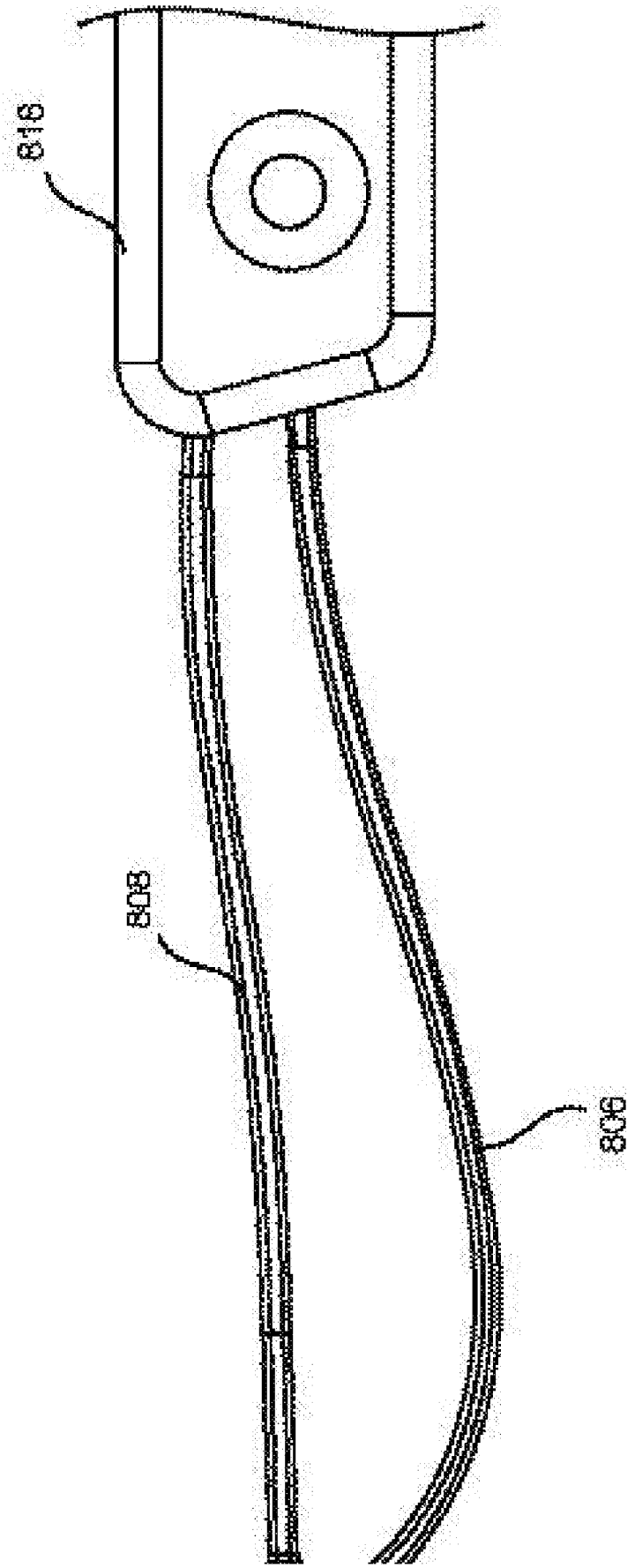
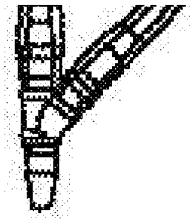


FIG. 8E

[Fig. 9]



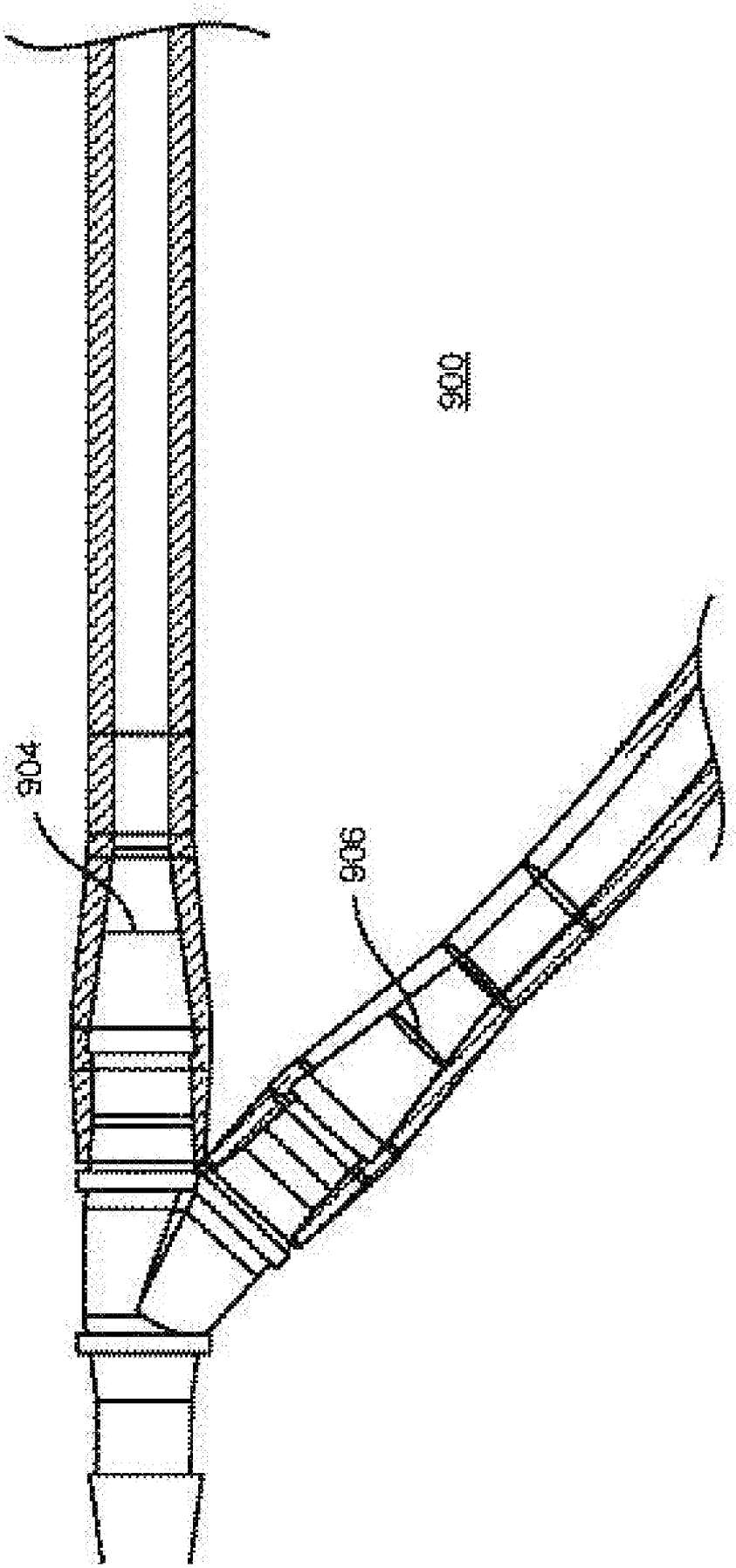


FIG. 9

[Fig. 10A]

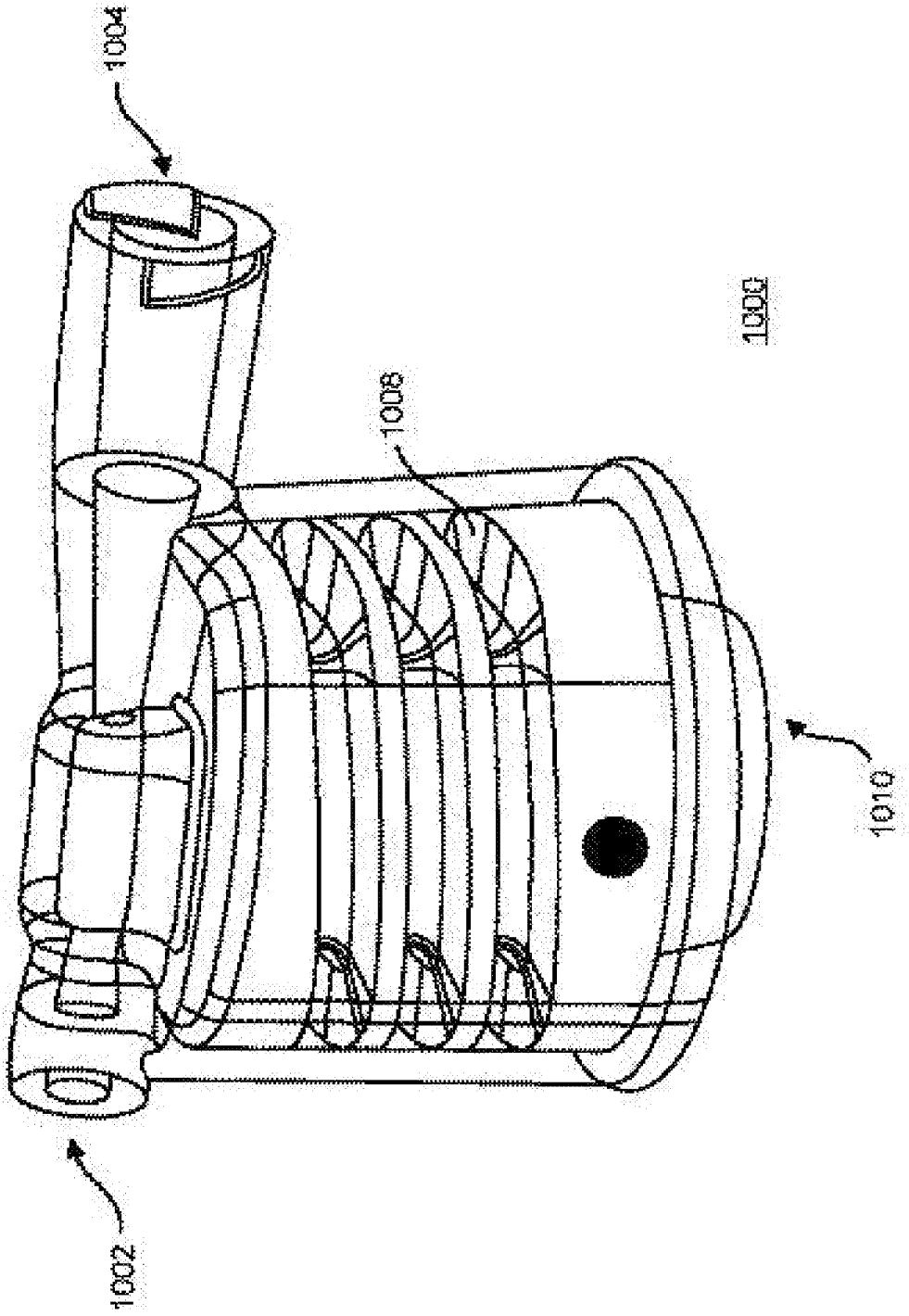


FIG. 10A

[Fig. 10B]

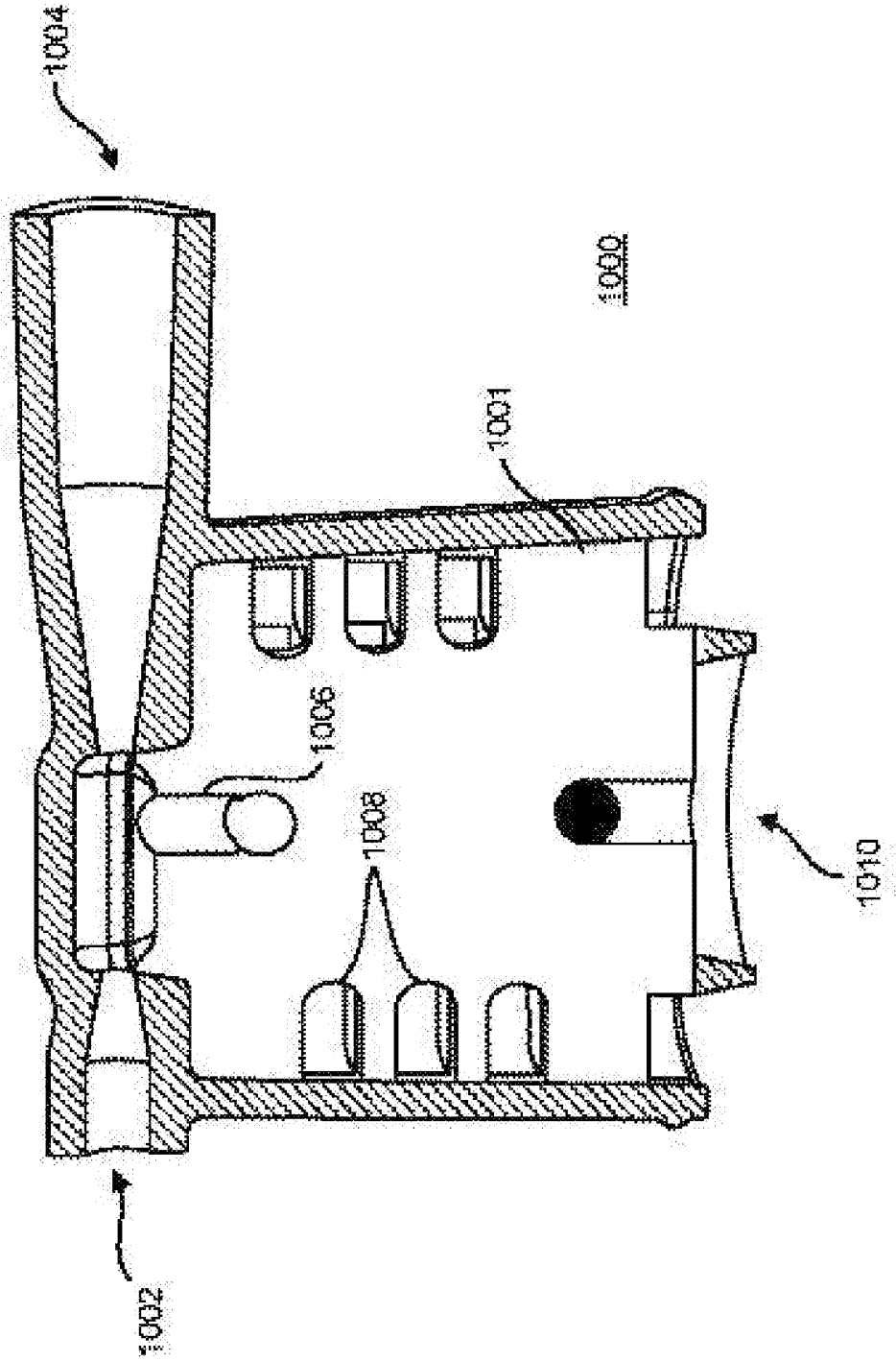
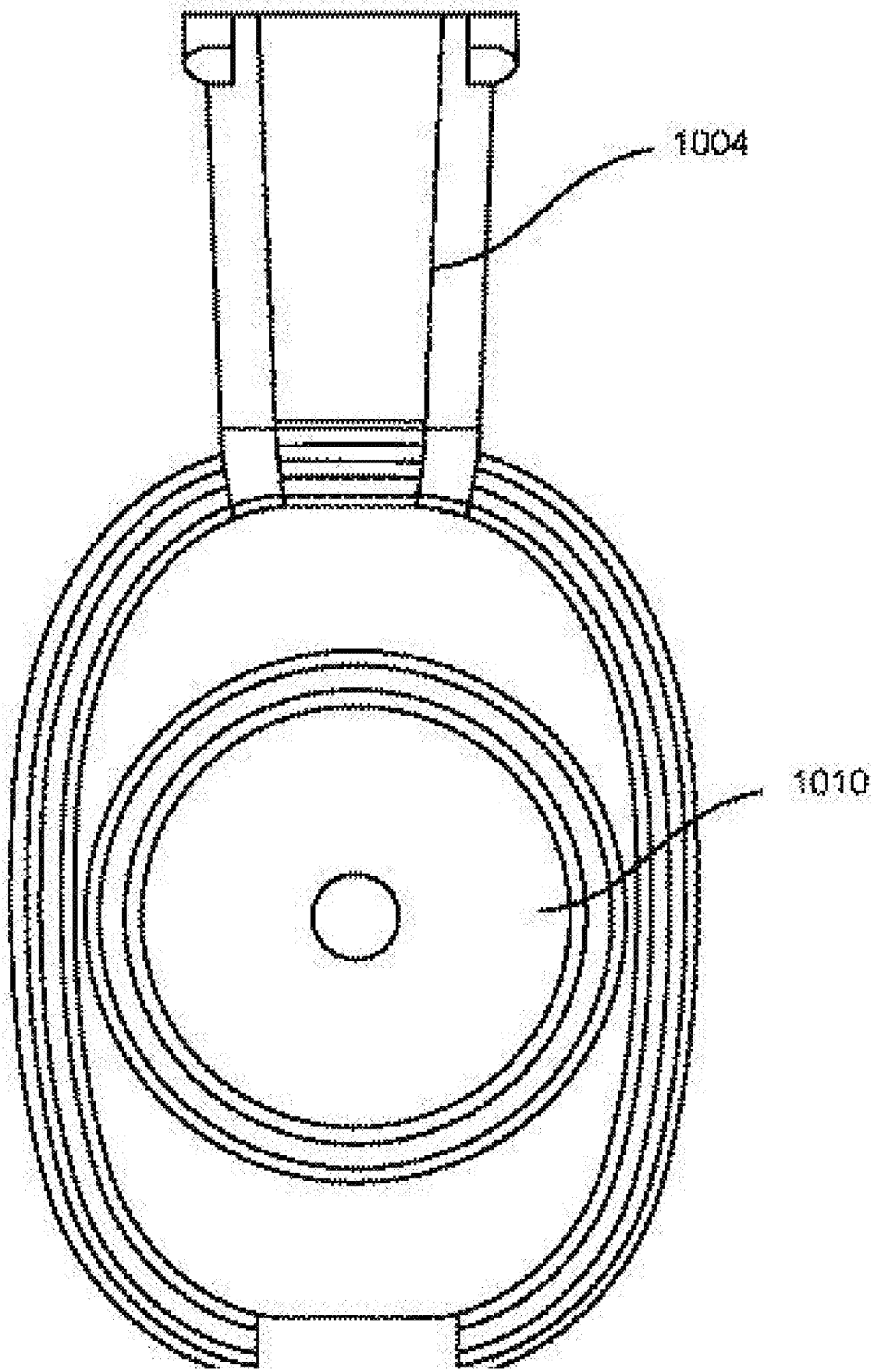


FIG. 10B

[Fig. 10C]


1004
1010

[Fig. 10D]

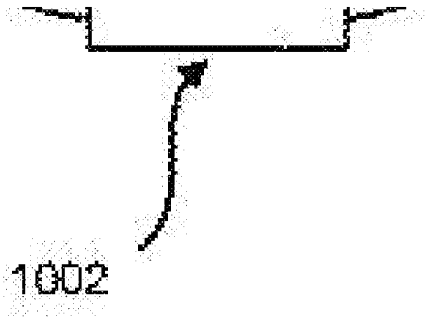
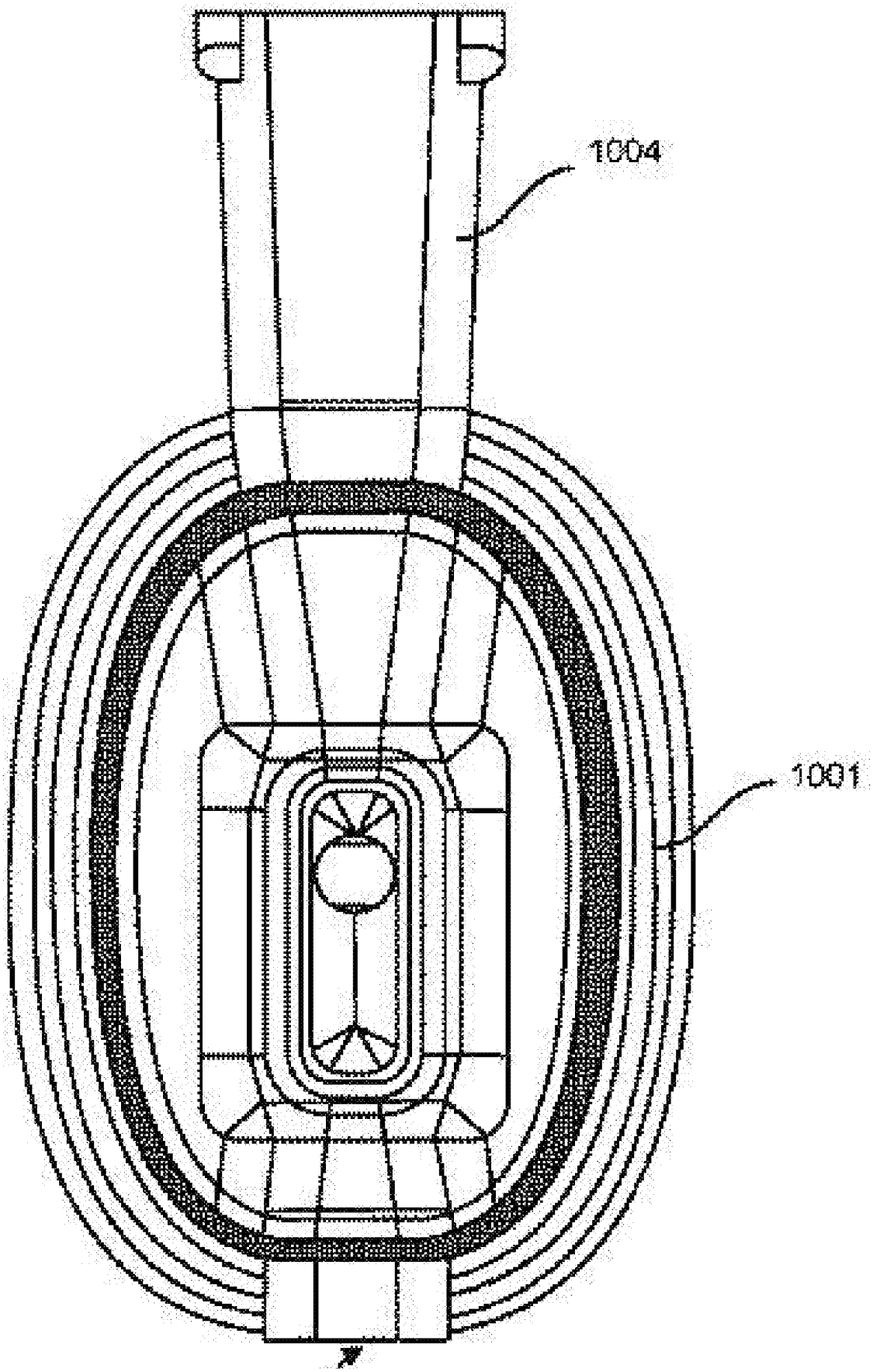


FIG. 10C


1004
1001

[Fig. 11A]

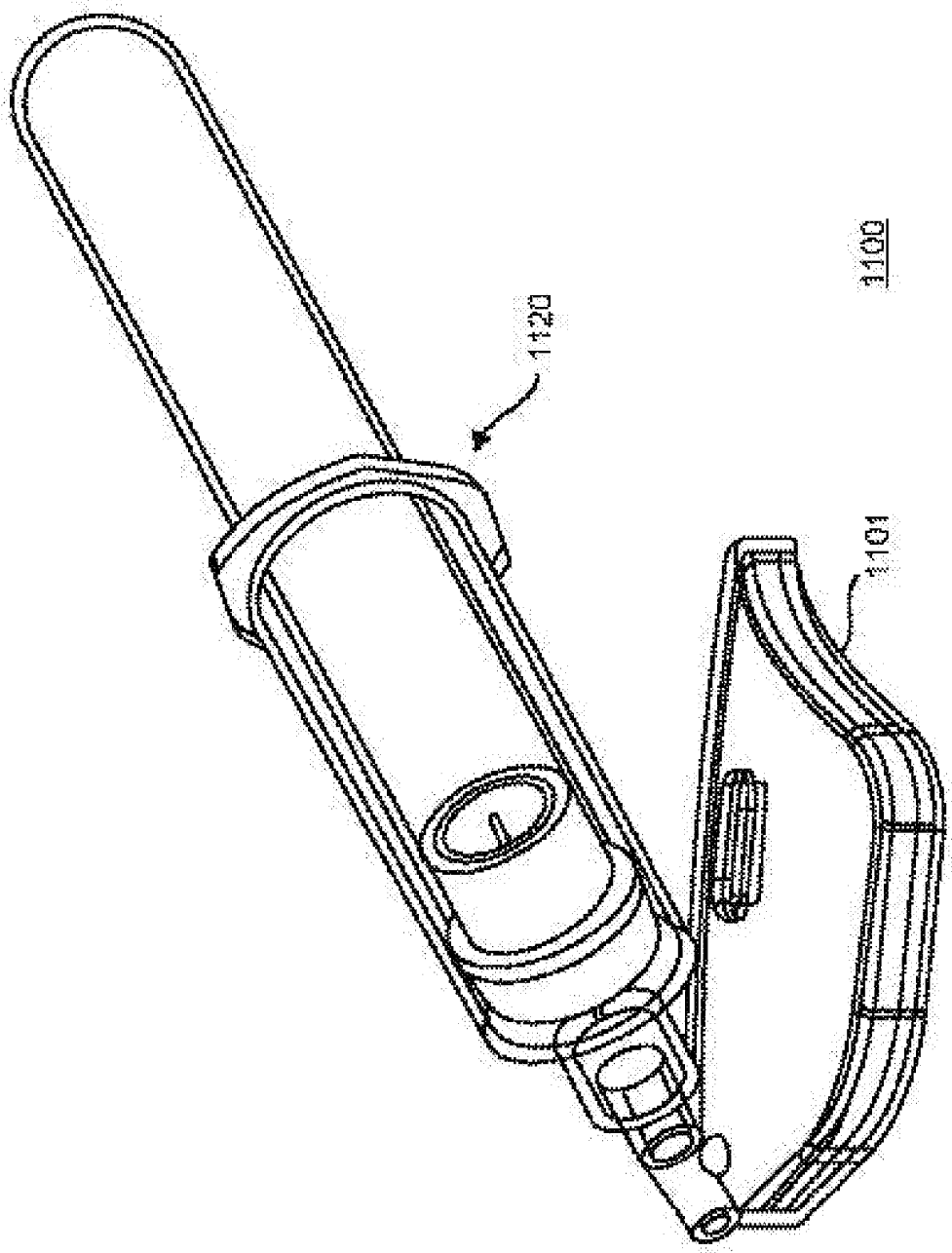


FIG. 11A

[Fig. 11B]

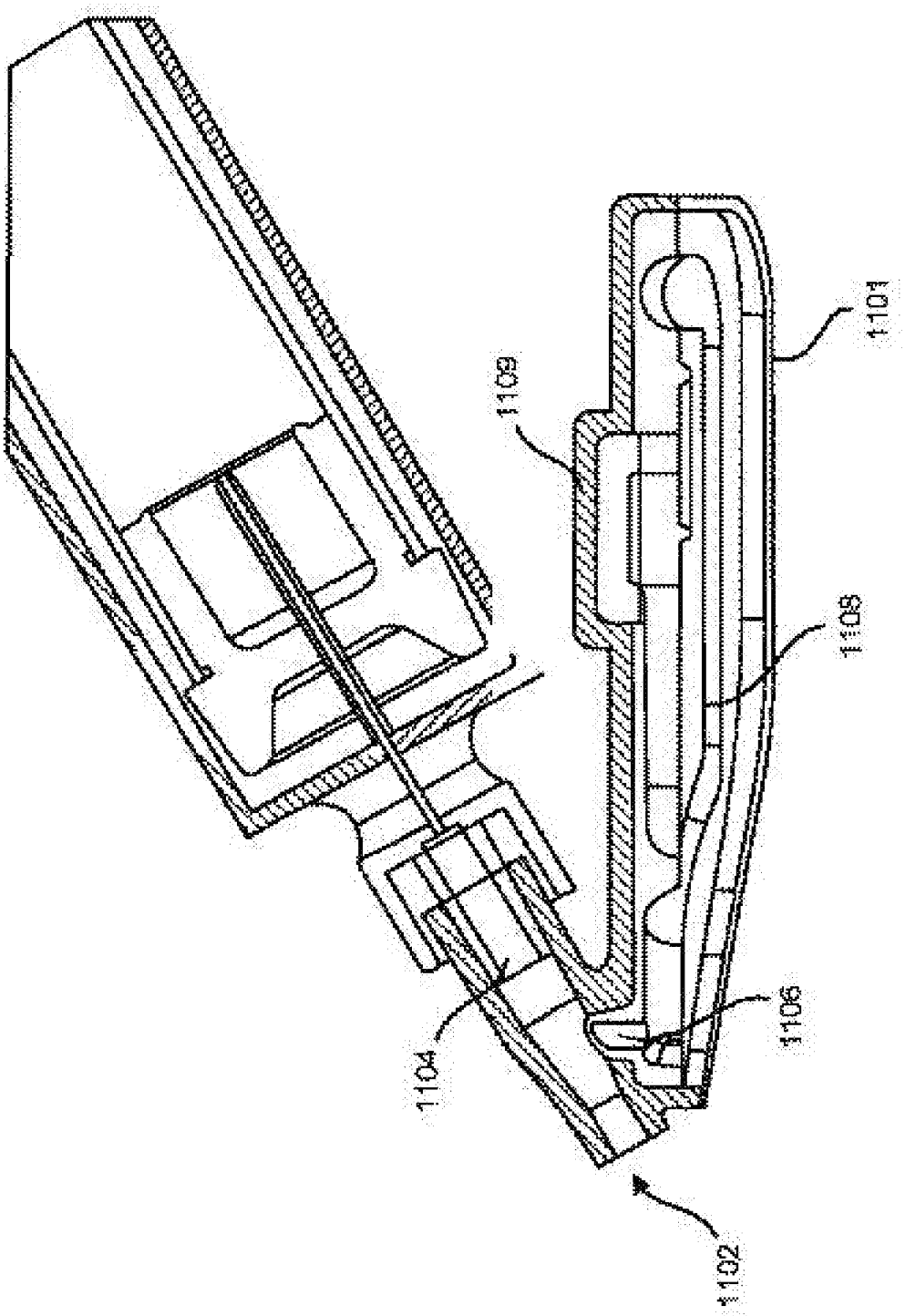
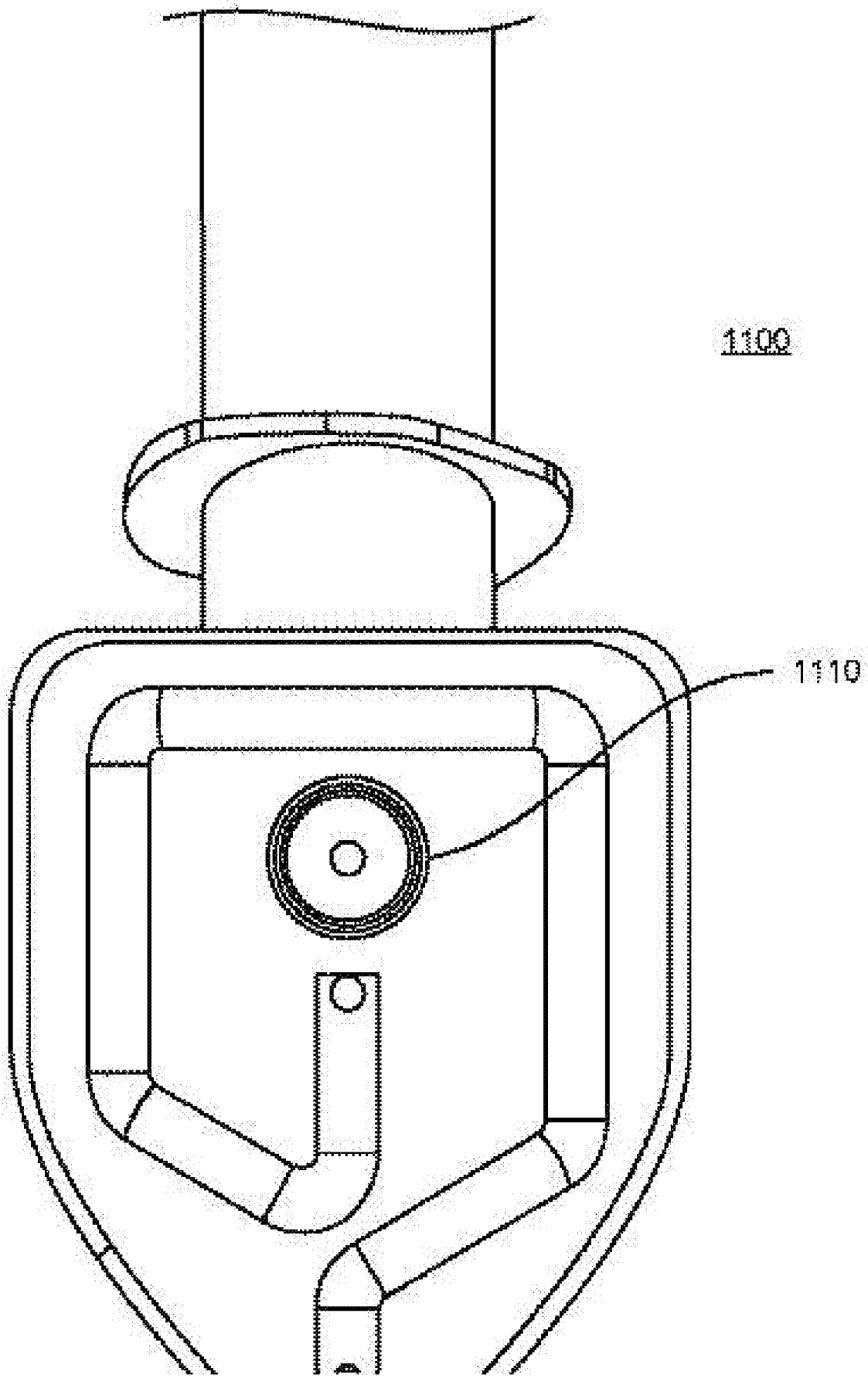


FIG. 11B

[Fig. 11C]


1100
1110

[Fig. 11D]

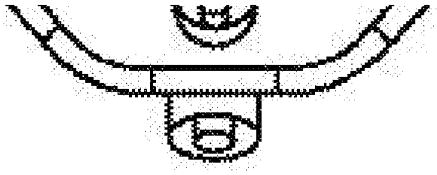
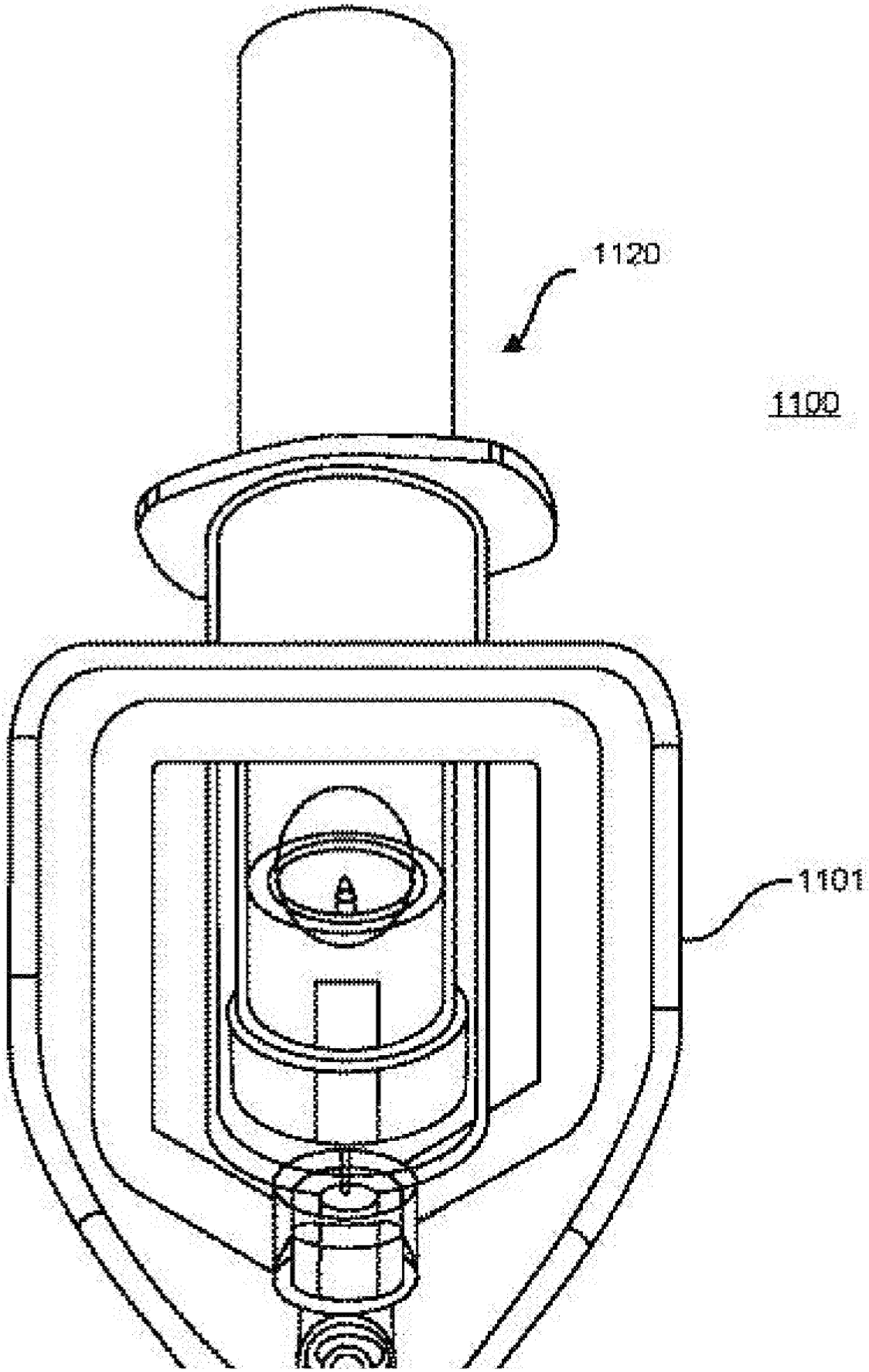


FIG. 11C


1120
1100
1101

[Fig. 11E]

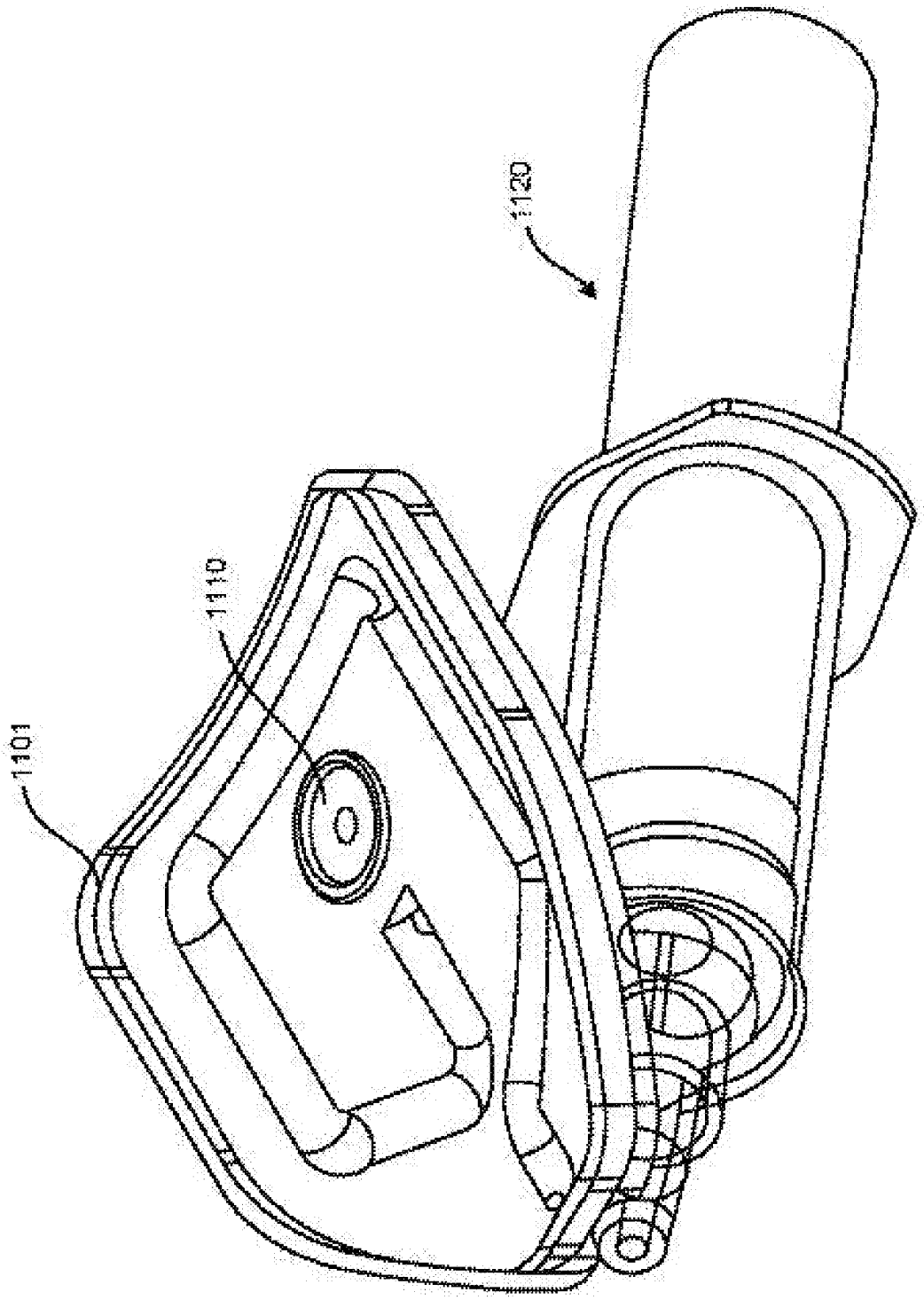


FIG. 11E

[Fig. 12A]

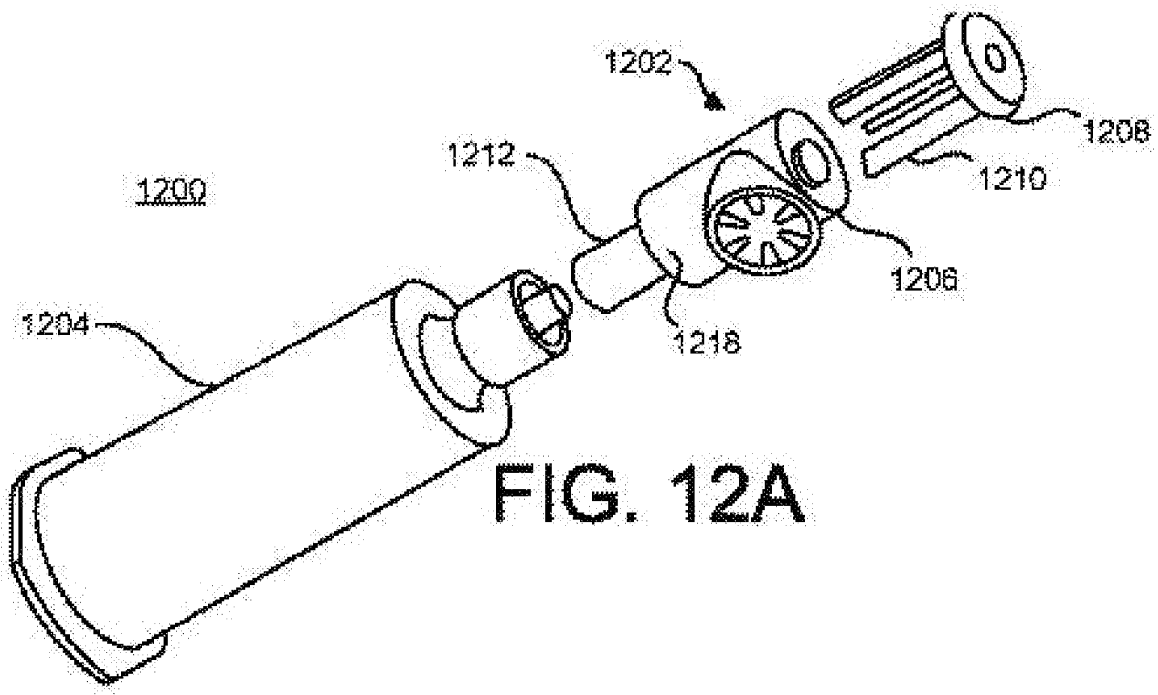


FIG. 12A

[Fig. 12B]

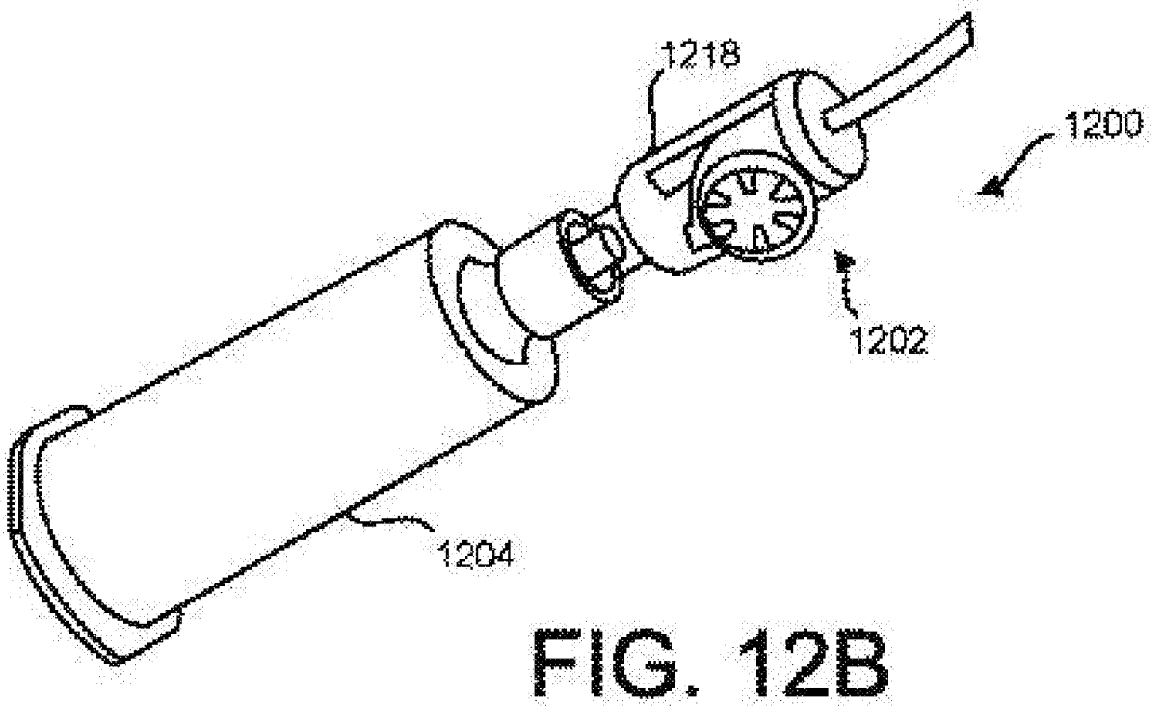


FIG. 12B

[Fig. 12C]

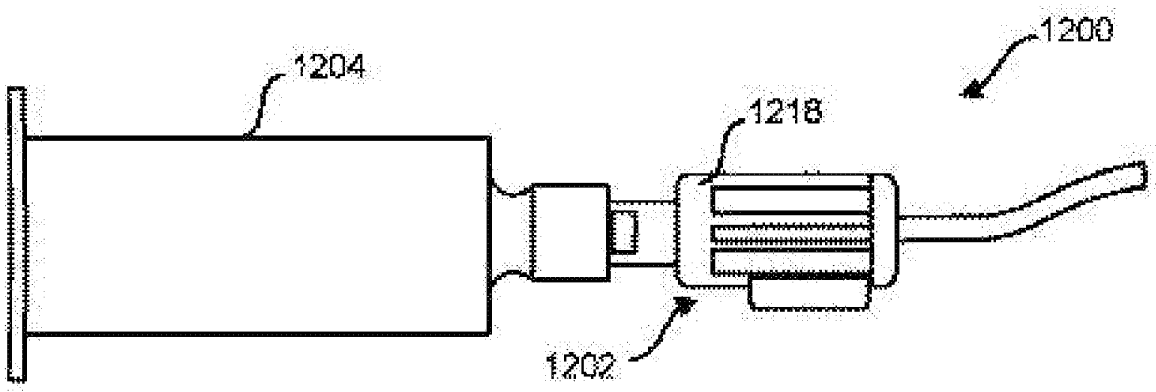


FIG. 12C

[Fig. 12D]

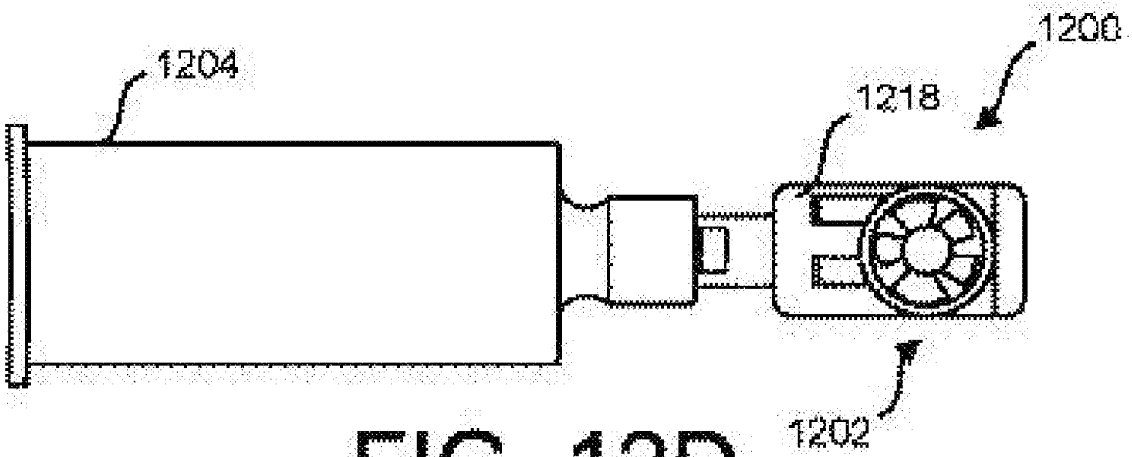


FIG. 12D

[Fig. 13A]

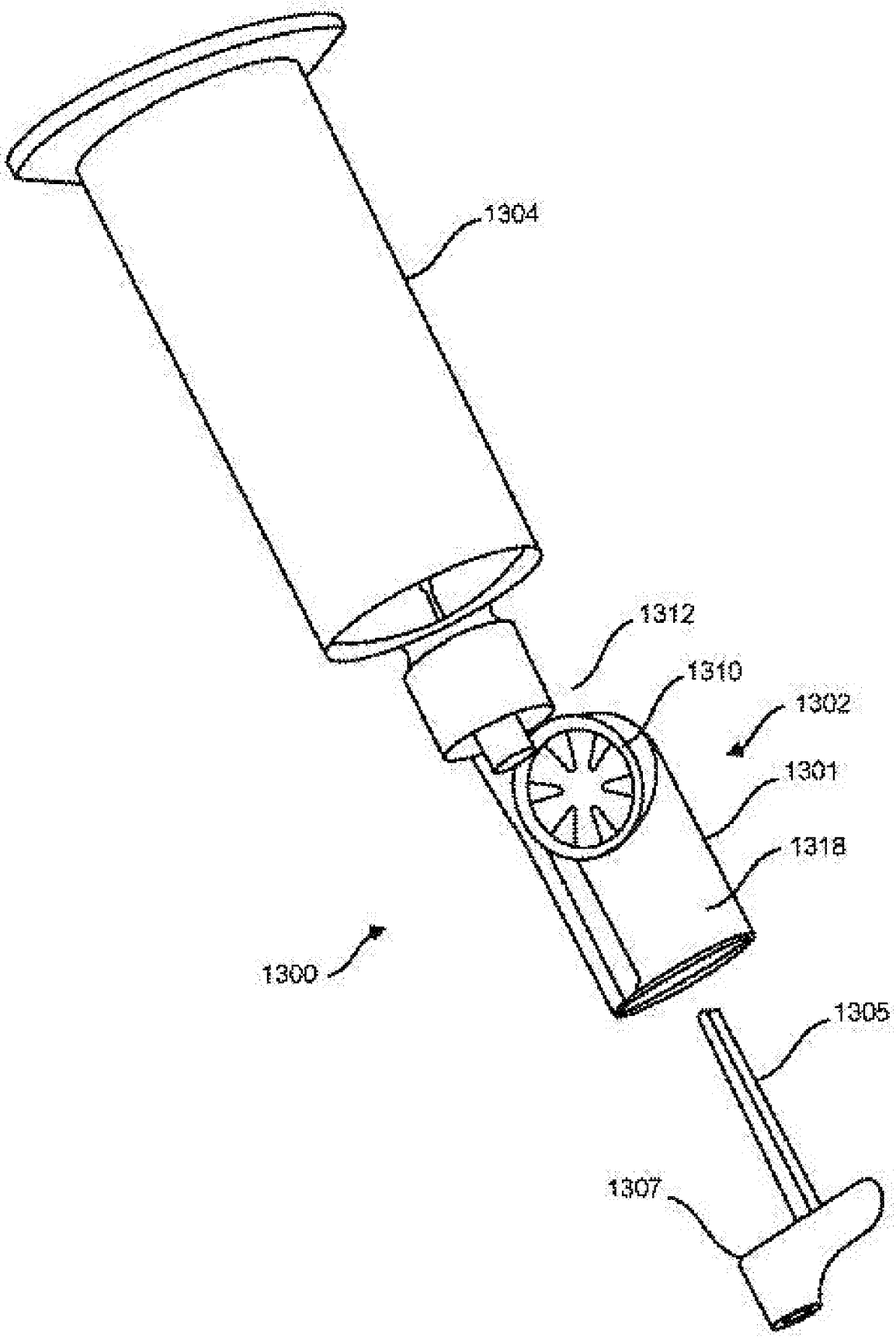


FIG. 13A

[Fig. 13B]

FIG. 13A

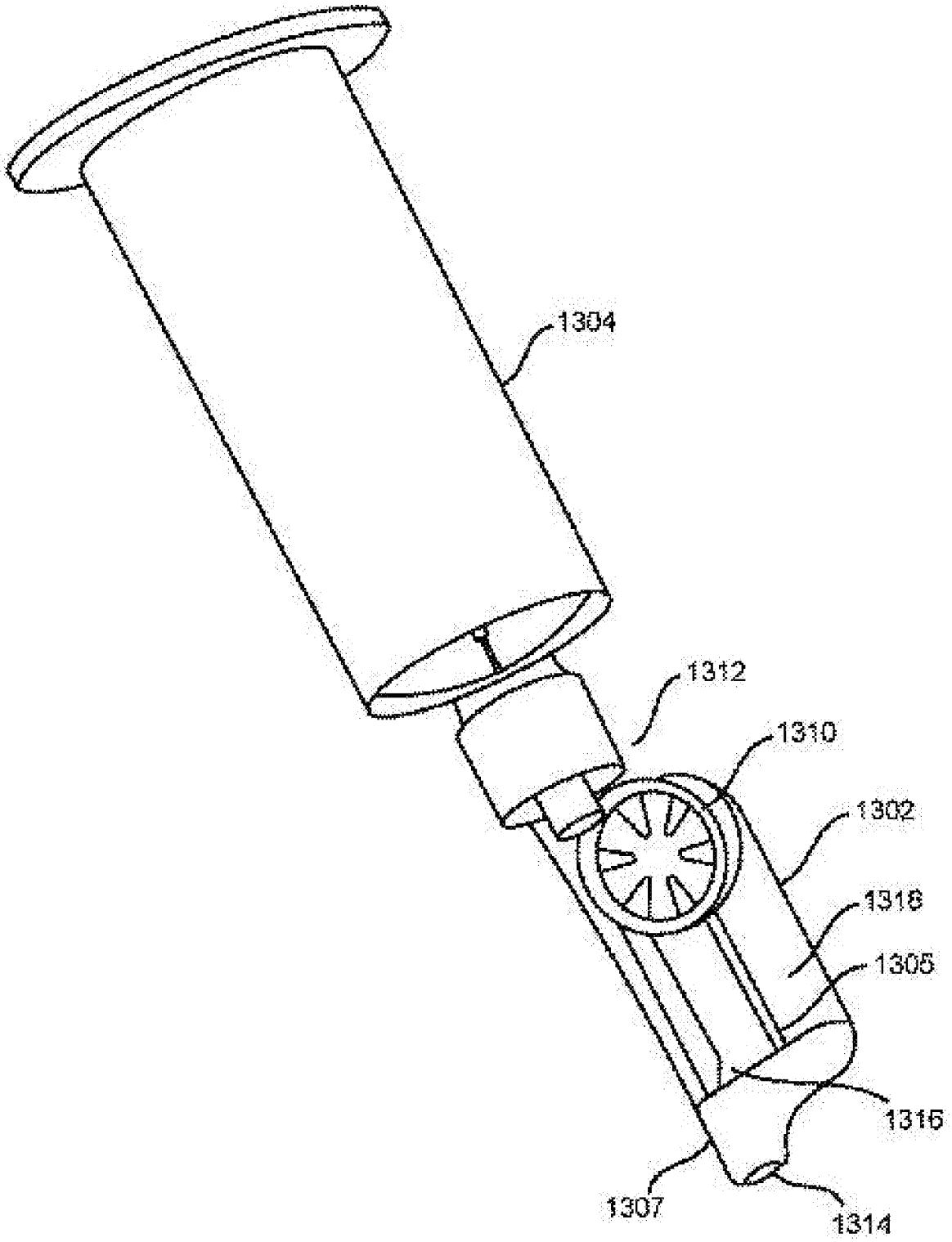


FIG. 13B

[Fig. 13C]

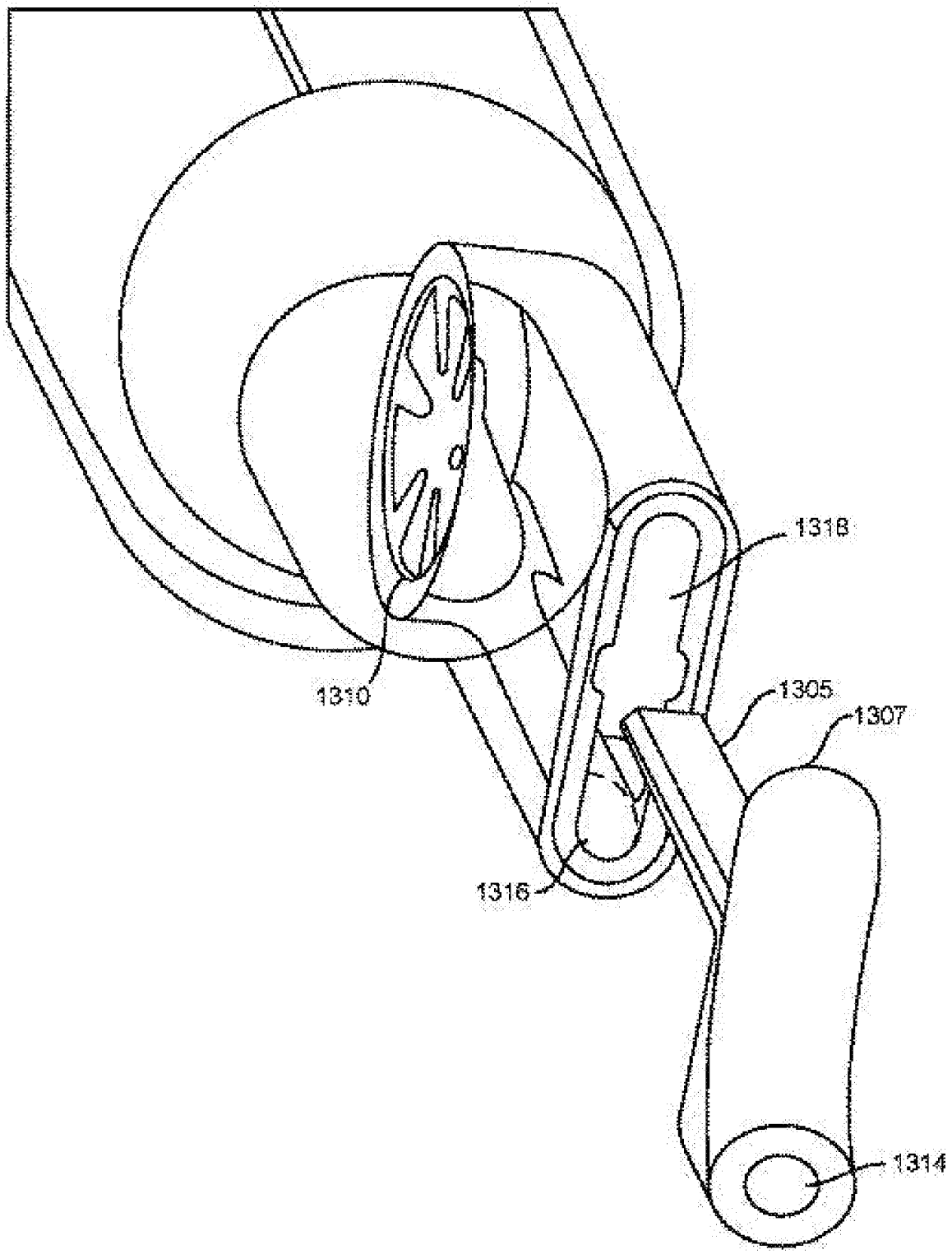
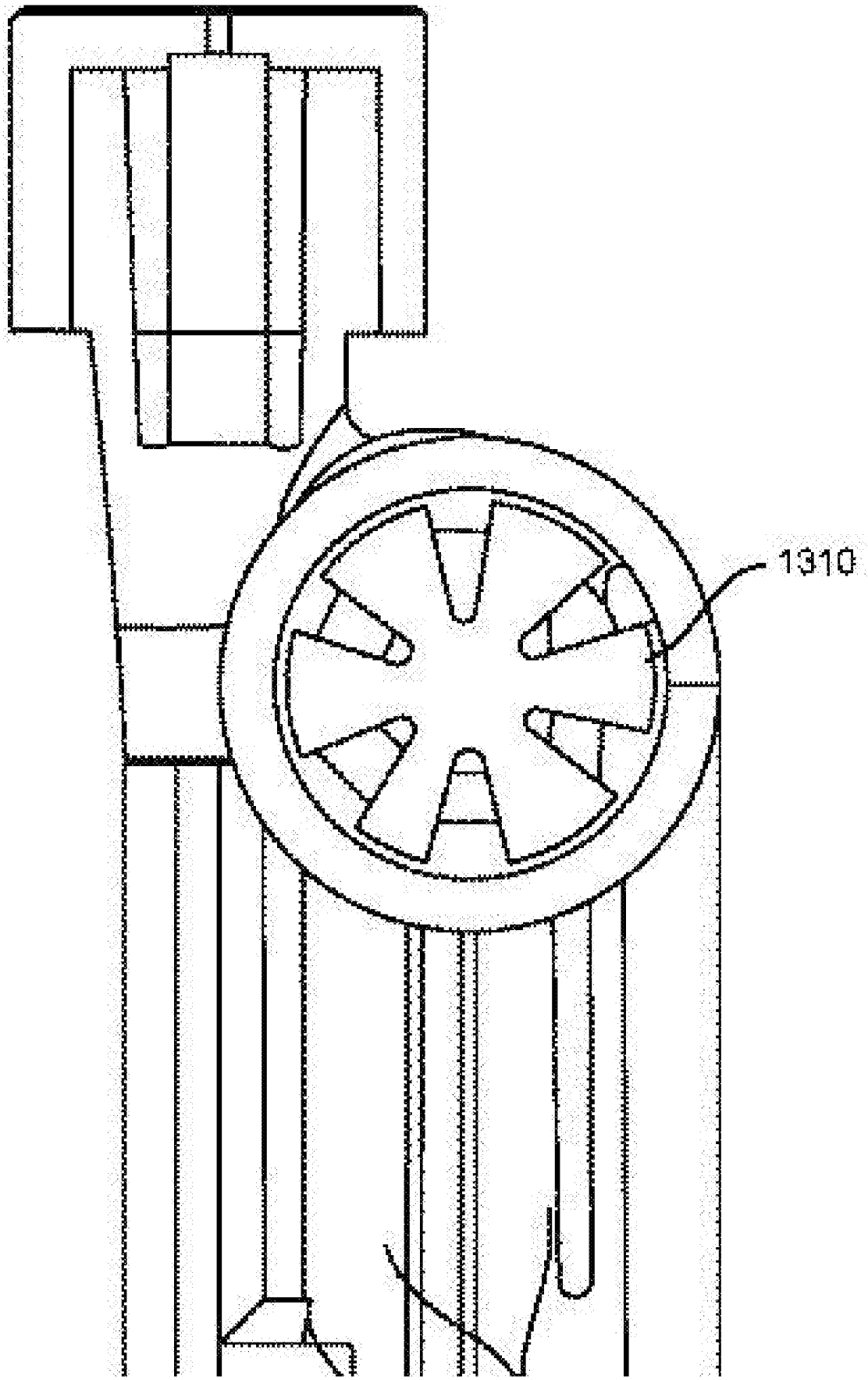


FIG. 13C

[Fig. 13D]


1310

[Fig. 14A]

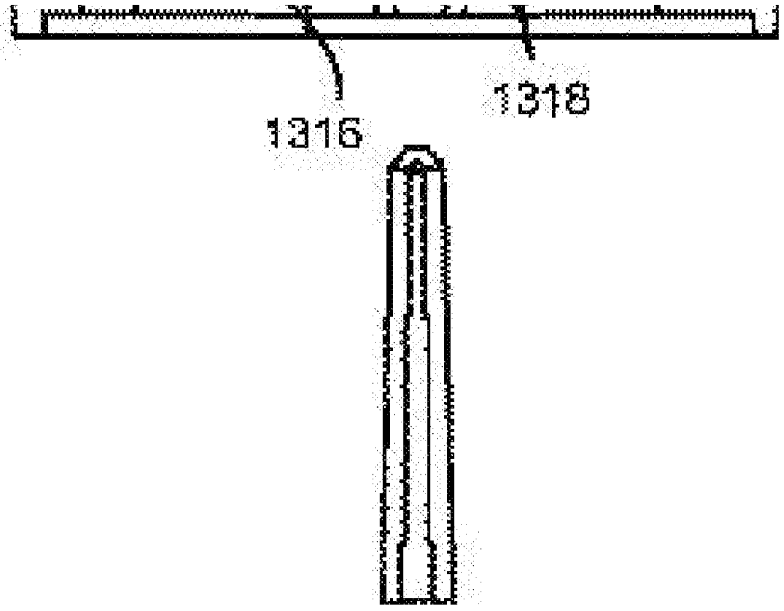
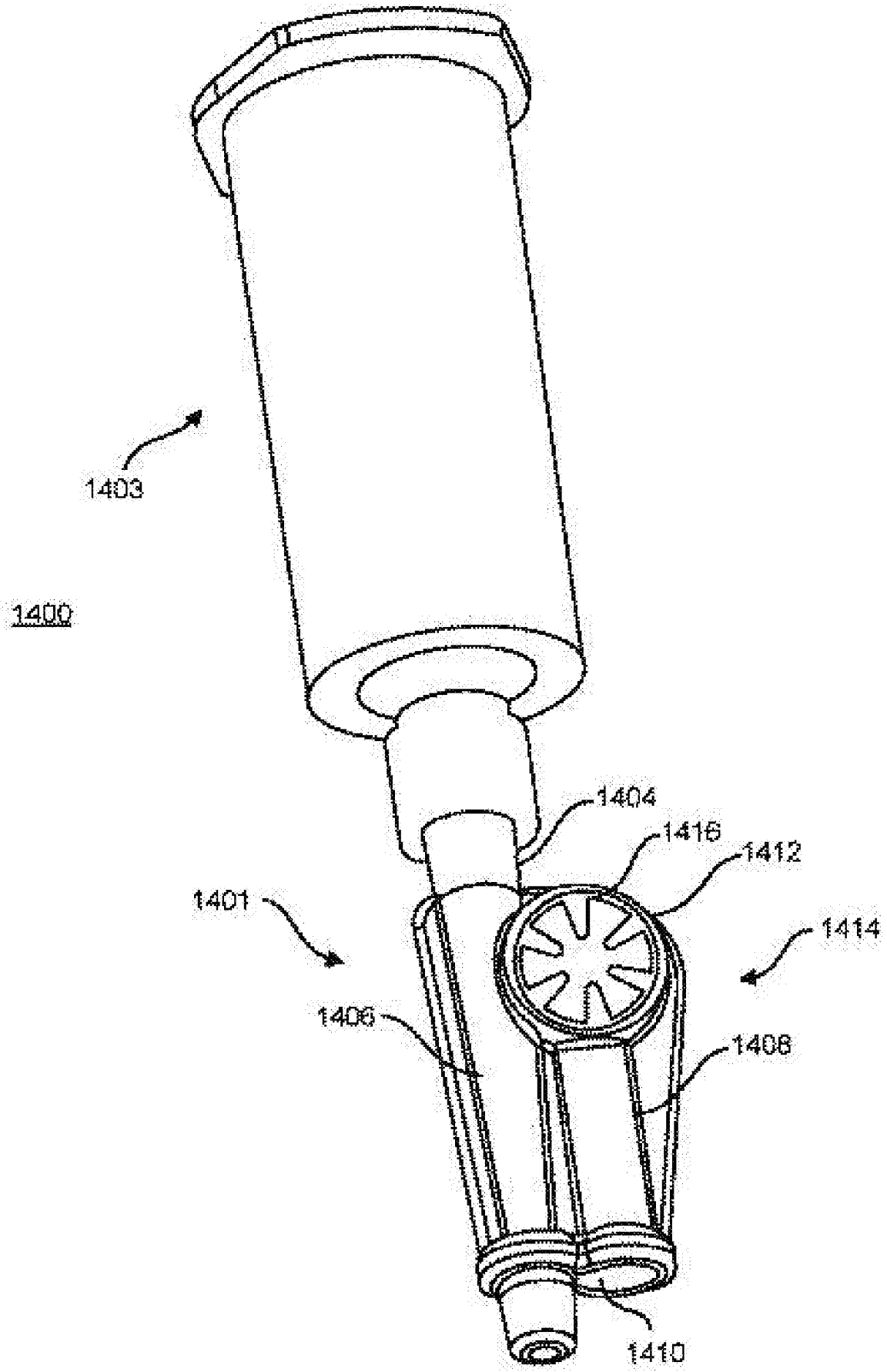


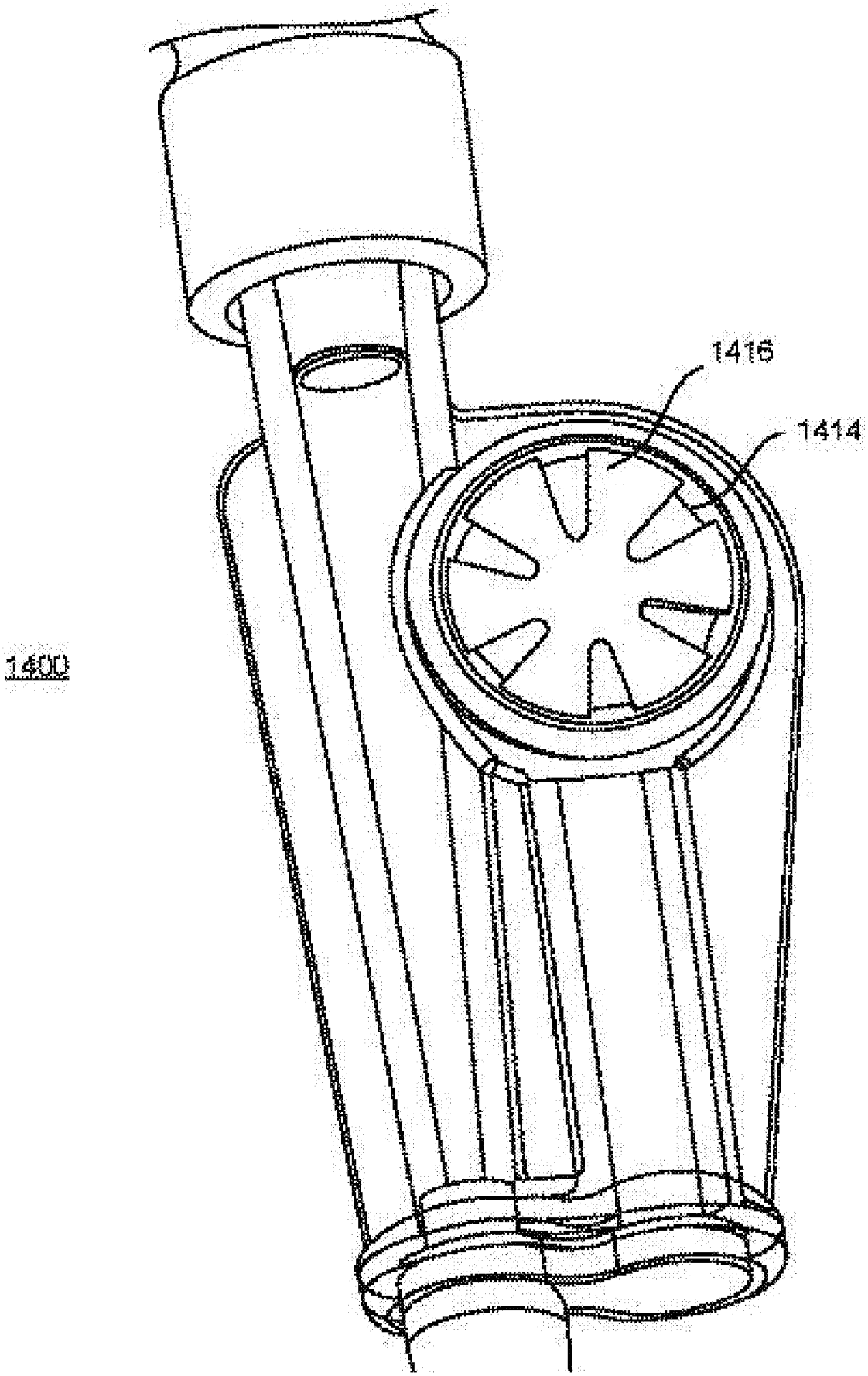
FIG. 13D


1403
1400
1404
1416
1412
1401
1414
1406
1408
1410

[Fig. 14B]



FIG. 14A


1416
1414
1400

[Fig. 14C]



FIG. 14B

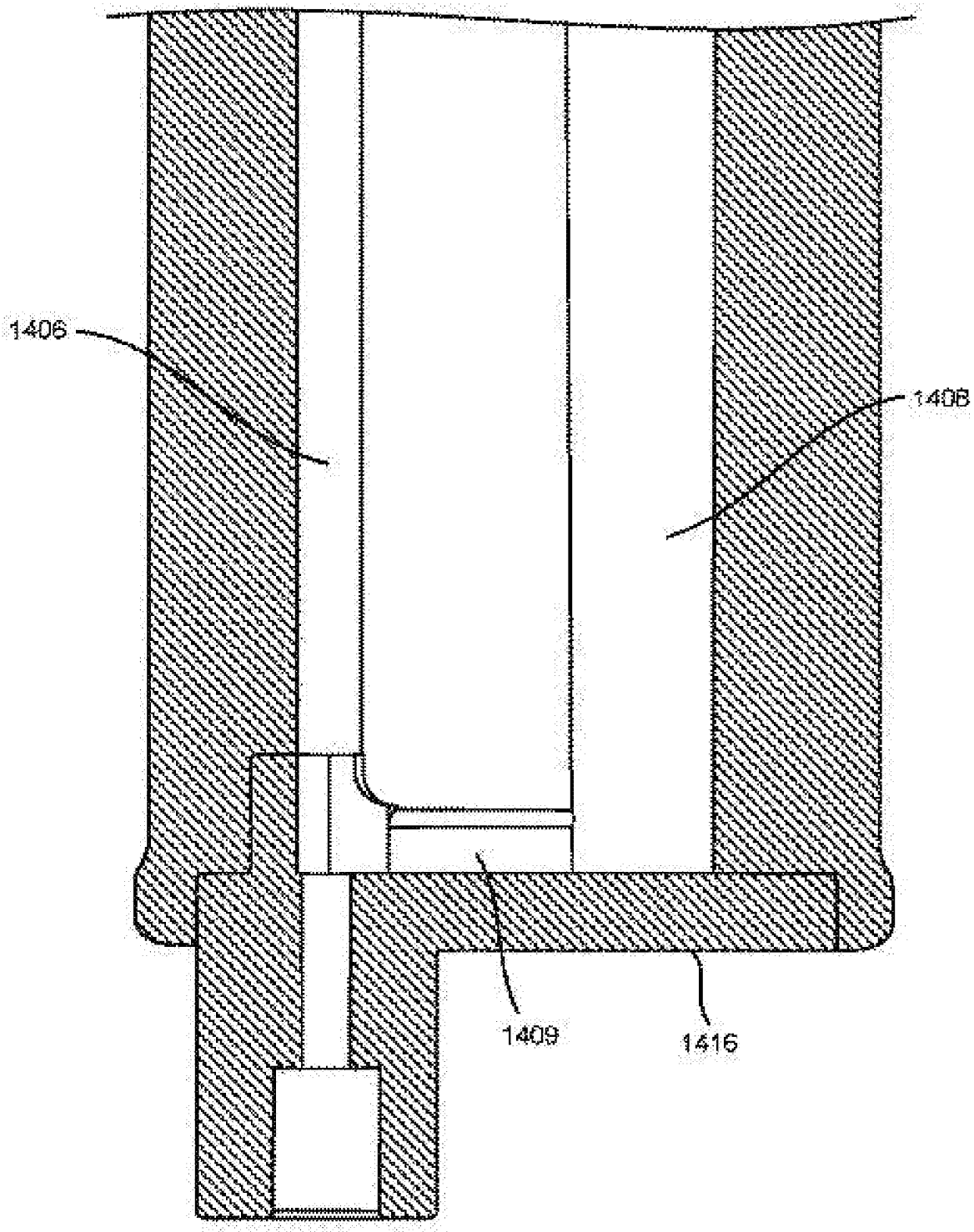
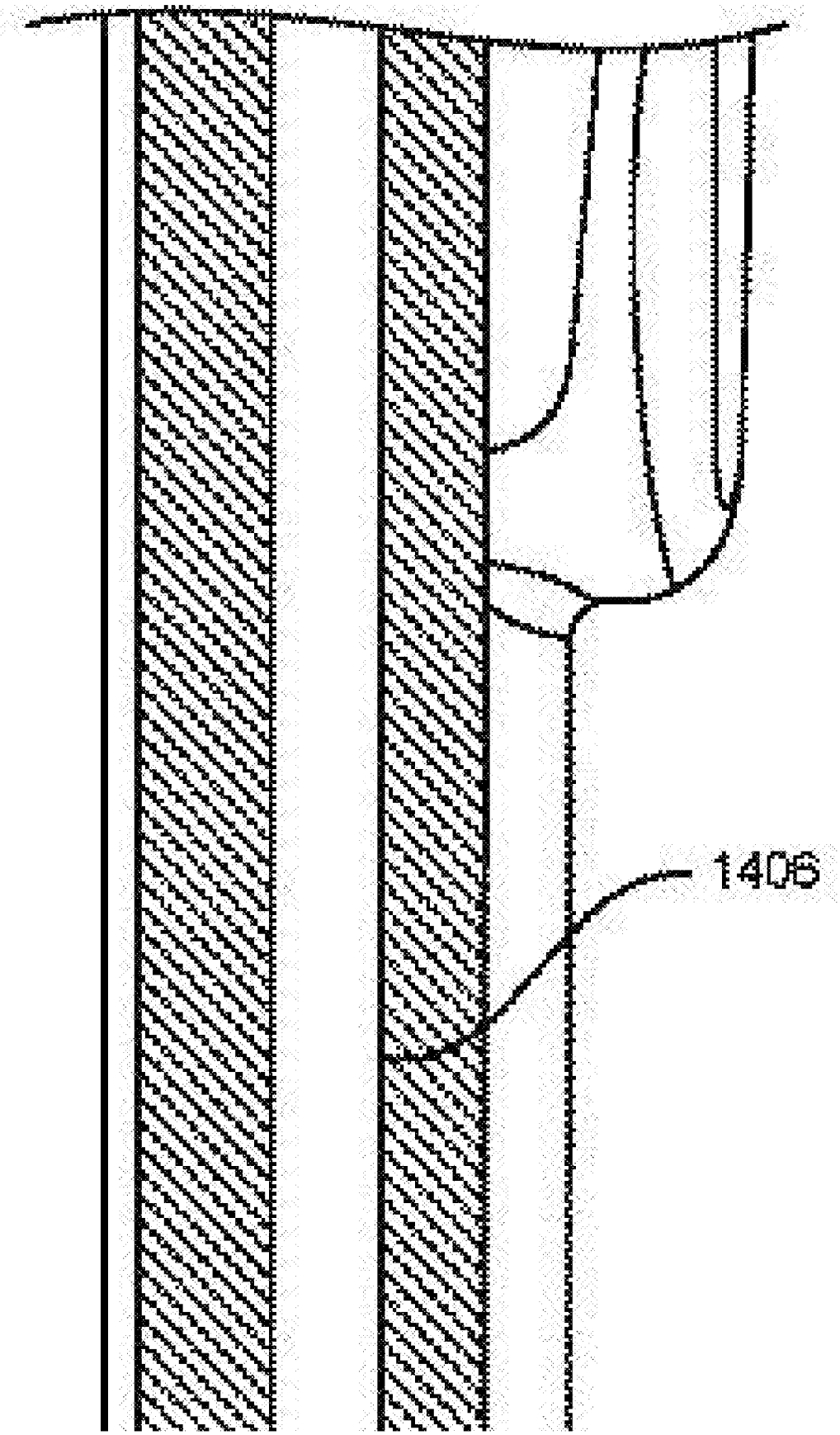


FIG. 14C

[Fig. 14D]


1406

[Fig. 14E]

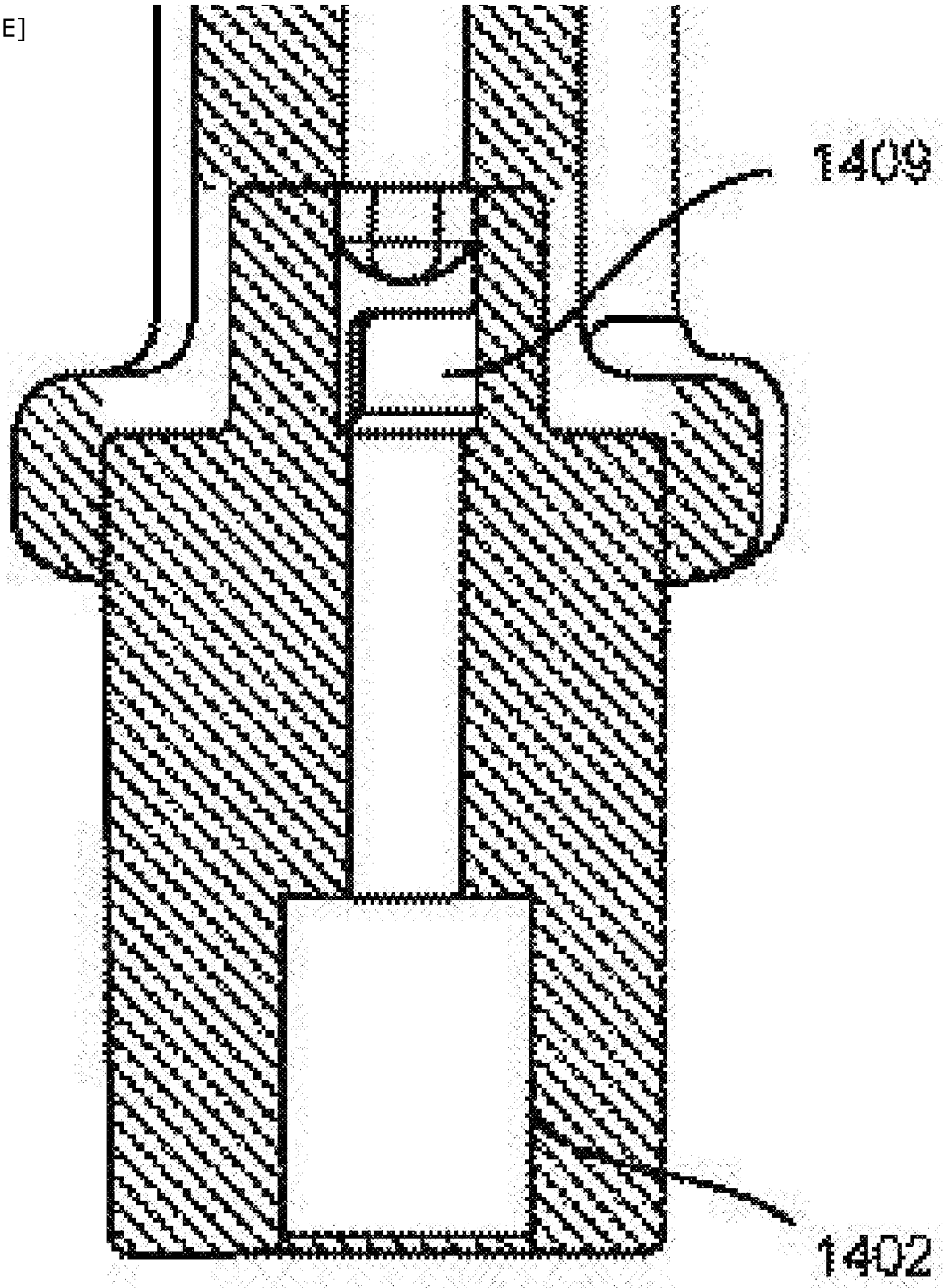


FIG. 14D

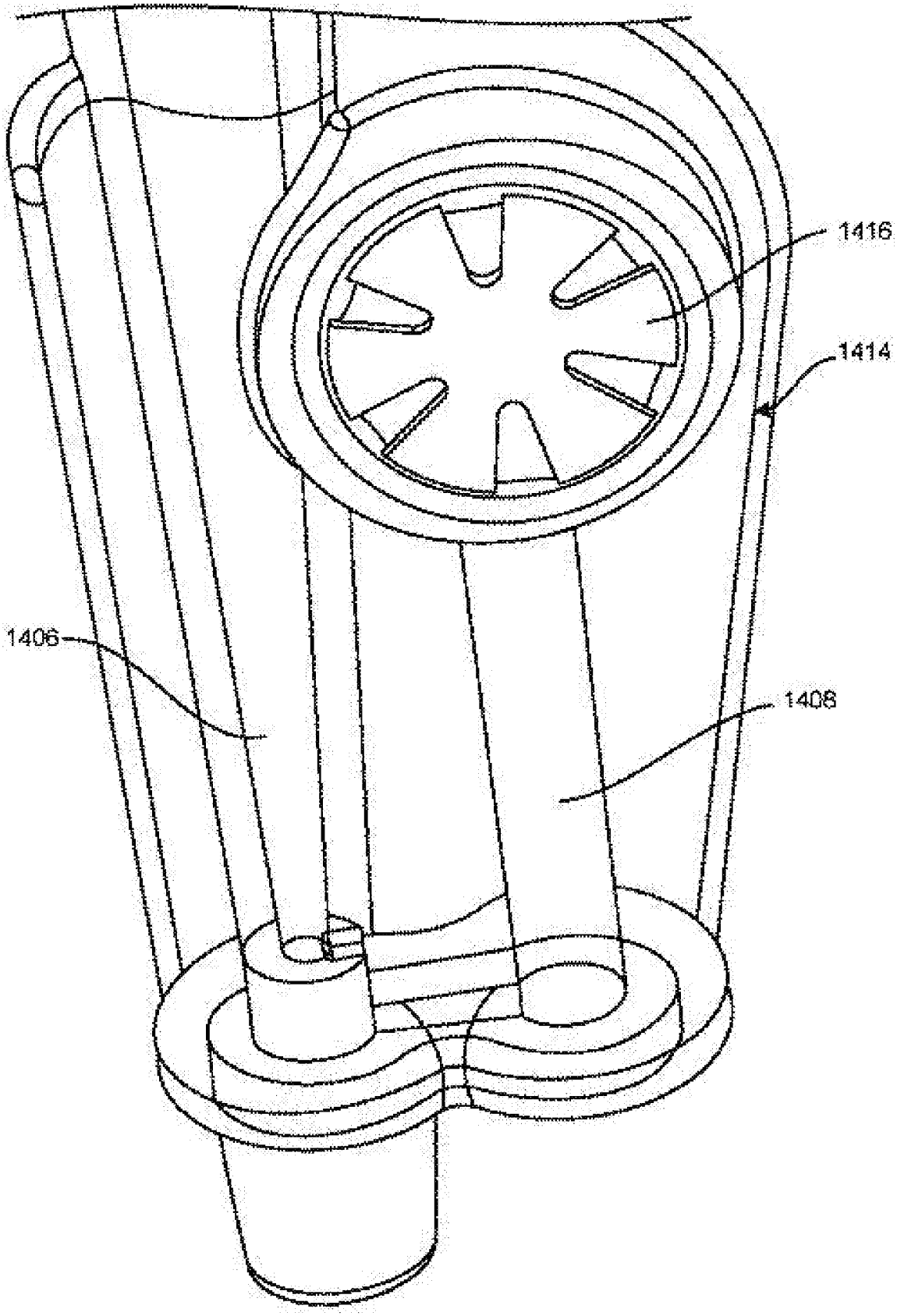


FIG. 14E

[Fig. 15A]

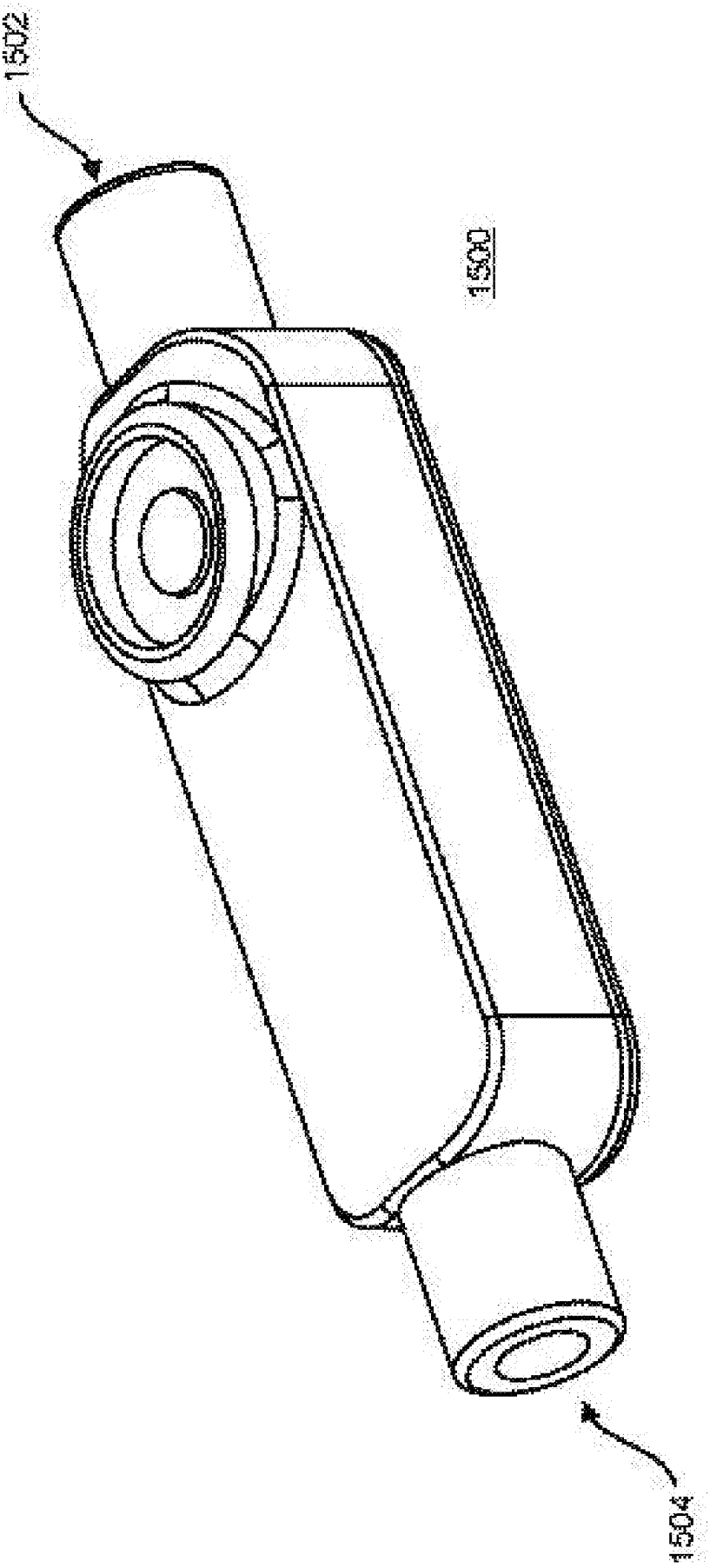


FIG. 15A

[Fig. 15B]

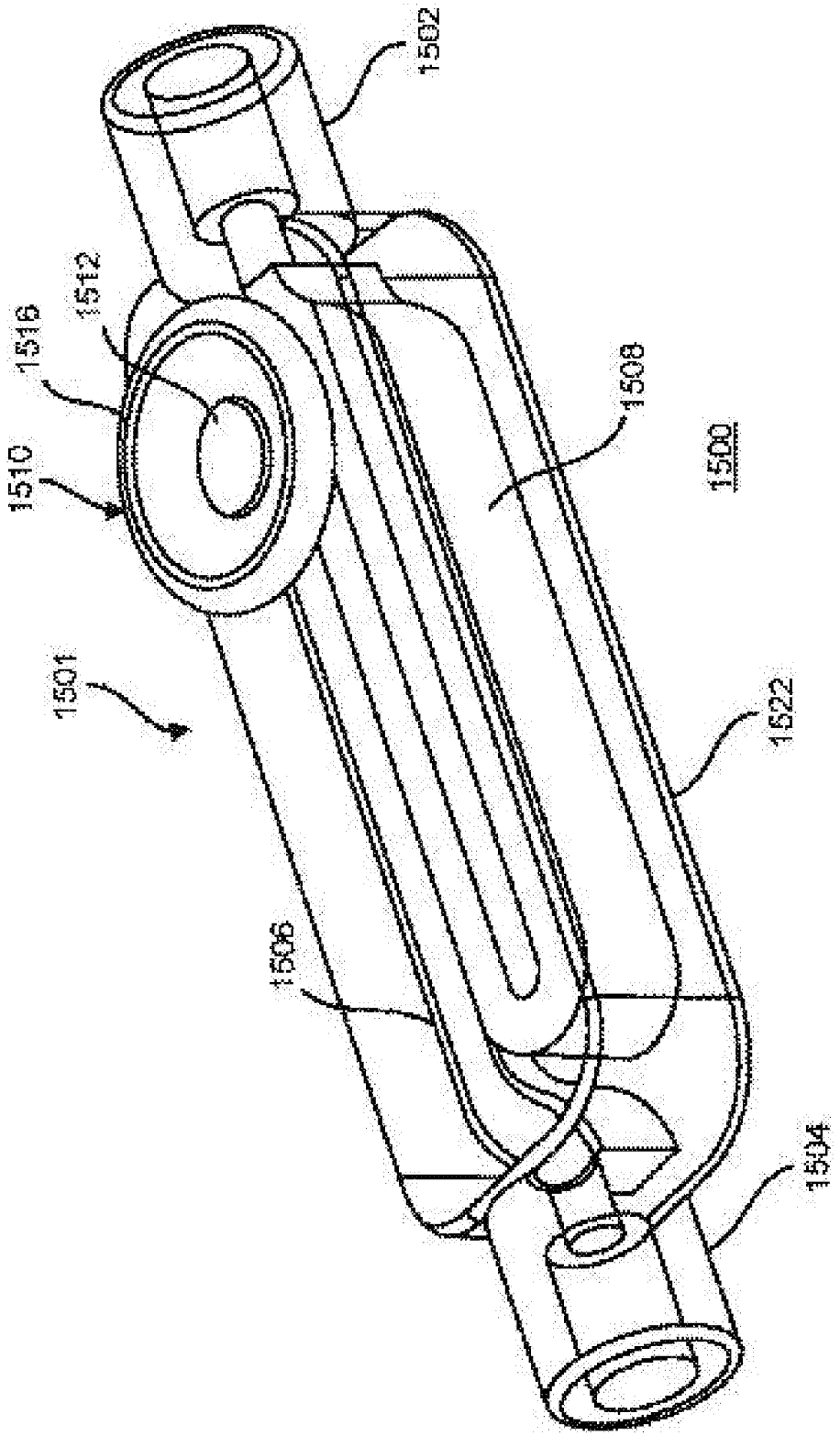


FIG. 15B

[Fig. 15C]

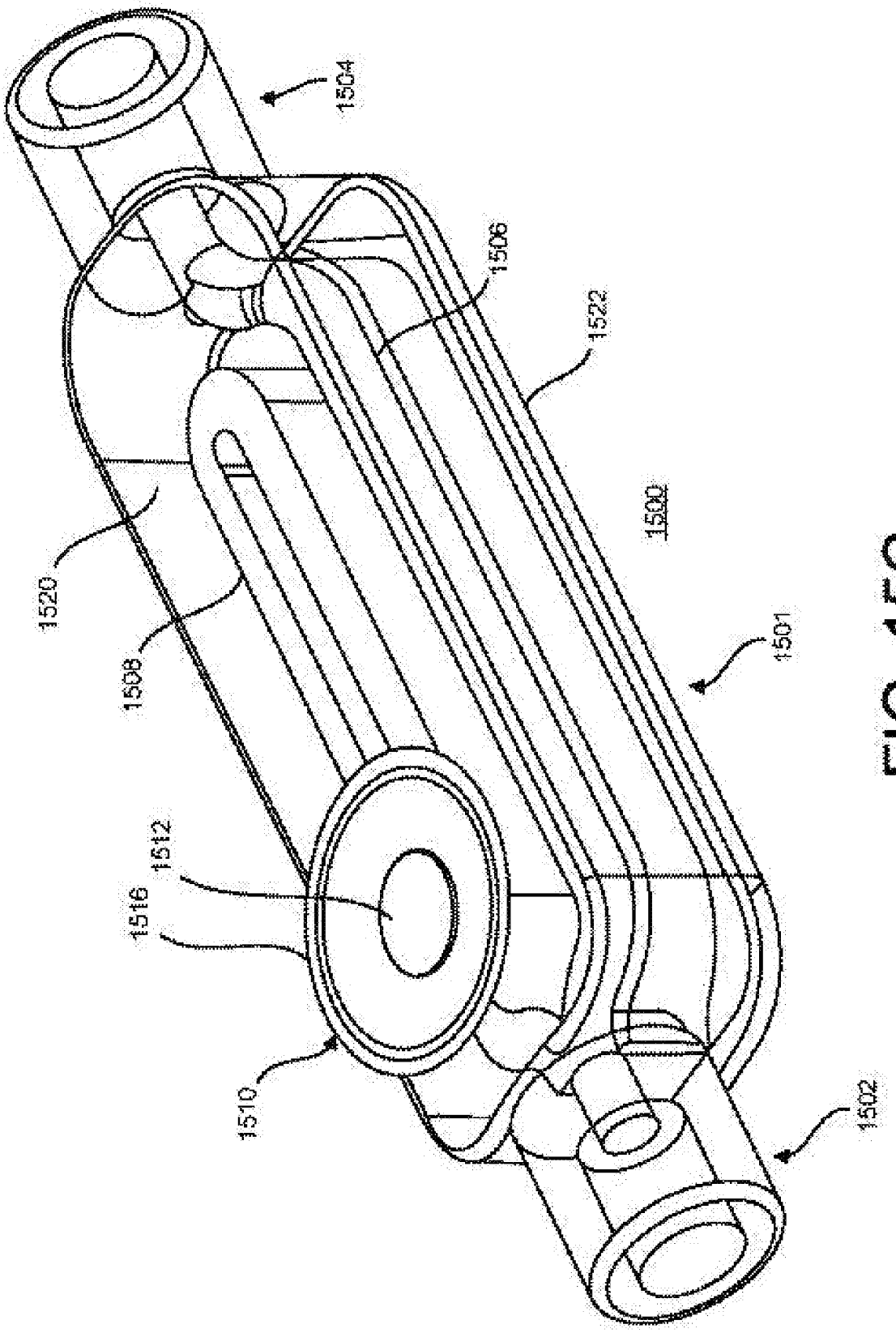


FIG. 15C

[Fig. 15D]

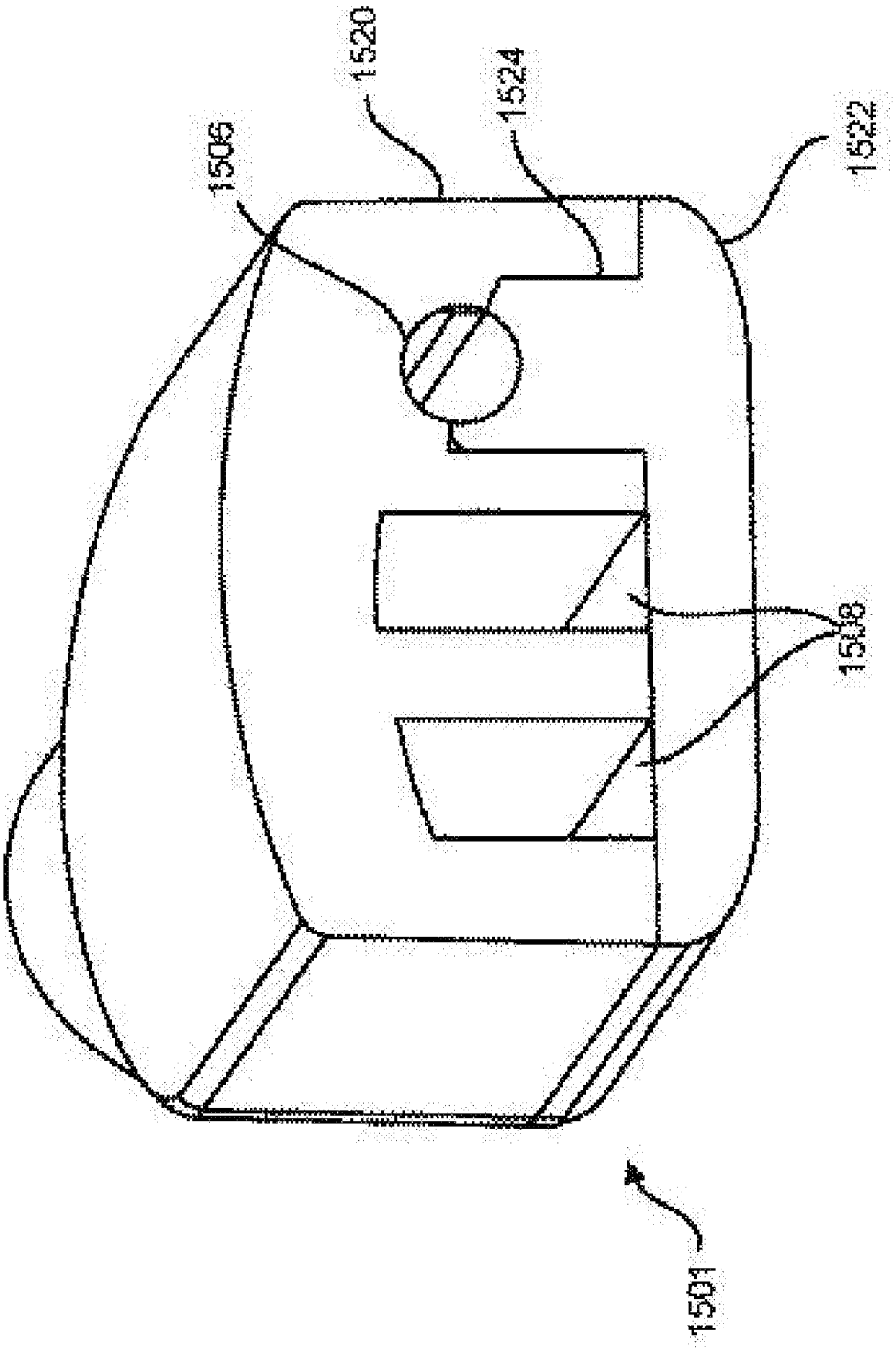


FIG. 15D

[Fig. 15E]

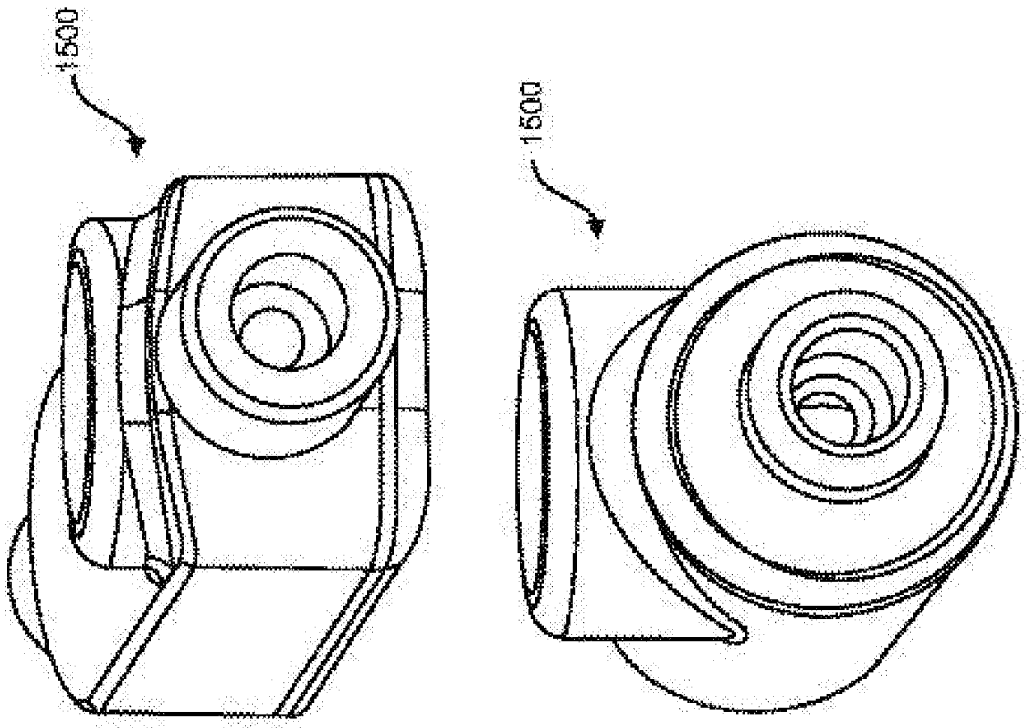


FIG. 15E

[Fig. 15F]

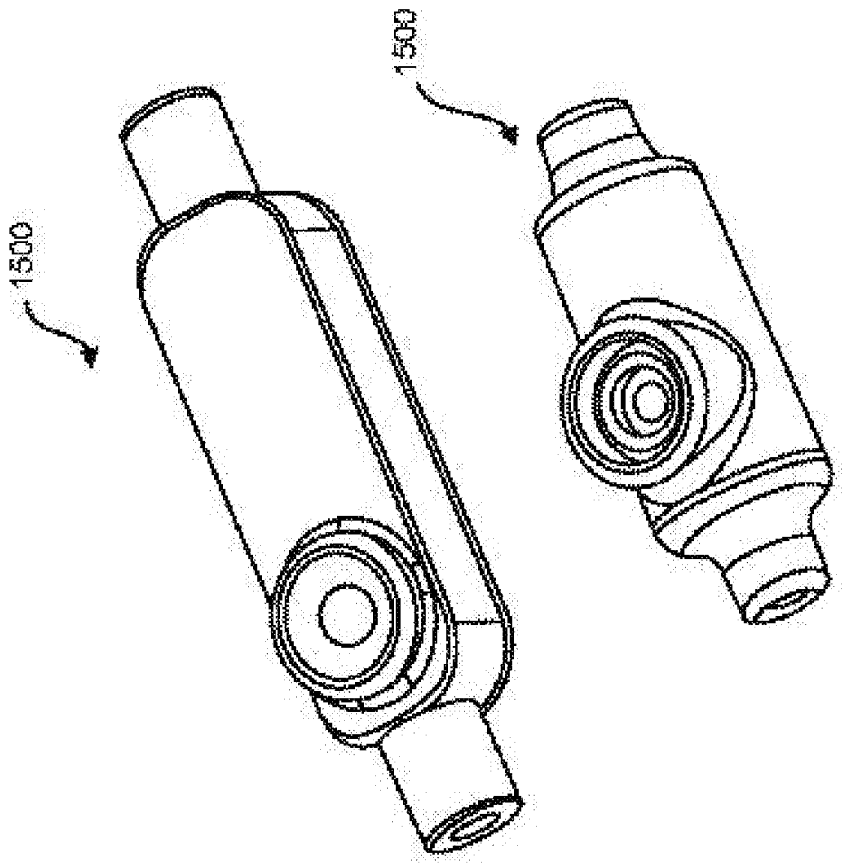


FIG. 15F

[Fig. 15G]

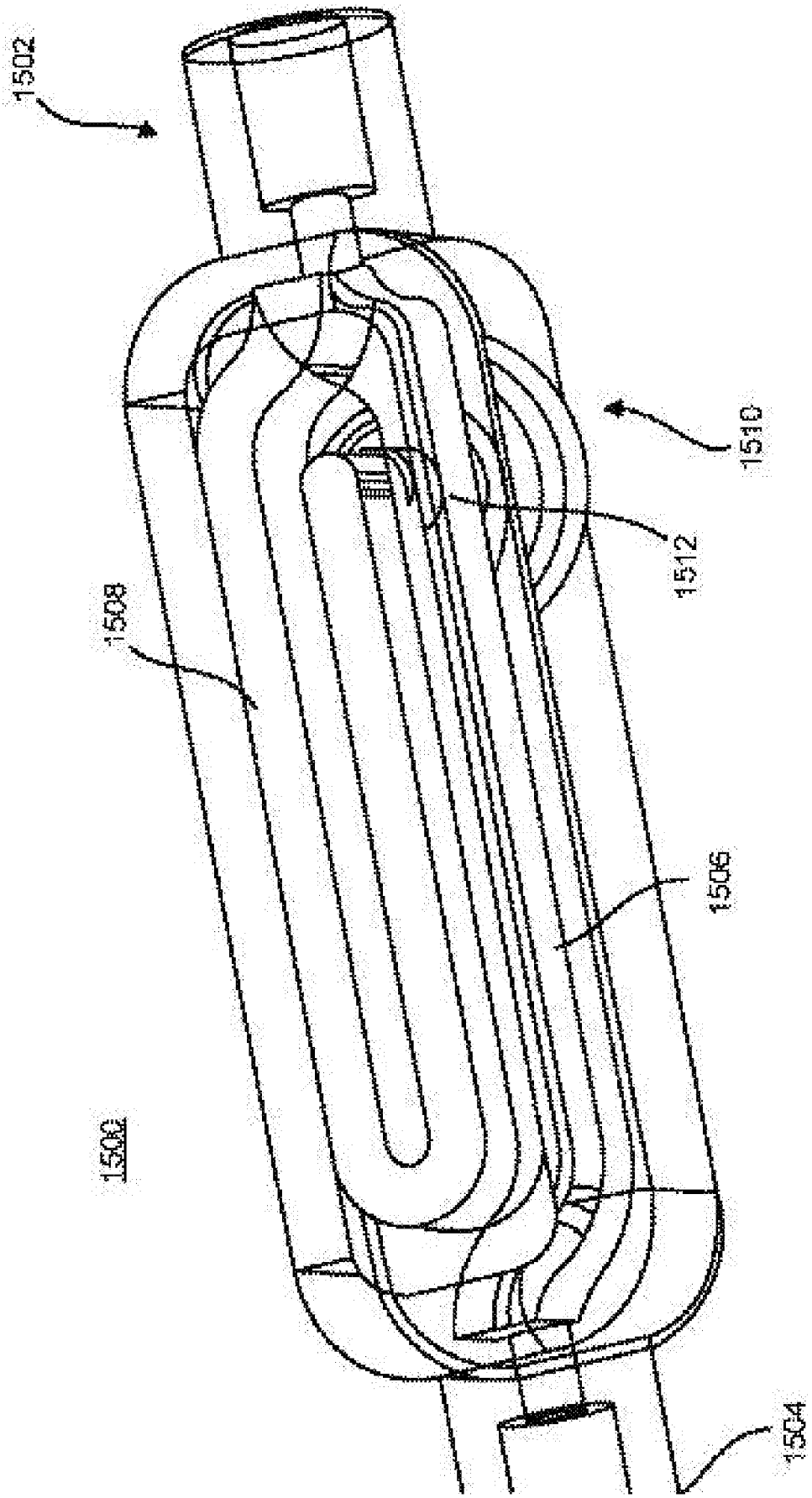


FIG. 15G

[Fig. 16A]



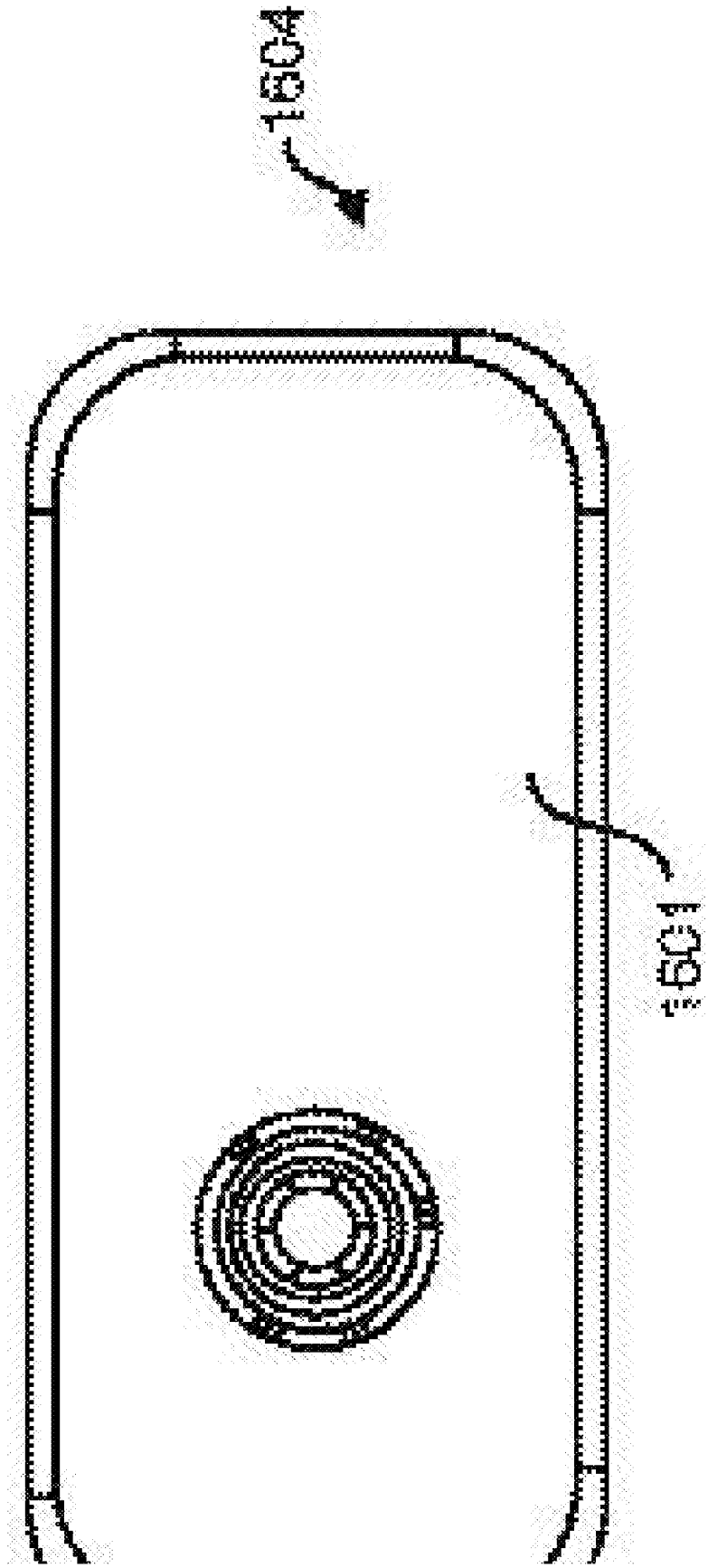
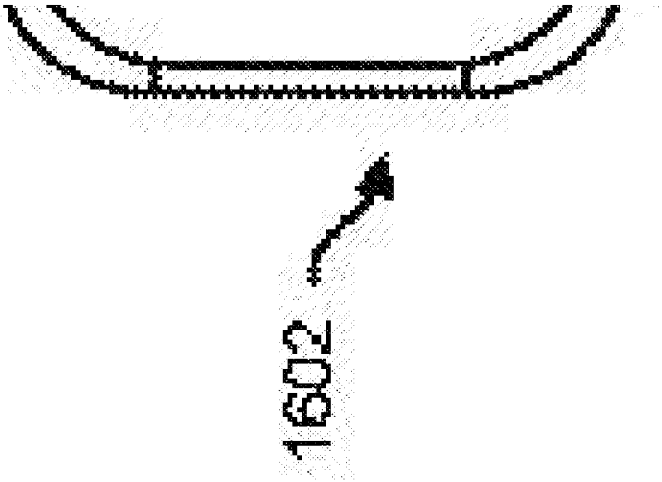
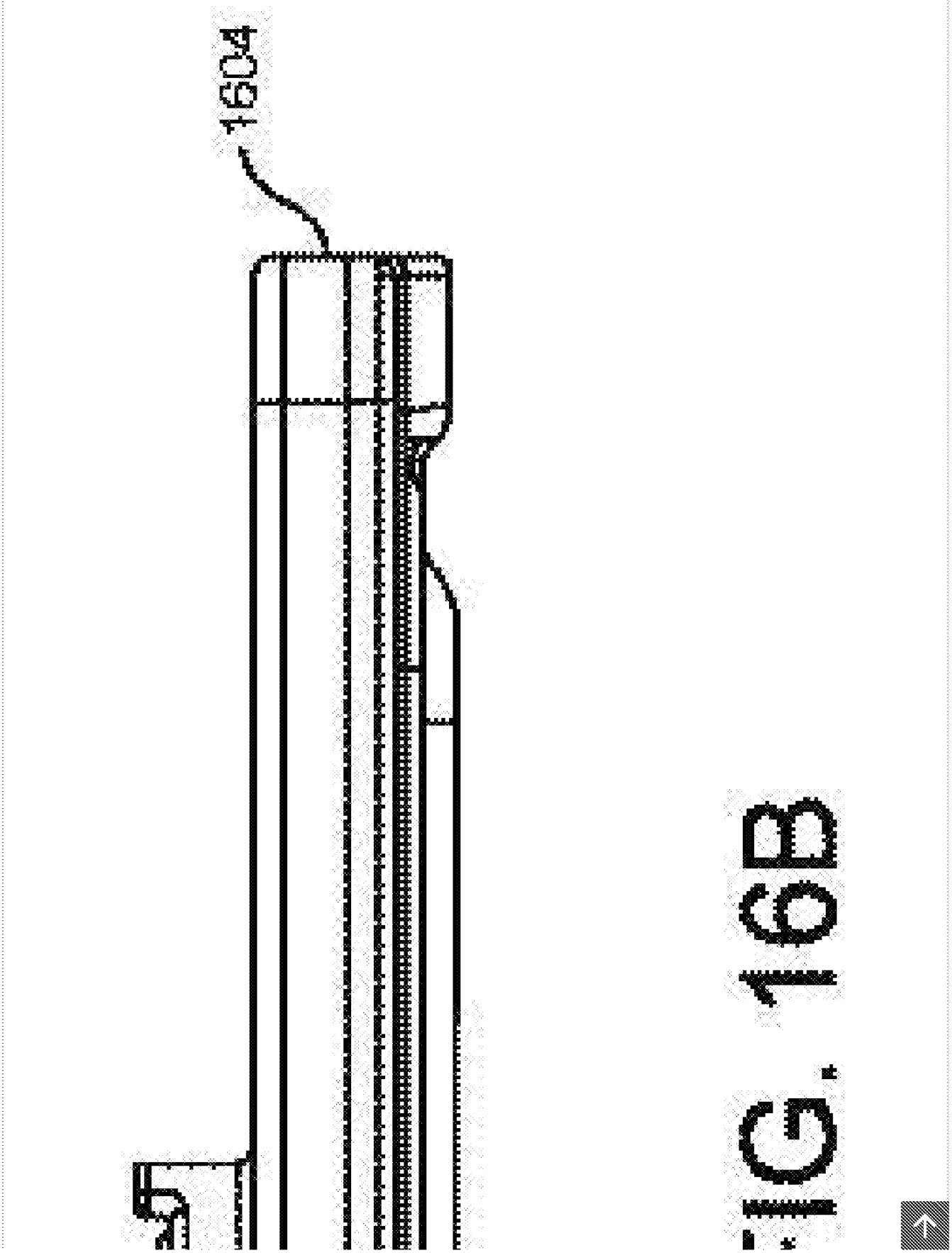


FIG. 16A

[Fig. 16B]




160a
160
160b

[Fig. 16C]

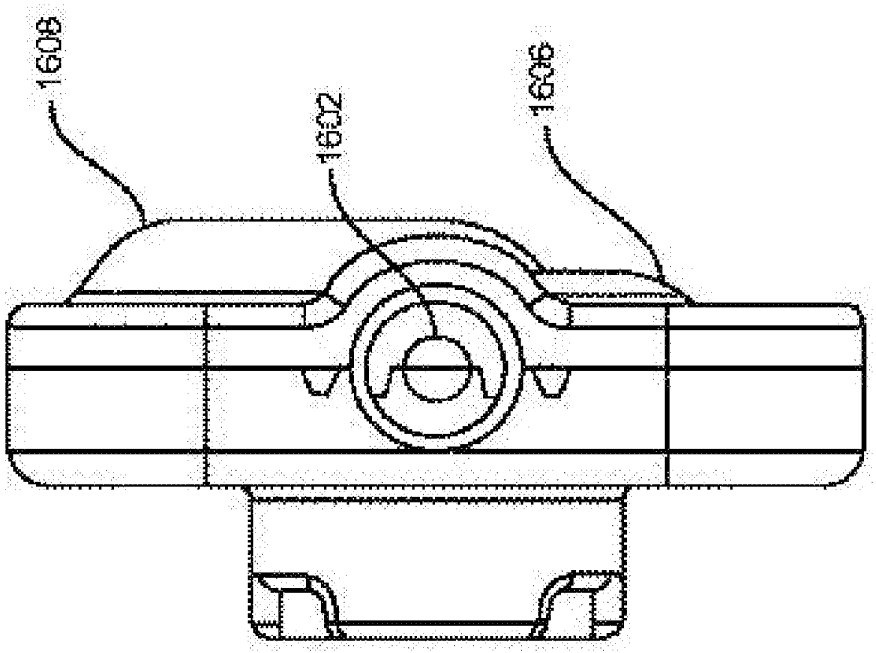
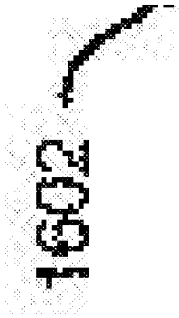


FIG. 16C

[Fig. 16D]



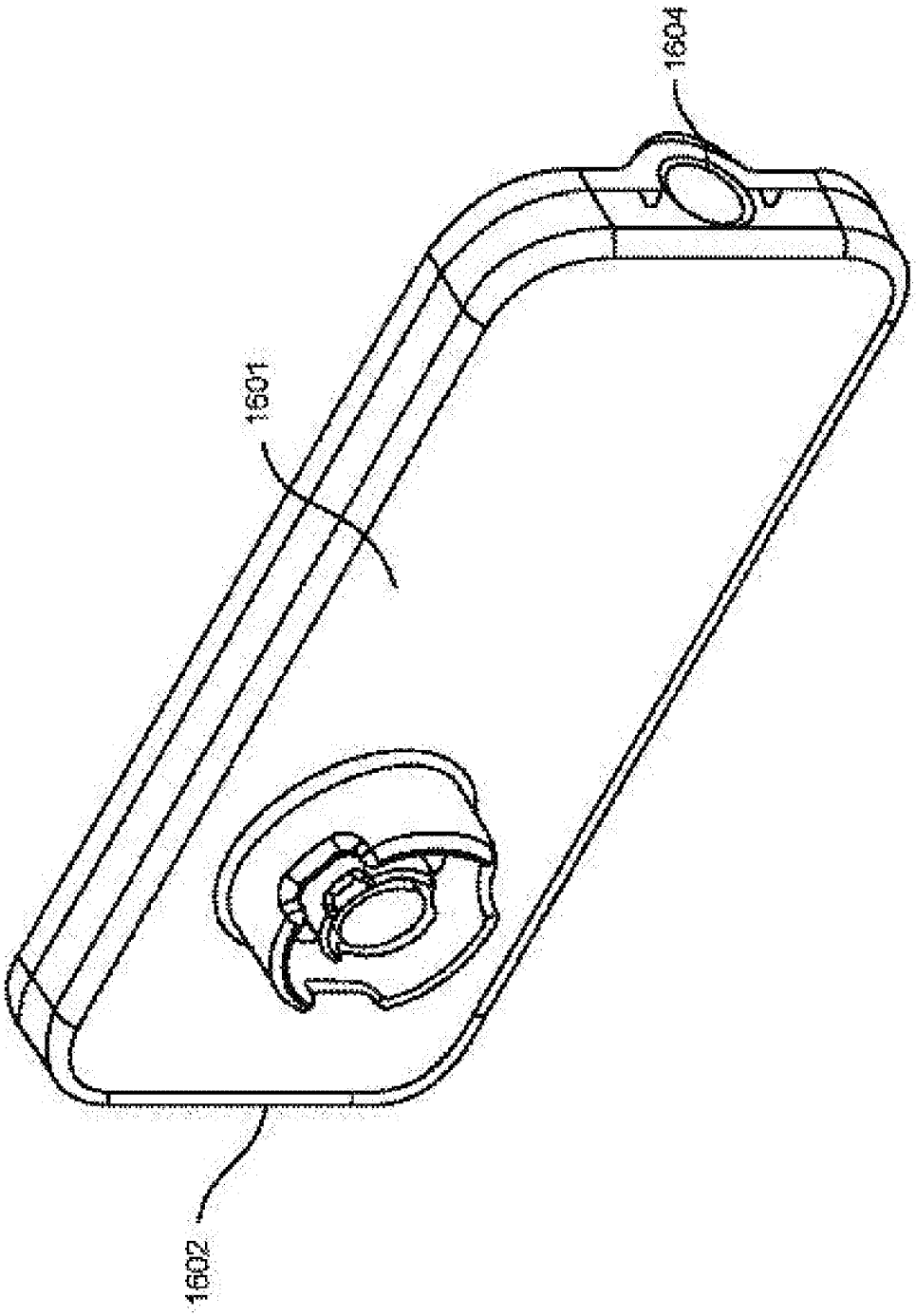


FIG. 16D

[Fig. 17A]

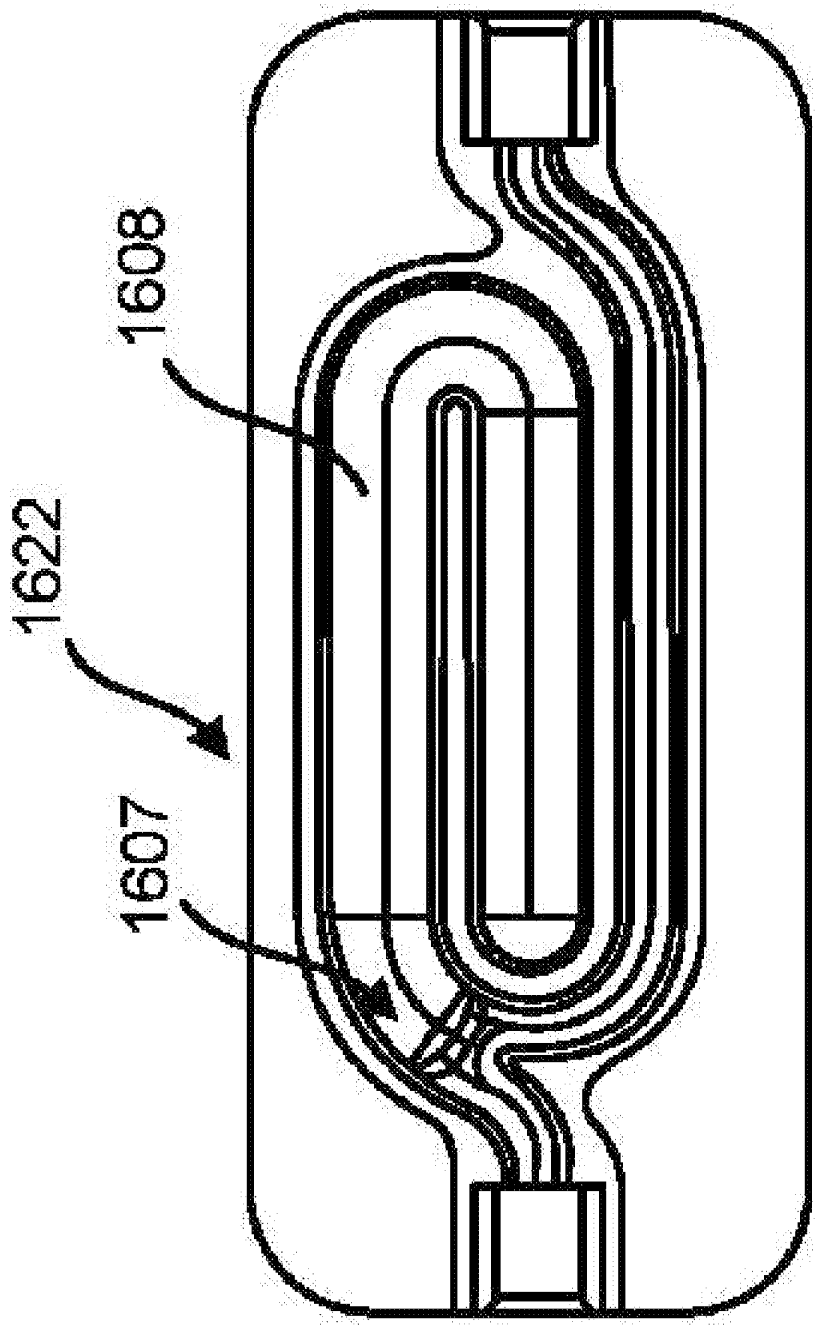


FIG. 17A

[Fig. 17B]

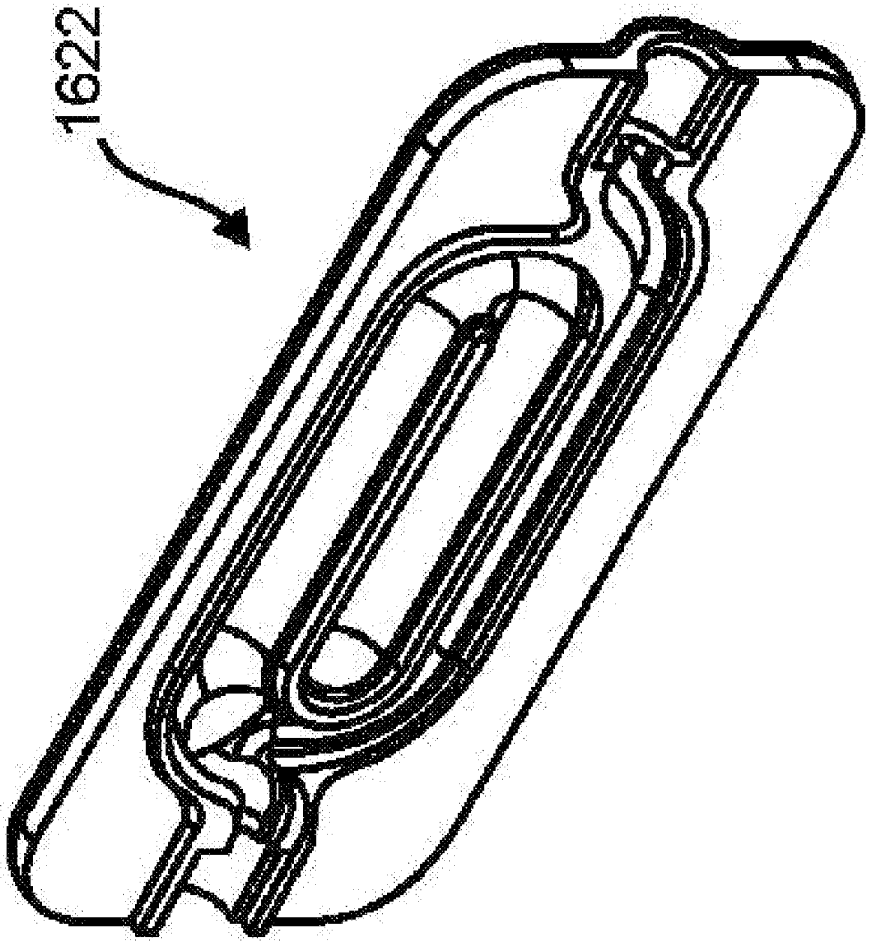


FIG. 17B

[Fig. 17C]

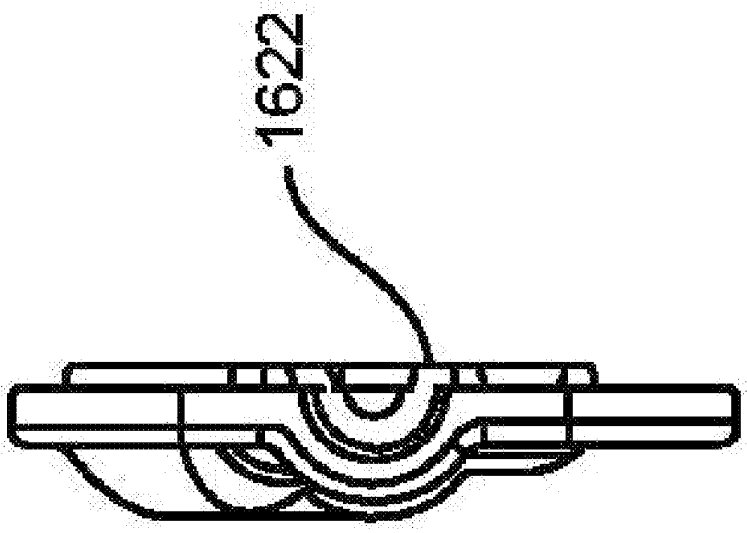


FIG. 17C

[Fig. 17D]

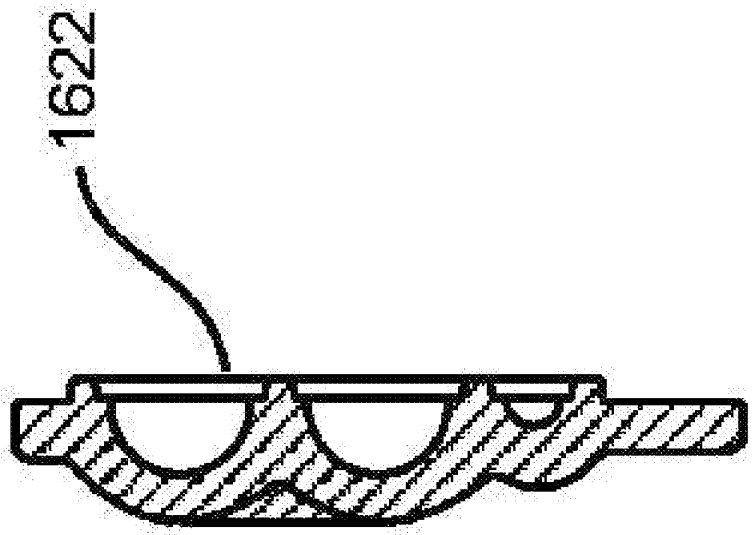


FIG. 17D

[Fig. 17E]



FIG. 17E

[Fig. 18A]

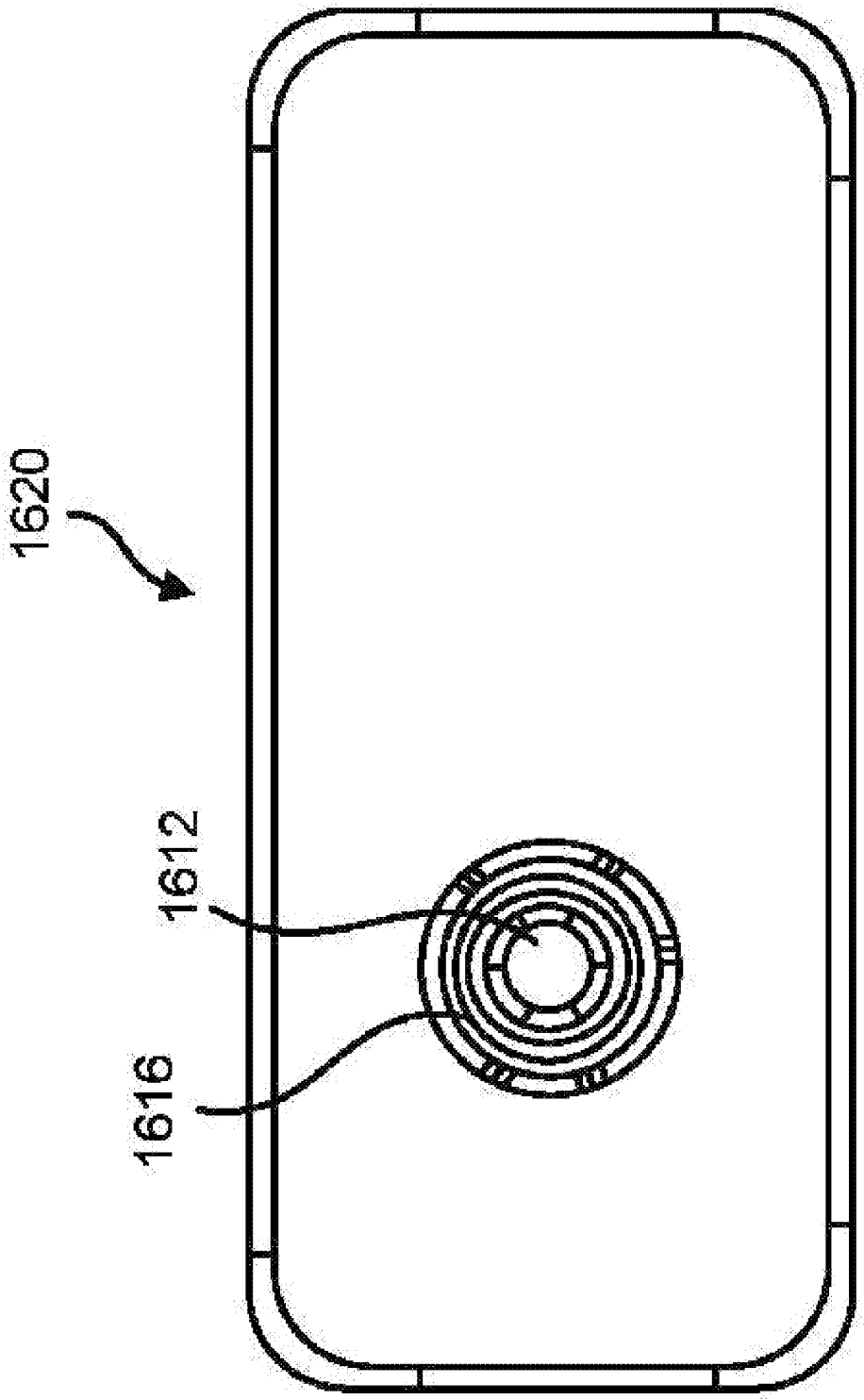


FIG. 18A

[Fig. 18B]

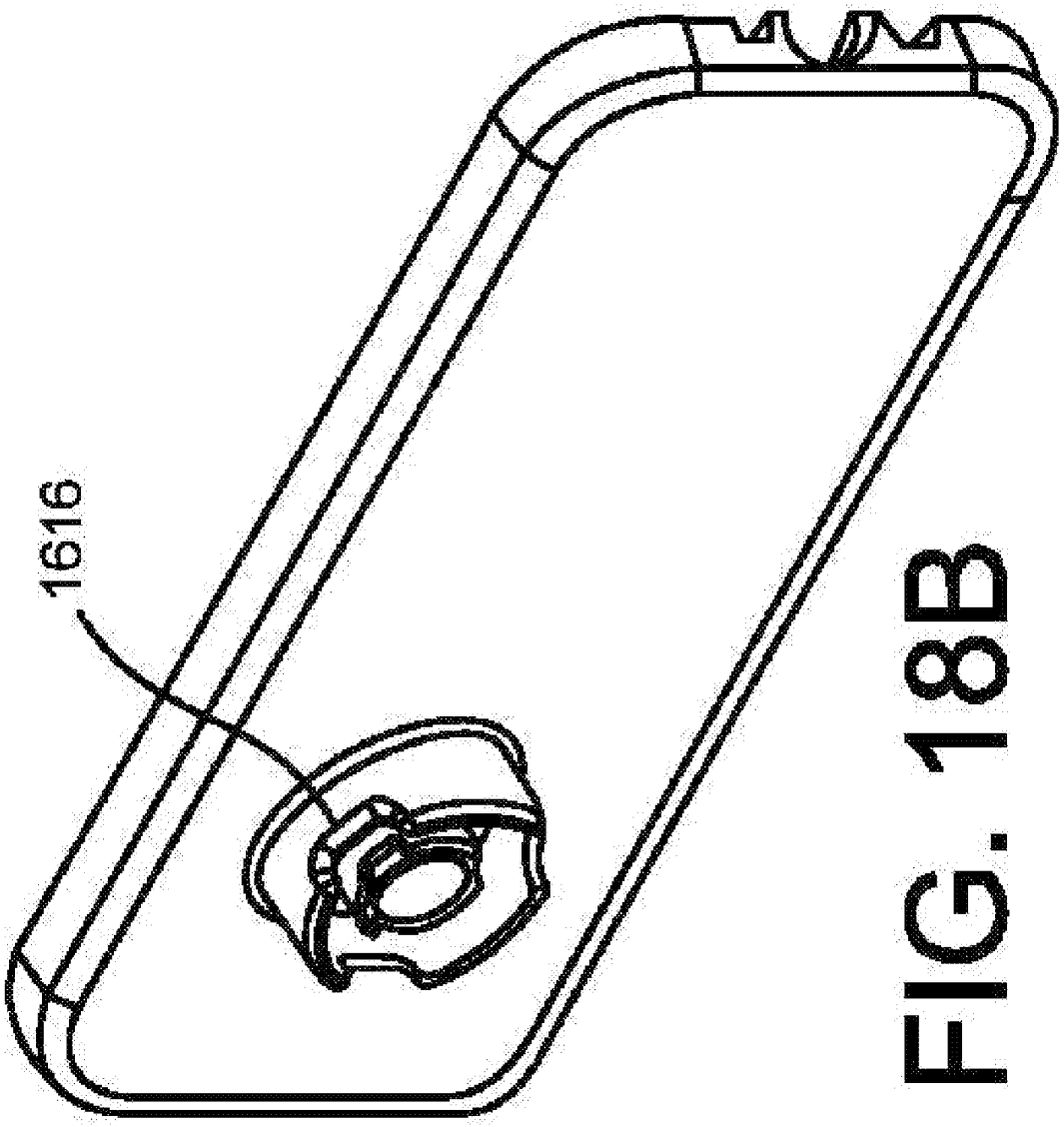


FIG. 18B

[Fig. 18C]

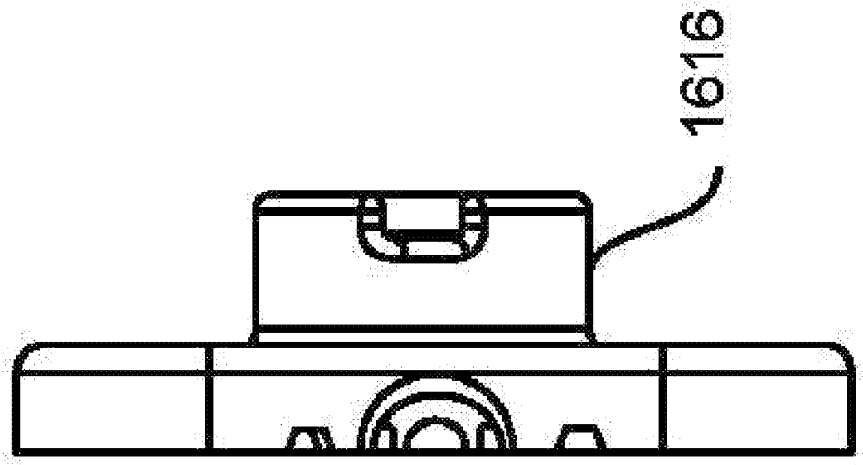


FIG. 18C

[Fig. 18D]

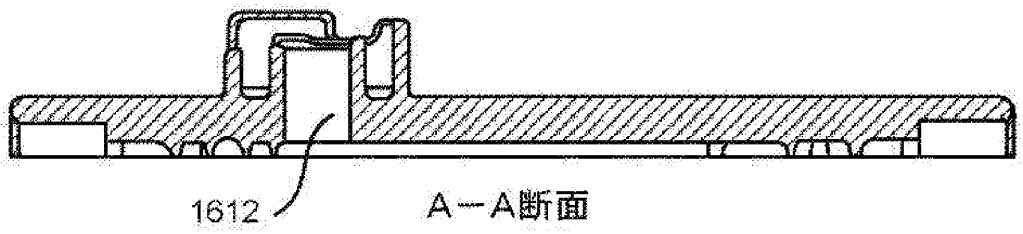


FIG. 18D

[Fig. 18E]

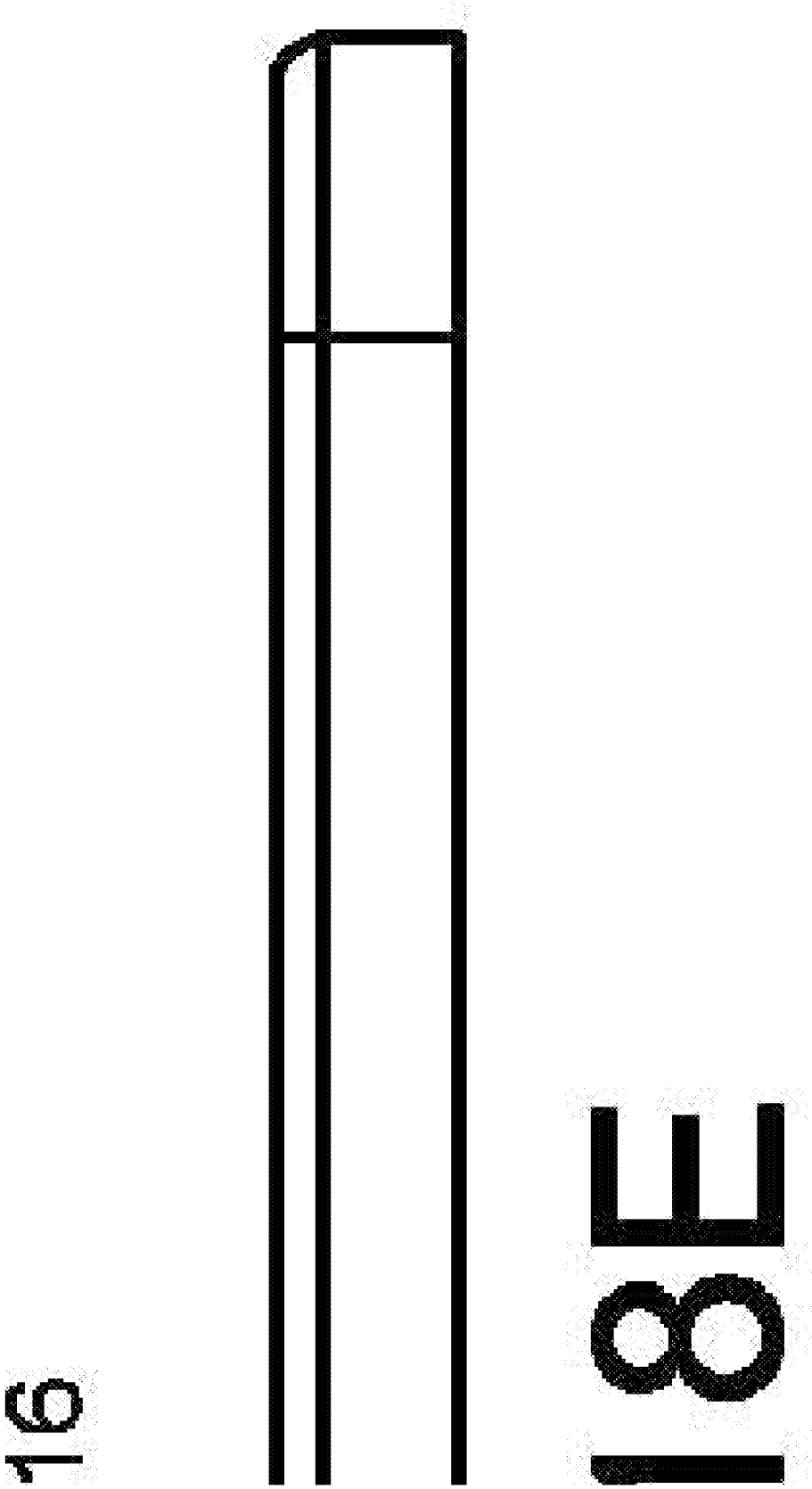
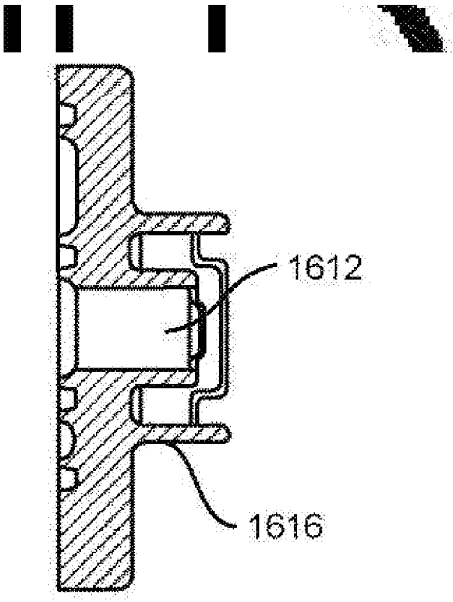


図18

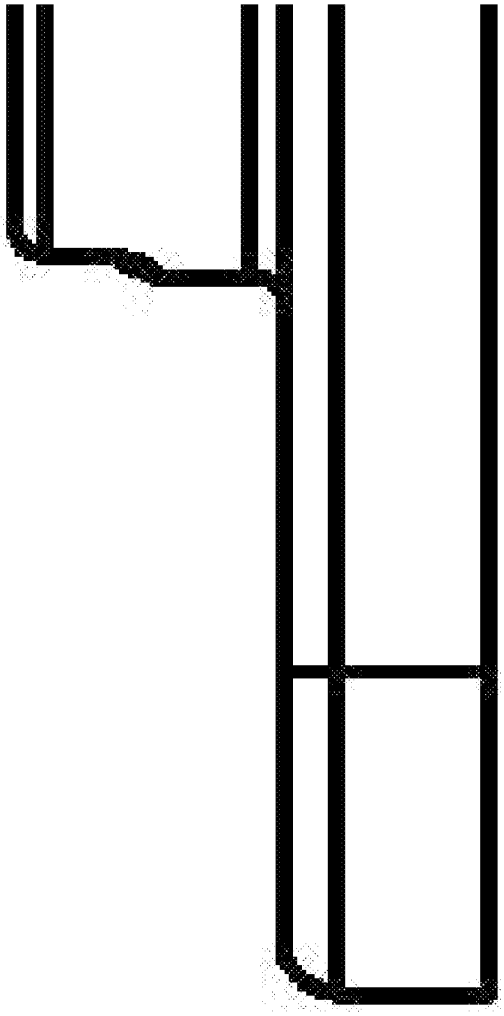
[Fig. 18F]



A－A断面

FIG. 18F

[Fig. 19A]



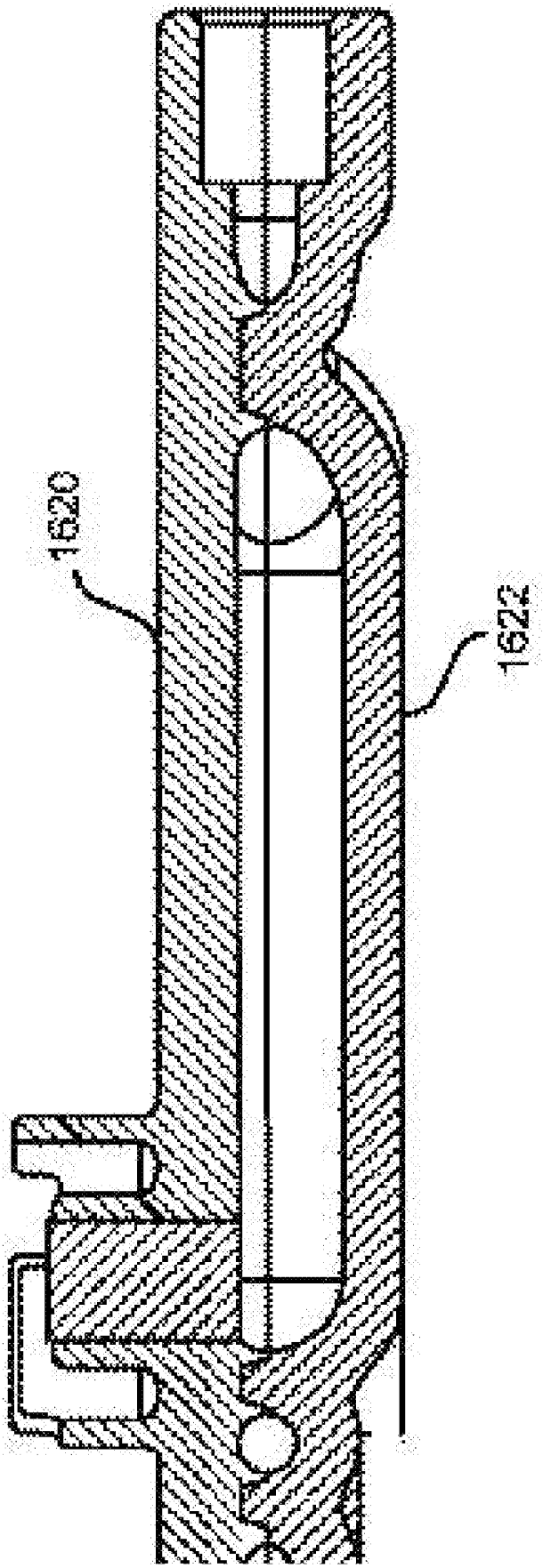


FIG. 19A

[Fig. 19B]

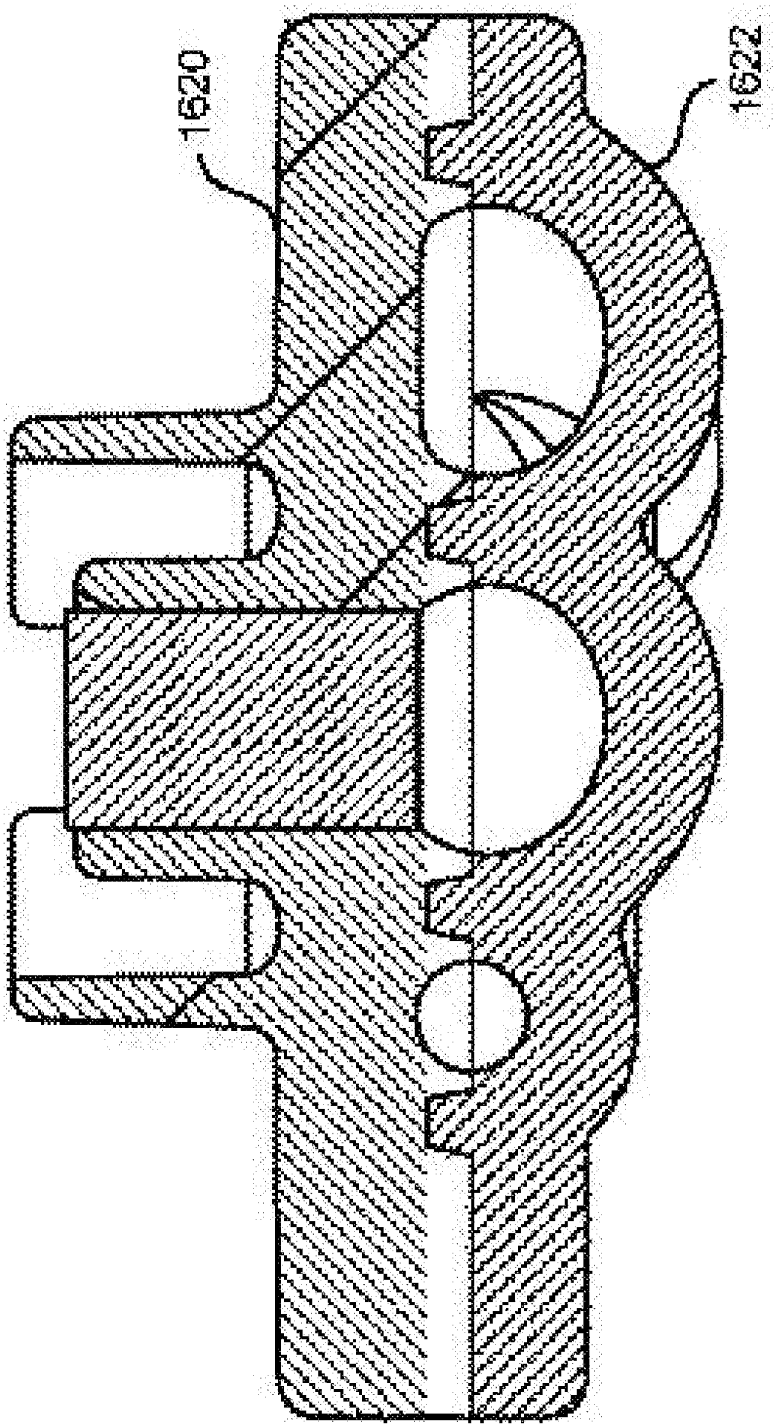


FIG. 19B

[Fig. 20]

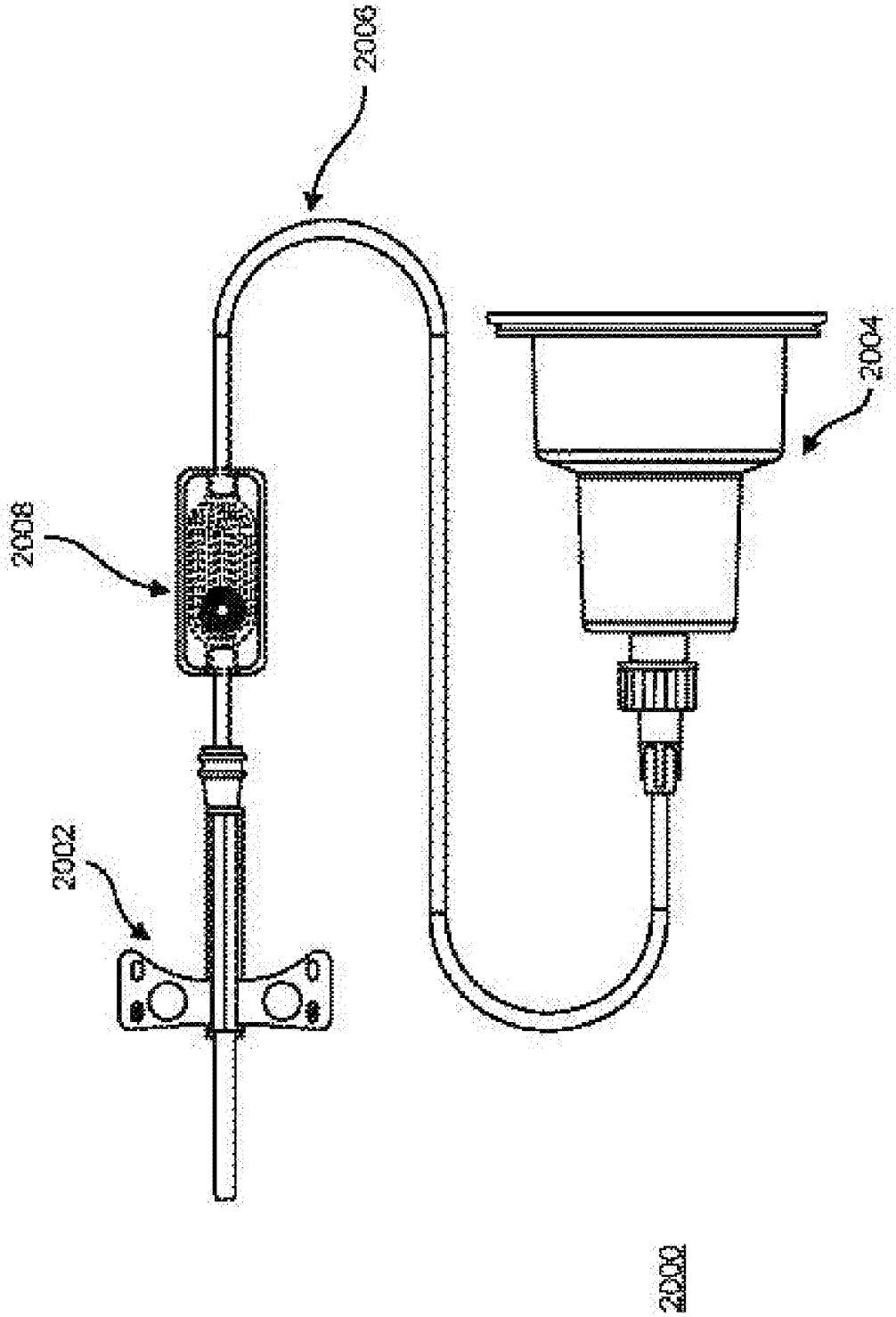


FIG. 20

[Fig. 21]

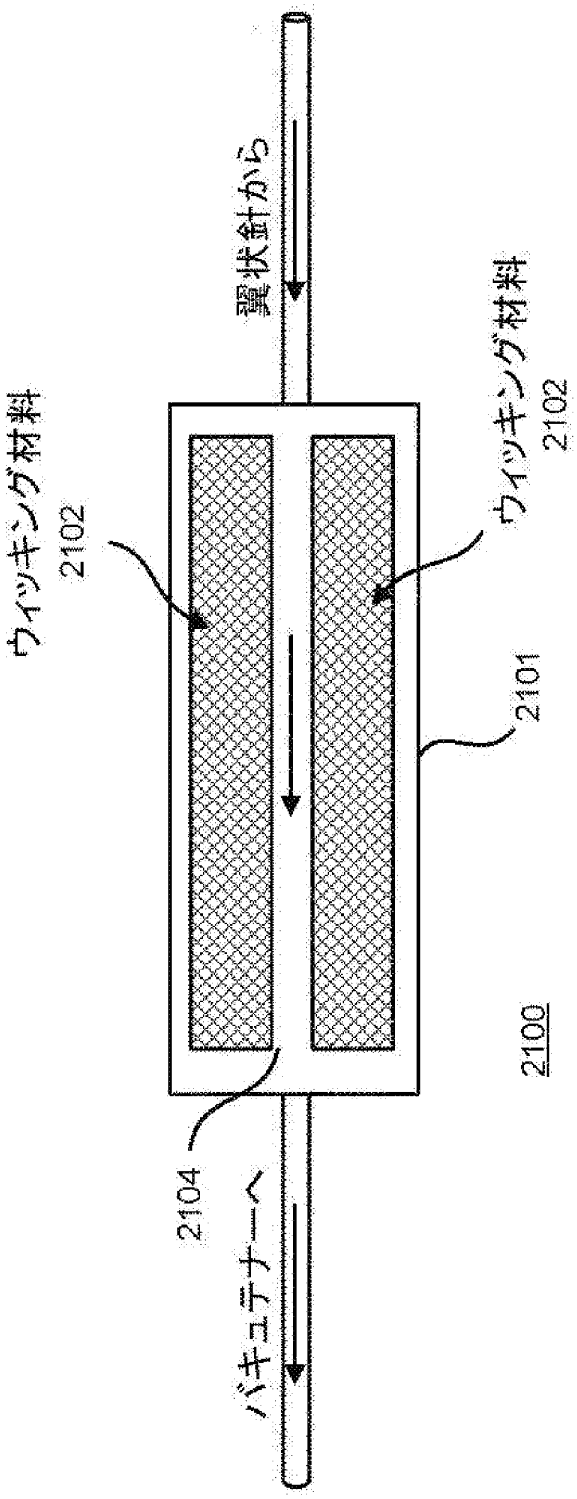


FIG. 21

[Fig. 22A]

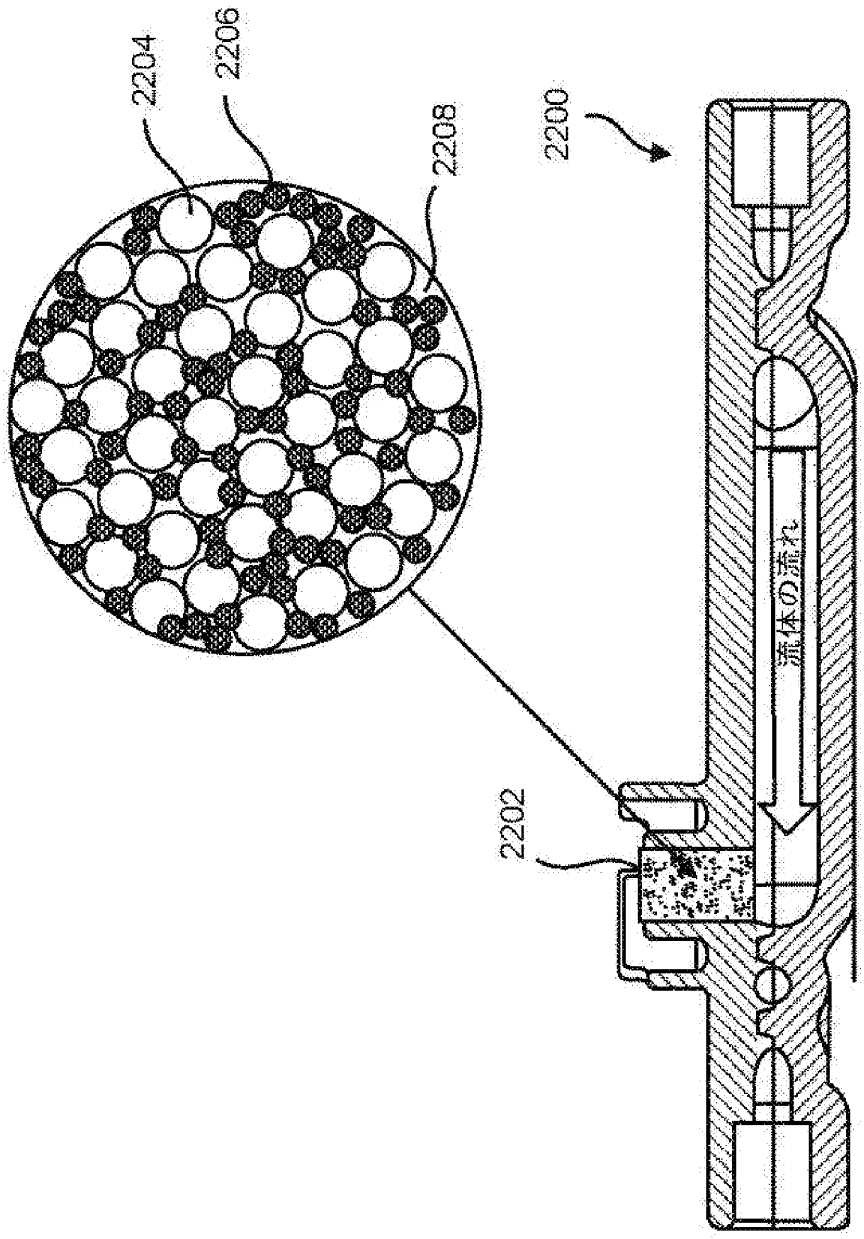


FIG. 22A

[Fig. 22B]

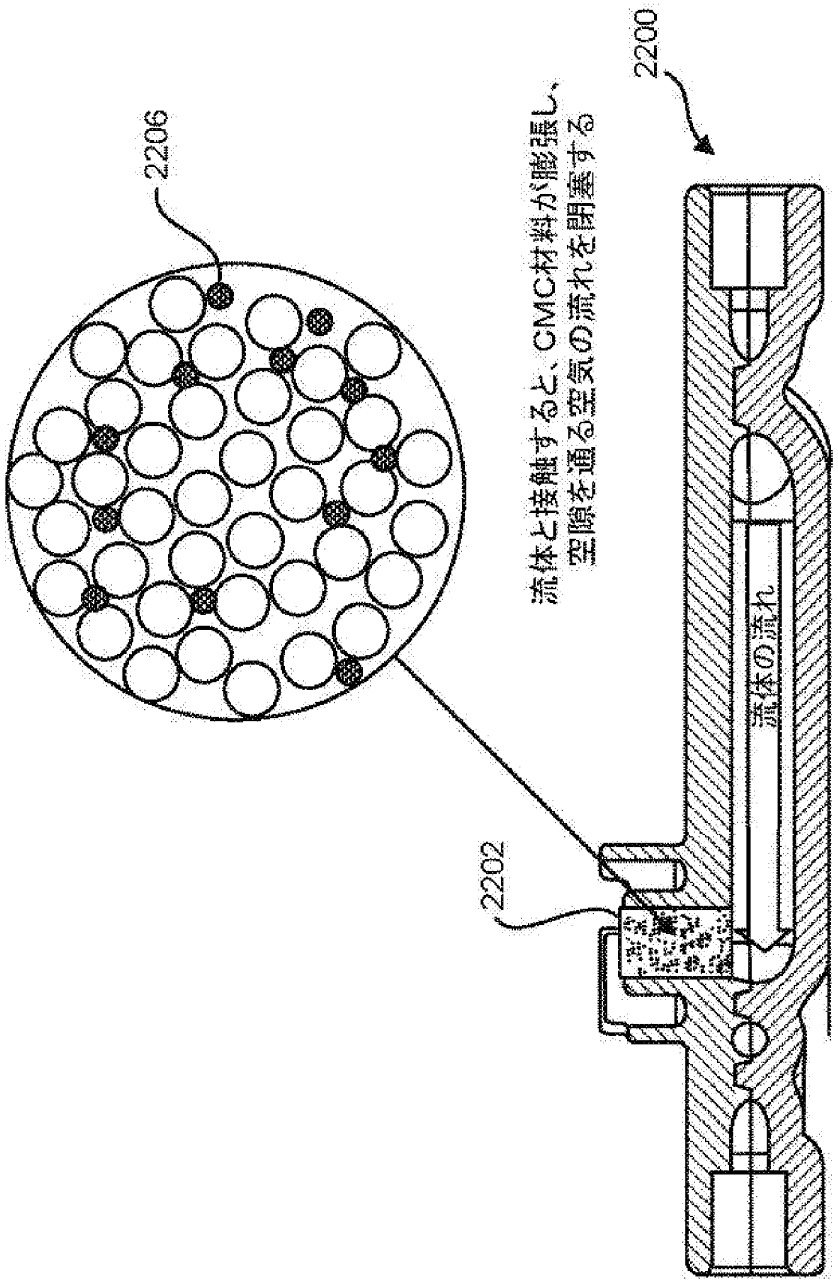


FIG. 22B

[Fig. 23A]

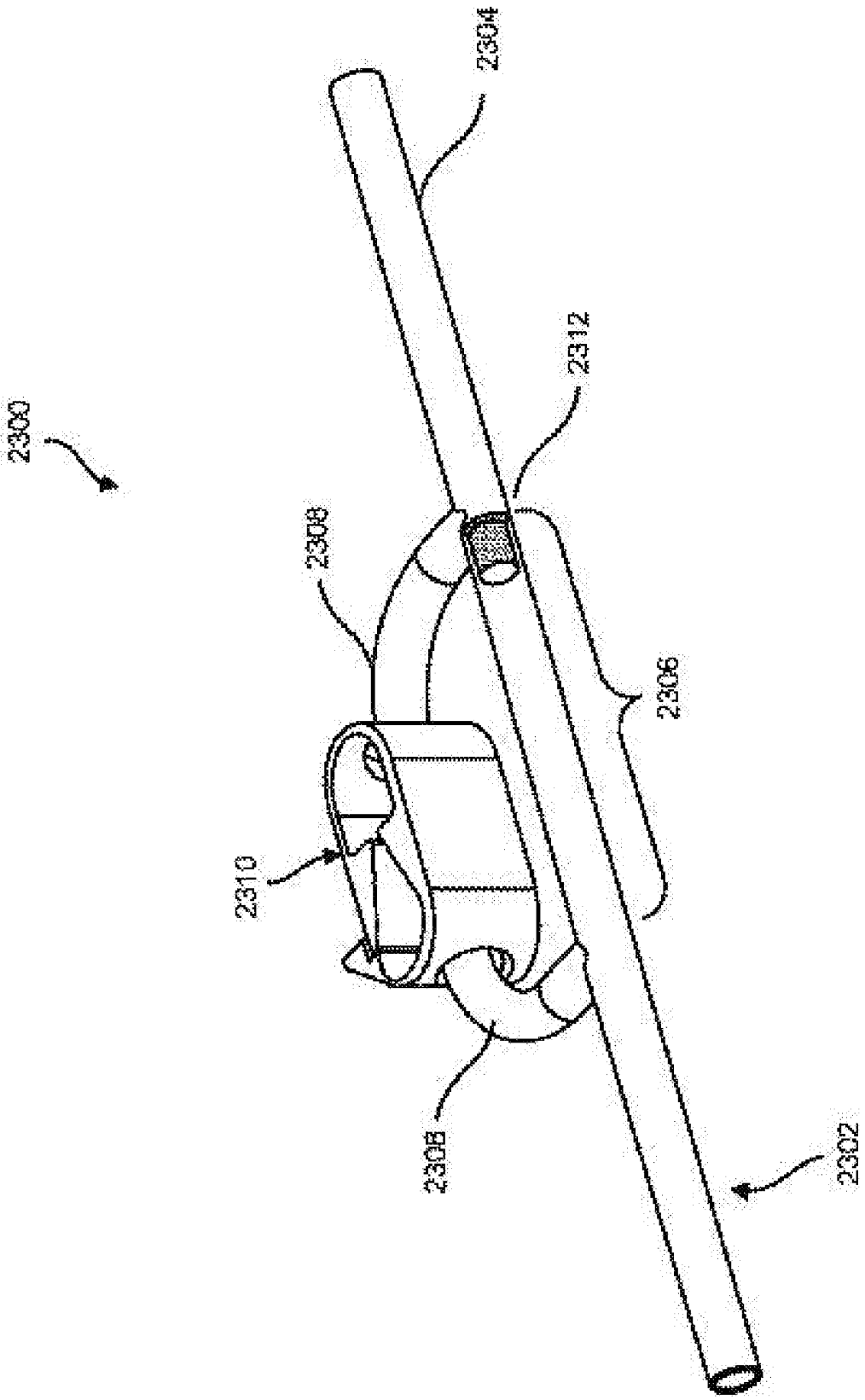


FIG. 23A

[Fig. 23B]

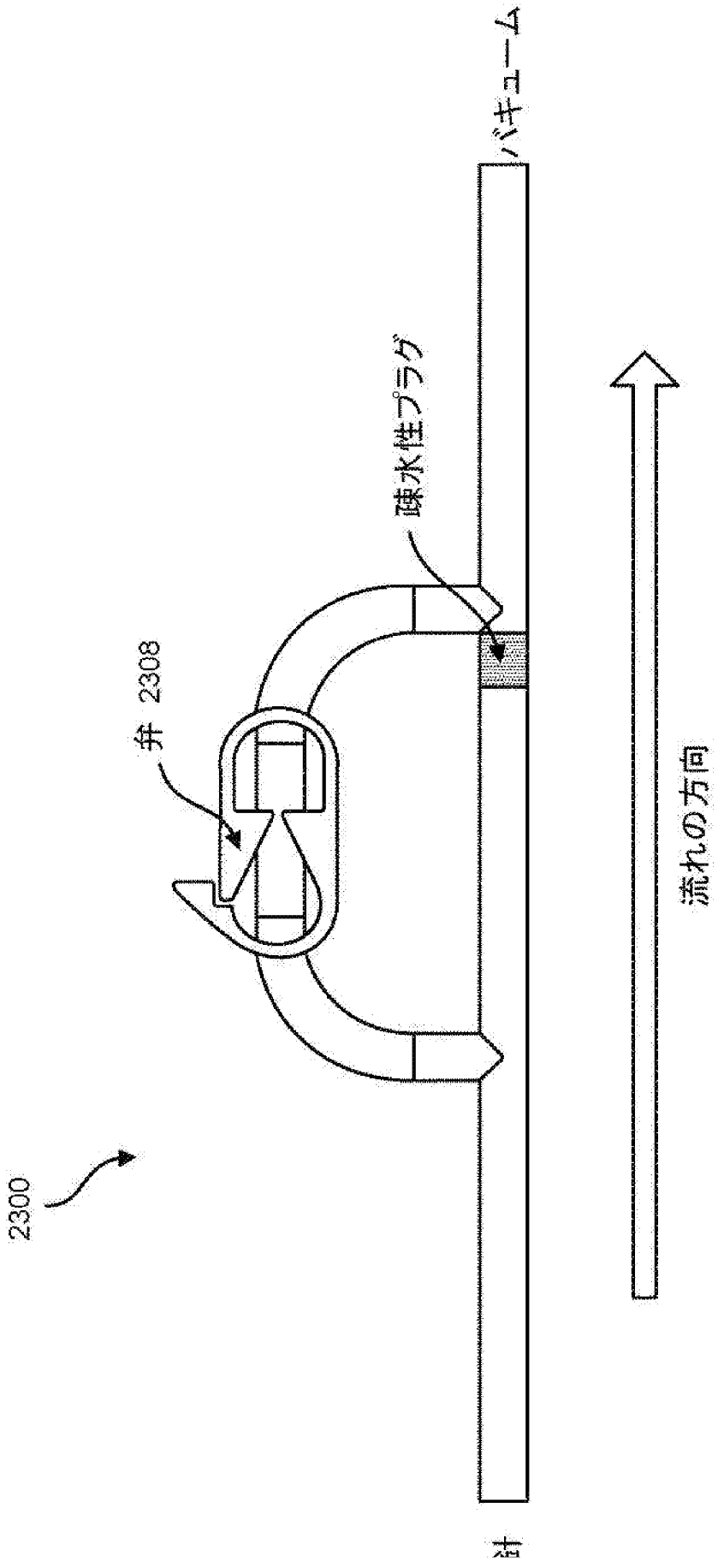


FIG. 23B

drawing open

1 2 3 Four Five 6 7 8A 8B 8C ...

Magnify and Rotate

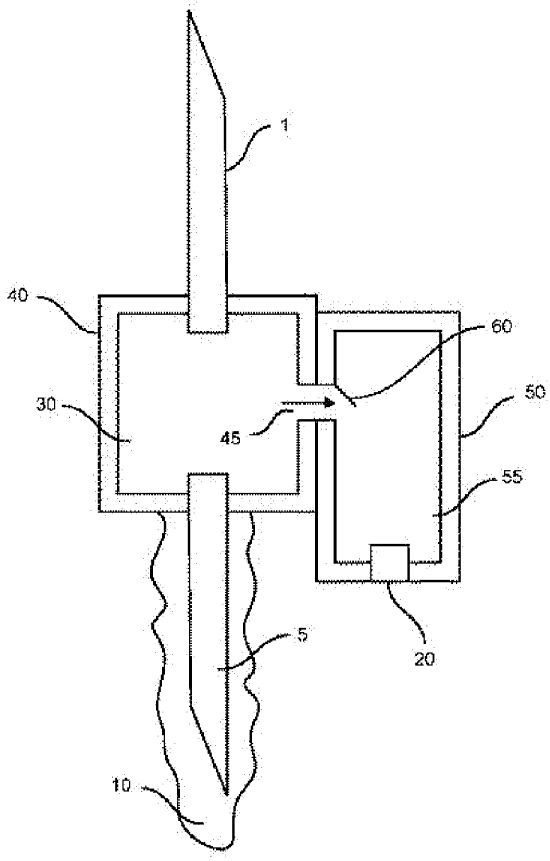


FIG. 1

Figure 1

1 / 1 display

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BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE AND METHOD

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Applicant(s): クリン インコーポレイテッド

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

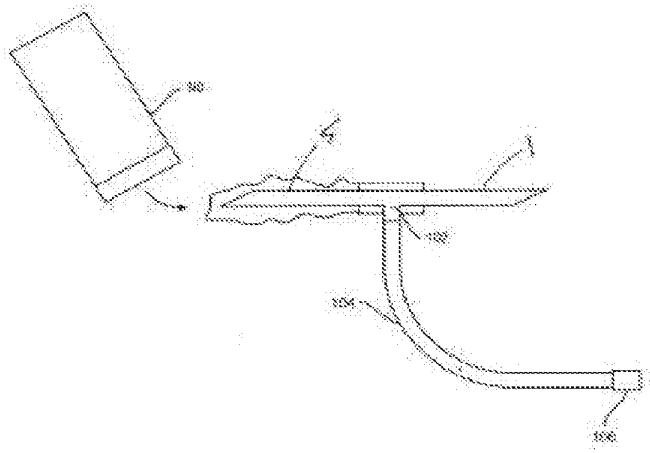
Application number: JP20180523384 20160722 Global Dossier

Priority number(s): US201562238636P 20151007 ; US201662318194P 20160404 ; US201562196797P 20150724 ; US201615140448 20160427 ; US201615140443 20160427 ; WO2016US43709 20160722

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Abstract of corresponding document: US2017020427 (A1)

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



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最終頁に続く

(54)【発明の名称】血液サンプル最適化システム及び血液隔離装置

(57)【特許請求の範囲】

【請求項１】

血液サンプル最適化システムであって、

採血システムであって、

患者の血液サンプルを取り出せるようにするために患者の静脈穿刺用に構成された患者針と、

前記患者針に接続され、前記血液サンプルを運ぶように構成された採血経路と、

前記血液サンプルの後続の部分を採取しかつ収容するために真空採血管を受け入れるように構成されたサンプル針と

を含む採血システムと、

前記患者針と前記サンプル針との間に前記採血経路に沿って接続された血液隔離装置であって、

前記血液サンプルを受け入れるように構成された入口ポートと、

前記入口ポートに接続されかつ空気透過性血液バリアを含む通気口を有する隔離チャンバであって、前記血液サンプルの最初の量を受け入れかつ前記血液サンプルの最初の量の少なくとも最初の部分を隔離するように構成された隔離チャンバと、

前記入口ポートに接続された近位端を有し、前記血液サンプルの後続の部分を受け入れるように構成されたサンプリング流路と

を含み、

前記隔離チャンバ、前記サンプリング流路及び前記入口ポートは、前記血液サンプル

の後続の部分が前記隔離チャンバ及び前記隔離チャンバ内に隔離された前記血液サンプルの最初の部分を迂回することを可能にしかつ前記血液サンプルの後続の部分を前記サンプリング流路の遠位端に接続された出口ポートに向かわせるように構成され、前記出口ポートは、前記血液サンプルの後続の部分を前記真空採血管に排出するように構成され、

前記入口ポート、前記出口ポート、前記隔離チャンバ及び前記サンプリング流路を収容しかつ画定するハウジングをさらに含む、血液隔離装置と

を含む、血液サンプル最適化システム。

【請求項２】

前記血液隔離装置の前記隔離チャンバは周囲空気圧であり、前記隔離チャンバは患者の血圧が前記隔離チャンバ内の周囲空気圧に打ち勝つことによって前記血液サンプルの最初の部分を受け入れる、請求項１に記載の血液サンプル最適化システム。

【請求項３】

前記サンプル針は、前記採血経路及び前記サンプリング流路を介した前記患者針へのアクセスを開くために前記真空採血管によって穿孔されるシールを含む、請求項２に記載の血液サンプル最適化システム。

【請求項４】

前記血液隔離装置の前記サンプリング流路は、前記サンプル針を開封する前記真空採血管によって真空圧力下で前記血液サンプルの後続部分を前記入口ポートに進入させる、請求項３に記載の血液サンプル最適化システム。

【請求項５】

前記血液隔離装置の前記空気透過性血液バリアは、血液と接触すると密封する空気透過性材料を含む、請求項１に記載の血液サンプル最適化システム。

【請求項６】

前記採血システムの前記採血経路はチューブを含む、請求項１に記載の血液サンプル最適化システム。

【請求項７】

患者から血液サンプルを取り出せるようにするように構成された患者針と、密封されたサンプル針であって、前記サンプル針を開封しかつ取り出せるようにされた血液サンプルを患者から採取するために真空採血管を受け入れるように適合されたサンプル針とを含む血液採取システムに接続された血液隔離装置であって、

前記患者針に接続され、患者からの血液サンプルを受け入れるように構成されたた入口ポートと、

前記入口ポートに接続された出口ポートと、

前記入口ポートに接続されかつ空気透過性血液バリアを含む通気口を有する隔離チャンバであって、前記サンプル針が前記真空採血管によって開封される前に前記血液サンプルの最初の部分を受け入れかつ隔離するように構成された隔離チャンバと、

前記入口ポートに接続された近位端を有し、前記血液サンプルの後続の部分を受け入れるように構成されたサンプリング流路と

を含み、

前記隔離チャンバ、前記サンプリング流路及び前記入口ポートは、前記血液サンプルの後続の部分が前記隔離チャンバ及び前記隔離チャンバ内に隔離された前記血液サンプルの最初の部分を迂回することを可能にしかつ前記血液サンプルの後続の部分を前記サンプリング流路の遠位端に接続された前記出口ポートに向かわせるように構成され、

前記入口ポート、前記出口ポート、前記隔離チャンバ及び前記サンプリング流路を収容しかつ画定するハウジングをさらに含む、血液隔離装置。

【請求項８】

前記隔離チャンバは周囲空気圧であり、前記隔離チャンバは患者の血圧が前記隔離チャンバ内の周囲空気圧に打ち勝つことによって前記血液サンプルの最初の部分を受け入れる、請求項７に記載の血液隔離装置。

【請求項９】

前記空気透過性血液バリアは、血液と接触すると密封する空気透過性材料を含む、請求項７に記載の血液隔離装置。
【請求項１０】
前記隔離チャンバは、前記ハウジング内に画定された隔離流路を含む、請求項７に記載の血液隔離装置。
【請求項１１】
血液サンプル最適化システムであって、
採血システムであって、
患者の血液サンプルを取り出せるようにするために患者の静脈穿刺用に構成された患者針と、
前記患者針に接続され、前記血液サンプルを運ぶように構成された採血経路と、
前記血液サンプルの後続の部分を採取しかつ収容するために真空採血管を受け入れるように構成されたサンプル針と
を含む採血システムと、
前記患者針と前記サンプル針との間に前記採血経路に沿って接続された血液隔離装置であって、
前記血液サンプルを受け入れるように構成された入口ポートと、
前記入口ポート及び前記採血システムのサンプル針に接続された出口ポートと、
前記入口ポートに接続されかつ空気透過性血液バリアを含む通気口を有する隔離チャンバであって、前記血液サンプルの最初の量を受け入れかつ前記血液サンプルの最初の量の少なくとも最初の部分を隔離するように構成された隔離チャンバと、
前記入口ポートに接続された近位端を有し、前記血液サンプルの後続の部分を受け入れるように構成されたサンプリング流路と
を含み、
前記隔離チャンバ、前記サンプリング流路及び前記入口ポートは、前記血液サンプルの後続の部分が前記隔離チャンバ及び前記隔離チャンバ内に隔離された前記血液サンプルの最初の部分を迂回することを可能にしかつ前記血液サンプルの後続の部分を前記サンプリング流路の遠位端に接続された前記出口ポートに向かわせるように構成され、
前記入口ポート、前記出口ポート、前記隔離チャンバ及び前記サンプリング流路を収容しかつ画定するハウジングをさらに含む、血液隔離装置と
を含む、血液サンプル最適化システム。
【請求項１２】
前記血液隔離装置の前記隔離チャンバは周囲空気圧であり、前記隔離チャンバは患者の血圧が前記隔離チャンバ内の周囲空気圧に打ち勝つことによって前記血液サンプルの最初の部分を受け入れる、請求項１１に記載の血液サンプル最適化システム。
【請求項１３】
前記サンプル針は、前記採血経路を介した前記患者針へのアクセスを開くために前記真空採血管によって穿孔されるシールを含む、請求項１１に記載の血液サンプル最適化システム。
【請求項１４】
前記血液隔離装置の前記空気透過性血液バリアは、血液と接触すると密封する空気透過性材料を含む、請求項１１に記載の血液サンプル最適化システム。
【請求項１５】
前記隔離チャンバは、前記ハウジング内に画定された隔離流路を含む、請求項１１に記載の血液サンプル最適化システム。
【請求項１６】
前記採血システムの前記採血経路はチューブを含む、請求項１１に記載の血液サンプル最適化システム。
【発明の詳細な説明】
【背景技術】

【０００１】
関連出願との相互参照
本出願は、２０１６年４月２７日に出願された「血液サンプル最適化システム及び血液汚染物質隔離装置及び方法」と題する米国非仮出願第１５／１４０，４４３号及び２０１６年４月２７日に出願された「血液サンプル最適化システム及び血液汚染物質隔離装置及び方法」と題する米国非仮出願第１５／１４０，４４８号の優先権の利益を主張するものであり、これらの米国非仮出願の両方が２０１５年７月２４日に出願された「血液培養改良システム及び方法」と題する米国仮特許出願第６２／１９６，７９７号、２０１５年１０月７日に出願された「非汚染採血用の血液隔離システム」と題する米国仮出願第６２／２３８，６３６号、及び２０１６年４月４日に出願された「血液サンプル最適化システム及び血液汚染物質隔離装置及び方法」と題する米国仮特許出願第６２／３１８，１９４号の優先権を主張しており、これらの開示はその全体が参照により本明細書に含まれるものとする。
【０００２】
菌血症は、血液中に微生物が存在することである。一方、敗血症は、発熱、頻脈、頻呼吸及び低血圧などの臨床症状及び臨床兆候がある場合の菌血症である。菌血症及び敗血症は、高い死亡率、入院発生率及び入院期間と関連する費用の増加とを伴う。多くの菌血症、敗血症、真菌血症及び他の病原体が実際に病院又は他の医療施設内で発生し、カテーテル及び静脈穿刺がこれらの病原体の潜在的なキャリアとしての汚染源である。
【０００３】
血液培養は、患者の血液中の菌血症及び敗血症に関連する微生物病原体を検出するのに使用される標準検査である。血液培養という用語は、血液が１つ以上の血液培養ボトル又は容器に接種される、末梢部位又は中心ライン又は動脈ラインからの１回の静脈穿刺を指す。１つのボトルが１つの血液培養と見なされ、２つ以上がセットと見なされる。複数のセットは複数の静脈穿刺から得られ、患者の異なる部位に関連する。
【０００４】
これらの方法は、敗血症を管理する上で重要な要素である微生物同定及び感受性検査を可能にするが、迅速な結果が得られないことと厄介な病原体に対する感度が低いことが、改良されたシステムの開発及び補助的な分子検査又はプロテオミクス検査につながっている。
【０００５】
血液培養を行うための血液サンプルの採取は、現代の患者ケアの重要な要素であり、正確な診断を提供することによって患者の結果に良い影響を与えることも、不必要な抗菌療法を長引かせ、入院期間を長くし、コストを増加させることによって結果に悪影響を与えることもある。
【０００６】
血液培養の採取の１つの結果は、汚染である。血液培養の汚染は、偽陽性の培養結果及び／又は医療関連コストの著しい増加につながる可能性がある。血液培養の汚染の原因は、不適切な皮膚消毒、不適切な採取管の消毒、最初の採血の汚染を含み、これらは結果を歪める可能性がある。
【０００７】
血液培養採取キットは、一般に、ＢＤ、スミス、ビー・ブラウンなどの会社によって提供される「バタフライ」セット、輸液セット、又は他のタイプの静脈穿刺装置と、好気性血液培養ボトル及び嫌気性血液培養ボトルとで構成される。様々な異なるボトルも検査要件に応じて利用可能である。これらのボトルは、好気性生物と嫌気性生物の両方の回収を最適化するように特別に設計されている。従来のキットでは、使用されるボトルは一般に「バキュテナー（登録商標）」として知られており、これは、所定の量の血液などの液体の採取を容易にするべく管の内部に真空を作り出すために排気される蓋を備える滅菌ガラス管又は滅菌プラスチック管から形成される採血管である。
【０００８】

偽陽性の血液培養は、一般的に、不十分なサンプリング技術の結果である。それらは、必要でないときに抗生物質を使用させ、病院費及び患者の不安を増大させる。血液培養は、皮膚内への針刺しから採取され、その後で血液のサンプルを取り込むためにバキュテナー（登録商標）が取り付けられる。汚染は、穿刺部位及びその周辺の皮膚領域の不適切又は不完全な消毒によって生じ得る。それはまた、挿入中の針による皮膚のくりぬきから、くりぬかれた皮膚細胞と関連する汚染物質とがサンプル中に引き込まれることで生じることもある。

【０００９】

皮下注射針を通る血流は層流であり、このため、皮下注射針に圧力降下が加えられるときに流管にわたって流速勾配が発生する。血液を強く吸引するか又は非常に小さな皮下注射針を使用すると、溶解及び赤血球からのカリウムの放出が起こり、それにより血液サンプルが異常になる可能性がある。

【００１０】

他の例では、一部の患者は繊細な静脈を有し、繊細な静脈は、特に患者の状態に対してあまりにも急速に引き出される注射器のプランジャによって加えられるような圧力低下又は真空の下で崩壊し得る。このような状態は事前に知ることが不可能であるため、このような静脈崩壊は危険であり、制御することは非常に困難である。

【００１１】

血液培養の汚染率を低下させるために、例えば、無歯採取技術に関するスタッフの訓練、汚染率に関するフィードバック、及び血液培養採取キットの導入など、様々な戦略が実施されている。皮膚消毒は汚染の心配を減らすことができるが、２０％以上の皮膚の微生物は真皮の深部に位置し、消毒の影響を受けない。ボトル接種の前に針を交換することは、汚染率を低下させることなく針刺し損傷を受ける危険性を高めるので推奨されない。

【００１２】

血液培養の汚染を低減するための一部の従来のシステム及び技術は、中心静脈カテーテル、静脈穿刺及び他の血管アクセスシステムから採取された最初のアリコートの血液を捨てることを含む。しかしながら、これらのシステムは、ユーザーが血管内装置を機械的に操作することを必要とするか又は確実にすることが困難な複雑な一連のステップを踏むこと必要とする。

【発明の概要】

【発明が解決しようとする課題】

【００１３】

本明細書は、血液培養の汚染、細胞の溶解、及び静脈崩壊を低減するためのシステム及び方法を提示する。一部の実施では、システム及び方法は、ユーザーの消毒のばらつきをなくし、また皮膚細胞が血液培養サンプルに入り込む危険性をなくすこともできる。本明細書に開示されたシステム及び方法は、汚染物質のない血液サンプルを採取するためにバキュテナー（登録商標）又は他の採血装置（すなわち、注射器）をいつ取り付けるべきかを潜在的に示す以外は、既存の臨床プロセスの変更を必要としない。

【００１４】

本明細書に開示されたシステム及び方法の一部の実施では、採血は、患者自身の血圧の使用によって受動的に成し遂げられ、それによって静脈崩壊の危険性を低減し、現行の実務を超える更なるユーザーのステップを排除する。システム及び方法は、短経路の直接刺し又はバタフライ静脈穿刺システムに適合するように適用されることができる。カテーテルを通して採取されたサンプルと共に使用されることもできる。

【課題を解決するための手段】

【００１５】

一態様では、血液隔離装置が提示されている。血液隔離装置は、入口ポートと出口ポートとを含む。血液隔離装置は、入口ポートと接続される隔離チャンバであって、空気透過性血液バリアを含む通気口を有する隔離チャンバを更に含む。血液隔離装置は、入口ポートと接続される近位端と、出口ポートと接続される遠位端とを有する、サンプリング流路

を更に含む。

【００１６】

別の態様では、採血経路と接続される血液隔離装置が記載されている。採血経路は、患者針とサンプル採取装置とを有する。血液隔離装置は、患者針と接続される入口ポートと、入口ポートと接続される隔離チャンバであって、空気透過性血液バリアを含む通気口を有する隔離チャンバとを含む。血液隔離装置は、入口ポートと接続される近位端を有するサンプリング流路と、サンプリング流路の遠位端及びサンプル採取装置と接続される出口ポートとを更に含む。

【００１７】

更に別の態様では、採血システムと接続される血液隔離装置が記載されている。採血システムは、患者から血液サンプルを取り出せるようにするための患者針と、密封され且つ真空採血管を受け入れるように適合されたサンプル針とを含む。血液隔離装置は、患者からの血液サンプルを受け入れるために患者針と接続される入口ポートを含む。血液隔離装置は、入口ポートと接続され且つ空気透過性血液バリアを含む通気口を有する隔離チャンバであって、サンプル針が真空採血管によって開封されるより前に血液サンプルの最初の部分を受け入れ且つ隔離する隔離チャンバを更に含む。血液隔離装置は、入口ポートと接続される近位端を有するサンプリング流路であって、真空採血管によってサンプル針が開封されると血液サンプルの後続の部分を運ぶサンプリング流路を更に含む。血液隔離装置は、血液サンプルの後続の部分をサンプル針に運ぶためにサンプリング流路の遠位端と接続される出口ポートを更に含む。

【００１８】

更に別の態様では、血液サンプル最適化システムが開示され、記載されている。血液サンプル最適化システムは、患者の血液の１つ以上のサンプルを取り出せるようにし且つ得るための採血システムと、静脈穿刺プロセスによって汚染されている恐れがあり且つ患者の血液中の病原体の偽陽性同定をもたらす可能性がある患者の血液の１つ以上のサンプルの最初の部分を受け入れ且つ隔離するための血液隔離装置とを含む。

【００１９】

採血システムは、患者の血液のサンプルを取り出せるようにするために患者の静脈穿刺用に構成された患者針と、血液サンプルを運ぶために患者針と接続される採血経路と、血液サンプルの後続の部分を採取し且つ収容するために真空採血容器を受け入れるように構成されたサンプル針とを含む。

【００２０】

更に別の態様では、血液隔離装置が開示され、記載されている。一部の実施では、血液隔離装置は、入口ポートと、入口ポートと接続される出口ポートと、入口ポートと接続される隔離チャンバとを含むことができる。隔離チャンバは、空気透過性血液バリアを含む通気口を有することができる。

【００２１】

血液隔離装置は、患者針とサンプル針との間で採血経路に沿って接続され、血液サンプルを受け入れるための入口ポートを含む。血液隔離装置は、血液サンプルの最初の量を受け入れるために入口ポートと接続される隔離チャンバであって、血液サンプルの最初の量の少なくとも最初の部分を隔離するために空気透過性血液バリアを含む通気口を有する隔離チャンバを更に含む。血液隔離装置は、入口ポートと接続される近位端を有するサンプリング流路であって、隔離チャンバが血液サンプルの最初の量の少なくとも最初の部分を隔離すると血液サンプルの後続の量を真空採血容器に運ぶサンプリング流路を更に含む。血液隔離装置は、サンプリング流路の遠位端と接続される出口ポートであって、血液サンプルの後続の量を出力する出口ポートを更に含む。

【００２２】

１つ以上の実施形態の詳細が、添付の図面及び以下の説明に記載されている。他の特徴及び利点は、明細書及び図面並びに特許請求の範囲から明らかになるであろう。

【図面の簡単な説明】

【００２３】
以下、これら及び他の態様について、以下の図面を参照して詳細に説明する。
【図１】血液サンプル最適化システムを示す。
【図２】代替的な実施に従う血液サンプル最適化システムを示す。
【図３】別の代替的な実施に従う血液サンプル最適化システムを示す。
【図４】別の代替的な実施に従う血液サンプル最適化システムを示す。
【図５】別の代替的な実施に従う血液サンプル最適化システムを示す。
【図６】代替的な実施に従う血液サンプル最適化システムを示す。
【図７】血液培養の質を最適化するための方法のフローチャートである。
【図８Ａ】一部の実施に従う非汚染採血用の血液隔離システムを示す。
【図８Ｂ】一部の実施に従う非汚染採血用の血液隔離システムを示す。
【図８Ｃ】一部の実施に従う非汚染採血用の血液隔離システムを示す。
【図８Ｄ】一部の実施に従う非汚染採血用の血液隔離システムを示す。
【図８Ｅ】一部の実施に従う非汚染採血用の血液隔離システムを示す。
【図９】血液隔離システムに用いる経路スプリッタを示す。
【図１０Ａ】代替的な実施に従う非汚染採血用の血液隔離システムを示す。
【図１０Ｂ】代替的な実施に従う非汚染採血用の血液隔離システムを示す。
【図１０Ｃ】代替的な実施に従う非汚染採血用の血液隔離システムを示す。
【図１０Ｄ】代替的な実施に従う非汚染採血用の血液隔離システムを示す。
【図１１Ａ】他の代替的な実施に従う非汚染採血用の血液隔離システムを示す。
【図１１Ｂ】他の代替的な実施に従う非汚染採血用の血液隔離システムを示す。
【図１１Ｃ】他の代替的な実施に従う非汚染採血用の血液隔離システムを示す。
【図１１Ｄ】他の代替的な実施に従う非汚染採血用の血液隔離システムを示す。
【図１１Ｅ】他の代替的な実施に従う非汚染採血用の血液隔離システムを示す。
【図１２Ａ】更に他の代替的な実施に従う血液隔離装置を含む血液サンプル最適化システムを示す。
【図１２Ｂ】更に他の代替的な実施に従う血液隔離装置を含む血液サンプル最適化システムを示す。
【図１２Ｃ】更に他の代替的な実施に従う血液隔離装置を含む血液サンプル最適化システムを示す。
【図１２Ｄ】更に他の代替的な実施に従う血液隔離装置を含む血液サンプル最適化システムを示す。
【図１３Ａ】更に別の代替的な実施に従う血液サンプル最適化システム１３００を示す。
【図１３Ｂ】更に別の代替的な実施に従う血液サンプル最適化システム１３００を示す。
【図１３Ｃ】更に別の代替的な実施に従う血液サンプル最適化システム１３００を示す。
【図１３Ｄ】更に別の代替的な実施に従う血液サンプル最適化システム１３００を示す。
【図１４Ａ】患者の血液サンプルに対して実施される血液培養又は検査における偽陽性を低減するために最初のアリコート又はサンプルの汚染物質を隔離する採血システムの更に別の実施を示す。
【図１４Ｂ】患者の血液サンプルに対して実施される血液培養又は検査における偽陽性を低減するために最初のアリコート又はサンプルの汚染物質を隔離する採血システムの更に別の実施を示す。
【図１４Ｃ】患者の血液サンプルに対して実施される血液培養又は検査における偽陽性を低減するために最初のアリコート又はサンプルの汚染物質を隔離する採血システムの更に別の実施を示す。
【図１４Ｄ】患者の血液サンプルに対して実施される血液培養又は検査における偽陽性を低減するために最初のアリコート又はサンプルの汚染物質を隔離する採血システムの更に別の実施を示す。
【図１４Ｅ】患者の血液サンプルに対して実施される血液培養又は検査における偽陽性を低減するために最初のアリコート又はサンプルの汚染物質を隔離する採血システムの更に

別の実施を示す。
【図１５Ａ】更に別の実施に従う血液隔離装置及びそれを使用する方法を示す。
【図１５Ｂ】更に別の実施に従う血液隔離装置及びそれを使用する方法を示す。
【図１５Ｃ】更に別の実施に従う血液隔離装置及びそれを使用する方法を示す。
【図１５Ｄ】更に別の実施に従う血液隔離装置及びそれを使用する方法を示す。
【図１５Ｅ】更に別の実施に従う血液隔離装置及びそれを使用する方法を示す。
【図１５Ｆ】更に別の実施に従う血液隔離装置及びそれを使用する方法を示す。
【図１５Ｇ】更に別の実施に従う血液隔離装置及びそれを使用する方法を示す。
【図１６Ａ】更に別の実施に従う血液隔離装置を示す。
【図１６Ｂ】更に別の実施に従う血液隔離装置を示す。
【図１６Ｃ】更に別の実施に従う血液隔離装置を示す。
【図１６Ｄ】更に別の実施に従う血液隔離装置を示す。
【図１７Ａ】血液隔離装置用のハウジングの下部部材を示す。
【図１７Ｂ】血液隔離装置用のハウジングの下部部材を示す。
【図１７Ｃ】血液隔離装置用のハウジングの下部部材を示す。
【図１７Ｄ】血液隔離装置用のハウジングの下部部材を示す。
【図１７Ｅ】血液隔離装置用のハウジングの下部部材を示す。
【図１８Ａ】血液隔離装置用のハウジングの上部部材を示す。
【図１８Ｂ】血液隔離装置用のハウジングの上部部材を示す。
【図１８Ｃ】血液隔離装置用のハウジングの上部部材を示す。
【図１８Ｄ】血液隔離装置用のハウジングの上部部材を示す。
【図１８Ｅ】血液隔離装置用のハウジングの上部部材を示す。
【図１８Ｆ】血液隔離装置用のハウジングの上部部材を示す。
【図１９Ａ】下部部材と嵌合する上部部材を有する血液隔離装置を示す。
【図１９Ｂ】下部部材と嵌合する上部部材を有する血液隔離装置を示す。
【図２０】血液隔離装置を含む血液サンプル最適化システムを示す。
【図２１】ウィッキング材料チャンバを使用する通気口付きでない血液隔離装置を示す。
【図２２Ａ】血液隔離装置の隔離チャンバ内の血液を隔離するためのフィルタの材料構成を示す。
【図２２Ｂ】血液隔離装置の隔離チャンバ内の血液を隔離するためのフィルタの材料構成を示す。
【図２３Ａ】採血装置による真空力を使用する血液隔離装置の別の実施を示す。
【図２３Ｂ】採血装置による真空力を使用する血液隔離装置の別の実施を示す。　様々な図面における同様の符号は同様の要素を示す。
【発明を実施するための形態】
【００２４】
本明細書は、採取される血液サンプル中の汚染物質を低減又は排除し、その結果、採取される血液サンプルの血液培養又は他の検査における偽陽性の判断を減少又は排除する血液サンプル最適化システム及び方法を記載している。一部の実施では、血液サンプル最適化システムは、患者の血流への血管アクセスのための患者針と、バキュテナー（登録商標）のような真空採血容器又は真空採血管などの採血容器か又は他のサンプリング装置に血液サンプルを供給するためのサンプル針と、患者針とサンプル針との間に位置する血液隔離装置とを含む。血液隔離装置は、汚染されている可能性のある最初のアリコートの血液を隔離するための隔離チャンバを含み、最初のアリコートの血液が隔離チャンバ内に隔離された後に患者針とサンプル針との間の汚染されていない可能性のある血液を運ぶために隔離チャンバを迂回するサンプリング流路を更に含むことができる。
【００２５】
図１は、一部の実施に従う血液サンプル最適化システムを示す。システムは、患者の皮膚を穿刺してその中の患者の静脈及び静脈内の血液にアクセスするための患者針１を含む。システムは、再密封可能なブーツ１０、ルアー作動弁、又は別の採取インターフェース

又は装置内に収容され且つ再密封可能なブーツ１０、ルアー作動弁、又は別の採取インターフェース又は装置によって当初は密封されていることができる、サンプル針（すなわち、バキュテナー（登録商標）などと共に使用するための再密封可能に密封された針）５を更に含む。再密封可能なブーツ１０は、患者の血液を採取するためのバキュテナー（登録商標）ボトル（図示せず）を用いることによって、サンプル針５のそばに又はサンプル針５の周りに押し付けることができる。システムは、サンプル針５に通じる低容量チャンバ３０を更に含むことができるが、ハウジング５０によって形成される隔離チャンバ５５に通じる穴又は１つ以上の流路４５も含む。

【００２６】

隔離チャンバ５５は、隔離チャンバ５５の容積に応じて、所定の又は測定された量であることができる、患者の血液の最初のアリコートを受け入れ且つ保持するためのチャンバ、流路、通路、ロック、又は他の構造である。最初の採血は、一般的に、後続の採血に比べて菌血症及び敗血症を引き起こす微生物又は他の病原体を含有しているか又はより含有の影響を受けやすい。隔離チャンバ５５は、硬いハウジング内に収容されるか、ハウジング自体に形成され又はハウジング自体によって画定された容器であることができ、或いはチューブ又は内腔として実現されることができる。隔離チャンバ５５は、どのように形成され且つ実施されるかにかかわらず、所定の容積を有することができる。一部の実施では、所定の容積は、患者針の容積に基づくこと、すなわち、患者針の容積よりも少ない容積から任意の容積から患者針の容積の２０倍以上大きい容積までの範囲であることができる。隔離チャンバ５５の所定の容積は、隔離され且つ処分される血液の量を節約又は最小化するように設定されることもできる。

【００２７】

隔離チャンバ５５は、チャンバハウジング５０内に形成、包含、又は収容されることができ、プラスチック、ゴム、鋼、アルミニウム又は他の適切な材料で作られることができる。例えば、隔離チャンバ５５は、可撓性チューブ又は他のエラストマー材料から形成されることができる。隔離チャンバ５５は、空気が隔離チャンバ５５から出ることを可能にする空気透過性血液バリア２０を更に含む。本明細書で使用される「空気透過性血液バリア」という用語は、空気透過性であるが実質的に血液不透過性の物質、材料又は構造体を意味する。代表的な例は、疎水性膜及び疎水性コーティング、疎水性膜又は疎水性コーティングと組み合わせた親水性膜又は親水性コーティング、メッシュ、フィルタ、機械的弁、抗菌性材料、又は隔離チャンバ５５が血液で満たされるときに隔離チャンバ５５から空気を追い出すことができる他の任意の手段を含むことができる。様々な例示的な実施形態において、空気透過性血液バリアは、空気が液体と接触するまで通過することを可能にする１つ以上の材料によって形成されることができ、このような材料は、空気及び／又は液体の通過を防止又は阻止するために完全に又は部分的に密封される。言い換えれば、液体との接触より前に、材料は空気透過性のバリアを形成している。液体との接触後、材料は、空気及び／又は液体の更なる通過を実質的に又は完全に防止する。

【００２８】

穴又は流路４５は、任意の所望の長さ、断面形状又はサイズであることができ、且つ／又は任意の所望の角度又は向きで低容量チャンバ３０から離れるように形成されることができる。穴又は流路４５はまた、最初のアリコートの血液サンプルを隔離チャンバ５５内に保持する一方向フラップ又は一方向弁６０を含むことができる。一部の特定の実施では、穴又は流路４５は、低容量チャンバ３０から隔離チャンバ５５への一方向の血液の流れのための「ダックビル」弁又はフラッパ弁６０などを含むことができる。空気透過性血液バリア２０は、空気が出ることを可能にするが血液と接触すると密封する材料で構成することもでき、それによって外気が隔離チャンバ５５に入ることを許容しない。この密封は弁を不要にする。

【００２９】

弁６０は、任意のタイプの弁又は開閉機構であることができる。チャンバ３０は、実質的に残留血液を保持しないように設計されており、特定の容積又は割合の血液を隔離チャ

ンバ５５に保持し又は通過させるように構成することができる。同様に、隔離チャンバ５５は、抗菌コーティングのような任意のタイプのコーティング、又は隔離された最初の採血の成分の同定及び／又は診断を支援するコーティングも含むことができる。

【００３０】

ハウジング５０及び４０は、アクリロニトリルブタジエンスチレン（ＡＢＳ）又は他の熱可塑性材料又はポリマー材料などのプラスチック、ゴム、鋼、又はアルミニウムを含む任意の適切な材料から形成されることができる。空気透過性血液バリア２０は、最初の採血による血液と接触すると又は空気の追い出しが停止されたときに、又は事象と隔離チャンバ５５内の血液との任意の組み合わせの場合に活性化される、色提供物質又は他の信号伝達機構を含むことができる。空気透過性のバリアはまた、外部流体源、しぶき等によるフィルタの不注意による又は早過ぎる密封を阻止又は防止する疎水性膜又はカバーなどの外層を含むことができる。隔離チャンバ５５はまた、チャンバが充填されたことをユーザーが視覚的に確認することを可能にするために半透明又は透明であることができる。

【００３１】

図２は、一部の代替的な実施に従う血液サンプル最適化システムを示す。図２に示す実施では、隔離チャンバ５５又は廃棄チャンバが患者針１を取り囲み、端部が開放されたカフ又はハウジングが廃棄チャンバと接続され、サンプル針ハウジングベース及びハウジングを取り囲んでいる。患者針１とサンプル針５とは、ブーツ５６によって互いと接続されており、ブーツ５６は、それを貫通する連続的な採血流路を形成している。ブーツ５６は、採血流路から隔離チャンバ５５に通じる単一の穴又は流路を含む。装置は、他の実施では、複数の穴又は流路を含むことができる。各穴又は流路は、一方向弁を含むことができ、所定の量の血流のために寸法設定され且つ適合されることができる。

【００３２】

隔離チャンバ５５は、空気透過性血液バリアを含む。フィルタは、所定容積の血液が隔離チャンバ５５に集められたときに、それぞれ、感知及び／又は指示するためのセンサ又は指標を更に含むことができる。その指示は、バキュテナー（登録商標）などの真空採血管又はボトルをサンプル針５に取り付けるようにユーザーに警告する。隔離チャンバ５５用のハウジングは、任意のサイズ又は形状であることができ、ハウジング内の内部空間又は容積を画定するために任意のタイプの材料を含むことができる。内部空間は、最初は空気のみで満たされているが、汚染除去剤、凝固剤などの薬剤又は物質でコーティングされることもできる。真空採血管がサンプル針５に取り付けられると、血液は自動的に患者針１に、採血流路及びサンプル針５を通ってボトルに流入する。サンプル針５は、採血ボトルがサンプル針に取り付けられていないときにサンプル針を密封する再密封可能なブーツ、コーティング又は膜によって覆われている。

【００３３】

図３は、一部の代替的な実施に従う血液サンプル最適化システムを示す。図示の実施では、サンプル針５は、再密封可能なブーツ又は膜によって取り囲まれ、更に患者針１と接続される。サンプル針及び患者針を通って血液流路が形成される。サンプル針と患者針との間の接続は、主血液流路から隔離チャンバ１０４へと導く流路、ポート又は開口部を含む「Ｔ」又は「Ｙ」コネクタ１０２を含む。

【００３４】

Ｔ又はＹコネクタ１０２は、フラップ又は一方向弁を含み、所定の流量の血液のために寸法設定され且つ適合された穴を有する。隔離チャンバ１０４は、チューブから形成され又は硬いハウジングによって形成されることができ、最初は空気で満たされている。隔離チャンバ１０４は、自動的に、すなわち、患者自身の血圧による圧力下で患者から流出する血液を受け入れる。隔離チャンバ１０４は、好ましくは隔離チャンバ１０４を形成し且つ近位端がＴ又はＹコネクタ１０２に接続されたチューブの遠位端に、空気透過性血液バリア１０６を含む。Ｔ又はＹコネクタ１０２は、最も効率的な血流のために任意の所望の角度で分岐することができ、最初のアリコートの血液と主要な採血サンプルとの混合を最小限に抑え又は排除するために、開口部及び流路と主血液流路との間の接合部分を最小化

するように形成されることができる。

【００３５】

一部の代替的な実施では、サンプル針は、図４に示すように、その反対側の端部がＴ又はＹコネクタ１０２と接続している任意の長さのチューブに取り付けられることができる。隔離チャンバ１０４は、最初のアリコートに所定量の血液サンプルを含む限り、任意の形状又は容積であることができる。Ｔ又はＹコネクタ１０２はまた、主血液流路に対して平行な開口部又は流路を含むことができる。空気透過性血液バリアは、所定量の血液が隔離チャンバに集められたとき、又は放出される空気が特定の閾値、すなわちゼロに達したときを示す指標１０７又は他の機構を更に含むことができる。チューブはまた、挟んでチューブを通る流体の流れを防止するのに使用することができるクリップ１０９を含むことができる。

【００３６】

空気透過性血液バリア及び一次チャンバが密封されると、最初のアリコートの血液が隔離チャンバ１０４に閉じ込められ、サンプルを得るためにバキュテナー（登録商標）ボトルのような真空採血管がサンプル針５に取り付けられる。採血管は取り外すことができ、サンプル針５は再密封される。更なる採血又はサンプルのために、任意の数の後続の採血管を取り付けることができる。全ての採血が完了すると、最初のアリコートの血液が隔離チャンバ１０４に閉じ込められたまま、システムは廃棄される。

【００３７】

図５は、一部の代替的な実施に従う血液サンプル最適化システムを示す。図示の実施では、サンプル針５が患者針とチューブによって接続されている。「Ｔ」又は「Ｙ」コネクタ１２０が、チューブに沿って任意の所望の位置に追加され、実質的に上記のように、隔離チャンバ２０４に通じる開口部、ポート又は流路を含む。

【００３８】

図６は、一次採取流路として形成された隔離チャンバ３０４が最初のアリコートの血液を受け入れ、採血流路に隣接して設けられている、一部の代替的な実施に従う血液サンプル最適化システムを示す。隔離チャンバ３０４は、採血流路、患者針１及び／又はサンプル針５を取り囲むことができる。一次採取流路は、Ｔ又はＹコネクタ１２０、又は他のタイプの開口部又は流路を含むことができる。隔離チャンバ３０４は空気透過性血液バリアを含み、上記のように、血液などの流体が接触したことの指標を含むこともできる。

【００３９】

一部の実施では、患者針１又はサンプル針５のいずれか又は両方をルアーロック雄コネクタ又はルアーロック雌コネクタで置き換えることができる。しかしながら、様々な実施で、血液サンプル最適化システムのサンプル針端部にあるコネクタを最初に密封し、周囲空気圧で加圧され且つ空気透過性血液バリアの空気出口を含む隔離チャンバへ最初のアリコートの血液をそらすことを可能にする。このようにして、システムは受動的且つ自動的に患者自身の血圧を用いて隔離チャンバの周囲空気圧に打ち勝ち、空気透過性血液バリアを通して空気を押し出し、隔離チャンバ内の空気を血液に置き換える。

【００４０】

図７は、血液培養の質を最適化するための例示的な方法のフローチャートである。７０２において、臨床医が患者の静脈に針を挿入する。７０４において、血液が隔離チャンバに流れ込み、隔離チャンバ内の空気を隔離チャンバから空気透過性血液バリアを通して押し出す。一部の実施では、隔離チャンバの容積は、０．１立方センチメートル（ｃｃ）未満から５立方センチメートル（ｃｃ）以上である。隔離チャンバは、血液サンプルの第２部分及び他の後続の部分又は後続の採取よりも汚染しやすい血液サンプルの第１部分を採取するように寸法設定され且つ適合されている。隔離チャンバは空気透過性血液バリアを有し、この血液バリアを通して空気を患者の静脈から押し出された血液で追い出すことができるので、このような血液は、血液サンプルを受け入れ且つ保管するためのバキュテナー（登録商標）又は他のボトルに引き込まれるか又は他の方法で入る前に、必然的に且つ自動的に隔離チャンバに流入する。

【００４１】
隔離チャンバがいっぱいになると、血液は、血液が通過するのを阻止又は防止する空気透過性血液バリアに集まるか、さもなければ接触する。７０６において、血液が空気透過性血液バリアの全内部表面積と接触すると、空気透過性血液バリアは閉じられ、空気はもはや流出又は流入しない。７０８において、臨床医は、バキュテナー（登録商標）などの真空採血管を取り付けることができることを示す指標を提供されるか又は満杯のチャンバを見ることができる。指標は、一次チャンバがいっぱいであるか否かを確認するための一次チャンバの可視性、例えば、色を変える血液バリア、又は他の指標を含むことができる。隔離チャンバの充填時間は、実質的に瞬間的であり得るので、このような指標は、存在する場合、隔離チャンバが満たされているというだけである可能性がある。

【００４２】
真空採血管が取り付けられる前、針、サンプリング流路、及び隔離チャンバの間の連通は、隔離チャンバの血液バリアの密封によって制限され、従って隔離によって空気がシステムに再び入ることを可能にしない。連通経路の密封は、機械的にねじること又は他の動作、小さな穴又は曲がりくねった経路によって達成され、臨床医による別個の弁又は機械的な動作又は操作の必要性をなくす。７１０において、真空採血管を取り外すと、自己密封式の膜がサンプル針を密封し、７１２で、更なる後続の真空採血管を取り付けることができる。７１４において、サンプルが採取されると、装置が患者から取り外され、廃棄される。

【００４３】
図８Ａ～８Ｅは、一部の実施に従う、非汚染採血用の例示的な血液サンプル最適化システム８００を示す。血液サンプル最適化システム８００は、チューブ、患者針（又は両方）、又は他の血管又は静脈アクセス装置に接続されることができる入口ポート８０２と、隔離チャンバチューブ８０６への第１出口とサンプル採取チューブ８０８への第２出口とを有する経路スプリッタ８０４とを含む。隔離チャンバチューブ８０６及びサンプル採取チューブ８０８の一方又は両方は、チューブから形成されることができる。一部の実施では、隔離チャンバチューブ８０６は、特定の量の当初血液サンプルを収容するように寸法設定される。サンプル採取チューブ８０８は、ひとたび隔離チャンバチューブ８０６が満たされると、血液サンプルを受け入れる。サンプル採取チューブ８０８は、バキュテナー（登録商標）ベース又はハウジング８１０、又は他の血液サンプル採取装置に接続されることができる。

【００４４】
血液隔離システム８００は血液隔離装置８１２を更に含み、血液隔離装置８１２は、図８Ｂ～８Ｄにより詳細に示すようにハウジング８１８を含み、ハウジング８１８は、非汚染サンプル採取チューブ８０８用の経路を画定するか又はいずれかの端部が非汚染サンプル採取チューブ８０８と接続されるサンプリング流路８２０を含む。サンプリング流路８２０は、非汚染サンプル採取チューブ８０８に沿った位置でハウジング８１８をより良好に固定し且つ安定させるように、ハウジング８１８を通って曲線状であることができる。

【００４５】
血液隔離装置８１２は、隔離チャンバチューブ８０６と接続される隔離チャンバ８２２又は他のチャンバを更に含む。隔離チャンバ８２２は、空気透過性血液バリア８２４で終端している。空気透過性血液バリア８２４はまた、血液サンプル（すなわち、非汚染血液サンプル）の正式な採取を開始することができる指標として、血液との完全な接触時に異なる色に変わる着色剤を含むことができる。小さい光、音発生機構などの他の指標を使用することができる。一部の実施では、空気透過性血液バリアは、隔離チャンバ８２２の方向から直角に配置されているが、ハウジング８１８に使用される空間及び材料を節約するために任意の距離又は向きに配置されることができる。ハウジング８１８及びその内容物は、任意の剛性材料又は半剛性材料又は一連の材料から形成されることができる。

【００４６】
図９は、例えば、図８Ａ～８Ｅに示すような血液隔離システムに用いる経路スプリッタ

９００を示す。経路スプリッタ９００は、入口ポート９０２と、主管路出口ポート９０４と、隔離流路出口ポート９０６とを含む。入口ポート９０２は、同様に患者針システムに接続される主チューブに、又は直接患者針に接続されることができる。主管路出口ポート９０４は、バキュテナー（登録商標）ベース又はハウジングなどの採血システムへの主管路チューブに、又は直接そのような採血システムに接続されることができる。隔離流路出口ポート９０６は、測定された量又は所定の閾値まで血液の第１サンプルを受け入れ且つ隔離するための隔離チューブに接続されることができる。代わりに、隔離流路出口ポート９０６は、隔離チャンバに接続することができる。隔離流路出口ポート９０６は、好ましくは、主管路出口ポート９０４から２０～７０度の角度に曲げられ、一方、主管路出口ポート９０４は、好ましくは、入口ポート９０２と一直線である。所定の量の最初の血液サンプルが、本明細書に記載された機構及び技術に従って隔離チューブ又は隔離チャンバ内に隔離されると、後続の血液サンプルは、入口ポート９０２に流入し、障害物なしで主管路出口ポート９０４から直接流出する。

【００４７】

図１０Ａ～１０Ｄは、別の実施に従う血液隔離装置１０００を示す。血液隔離装置１０００は、入口ポート１００２と、主出口ポート１００４と、隔離流路ポート１００６とを含む。入口ポート１００２は、患者針又は関連するチューブと接続されることができる。主出口ポート１００４は、バキュテナー（登録商標）、関連するチューブ、又はルアー作動弁などの血液サンプル採取装置に接続されることができる。隔離流路ポート１００６は、主出口ポート１００４から隔離チャンバ１００８に分離する。一部の実施では、隔離チャンバ１００８は、ハウジング又は他の容器１００１内に螺旋流路として形成される。

【００４８】

隔離チャンバ１００８は、実質的に上記のように、遠位端が空気透過性血液バリア１０１０に接続される。隔離チャンバ１００８内の空気は、空気透過性血液バリア１０１０を通して、隔離流路ポート１００６内に案内される最初のアリコートの血液によって追い出される。ひとたび隔離チャンバ１００８が満たされると、主出口ポート１００４を通る更なる採血が成し遂げられ、これらのサンプルは汚染されていない。

【００４９】

図１１Ａ～１１Ｅは、他の代替的な実施に従う血液隔離装置１１００を示す。血液隔離装置１１００は、上述の入口ポートと同様の入口ポート１１０２と、主出口ポート１１０４と、主出口ポート１１０４及び入口ポート１１０２から分離する隔離流路ポート１１０６とを含む。隔離流路ポートは、隔離チャンバ１１０８に接続されている。図１１Ａ～１１Ｅに示す実施では、血液隔離装置は、隔離チャンバ１１０８として機能する流路を内部に有するベース部材１１０１を含む。流路は、ベース部材１１０１を通る曲がりくねった経路として形成されることができ、一方、ベース部材１１０１は、患者の四肢に載るように成形され且つ形成される。

【００５０】

隔離チャンバ１１０８の一部は、血液隔離指標１１０９として機能するように、空気透過性血液バリア１１１０に出る直前に、ベース部材から又はベース部材の上面付近に突出することができる。指標１１０９は、透明な材料、又は血液と接触すると変色する材料で形成されることができる。

【００５１】

一部の実施では、血液隔離装置１１００は、常時閉じている針、バキュテナー（登録商標）シールド又は他の採取装置などの採血装置１１２０を含むことができる。採血装置１１２０は、患者針の挿入プロセスによって汚染される恐れがある最初のアリコートの血液を隔離することができるように、効率及び利便性のために血液隔離装置１１００と共に製造及び販売されることができる。従って、採血装置１１２０は、偽陽性の検査のリスクを低減するように非汚染血液サンプルを採取し且つ非汚染サンプルを確実にすることができる。

【００５２】

図１２Ａ～１２Ｄは、更に他の代替的な実施に従う血液サンプル最適化システム１２００を示す。システム１２００は、バキュテナー（登録商標）又は他の採取及びサンプリング装置のような採血装置１２０４に取り付けるための血液隔離装置１２０２を含む。血液隔離装置１２０２は、バキュテナー（登録商標）容器又はバイアルが採血装置１２０４の採取針に取り付けられる前に、最初のアリコート又は量の血液を受け入れ、且つその最初のアリコート又は量を血液隔離装置１２０２の隔離流路内に隔離するように、構成され且つ配置されている。

【００５３】

一部の実施では、血液隔離装置１２０２は、入口ポート１２１２と、主出口ポートと、隔離流路ポートとを含むことができる。入口ポート１２１２は、患者針又は関連するチューブに接続されることができる。主出口ポート１２１４は、真空採血容器又はバキュテナー（登録商標）などの他の採取装置、関連するチューブ、ルアーコネクタ、注射器、ルアー作動弁との接続を可能にするために、常時閉じている針又は装置に接続されることができる。隔離流路ポートは、主出口ポートから隔離チャンバ１２１８に分離する。

【００５４】

一部の実施では、隔離チャンバ１２１８は、隔離装置１２０２の本体内の流路として形成される。隔離チャンバ１２１８は、Ｕ字形流路、Ｓ字形流路、螺旋流路、又は任意の他の曲がりくねった流路などの曲がりくねった流路であることができる。隔離装置１２０２は、ハウジング又は他の収容体、及びその中に形成された１つ以上の流路を含むことができる。図１２Ａ及び１２Ｂに示すように、隔離装置１２０２は、本体１２０６とキャップ１２０８とを含む。本体１２０６には１つ以上の空洞又は流路が形成され、空洞又は流路にはキャップ１２０８から延びる１つ以上のアーム１２１０が更に形成され、１つ以上のアーム１２１０は、本体１２０６の空洞又は流路に当接して一次採取ポート及び主出口ポートを形成している。

【００５５】

図１３Ａ～１３Ｄは、更に他の代替的な実施に従う血液サンプル最適化システム１３００を示す。システム１３００は、バキュテナー（登録商標）又は他の体液採取及びサンプリング装置などの採血装置１３０４に取り付けるための血液隔離装置１３０２を含む。血液隔離装置１３０２は、バキュテナー（登録商標）容器又はバイアルが採血装置１３０４の採取針に取り付けられる前に、最初のアリコート又は量の血液を受け入れ、且つその最初のアリコート又は量の血液又は他の体液を血液隔離装置１３０２の隔離流路内に隔離するように、構成され且つ配置されている。

【００５６】

血液隔離装置１３０２は、入口ポート１３１４と、主出口ポート１３１２と、隔離流路ポート１３１６とを有するハウジング１３０１を含む。入口ポート１３１４は、患者針又は関連するチューブに接続されることができる。主出口ポート１３１２は、真空採血容器又はバキュテナー（登録商標）などの他の採取装置、関連するチューブ、ルアーコネクタ、注射器、ルアー作動弁との接続を可能にするために、常時閉じている針又は装置に接続されることができる。隔離流路ポート１３１６は、主入口ポート１３１４から隔離チャンバ１３１８に分離する。

【００５７】

図１３Ａ～１３Ｄに示す実施例では、隔離チャンバ１３１８は、ハウジング１３０１内の空洞又はチャンバとして形成され、又はハウジング１３０１を画定する壁によって形成される。隔離チャンバ１３１８は、Ｕ字形流路、Ｓ字形流路、螺旋流路などの曲がりくねった流路、又はハウジング１３０１とキャップ１３０７との協働及び接続によって画定される任意の他の曲がりくねった流路であることができ、キャップ１３０７は、隔離チャンバ１３１８内の曲がりくねった流路のための１つ以上の壁又はディレクタを提供する突出部１３０５を含むことができる。キャップ１３０７からの突出部１３０５は、真っ直ぐであるか湾曲していることができ、様々な流路、開口部又は溝が埋め込まれていることができ、キャップ１３０７から任意の角度又は向きで延びることができる。隔離チャンバ１３

１８の形成を完了するためにキャップ１３０７がハウジング１３０１と接続されると、突出部１３０５は曲がりくねった流路の少なくとも一部を形成し、隔離チャンバ１３１８内に曲がりくねった流路によって形成される隔離流路に最初のアリコート又は量の血液又は他の体液を隔離する。

【００５８】

隔離チャンバ１３１８は、実質的に上記のように空気透過性血液バリア１３１０を含む。隔離チャンバ１３１８内の空気は、患者の血圧によって隔離チャンバ１３１８内に供給される最初のアリコートの血液によって空気透過性血液バリア１３１０を通して追い出される。隔離チャンバ１３１８が満たされ、隔離チャンバ１３１８内の空気が追い出されると、バキュテナー（登録商標）のような血液サンプル採取装置によって提供されるような真空又は他の圧力のような力が次のアリコート又は量の血液又は体液を引き抜くために提供されるまで、患者の血圧は、血液隔離装置１３０２、特に、出口ポート１３１２に更なる血液を追い込み又は提供するのには不十分である。主出口ポート１３１２を通して更なる採血を行うことができ、あらゆる汚染物質が最初のアリコートの血液と共に隔離チャンバ１３１８内に隔離されているので、これらのサンプルは汚染されない。

【００５９】

図１４Ａ～１４Ｅは、患者の血液サンプルに対して実施される血液培養又は検査における偽陽性を低減するために最初のアリコート又はサンプルの汚染物質を隔離する採血システム１４００の更に別の実施を示す。採血システム１４００は、血液サンプル採取装置１４０３と患者針（図示せず）との間に接続されることができる血液隔離装置１４０１を含む。血液サンプル採取装置１４０３は、バキュテナー（登録商標）などであることができる。血液隔離装置１４０１は、血液サンプルへのアクセス及び血液サンプルの採取のために患者の血管系に挿入される患者針と接続されることができる入口ポート１４０２を含む。入口ポート１４０２は、同様に患者針と接続されるチューブ又は他の導管と接続されることもできる。

【００６０】

入口ポート１４０２は、血液隔離装置１４０１への開口部を画定し、この開口部は、患者針と接続されるチューブ又は他の導管又は患者針自体と同じ断面寸法であることができる。例えば、開口部は、約０．０４５インチ（１．１４３ｍｍ）の直径を有する円形であることができるが、０．０１インチ（０．２５４ｍｍ）から０．２インチ（５．０８ｍｍ）又はそれ以上の直径を有することができる。血液隔離装置１４０１は、血液隔離装置１４０１から及び血液サンプル採取装置１４０３への開口部を画定する出口ポート１４０４を更に含む。出口ポート１４０４は、同様に血液隔離装置１４０３と接続されるチューブ又は他の導管と接続されることもできる。出口ポート１４０４は、ねじ付きキャップ、ルアーコネクタ（雄型又は雌型）、チューブなどを含むがそれらに限定されない様々な装置の取り付け用のねじが切られていない締め代又は接着継手などのコネクタ装置を更に含むことができる。

【００６１】

血液隔離装置１４０１は、入口ポート１４０２と出口ポート１４０４との間にサンプリング流路１４０６を更に含み、サンプリング流路１４０６は、最初のアリコートの血液が隔離されると血液サンプル経路として機能する。サンプリング流路１４０６は、任意のサイズ、形状又は構成の流路又は導管であることができる。一部の実施では、サンプリング流路１４０６は、入口ポート１４０２の開口部と実質的に同様の断面積を有する。他の実施では、サンプリング流路１４０６は、入口ポート１４０２から出口ポート１４０４まで徐々に広がることができる。

【００６２】

血液隔離装置１４０１は隔離チャンバ１４０８を更に含み、隔離チャンバ１４０８は、入口ポート１４０２と出口ポート１４０４との間の任意の位置でサンプリング流路１４０６に接続され且つサンプリング流路１４０６から分離又は方向転換されるが、好ましくは入口ポート１４０２の近くのサンプリング流路１４０６の近位端に接続され且つ近位端か

ら分離又は方向転換される。隔離チャンバ１４０８は、最初は大気圧に維持され、サンプリング流路１４０６からの方向転換点と反対側の隔離チャンバ１４０８の遠位端又はその近傍に空気出口１４１２を含む。空気出口１４１２は、空気透過性血液バリア１４１２を含む。図１４Ｂに示すように、空気透過性血液バリア１４１２は、保護カバー１４１６で覆われていることができる。保護カバー１４１６は、ユーザーが彼らの指又は他の外部器具で空気透過性血液バリア１４１２に触れるのを妨げるように寸法設定され且つ構成されることができ、一方それでも患者自身の血圧によって隔離チャンバ１４０８内に強制的に血液が供給されることによって空気が隔離チャンバから追い出されるときに空気が空気透過性血液バリア１４１２から出ることを可能にする。また、保護カバー１４１６は、空気透過性血液バリアが周囲の流体又は飛沫に偶発的に曝されるのを阻止又は防止するように構成されることができる。これは、保護カバーに疎水性膜を追加することを含むがそれに限定されない、様々な機械的方法で行うことができる。

【００６３】

図１４Ｃ及び１４Ｄに示すように、サンプリング流路１４０６は、赤血球を溶解する可能性を最小限に抑えるために、より小さい直径からより大きい直径になる円筒形又は円錐台形であることができる。同様に、サンプリング流路１４０６は、赤血球を溶解する可能性がある急カーブ又は鋭角が最小限の量で又はなしで形成される。サンプリング流路１４０６は、方向転換経路１４０９を通して入口ポート１４０２の近くで隔離チャンバ１４０８へと分離する。方向転換経路１４０９は、任意の断面形状又はサイズを有することができるが、好ましくは、入口ポート１４０２の少なくとも一部の断面形状と同様である。

【００６４】

一部の実施では、サンプリング流路１４０６及び隔離チャンバ１４０８は、ハウジング１４１４に形成された溝、流路、ロック又は他の経路によって形成される。ハウジング１４１４は、プラスチック、金属又は他の剛性又は半剛性材料で作られることができる。ハウジング１４１４は、上部部材と密封可能に嵌合する下部部材を有することができる。下部部材及び上部部材の一方又は両方は、サンプリング流路１４０６及び隔離チャンバ１４０８、並びに方向転換経路１４０９、入口ポート１４０２、及び出口ポート１４０４を含むことができる。一部の他の実施態様では、方向転換経路１４０９、入口ポート１４０２、及び／又は出口ポート１４０４のうちの１つ以上が、ハウジング１４１４のいずれかの端部に接続されるキャップ部材によって少なくとも部分的に形成されることができる。一部の実施では、上部部材及び下部部材、並びにキャップ部材は、レーザ溶接、ヒートシール、接着、スナップ止め、ねじ止め、ボルト止めなどによって互いに連結されることができる。他の実施では、方向転換経路１４０９及び／又は隔離チャンバ１４０８の内面の一部又は全部が、汚染除去剤、凝固剤などの薬剤又は物質でコーティング又は充填されることができる。例えば、隔離チャンバ１４０８が満たされて最初のアリコートの血液が方向転換経路１４０９に戻るとき、隔離された血液の最後の量が凝固し、隔離チャンバ１４０８とサンプリング流路１４０６との間に障壁を作り出すように、方向転換経路１４０９に凝固剤を設けることができる。

【００６５】

図１５Ａ～１５Ｇは、血液隔離装置１５００を示す。血液隔離装置１５００は、真空採血容器又はバキュテナー（登録商標）などの他の採取装置、関連するチューブ、ルアーコネクタ、注射器、ルアー作動弁などとの接続を可能にするために常時閉じている針又は装置に接続されることができる。

【００６６】

血液隔離装置１５００は、血液サンプルへのアクセス及び血液サンプルの採取のために患者の血管系に挿入される患者針と接続されることができる入口ポート１５０２を含む。入口ポート１５０２は、同様に患者針と接続されるチューブ又は他の導管と接続されることもできる。入口ポート１５０２は、血液隔離装置１５００への開口部を画定し、この開口部は、患者針と接続されるチューブ又は他の導管又は患者針自体と同じ断面寸法であることができる。例えば、開口部は、約０．０４５インチ（１．１４３ｍｍ）の直径を有す

る円形であることができるが、０．０１インチ（０．２５４ｍｍ）から０．２インチ（５．０８ｍｍ）又はそれ以上の直径を有することができる。

【００６７】

入口ポート１５０２はまた、ねじ切り又はルアーフィッティングなどのような密封又は流体密封のコネクタ又は接続部を含むことができる。一部の実施では、患者針に結合されているチューブ又は他の導管は、部品同士の共成形、接着、レーザ溶接、又は熱接合などによって、入口ポート１５０２と一体化されることができる。これによって、血液隔離装置１５００は、患者針と共に単一ユニットとして製造及び販売され、採血又はサンプリングの際に患者針を血液隔離装置１５００に接続する必要性をなくすことができる。

【００６８】

血液隔離装置１５００は、血液隔離装置１５００から及び血液サンプル採取装置への開口部を画定する出口ポート１５０４を更に含む。出口ポート１５０４は、同様に血液隔離装置と接続されるチューブ又は他の導管と接続されることもでき、ねじ切り又はルアーフィッティングなどの密封又は流体密封コネクタ又は接続部を含むことができる。したがって、上記のように、血液隔離装置１５００は、患者針及び／又はチューブ及び血液サンプル採取装置と共に単一ユニットとして製造及び販売され、採血又はサンプリングの際に患者針及び血液サンプル採取装置を血液隔離装置１５００に接続する必要性をなくすことができる。

【００６９】

血液隔離装置１５００は、入口ポート１５０２と出口ポート１５０４との間にサンプリング流路１５０６を更に含み、サンプリング流路１５０６は、最初のアリコートの血液が隔離されると血液サンプル経路として機能する。サンプリング流路１５０６は、任意のサイズ、形状、又は構成の流路又は導管であることができる。一部の実施では、サンプリング流路１５０６は、入口ポート１５０２の開口部と実質的に同様の断面積を有する。他の実施では、サンプリング流路１５０６は、入口ポート１５０２から出口ポート１５０４まで徐々に広がることができる。

【００７０】

血液隔離装置１５００は隔離チャンバ１５０８を更に含み、隔離チャンバ１５０８は、入口ポート１５０２と出口ポート１５０４との間の任意の位置でサンプリング流路１５０６に接続され且つサンプリング流路１５０６から分離又は方向転換されるが、好ましくは入口ポート１５０２の近くのサンプリング流路１５０６の近位端に接続され且つ近位端から分離又は方向転換される。一部の実施では、分水路はＹ字路を含む。隔離チャンバ１５０８は、好ましくは大気圧に維持され、隔離チャンバ１５０８の遠位端又はその近傍に通気口１５１０を含む。通気口１５１０は、空気透過性血液バリア１５１２を含む。図１５Ｃは、隔離チャンバ１５０８が患者からの血液の最初のアリコート又はサンプルで満たされた血液隔離装置１５００を示す。

【００７１】

空気透過性血液バリア１５１２は、保護カバー１５１６で覆されていることができる。保護カバー１５１６は、ユーザーが彼らの指又は他の外部器具で空気透過性血液バリア１５１２に触れるのを妨げるように寸法設定され且つ構成されることができ、一方それでも患者自身の血圧によって隔離チャンバ１５０８内に強制的に血液が供給されることによって空気が隔離チャンバから追い出されるときに空気が空気透過性血液バリア１５１２から出ることを可能にする。保護カバー１５１６は、フィルタが周囲の流体又は飛沫に偶発的に曝されるのを阻止又は防止するように構成されることができる。これは、保護カバーに疎水性膜を追加することを含むがそれに限定されない、様々な機械的方法で行うことができる。

【００７２】

図１５Ｂは、血液隔離装置１５００の出口ポート１５０４及び通気口１５１０を含むハウジング１５０１の上面からの血液隔離装置１５００の斜視図であり、サンプル採取装置が起動される前、サンプリング流路１５０６が空である間に最初のアリコートの血液が隔

離チャンバ１５０８を満たすことを示す。図１５Ｇは、血液隔離装置１５００の出口ポート１５０４及びハウジング１５０１の底面からの血液隔離装置１５００の斜視図であり、サンプル採取装置が起動される前、サンプリング流路１５０６が空である間に最初のアリコートの血液が隔離チャンバ１５０８を満たすことを示す。図１５Ｃは、血液隔離装置１５００の入口ポート１５０２及び通気口１５１０を含むハウジング１５０１の上面からの血液隔離装置１５００の別の斜視図であり、隔離された血液は実質的に隔離チャンバ１５０８内にとどまっている間に血液がサンプリング流路１５０６を通って採取されることを示す。

【００７３】

図１５Ｄは、一部の実施に従う血液隔離装置１５００の断面図であり、サンプリング流路１５０６及び隔離チャンバ１５０８を画定するハウジング１５０１を示す。図１５Ｅ及び１５Ｆは、本明細書に記載される１つ以上の実施に従う血液隔離装置用のハウジングの様々なフォームファクタを示す。

【００７４】

隔離チャンバ１５０８は、サンプリング流路１５０６よりも大きい断面積を有することができ、断面積又は長さは、所定の又は特定の血液量が隔離又はロックされるように構成されることができる。サンプリング流路１５０６は、患者針のチューブ又は採血装置のチューブのいずれか又は両方のためのチューブに適合するように寸法設定されることができる。

【００７５】

ハウジング１５０１は、複数の部品又は単一の一体部品から形成されることができる。一部の実施では、図１５Ｄに示すように、ハウジング１５０１は、互いに嵌合する上部部材１５２０と下部部材１５２２とを含み、それらの一方又は両方は、例えば、射出成形プロセスによって又はエッチング、切削、穿孔などによって予め形成された溝、流路、ロック、導管又は他の経路を有する。上部部材１５２０は、レーザ溶接、熱接合、超音波溶接、接着、ねじ、リベット、ボルトなどを使用することなどの任意の嵌合又は接続機構によって、又はラッチ、溝、舌状部、ピン、フランジなどの他の嵌合機構によって、下部部材１５２２と接続されることができる。

【００７６】

一部の実施では、図１５Ｄに示すように、上部部材１５２０は、溝、流路、ロック、導管又は他の経路を含むことができ、一方、下部部材１５２２は、上部部材１５２０の溝、流路、ロック又は他の経路のうちの少なくとも１つに嵌合するように寸法設定され且つ適合された突出部１５２４を含むことができる。突出部１５２４は、例えば、サンプリング流路１５０６及び／又は隔離チャンバ１５０８のいずれかの形成を完了させるために、部分的な溝又は部分的な流路などの表面特徴を提供することができる。一部の実施では、突出部１５２４は、対応する溝、流路、ロック又は他の経路内によりぴったりと嵌合するために、１つ以上の傾斜した側面又は面を形成されることができる。更に他の実施では、上部部材１５２０と下部部材の両方が、溝、流路、ロック又は他の経路、並びに１つ以上の突出部１５２４を含むことができる。

【００７７】

一部の実施では、サンプリング流路１５０６及び隔離チャンバ１５０８は、ハウジング１５０１に形成された溝、流路、ロック又は他の経路によって形成される。ハウジング１５０１は、ゴム、プラスチック、金属又は他の材料を含む任意の適切な材料で作られることができる。ハウジング１５０１は、透明又は半透明の材料から、又は不透明又は非半透明の材料から形成されることができる。他の実施では、ハウジング１５０１は、大部分が不透明又は非透明であることができるが、サンプリング流路１５０６及び／又は隔離チャンバ１５０８に直接隣接するハウジング表面は、透明又は半透明であり、最初に隔離チャンバ１５０８が必要又は所望の程度まで満たされているという視覚的な合図又はサイン、及び／又は、次に汚染されていない血液サンプルがサンプリング流路１５０６を通して採取される間、隔離された血液が隔離されたままであるという視覚的な合図又はサインを施

術者に与える。隔離の他の視覚的な合図又はサインは、以下に限定されるものではないが、血液の接触、浸透、又は部分的な浸透で空気透過性血液バリア１５１２が異なる色に変わること、隔離チャンバに沿った又は隔離チャンバに隣接する任意の位置にある色分けされたタブ又は指標、可聴信号、振動信号、又は他の信号を含むことができる。

【００７８】

患者の皮膚から多数の病原体を集める可能性がある患者針（図示せず）による静脈穿刺の後、患者自身の血圧が隔離チャンバ１５０８内の大気圧に打ち勝って空気透過性血液バリア１５１２を通して隔離チャンバ１５０８内の空気を追い出すので、これらの病原体を有する患者の血液の最初の量が、血液隔離装置１５００入口ポート１５０２に入り、最も抵抗の少ない経路をたどることによって隔離チャンバ１５０８に流入する。患者の血圧は、密封されたサンプリング流路１５０６内で高まっている空気圧に打ち勝つのに十分ではない。最終的に、所定の容積を有する隔離チャンバ１５０８は、空気透過性血液バリア１５１２を通して空気を追い出す血液で満たされる。血液が空気透過性血液バリアに衝突すると、血液は空気透過性血液バリア１５１２の材料と相互作用して、通気口１５１０を完全に又は部分的に密封する。施術者がいまやバキュテナー（登録商標）カプセル又は他の血液サンプル採取装置を利用してサンプリングのために患者の血液の次の量を得ることができるという信号又は表示を提供することができる。隔離チャンバ１５０８内の血液は、このとき隔離チャンバ内で事実上隔離されている。

【００７９】

血液隔離経路１５０８を満たすと、バキュテナー（登録商標）又は他の血液サンプル採取装置の使用より前に、患者の血圧は、サンプリング流路１５０６内の空気の圧縮を引き起こし、場合によっては少量の血液が隔離チャンバ１５０８への方向転換点を過ぎてサンプリング流路１５０６に移動し、サンプリング流路１５０６を通して採取される汚染されていない血液を待ち行列に入れる。

【００８０】

図１６～１９は、血液隔離装置の更に別の実施を示す。図１６Ａ～１６Ｄは、バキュテナー（登録商標）（図示せず）のような真空採血容器のような血液サンプル採取装置と患者針（図示せず）及び／又は関連するチューブとの間に接続されることができる血液隔離装置１６００を示す。図１７は、血液隔離装置の下部部材を示し、図１８は、血液隔離装置の上部部材を示し、上部部材及び下部部材は、以下でより詳しく説明するように、相互に嵌合して、入口ポート、出口ポート、隔離チャンバ及びサンプリング流路を形成することができる。図１９Ａ及び１９Ｂは、互いに嵌合する上部部材及び下部部材を示す。図１６～１９は本明細書に記載される血液隔離装置を構成する１つの例示的な方法を示しており、他の形態の構成も可能であることを理解されたい。

【００８１】

図１６Ａ～１６Ｄを参照すると、血液隔離装置１６００は、血液サンプルへのアクセス及び血液サンプルの採取のために患者の血管系に挿入される患者針と接続されることができる入口ポート１６０２を含む。入口ポート１６０２は、同様に患者針と接続されるチューブ又は他の導管と接続されることもできる。入口ポート１６０２は、血液隔離装置１６００への開口部を画定し、この開口部は、患者針と接続されるチューブ又は他の導管又は患者針自体と同じ断面寸法であることができる。例えば、開口部は、約０．０４５インチ（１．１４３ｍｍ）の直径を有する円形であることができるが、０．０１インチ（０．２５４ｍｍ）から０．２インチ（５．０８ｍｍ）又はそれ以上の直径を有することができる。

【００８２】

入口ポート１６０２はまた、ねじ切り又はルアーフィッティングなどのような密封又は流体密封コネクタ又は接続部を含むことができる。一部の実施では、患者針に結合されているチューブ又は他の導管は、部品同士の共成形、接着、レーザー溶接、又は熱接合などによって、入口ポート１６０２と一体化されることができる。これによって、血液隔離装置１６００は、患者針及び／又はチューブと共に単一ユニットとして製造及び販売され、

採血又はサンプリングの際に患者針を血液隔離装置１６００に接続する必要性をなくすことができる。

【００８３】

血液隔離装置１６００は、血液隔離装置１６００から及び血液サンプル採取装置への開口部を画定する出口ポート１６０４を更に含む。出口ポート１６０４は、同様に血液隔離装置と接続されるチューブ又は他の導管と接続されることもでき、ねじ切り又はルアーフィッティングなどの密封又は流体密封コネクタ又は接続部を含むことができる。したがって、上記のように、血液隔離装置１６００は、患者針及び／又はチューブ及び血液サンプル採取装置と共に単一ユニットとして製造及び販売され、採血又はサンプリングの際に患者針及び血液サンプル採取装置を血液隔離装置１６００に接続する必要性をなくすことができる。

【００８４】

血液隔離装置１６００は、入口ポート１６０２と出口ポート１６０４との間のサンプリング流路１６０６と、入口ポート１６０２と出口ポート１６０４との間の任意の位置でサンプリング流路１６０６に接続され且つサンプリング流路１６０６から分離又は方向転換される隔離チャンバ１６０８とを更に含む。サンプリング流路１６０６は、最初のアリコートの血液が隔離チャンバ１６０８内に隔離されると、採血経路として機能する。サンプリング流路１６０６は、任意のサイズ、形状又は構成の流路又は導管であることができる。一部の実施では、サンプリング流路１６０６は、入口ポート１６０２の開口部と実質的に同様の断面積を有する。他の実施では、サンプリング流路１６０６は、入口ポート１６０２から出口ポート１６０４まで徐々に広がることができる。隔離チャンバ１６０８は、図１７及び１９により詳しく示すように、血液がサンプリング流路１６０６のより小さい直径に入るのに対して、まずリザーバに入ろうとするように、隔離流路の経路に向かって大きいリザーバを形成するべくより大きい断面を有することができる。

【００８５】

一部の例示的な実施では、サンプリング流路１６０６と隔離チャンバ１６０８との間の方向転換は、方向転換分岐点１６０７によって行われる。方向転換分岐点１６０７は、実質的にＹ字形、Ｔ字形、又はＵ字形であることができる。一部の好ましい例示的な実施では、図１７Ａ～１７Ｂに示すように、方向転換分岐点１６０７は、入口ポート１６０２からの流れが優先的に隔離チャンバ１６０８に向けられるように構成される。隔離チャンバ１６０８はまた、最初の血液流を隔離チャンバ１６０８に向かって且つ隔離チャンバ１６０８内に移動させるための湾曲部又は傾斜路を含むか又は形成することができる。

【００８６】

隔離チャンバ１６０８は、好ましくは大気圧に維持され、隔離チャンバ１６０８の遠位端又はその近傍に通気口１６１０を含む。通気口１６１０は、上記のように空気透過性血液バリア１６１２を含むことができる。

【００８７】

血液隔離装置１６００は、複数の部品又は単一の一体部品から形成されることができるハウジング１６０１を含むことができる。一部の実施では、図１７Ａ～１７Ｄ及び図１８Ａ～１８Ｆに示すように、ハウジング１６０１は、互いに嵌合する上部部材１６２０と下部部材１６２２とを含む。血液隔離装置１６００は、上部部材１６２０が下部部材１６２２に機械的に取り付けられたときに、両者の間の接合部分がガスケット又は密封部材によって密封されるように、ガスケット又は他の密封部材（図示せず）を含むこともできる。図１７Ａ～１７Ｄは、血液隔離装置１６００用のハウジングの下部部材１６２２を示す。下部部材１６２２は、サンプリング流路１６０６、隔離チャンバ１６０８、及び方向転換分岐点１６０７を形成するために、射出成形プロセスによって又はエッチング、切削、穿孔などによって予め形成された溝、流路、ロック、導管又は他の経路を含むことができる。

【００８８】

隔離チャンバ１６０８は、血液がサンプリング流路１６０６のより小さい直径に入るの

に対して、まず隔離チャンバ内に優先的に移動するように、サンプリング流路１６０６よりも大きい断面を有することができる。

【００８９】

図１８Ａ～１８Ｆは、レーザ溶接、熱接合、接着、ねじ、リベット、ボルトなどを使用することなどの任意の嵌合又は接続機構によって、又はラッチ、溝、舌状部、ピン、フランジなどの他の嵌合機構によって、下部部材１６２２と接続可能な上部部材１６２０を示す。上部部材１６２０は、サンプリング流路１６０６、隔離チャンバ１６０８、及び方向転換分岐点１６０７を形成するために、溝、流路、ロック、導管又は他の経路の一部又はすべてを含むことができる。更に他の実施では、上部部材１６２０と下部部材１６２２の両方が、溝、流路、ロック又は他の経路を含むことができる。

【００９０】

一部の実施では、サンプリング流路１６０６及び隔離チャンバ１６０８は、ハウジング１６０１に形成された溝、流路、ロック又は他の経路によって形成される。ハウジング１６０１は、ゴム、プラスチック、金属又は任意の他の適切な材料で作られることができる。ハウジング１６０１は、透明又は半透明の材料から、又は不透明又は非半透明の材料から形成されることができる。他の実施では、ハウジング１６０１は、大部分が不透明又は非半透明であることができるが、サンプリング流路１６０６及び／又は隔離チャンバ１６０８に直接隣接するハウジング表面は、透明又は半透明であることができ、最初に隔離チャンバ１６０８が必要又は所望の程度まで満たされているという視覚的な合図又はサイン、及び／又は、次に汚染されていない血液サンプルがサンプリング流路１６０６を通して採取される間、隔離された血液が隔離されたままであるという視覚的な合図又はサインを施術者に与える。隔離の他の視覚的な合図又はサインは、以下に限定されるものではないが、血液の接触、浸透、又は部分的な浸透で空気透過性血液バリア１６１２が異なる色に変わること、隔離チャンバに沿った又は隔離チャンバに隣接する任意の位置にある色分けされたタブ又は指標、可聴信号、振動信号、又は他の信号を含むことができる。

【００９１】

図１８Ａ～１８Ｆに示すように、空気透過性血液バリア１６１２は、保護部材１６１６で覆われているか又は保護部材１６１６によって包囲されていることができる。保護部材１６１６は、ユーザーが彼らの指又は他の外部器具で空気透過性血液バリア１６１２に触れるのを妨げるように寸法設定され且つ構成されることができ、一方それでも空気が隔離チャンバ１６０８から追い出されるときに空気が空気透過性血液バリア１６１２から出ることを可能にする。一部の実施では、保護部材１６１６は、上部部材１６２０の上面から上に空気透過性血液バリア１６１２の周りに延びる突出部を含む。保護カバー１６１６は、フィルタが周囲の流体又は飛沫に偶発的に曝されるのを阻止又は防止するように構成されることができる。これは、保護カバーに疎水性膜を追加することを含むがそれに限定されない、様々な機械的方法で行うことができる。

【００９２】

使用時、血液隔離装置１６００は、サンプリング流路１６０６と隔離チャンバ１６０８とを含む。両方の経路が、最初は大気圧で空気を充填されているが、サンプリング流路１６０６は、最初はバキュテナー（登録商標）又は他のこのような密封された採血装置によって密封されている出口ポート１６０４に向けられ、隔離チャンバ１６０８は、空気透過性血液バリア１６１２を含む大気への通気口１６１０で終端している。

【００９３】

患者の皮膚から多数の病原体を集める可能性がある患者針（図示せず）による静脈穿刺の後、これらの病原体を有する患者の血液の最初の量が、血液隔離装置１６００の入口ポート１６０２を通過する。この汚染されている可能性のある血液の最初の量は、最も抵抗の少ない経路を見出すことによって、隔離チャンバ１６０８に優先的に流入する。患者自身の血圧は、通気口付きの隔離チャンバ１６０８内の大気圧に打ち勝ち、空気透過性血液バリア１６１２を通して隔離チャンバ１６０８内の空気を追い出すが、密封されたサンプリング流路１６０６内で高まっている空気圧に打ち勝つには不十分である。様々な例示的

な実施形態では、隔離チャンバ１６０８及びサンプリング流路１６０６は、患者の血圧によって生じた力が、血液隔離装置の向きに関わらず、重力の影響に打ち勝つのに十分であるように構成されることができる。

【００９４】

最終的に、隔離チャンバ１６０８は、空気透過性血液バリア１６１２を通して空気を追い出す血液で満たされる。血液が空気透過性血液バリアと接触すると、血液は空気透過性血液バリア１６１２の材料と相互作用して通気口１６１０を完全に又は部分的に密封する。施術者がいまやバキュテナー（登録商標）又は他の採血装置を利用することができるという信号又は表示を提供することができる。

【００９５】

血液隔離経路１６０８を満たすと、バキュテナー（登録商標）又は他の血液サンプル採取装置の使用より前に、患者の血圧は、サンプリング流路１６０６内の空気の圧縮を引き起こし、場合によっては少量の血液が方向転換点を過ぎてサンプリング流路１６０６に移動しサンプリング流路１５０６を通して採取される汚染されていない血液を待ち行列に入れる。

【００９６】

図１９Ａは、血液隔離装置１６００の側面図であり、図１９Ｂは、血液隔離装置１６００の断面図であり、下部部材１６２２と嵌合する上部部材１６２０を示す。

【００９７】

図２０は、患者の血流への血管アクセスのための患者針２００２と、１つ以上の血液サンプルの採取を容易にする血液サンプル採取装置２００４と、患者針２００２と血液サンプル採取装置２００４との間の流体接続を提供する導管２００６とを含む血液サンプル最適化システム２０００を示す。一部の実施では、血液サンプル採取装置２００４は、密封された採取針を含む保護シールドを含み、採取針に密封された真空容器が置かれ、容器は採取針によって一度穿孔されると、患者針２００２から導管２００６を通して真空圧力又は真空力で血液サンプルを吸い込む。

【００９８】

血液サンプル最適化システム２０００は、本明細書で説明するように、患者針２００２と血液サンプル採取装置２００４との間の導管２００６上の任意の点に位置する血液隔離装置２００８を更に含む。

【００９９】

図２１は、ウィッキング材料チャンバを使用する通気口付きでない血液隔離装置２１００を示す。血液隔離装置２１００は、ウィッキング材料で満たされた隔離チャンバ２１０２によって少なくとも部分的に囲まれ又は当接されるサンプリング流路２１０４を有するハウジング２１０１を含む。最初のアリコートの血液が患者針からサンプリング流路２１０４に引き込まれ、サンプリング流路２１０４において隔離チャンバ２１０２のウィッキング材料の中に直ちに逃がされる。ウィッキング材料及び／又は隔離チャンバ２１０２は、後続の又はそれ以降の採血がウィッキング材料を通り過ぎ、サンプリング流路２１０４を通って直接バキュテナー（登録商標）などのサンプリング装置に流れるように、所定量の血液を受け入れ且つ保持するように寸法設定され且つ適合されている。ウィッキング材料は、固化剤、汚染除去剤、又は他の添加剤などの物質を含むことができる。

【０１００】

本明細書に記載されるように、空気透過性血液バリアは、多種多様な異なる構造及び材料を用いて作られることができる。図２２Ａ及び２２Ｂに示すように、血液隔離装置２２００の空気透過性血液バリア２２０２は、少なくとも一部のビーズが親水性になるように処理されたポリマービーズマトリックス２２０４を含むことができる。空気透過性血液バリア２２０２は、カルボキシメチルセルロース（ＣＭＣ）又はセルロースガムなどの自己密封材料２２０６、又は他の密封材料を更に含む。空気透過性血液バリア２２０２は、血液などの流体との接触前又は部分接触中の空気の流れを可能にする空隙２２０８を更に含むことができる。図２２Ｂに示すように、流体と接触すると、自己密封材料２２０６が膨

張して空隙２２０８を閉鎖し、空隙２２０８を通る空気の流れを閉塞し、完全に又は部分的に密封する。

【０１０１】

図２３Ａ及び２３Ｂは、患者針と接続するための入口ポート２３０２と、血液サンプル採取装置と接続するための出口ポート２３０４と、隔離チャンバ２３０６と、隔離チャンバ２３０６と、隔離するべき汚染されている可能性のある血液の最初のアリコートまで隔離チャンバが満たされると隔離チャンバ２３０６を迂回するサンプリング流路２３０８とを有する、血液隔離装置２３００の更に別の実施を示している。隔離チャンバ２３０６は、入口ポート２３０２から最も遠い隔離チャンバ２３０６の遠位端に疎水性プラグ２３１２を含む。バキュテナー（登録商標）などからのような、出口ポート２３０４から加えられる真空力又は他の吸引力は、血液を入口ポート２３０２内に、そして隔離チャンバ２３０６内に直接吸い込み、そこで最初のアリコートの血液が疎水性プラグ２３１２に接触し、最初のアリコートの血液を隔離チャンバ２３０６に戻してそこで隔離させる。少量の血液が、最初は弁２３０８によって閉鎖されているサンプリング流路２３０８に入ることができる。弁２３０８が解放されると、真空の更なる力又は他の力の下で、後続の量の血液が入口ポート２３０２に流れ、隔離チャンバ２３０６を迂回し、サンプリング流路２３０８を通り抜けて出口ポート２３０４に向かって流れ、採取装置に送られる。

【０１０２】

サンプリング流路２３０８は、任意の適切な幾何学的形状を有することができ、プラスチックチューブ又は任意の他の適切な材料から形成されることができる。弁２３０８は、最初のアリコートの血液が隔離チャンバ２３０６内に隔離される前にサンプリング流路を挟み、脇へそらし、曲げ、又は他の方法で閉じるためにクリップ又は他の包囲装置であることができる。

【０１０３】

様々な実施形態を上記で詳細に説明してきたが、他の変更も可能である。他の実施形態は、添付の特許請求の範囲内に含まれ得る。

【図１】

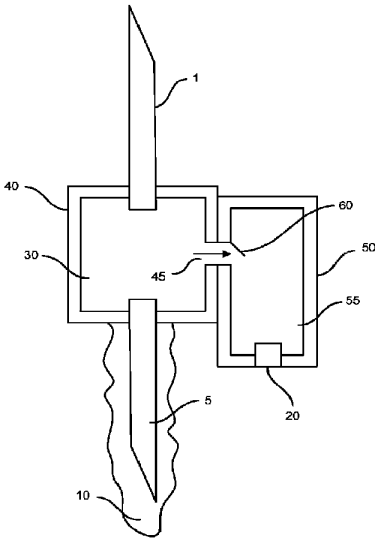


FIG. 1

【図２】

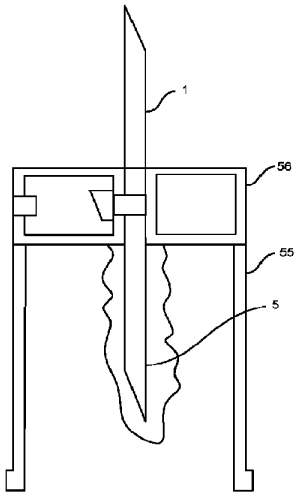


FIG. 2

【図３】

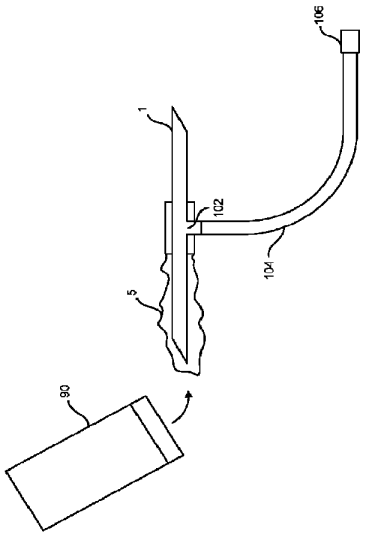


FIG. 3

【図４】

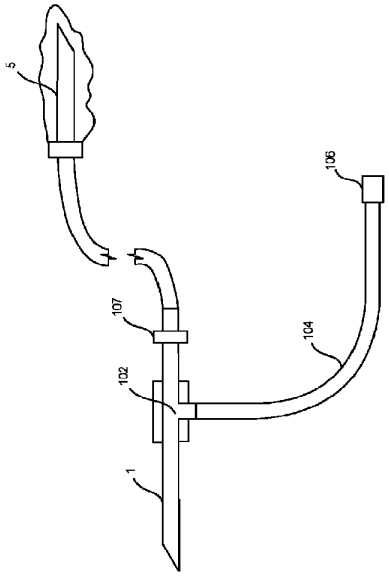


FIG. 4

【図５】

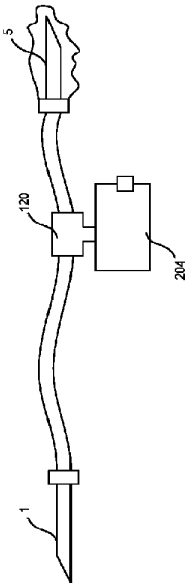


FIG. 5

【図６】

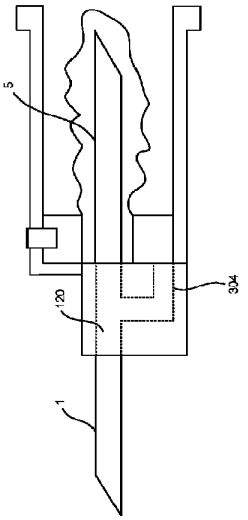


FIG. 6

【図７】

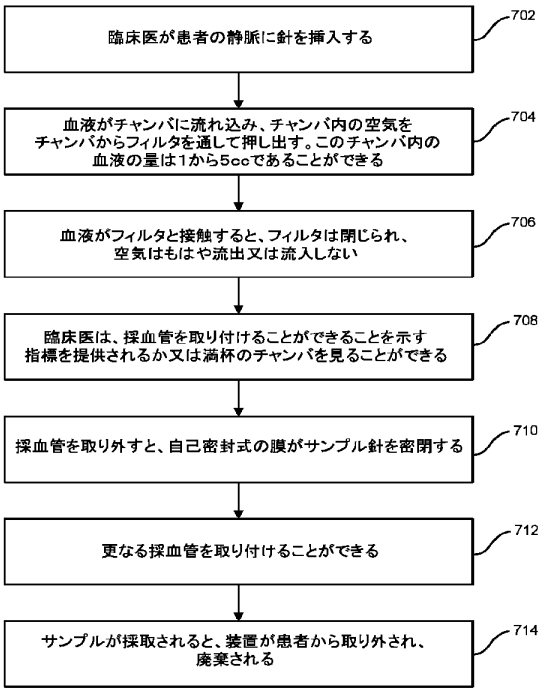


FIG. 7

【図８Ａ】

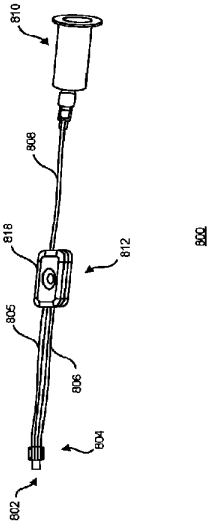


FIG. 8A

【図８Ｂ】

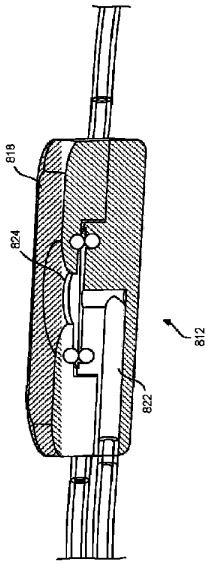


FIG. 8B

【図８Ｃ】

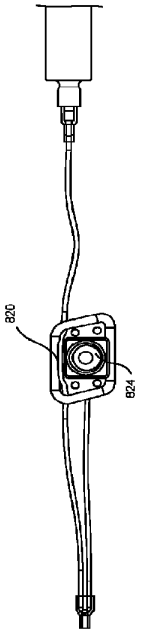


FIG. 8C

【図８Ｄ】

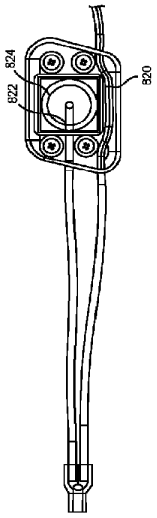


FIG. 8D

【図８Ｅ】

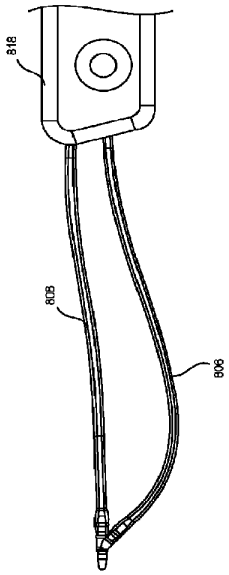


FIG. 8E

【図９】

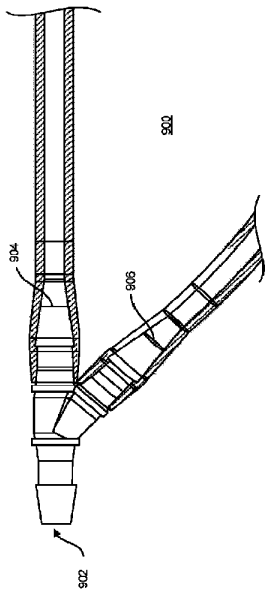


FIG. 9

【図１０Ａ】

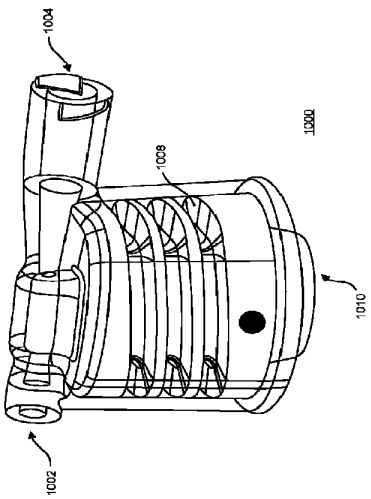


FIG. 10A

【図１０Ｂ】

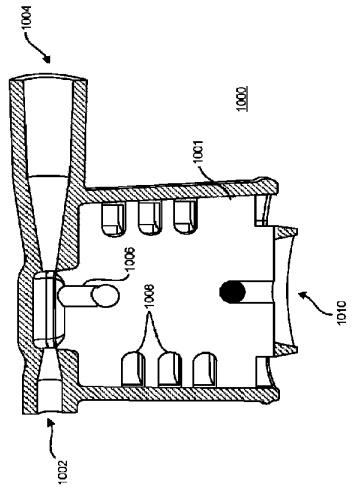


FIG. 10B

【図１０Ｃ】

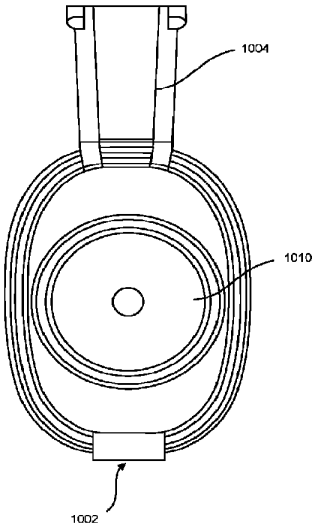


FIG. 10C

【図１０Ｄ】

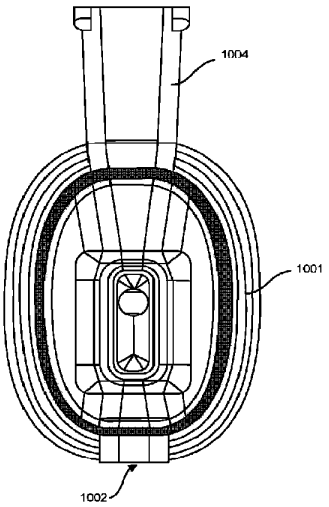


FIG. 10D

【図１１Ａ】

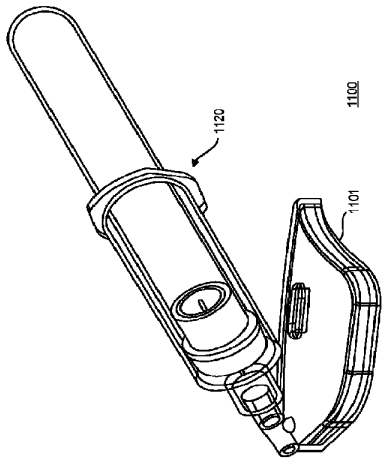


FIG. 11A

【図１１Ｂ】

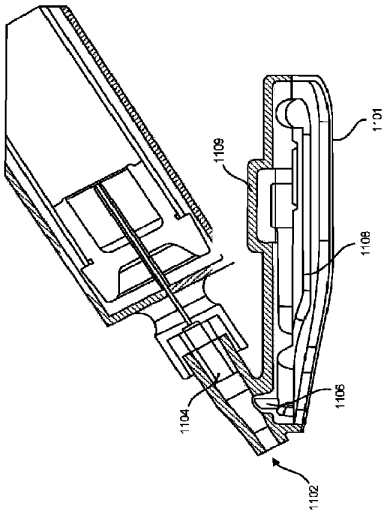


FIG. 11B

【図１１Ｃ】

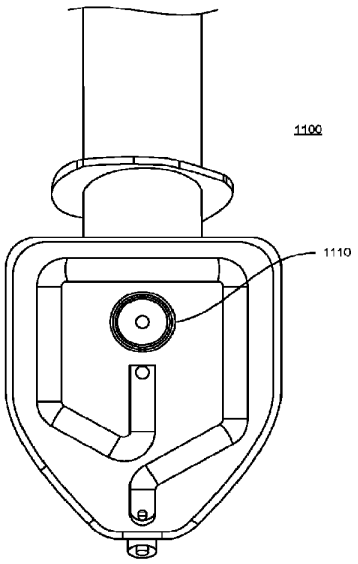


FIG. 11C

【図１１Ｄ】

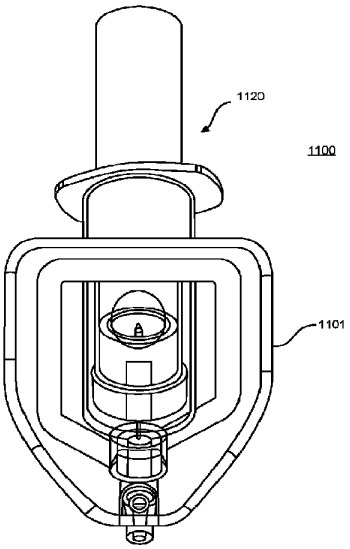


FIG. 11D

【図１１Ｅ】

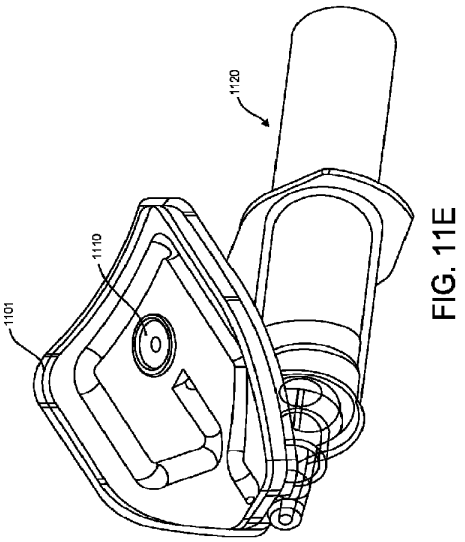


FIG. 11E

【図１２Ａ】

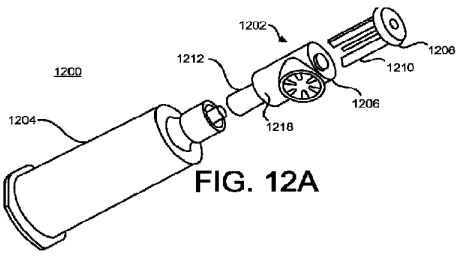


FIG. 12A

【図１２Ｂ】

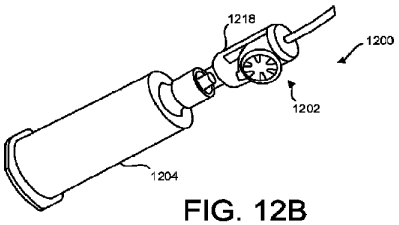


FIG. 12B

【図１２Ｃ】

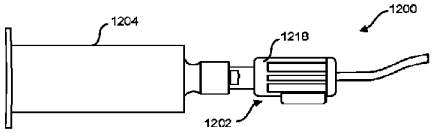


FIG. 12C

【図１２Ｄ】

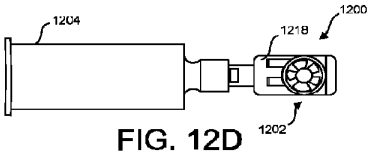


FIG. 12D

【図１３Ａ】

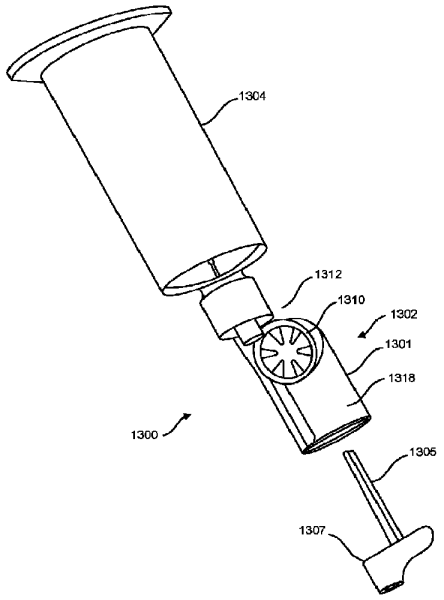


FIG. 13A

【図１３Ｂ】

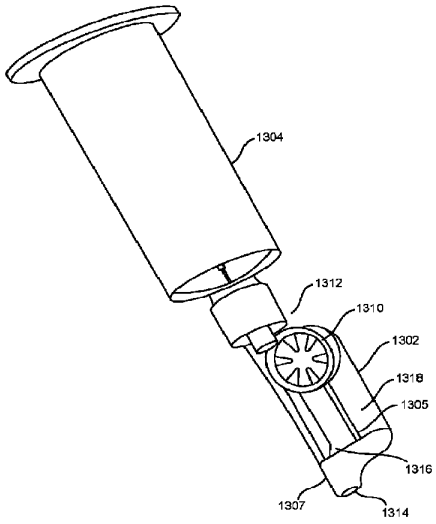


FIG. 13B

【図１３Ｃ】

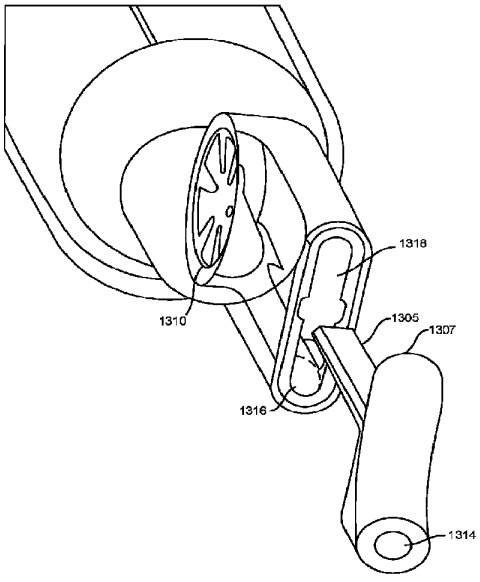


FIG. 13C

【図１３Ｄ】

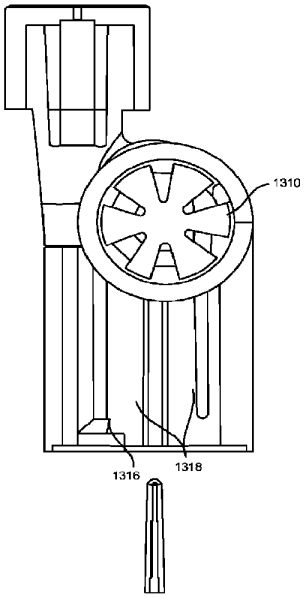


FIG. 13D

【図１４Ａ】

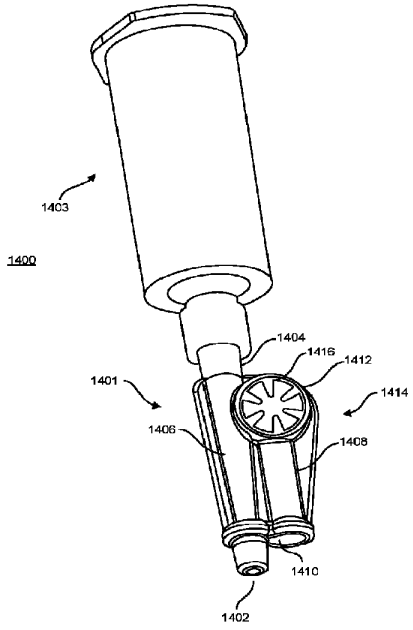


FIG. 14A

【図１４Ｂ】

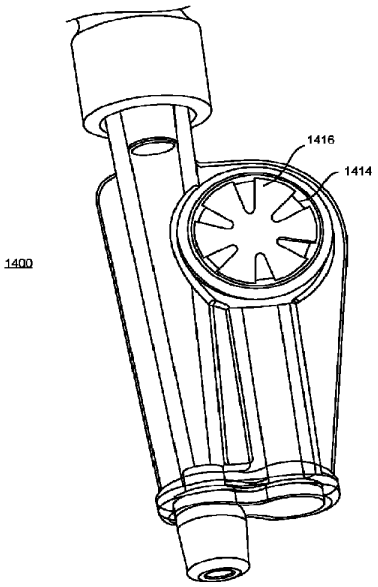


FIG. 14B

【図１４Ｃ】

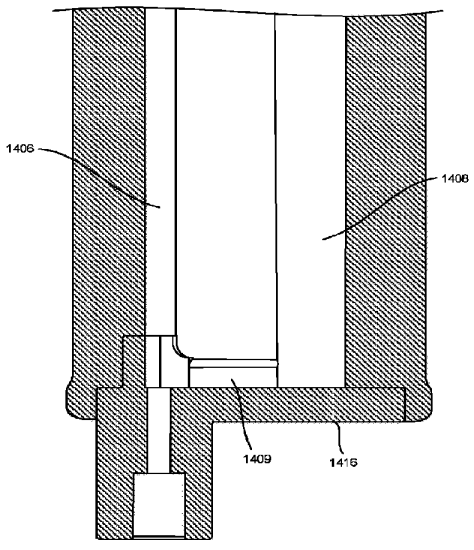


FIG. 14C

【図１４Ｄ】

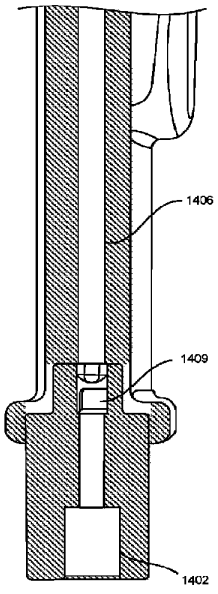


FIG. 14D

【図１４Ｅ】

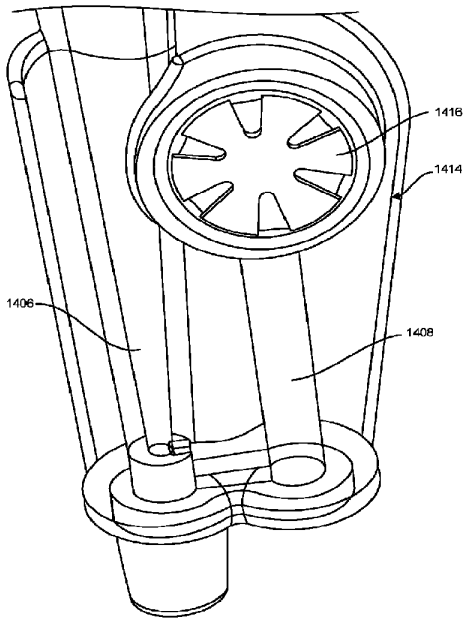


FIG. 14E

【図１５Ａ】

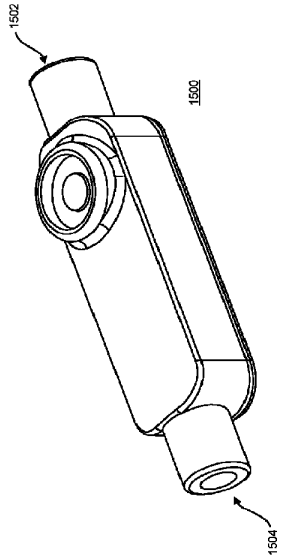


FIG. 15A

【図１５Ｂ】

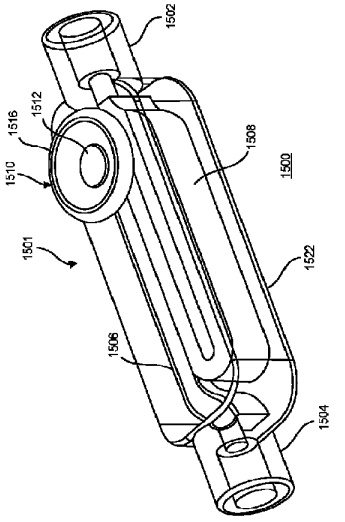


FIG. 15B

【図１５Ｃ】

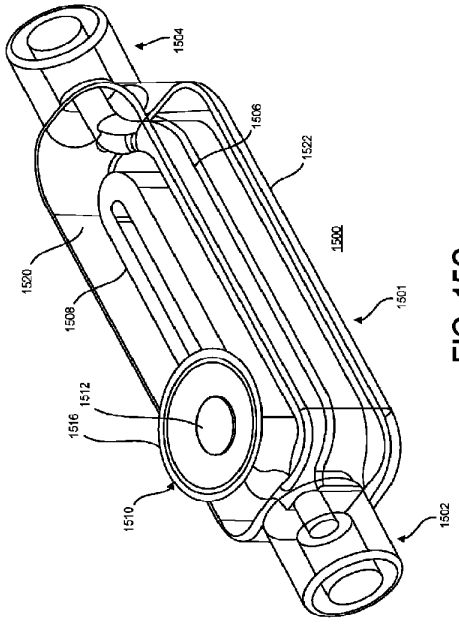


FIG. 15C

【図１５Ｄ】

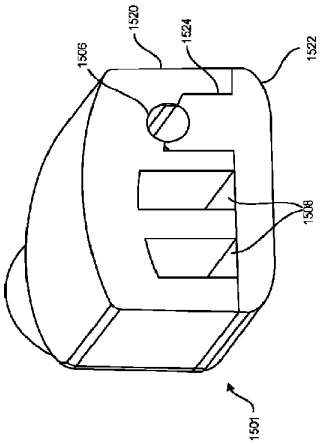


FIG. 15D

【図１５Ｅ】

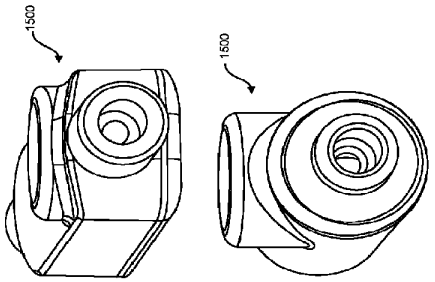


FIG. 15E

【図１５Ｆ】

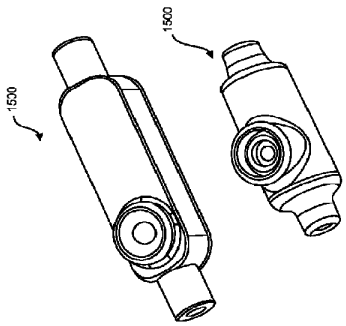


FIG. 15F

【図１５Ｇ】

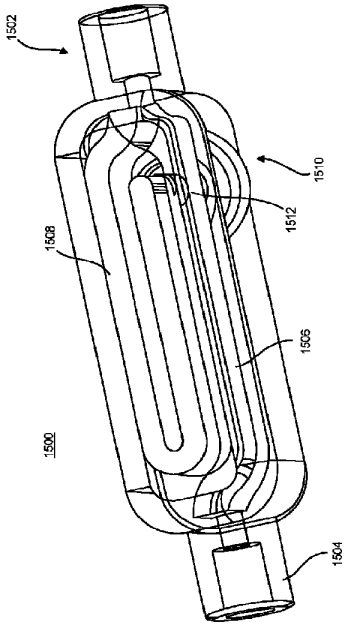


FIG. 15G

【図１６Ａ】

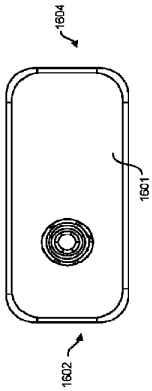


FIG. 16A

【図１６Ｂ】

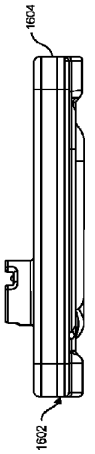


FIG. 16B

【図１６Ｃ】

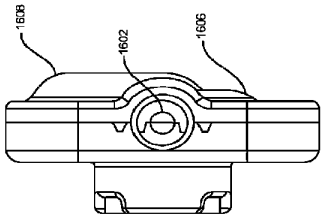


FIG. 16C

【図１６Ｄ】

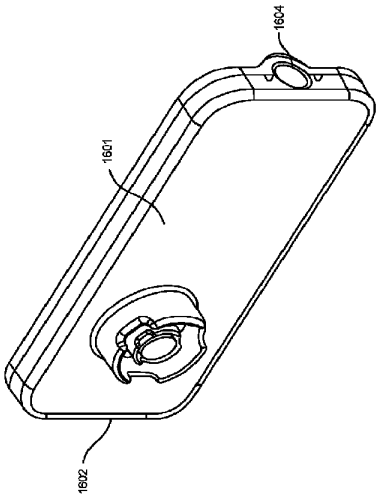


FIG. 16D

【図１７Ａ】

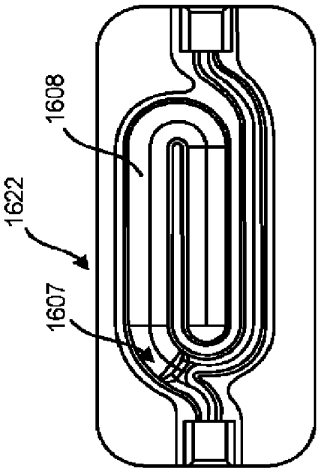


FIG. 17A

【図１７Ｂ】

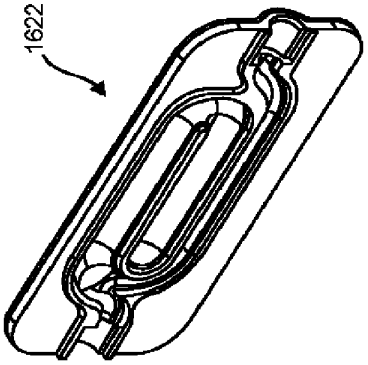


FIG. 17B

【図１７Ｃ】

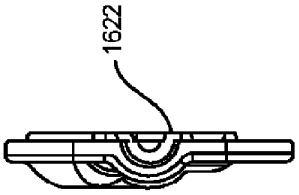


FIG. 17C

【図１７Ｄ】

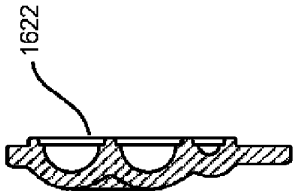


FIG. 17D

【図１７Ｅ】

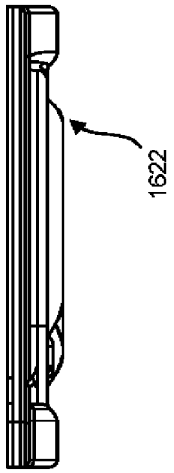


FIG. 17E

【図１８Ａ】

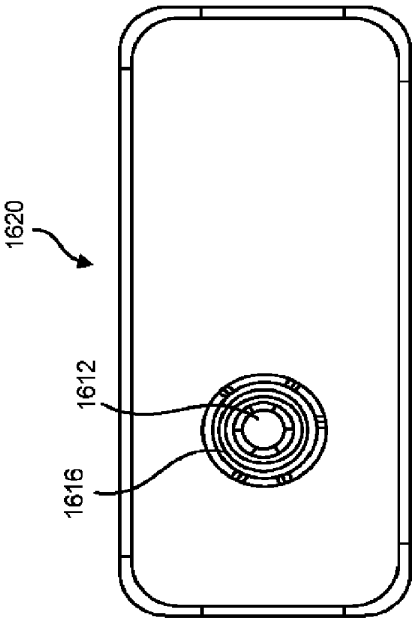


FIG. 18A

【図１８Ｂ】

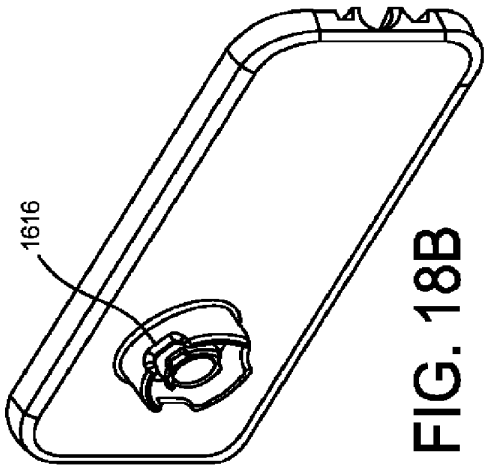


FIG. 18B

【図１８Ｃ】

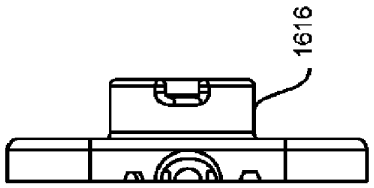


FIG. 18C

【図１８Ｄ】

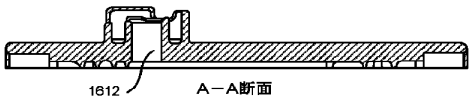


FIG. 18D

【図１８Ｅ】

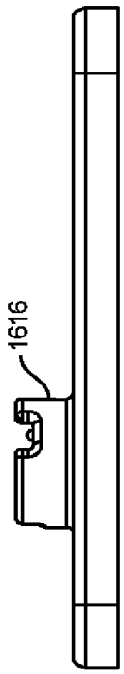


FIG. 18E

【図１８Ｆ】

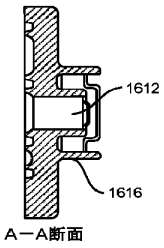


FIG. 18F

【図１９Ａ】

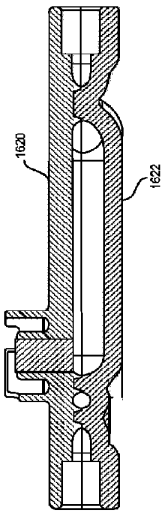


FIG. 19A

【図１９Ｂ】

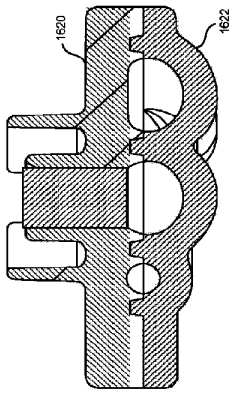


FIG. 19B

【図２０】

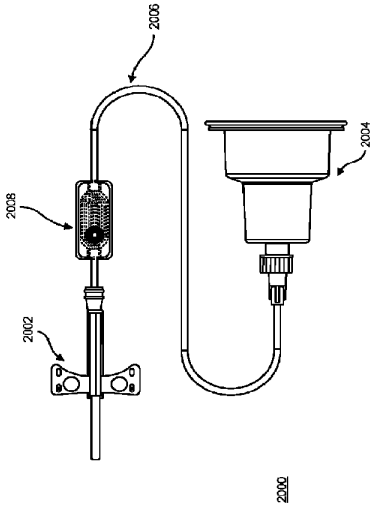


FIG. 20

【図２１】

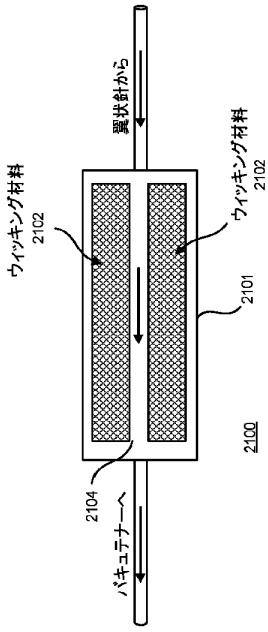


FIG. 21

【図２２Ａ】

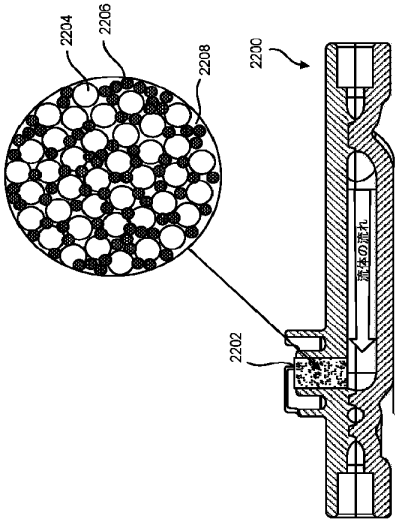


FIG. 22A

【図２２Ｂ】

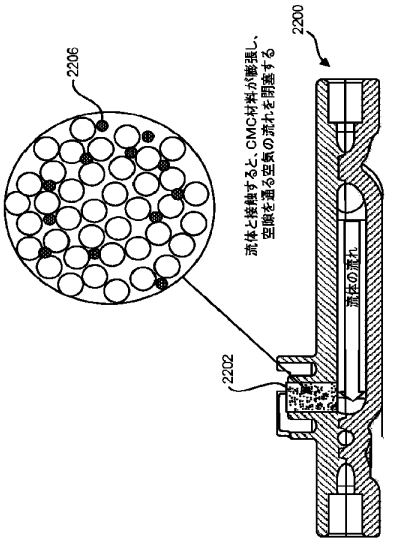


FIG. 22B

【図２３Ａ】

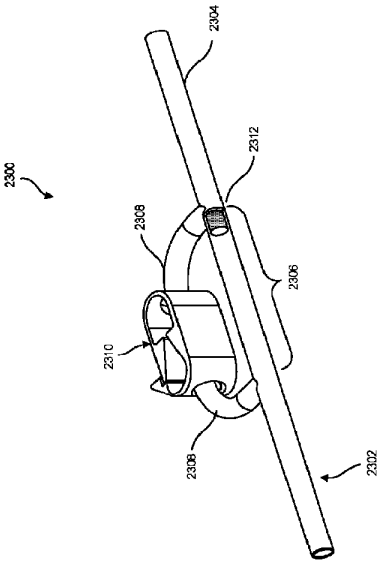


FIG. 23A

【図２３Ｂ】

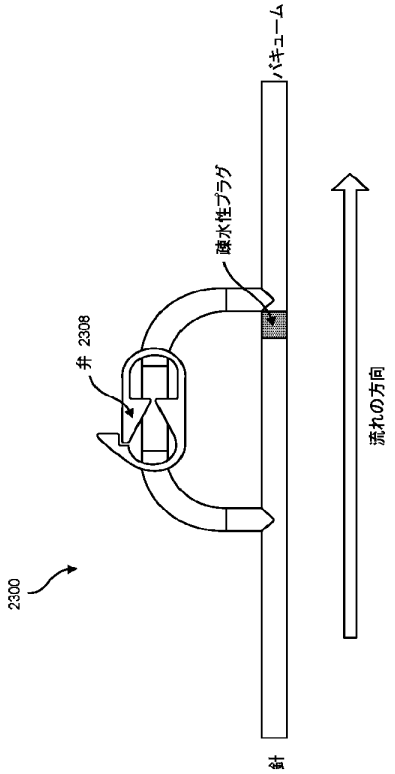


FIG. 23B

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(56)参考文献 特開昭５８－０２５１４６（ＪＰ，Ａ）
特開昭５８－０６７２３８（ＪＰ，Ａ）
特開２０１２－０１６４９６（ＪＰ，Ａ）
特開昭５７－０８９８６９（ＪＰ，Ａ）
特表平０９－５０４７２６（ＪＰ，Ａ）
特開平０２－２２４７４２（ＪＰ，Ａ）
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Differential Quantitative Blood Cultures in the Diagnosis of Catheter-Related Sepsis in Intensive Care Units

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The aim of this prospective study was to compare differential blood cultures and quantitative catheter tip cultures for the diagnosis of catheter-related sepsis. Over a period of 2 years, 283 central venous catheters were inserted in 190 adult patients. Catheters were removed when they were no longer needed or when infection was suspected. Immediately before removal of the central venous catheters, blood cultures were performed, with blood drawn simultaneously from the catheter and the peripheral vein. After removal, quantitative catheter culture was performed according to the Brun-Buisson modified Cleri technique. Fifty-five quantitative catheter cultures were positive. They were classified as contaminated (n = 18), colonized (n = 23), or infected (n = 14). Differential blood cultures correctly identified 13 infections. With a catheter/peripheral cfu ratio of 8, differential blood cultures had a sensitivity of 92.8% and a specificity of 98.8%. When the catheters were removed because of suspected infection, differential blood cultures had a sensitivity of 92.8% and a specificity of 100%. Differential blood culture, a technique that does not necessitate catheter removal, seems effective in the diagnosis of catheter-related sepsis in patients in the intensive care unit.

Infection is the main complication related to the use of central venous catheters (CVCs). Catheter-related infection (CRI) is a major cause of nosocomial infection and may be life-threatening [1]. The diagnosis of CRI remains difficult. Clinical signs lack sensitivity and specificity. It is widely accepted that when a patient in the intensive care unit (ICU) becomes febrile, infection of the CVC is suspected and it is removed [2]. However, 70%–85% of CVCs are removed unnecessarily [2–4]. Moreover, the insertion of a new CVC is not without complications, especially mechanical [5]. Therefore, a technique allowing the diagnosis of CRI without removal of the catheter would be of great interest.

Differential quantitative blood cultures (DBCs) of blood withdrawn from the CVC and from a peripheral vein have been evaluated in hematology and oncology patients and in patients receiving long-term parenteral nutrition [6–10]. The few studies comparing this technique to a "gold standard" have given conflicting results [11–14]. Moreover, few data are available concerning ICU patients. The aim of our study was to compare DBC with a reference technique for the diagnosis of CRI in patients treated in ICUs.

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Informed consent was obtained from all patients or their next of kin.
This study followed the guidelines of the Institutional Review Board.
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Patients and Methods

The study was approved by the hospital's Institutional Review Board. Informed consent was obtained from all patients or their next of kin. Patients hospitalized in a surgery-trauma ICU and in a medical ICU were included during the 25-month period of November 1992 through November 1994. Patients were eligible if a CVC (either single or multiple lumen) inserted while the patient was in the ICU was scheduled to be removed. Several CVCs inserted in the same patient could be included in the study. Many patients in the study units were not eligible because they entered the units with a CVC inserted elsewhere or were discharged with their CVC still in place. People who died in the units with their CVC in place were not included. Arterial and pulmonary catheters were excluded, but introducer sheaths were included. All inserted CVCs were polyurethane. The insertion site was the jugular, subclavian, or femoral vein. None of the CVCs were tunneled.

Physicians of both ICUs inserted the CVCs after surgical hand-washing and the donning of masks, sterile gowns, and gloves. The puncture site was prepared first with a solution of quaternary ammonium, then ether, and then iodine/alcohol. The surrounding areas were covered with sterile drapes. After insertion of the CVC, an occlusive gauze dressing was placed following application of povidone-iodine. The dressings were changed every 48 hours.

When it was decided to remove the CVC, the connection of the CVC and the venous line were externally disinfected with iodine/alcohol. Then the line was disconnected and a sterile syringe was inserted in order to withdraw 5 mL of blood. For multiple-lumen CVCs, blood was withdrawn from each port.

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Immediately after, 5 mL of blood was obtained from a peripheral vein by standard venipuncture and placed in a heparinized tube. Then each intravascular device was removed aseptically after sterilization of the skin-puncture site. The distal segment of the catheter tip (5 cm) was cut off with sterile scissors, dropped into a tube, and sent to the laboratory.

The catheter tip was cultured according to the technique described by Brun-Buisson et al. [15], adapted from Cleri et al. [16]. In brief, 1 mL of sterile water was added into the tube containing the catheter tip. The contents were mixed for 1 minute, and 0.1 mL was sampled and plated on the surface of 5% horse blood agar. The agar plates were incubated at 37°C for 5 days. If colonies were observed, the number was recorded. The culture was considered positive when bacterial growth was observed. Identification and antimicrobial susceptibility assessment were conducted according to standard laboratory methods.

Blood withdrawn from the CVC and the peripheral vein was treated with use of the pour-plate technique [6–12]: 1 mL of nondiluted blood and 1 mL of serial blood dilutions (10^{-1}, 10^{-2}, 10^{-3}) were added to 19 mL of melted brain-heart infusion agar cooled to 45°C and poured into petri dishes. All plates were incubated for 5 days, and cfu were counted. When no growth was observed, the count was taken as 1 for the calculation of catheter/peripheral ratio. The DBC was considered positive when the catheter/peripheral cfu ratio was greater than 1.

Catheter findings were divided into three categories [4–15]. Catheter contamination was defined as the presence of $<10^3$ cfu/mL by the quantitative catheter-tip technique, without any local or general sign of infection. Catheter colonization was defined as the presence of $>10^3$ cfu/mL by the quantitative technique, without any local sign of infection. In this category, general signs of infection might be present and related to a remote septic focus, and clinical sepsis did not resolve within 48 hours after catheter removal. CRI was defined as a positive tip culture with a bacterial count of $>10^3$ cfu/mL, in association with general signs of infection (which disappeared after catheter removal), without any focus of infection with the same microorganism. The CRI could be accompanied by bacteremia.

Statistical Analysis

Published studies were analyzed to estimate the sample size for catheters. Assuming a prevalence of CRI in ICU patients of 5%–10%, and using data from a preliminary study indicating sensitivity of 90% and specificity of 94%, we decided 250–300 catheters would be required to obtain a positive predictive value between 60% and 80% with a precision of 5% α level. Thus, 300 catheters were included.

Using the quantitative catheter-tip culture as a reference, the sensitivity, specificity, and positive and negative predictive values were calculated at different catheter/peripheral cfu ratios. Sensitivity was plotted against specificity with use of a receiver operating characteristic (ROC) curve [17]. Quantitative results were expressed as mean ± standard deviation. Categorical results were given with their 95% confidence interval.

Results

During the 2 years, 283 CVCs were inserted in 190 adult patients.

Quantitative cultures of the catheter tip. One hundred and fifteen patients were hospitalized in the surgical unit and 75 in the medical unit. They were comparable with respect to age (45.9 ± 19.2 vs. 56.6 ± 19.6 years), sex, simplified acute physiologic score (SAPS) (11 ± 5 vs. 14 ± 4) [18], length of ICU stay (24 ± 16 vs. 21 ± 22 days), and antibiotic treatment (112/115 vs. 73/75).

Of the 283 studied catheters, 55 (19%) were positive in quantitative catheter-tip cultures. Of these positive results, 18 were considered contaminations; 23, colonizations; and 14, infections (table 1). The organism distribution pattern was similar among contaminated, colonized, and infected catheters, with a large predominance of staphylococci (76% of all isolates).

Fourteen catheters from different patients were considered infected. These catheters were inserted in 14 patients (age, 56.9 ± 18.4 years; SAPS, 13 ± 5; ICU stay, 36 ± 18 days), of whom 12 were treated with antibiotics for a remote septic focus. Bacteremia was associated with nine of these catheters. None of the bacteria were susceptible to the antibiotics previously prescribed. For the patients with infected catheters, the quantitative cultures, indicative of infection, were positive within 18–36 hours.

Differential blood cultures. Among the 283 catheters, 19 (from 19 patients) were DBC-positive (table 2). Among the catheters, 8 were inserted in the jugular vein, 7 in the femoral vein, and 4 in the subclavian vein. Of the 14 CRIs according to the quantitative catheter-tip cultures, 13 were associated with a positive DBC.

ROC curve analysis was carried out by varying the catheter/peripheral cfu ratio (figure 1). The combined sensitivity and specificity were most satisfactory at a ratio of 8. With use of this threshold, the DBCs were positive for 16 catheters as well as for the 13 catheters previously considered infected. Sensitivity, specificity, and predictive values are reported in table 3.

Discussion

When CRI is suspected in ICU patients, the removal of the catheter is generally proposed. However, as many as 80% of the catheters removed will be sterile [4]. Furthermore, the insertion of a new catheter carries its own risk of complications, especially mechanical. In a study of 160 ICU patients, insertion of CVCs at new sites has been shown to lead to complications such as pneumothorax or arrhythmias in 9% of patients [5].

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Table 1. Characteristics of the catheters removed from ICU patients and analyzed in the study.

	Positive in catheter tip culture			Negative in culture (n = 228)	All catheters (n = 283)
	Contaminated (n = 18)	Colonized (n = 23)	Infected (n = 14)		
Insertion site					
Jugular	13	15	6	143	177
Subclavian	4	3	2	46	55
Femoral	1	5	6	39	51
Mean (±SD) duration of stay (d)	10 ± 5	10 ± 3	13 ± 5	10 ± 6	10 ± 5
Reason for catheter removal					
Infection suspected	7	11	14	86	118
No longer useful	11	12	0	142	165
Organism(s) identified					
Staphylococcus aureus	5	8	7		
Coagulase-negative staphylococci	8	10	4		
Other gram-positives	3	1	1		
Enteric gram-negatives	2	4	2		

Therefore, a technique allowing for the diagnosis of CRI without catheter removal would be useful in clinical practice. The ideal technique should have good specificity to prevent the removal of sterile catheters, but, more important, it should have good sensitivity. Indeed, this technique needs to be safe, presenting minimal risk of leaving an infected catheter in place. False-negative results should be minimized.

In 1979 Wing et al. first had the idea of performing cultures of blood withdrawn from the CVC and from a peripheral vein [6]. They compared both results and could establish the diagnosis of CRI in a patient. This observation led to the development of differential blood cultures for the diagnosis of CRI.

The aim of our study was to evaluate DBCs for ICU patients. As the ''gold standard'' for the microbiological diagnosis technique, we chose that proposed by Brun-Buisson et al. [15], adapted from Cleri et al. [16]. This technique allows for the detection of colonization of the external surface of the catheter tip and of its internal lumen. To identify false-negatives in the

Table 2. Data concerning the 19 positive differential blood cultures.

Catheter classification	Insertion site	Isolate	Differential blood cultures: cfu/mL in indicated specimen		
			CVC	P	CVC/P ratio
Sterile	Jugular	*Klebsiella oxytoca*	10^2	<1	10^2
Sterile	Subclavian	*Klebsiella oxytoca*	16	<1	16
Sterile	Femoral	*Enterobacter cloacae*	10^2	<1	10^2
Sterile	Subclavian	*Staphylococcus epidermidis*	2	<1	2
Colonized	Jugular	*Staphylococcus aureus*	2	<1	2
Colonized	Jugular	*Escherichia coli*	4.4×10^3	<1	4.4×10^3
Infected	Jugular	*Staphylococcus aureus*	10^4	20	5×10^2
Infected	Jugular	*Staphylococcus aureus*	5×10^3	10	5×10^2
Infected	Femoral	*Staphylococcus aureus*	10^4	3	3.3×10^3
Infected	Jugular	*Staphylococcus aureus*	4.6×10^3	<1	4.6×10^3
Infected	Subclavian	*Staphylococcus aureus*	7×10^2	90	8
Infected	Femoral	*Staphylococcus aureus*	3×10^5	2×10^3	1.5×10^2
Infected	Femoral	*Staphylococcus epidermidis*	8×10^2	<1	8×10^2
Infected	Femoral	*Staphylococcus epidermidis*	4×10^6	10^3	4×10^3
Infected	Femoral	*Staphylococcus epidermidis*	1.5×10^6	<1	1.5×10^6
Infected	Jugular	*Staphylococcus epidermidis*	5×10^2	<1	5×10^2
Infected	Subclavian	*Escherichia coli*	4×10^3	<1	4×10^3
Infected	Jugular	*Escherichia coli*	3.5×10^3	<1	3.5×10^3
Infected	Femoral	*Corynebacterium* species	6×10^4	<1	6×10^4

NOTE. CVC = central venous catheter; P = peripheral vein. When the number of cfu in the peripheral vein was <1, it was considered as 1 for the calculation of the CVC/P ratio.

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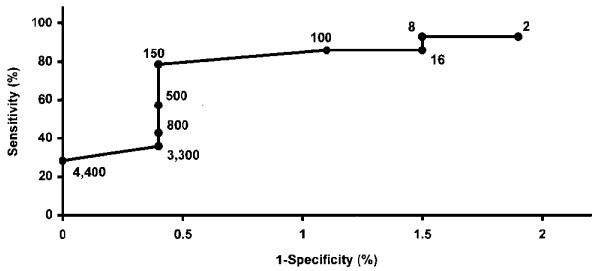


Figure 1. Receiver operating characteristic curve for ratio of bacterial counts in culture of the blood withdrawn from the catheter and culture of blood from a peripheral vein. The numbers on the curve are respective cutoffs in the differential blood cultures.

microbiological techniques, local and general signs of infection were noted at the time of the sepsis suspicion and after catheter removal. The reason for removal could be either that infection was suspected because of local signs (local inflammation or infection) or general signs (fever, chills, etc.), or else that the catheter was no longer needed.

We found a rate of 4.9% of infected catheters and 7.3% of patients with CRI. Bacteremia followed catheter infection in 3.1% of catheterized patients. *Staphylococcus aureus* was the predominant organism associated with bacteremia. This is in accordance with findings in other studies of ICU patients [11, 12, 15]. Although yeast may be responsible for CRI in the ICU, especially in immunocompromised patients, no fungal infection was identified.

DBCs have been evaluated in several studies, including a comparison with another microbiological technique. In a group of 24 patients receiving parenteral nutrition, Fan et al. found that DBC correctly identified seven of nine infected catheters [12]. They used an arbitrary threshold of seven for the catheter/peripheral cfu ratio. Sensitivity was 77.8% and specificity was 100%, with no false-positive results.

These interesting findings were brought into question by the results from Paya et al. [13]. In a study including 44 patients in a surgical ICU with suspected CRI, 15 catheters were considered infected according to a semiquantitative technique; DBC identified only 7 of these catheters. In that study, with regard to six catheters classified as DBC-false-negative, high organism concentrations (>100 cfu/mL) were observed in the blood withdrawn from the catheter and from the vein. In fact, a dilution of these samples might have yielded a positive DBC. In addition, the investigators did not include any clinical information in the definition of CRI. Thus, it was impossible to separate colonizations and infections of the catheters.

Finally, bacteria responsible for CRI were different from those found in other studies, including ours. *Pseudomonas aeruginosa* was found in more than half of the CRIs, and *S. aureus* accounted for only 6% of the isolated organisms. This difference may be explained by variations in the pathogenesis of the infections and may reflect differences in the efficiency of DBC.

In another study of patients hospitalized in internal medicine and surgical wards and the ICU, 107 catheters were evaluated, and DBCs identified 16 of 17 CRIs. DBC was found to be reliable, with a sensitivity of 94% and a specificity of 100% [11]. Recently, in patients with cancer (n = 31) and in the ICU (n = 27), DBC identified correctly 30 of 36 CRIs; the 6 remaining cases were false-negatives because removal of these catheters led to resolution of clinical signs of infection [14]. It is interesting that 16 patients with CRI had a negative tip culture, and CRIs were found to be related to hub infection. If this finding is confirmed, the efficacy of DBC as compared with that of tip cultures would be reinforced.

In all of these studies the catheter/peripheral cfu ratio was chosen arbitrarily. The range of this ratio was wide, between 2 and 30. In our study, the ROC curve technique was used to determine the ratio of the DBC that gives the best performance in diagnosis of CRI. With a threshold of 8, sensitivity was maximal, decreasing the number of false-negatives with the technique. This value is close to those chosen arbitrarily in other studies [11–14]. With this cutoff, sensitivity and specificity of DBC were very high. The few false-positive results led to the removal of sterile catheters, but these cases are few in contrast to the large number of catheters that can be safely left in place.

The DBC technique may have some potential drawbacks. First, the one false-negative result of the study raises an important issue because an infected catheter may remain inserted. All the studies of DBC have found false-negative results, but sensitivity remained up to 80%. These results may be explained by strictly external contamination of the catheter, missed by the DBC. However, to our knowledge, a method of diagnosis of CRI with 100% sensitivity and 100% specificity does not

Table 3. Sensitivity, specificity, and predictive values of differential blood cultures for all catheters and for catheters removed for a suspected infection. (Percentages and 95% confidence limits are given.)

Catheters removed	Sensitivity	Specificity	PPV	NPV	Accuracy
All (n = 283)	92.8 ± 3.0	98.8 ± 1.2	81.2 ± 4.5	99.6 ± 0.7	98.5 ± 1.4
For suspected infection (n = 118)	92.8 ± 3.0	100	100	99.0 ± 0.9	99.1 ± 1.7

NOTE. NPV = negative predictive value; PPV = positive predictive value.

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exist. In all circumstances, the results of the technique must be interpreted cautiously and clinical evaluation must remain the first criterion of CRI diagnosis, leading to the removal of the catheter if there is any doubt.

The second problem is related to the time necessary to obtain results from quantitative cultures, generally between 24 and 48 hours. In some circumstances, this delay will be too long for a patient with signs of severe infection. In this case, the catheter has to be removed. In our study, the catheters were cultured over 5 days to be certain not to miss late bacterial growth. However, no culture was positive after 48 hours.

Finally, the technique of DBC has a cost. However, this is balanced by the savings due to the limitation in wasting sterile catheters. In our study, 14 of 118 patients with a suspected CRI had a positive DBC, so 104 catheters were removed unnecessarily. Their replacement could have been avoided. A cost-benefit evaluation of the DBC technique must be done.

In conclusion, for ICU patients, DBC may be considered a useful tool for diagnosis of CRI without removal of the catheter. The possibility of false-negative results, although uncommon, must be kept in mind, and the persistence of sepsis syndrome without any evidence of other sources of infection must lead to the removal of the catheter. The technique cannot be used for all ICU patients, especially because of the time lag in obtaining culture results. However, this technique seems to decrease the waste of sterile catheters removed when ICU patients become febrile.

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Bacterial Contamination of Platelets for Transfusion: Recent Advances and Issues

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- 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.[2,3] 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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wrap up close —

(57) [Abstract] Since this gazette is application data before electronic filing, abstract data is n ot recorded.

The scope of the claims open —

Claims:
(1) In a coupling used by medical personnel in drawing and storing blood from a patient to ins ert the needle of the needle assembly into the patient to draw the blood sample, the coupling comprises first
and an elongated hollow shaft having a second end; and a
first portion of the shaft fixedly connecting the needle assembly to the shaft so that blood dra wn by the needle can be delivered to the shaft. and an adapter sleeve attached to a second e nd of said shaft for
connecting said shaft to a blood storage means,
for communicating blood received by said shaft; an opening connected to said shaft between an adapter sleeve and said connecting member and communicating with said connecting mem ber.
(2) The coupling of claim 1, further comprising means for blocking blood flow and exhausting air trapped within said shaft.
(3) intermediate the opening and the adapter sleeve, wherein the means for evacuating air re stricts blood flow from the shaft to the adapter sleeve while permitting air flow from the shaft to the adapter sleeve; 3. A coupling according to claim 2, comprising flow control means locat ed within said shaft of.
(4) The coupling of Claim 3, wherein said flow control means comprises a microporous hydrop hobic plug.
(5) The coupling of claim (4) further comprising needle guide means for guiding a needle coup

led to blood reservoir means through said plug and for coaxially fitting said needle with said s haft.

(6) The cup according to (2), further comprising blood storage means for temporarily storing a portion of blood drawn from a patient, said blood storage means being sealably connectable to said opening. ring.

(7) The coupling of claim (6), wherein said blood storage means comprises a syringe.

(8) Further comprising valve means fixedly positioned intermediate said opening and said shaf t for enabling selective communication between said shaft and said opening. coupling.

(9) The coupling of claim 2, further comprising means for sealing said opening.

(10) In a blood collection device used by medical personnel to withdraw and store a blood sa mple from a patient, needle means adapted to be inserted into the patient to withdraw the blo od

sample

; coupling means for connecting the means to the blood storage means,

said coupling means having first and second openings;and adapted to direct blood from said n eedle means to said first and second openings.

(11) The coupling of claim 10, further comprising means for blocking blood flow to exhaust air trapped within said coupling means.

(12) the means for evacuating air restricts blood flow from the needle means to the first openi ng while permitting air flow from the needle means to the first opening; 12. The blood collecti on device of claim 11, comprising flow control means positioned within said coupling means b etween said first and second openings.

(13) The blood collection device of Claim 12, wherein said flow control means comprises a mic roporous hydrophobic plug.

(14) The blood collection device of (13) further comprising needle guide means for guiding a n eedle coupled to blood reservoir means through said plug and coaxial with said coupling mean s.

(15) The method according to (14), further comprising blood storage means for temporarily st oring a portion of the blood drawn from the patient, said blood storage means being sealingly connectable to said second opening. A blood collection device as described.

(16) The blood collection device of (12), wherein said blood storage means comprises a syring e.

(17) The blood collection device of (12) further comprising means for sealing said second ope ning.

(18) further comprising valve means disposed intermediate said needle means and said secon d opening for enabling selective communication between said needle means and said second opening. The blood sampling device according to (12).

(19) said needle means is an elongate needle for insertion into a patient and leading from sai d needle to said coupling means;

13. The blood collection device of claim 12, comprising: a tube, said tube being generally tran sparent so that medical personnel can see blood being directed therethrough.

(20) A blood collection device for use by medical personnel in drawing and collecting blood sa mples from a patient, comprising needle means for drawing blood from a patient and coupling means for selectively connecting blood reservoir means to

said

needle means. wherein

said coupling means is secured to said needle means, said coupling means being positioned b etween said first opening and said needle means and a first opening for receiving blood storag e means; a hollow shaft, said coupling means further comprising a second opening for receivi ng blood storage means, said second opening being connected to said first opening and said n eedle; Mounted on the shaft between means,

the blood sampling device restricts the flow of blood from the shaft to the first opening, but re stricts the flow of blood from the shaft to the first opening.The blood collection device further comprising a flow control device located within the shaft intermediate the first and second ope nings to allow gas flow to the first opening.

(21) further comprising blood storage means for temporarily storing a portion of blood, said bl ood storage means being sealed to said second opening for receiving blood delivered from sai d needle means to said shaft; 21. A blood collection device according to claim 20, adapted for coupling.

(22) said blood storage means comprises a syringe having a blood storage chamber and a plu nger located within said blood storage chamber, said syringe sealing said blood storage chamb er to said second opening; 22. A blood collection device according to claim 21, further compri sing means for connecting with.

(23) The blood collection device of Claim 20, wherein said flow control means comprises a mic roporous hydrophobic plug.

(24) further comprising blood storage means for storing a blood sample, said blood storage m eans being sealingly attachable to said first opening for insertion through said plug, thereby 2 4. A blood collection device according to claim 23, comprising a needle adapted to lead blood f rom the shaft to said blood storage means.

(25) guiding means located within said shaft between said plug and said first opening for guidi ng said needle of said blood storage means through said plug and making said needle coaxial with said shaft; 25. The blood collection device of claim 24, further comprising:

(26) within said shaft between said flow control means and said first opening for guiding a ne edle coupled to said blood storage means through said flow control means and coaxial with sai d shaft; 21. A blood collection device according to claim 20, further comprising guide means l ocated at the .

(27) The blood collection device of Claim 20, further comprising valve means for selectively all owing communication between said shaft and said second opening.

(28) said needle means comprises a needle for insertion into a patient to withdraw a blood sa mple and an elongated tube for guiding blood withdrawn from a patient to said coupling mean s, said tube being flexible

; 21. A blood collection device according to claim 20, and wherein the blood being conducted by said tube is generally transparent so as to be visible to medical personnel.

(29) further comprising a syringe having a blood storage chamber and a plunger positioned wi thin the blood storage chamber, the syringe having means for sealingly connecting the blood s torage chamber to the second opening; 29. A blood collection device according to claim 28, fu rther comprising.

(30) The blood collection device of (11) further comprising cap means for sealing said second opening.

(31) in drawing and collecting a blood sample from a patientA blood collection device for use by medical personnel comprising a

first elongated needle member having an insertion end and an attachment end, said insertion end adapted for insertion into a patient, said first needle member comprising: has a coaxial p assageway for carrying blood drawn from a patient from the insertion end to the attachment e nd and includes a

needle receiving end, a mating end, and from the needle receiving end to the mating end. an d said mounting of said first needle member

such that blood drawn from a patient is conveyed by said first needle member to said first fe male connector. means for fixedly and sealingly connecting an end to a receiving end of said fi rst female connector; a

mating end; a mounting end; and a coaxial extending from said mating end to said mounting end. further comprising a first male connector having a passageway, wherein the mating end of the first male connector is adapted to receive blood conveyed to the first female connector by the first male connector;

first and second ends and a passage extending from the first end to the second end sealingly mated to the mating end of the first female connector; and wherein the first end of the tube i s connected to the attachment end of the first male connector such that blood received by the first male connector is carried by the tube. sealingly attached to the portion, the tube being fl exible and generally transparent so that blood received by the tube is visible to medical perso nnel;

Further comprising a coupling having an elongated hollow shaft and a connecting member att ached to a first end of said shaft, said coupling securing a second end of said tube to said cou pling. to sealably connect to a second end of the shaft, thereby conveying blood received by t he tube to the coupling, the coupling being attached to a second end of the shaft connecting t he shaft to blood storage means. and the coupling is fixedly attached to the shaft between the adapter sleeve and the connecting member such that blood received by the coupling flows int o and out of the second female connector. a plug communicatively further comprising a secon

d female connector in communication with said connecting member and positioned within said shaft of said coupling between said second female connector and said adapter sleeve; wherein said plug is adapted to allow gas to escape from said shaft to effectively block blood flow from said shaft to said adapter sleeve.

(32) a second needle member having an insertion end, a connecting end, a coaxial passageway extending from said insertion end to said connecting end, and a vacutainer means for storing blood drawn from a patient

; The vacutainer means is fixedly attached to the second needle member, the adapter sleeve is positioned such that the vacutainer means is press fit into the adapter sleeve, and the second 32. A blood collection device according to claim 31, wherein a needle member is configured to be inserted through said plug, thereby conveying blood received by said shaft of said coupling to said vacutainer means.

(33) located within said coupling between said plug and said adapter sleeve for guiding said second needle member to insert said second needle member into said plug coaxial with said coupling; 33. A blood collection device according to claim 32, further comprising a needle guide means for receiving the blood.

(34) needle guide means located within said coupling between said plug and said adapter sleeve for guiding a needle coupled to blood storage means for coaxial insertion of said needle into said coupling; 32. The blood collection device of claim 31, further comprising:

(35) further comprising cap means adapted to engage said second female connector and thereby seal said second female connector to prevent blood from flowing out of said second female connector; A blood sampling device according to claim (31).

(36) Further comprising a syringe for temporarily storing blood, said syringe having a blood storage chamber and a plunger located within said blood storage chamber, said syringe being in communication with said blood storage means. (31) adapted to mate with said second female connector such that blood received by said coupling is stored within said syringe.

(37) located within said coupling between said plug and said adapter sleeve for guiding said second needle member to insert said second needle member into said plug coaxial with said coupling; 37. A blood collection device according to claim 36, further comprising a needle guide means for receiving the blood.

(38) a second needle member having an insertion end, a connecting end, a coaxial passageway extending from said insertion end to said connecting end, and a vacutainer means for storing blood drawn from a patient

; The vacutainer means is fixedly attached to the second needle member, the adapter sleeve is positioned such that the vacutainer means is press fit into the adapter sleeve, and the second A needle member is configured to be inserted through said plug, thereby carrying blood received by said shaft of said coupling to said vacutainer means.38. The blood collection device of claim 37.

(39) The blood collection of claim (37) further comprising first, second and third cap means re

spectively sealing said first needle means, said second female connector and said adapter slee ve. Device.

(40) The blood collection device of claim (31) further comprising valve means coupled to said second female connector for selectively communicating between said second female connector and said shaft.

(41) needle means for withdrawing blood from a patient

and

temporarily storing a first blood portion withdrawn from the patient in a blood collection devic e used by medical personnel to withdraw and store a blood sample from a patient; syringe me ans and

coupling means sealingly connecting said needle means to said syringe means, said coupling means including flow control means for venting air trapped within said needle means and said coupling means. said coupling means further comprising adapter means adapted to receive bl ood storage means and direct blood to said coupling means for storage; A blood collection dev ice wherein the means are further configured to return said first blood portion to the patient.

(42) said coupling means comprises a coupling having an elongated hollow shaft, said couplin g means attached to a first end of said shaft fixedly connecting said needle means to said cou pling; further comprising a connecting member, said adapter means being attached to a secon d end of said shaft, said coupling receiving said syringe means, said shaft between said adapt er means and said connecting member; 42. A blood collection device according to claim 41, fu rther comprising a connecting member fixedly attached to.

(43) The blood collection device of Claim 42, wherein said flow control means comprises a plu g positioned within said shaft of said coupling between said connecting member and said adap ter means.

(44) The blood collection device of Claim 43, wherein said plug comprises a microporous hydr ophobic plug.

(45) said needle means comprises a needle for insertion into a patient to withdraw a blood sa mple and an elongated tube for conducting blood withdrawn from the patient to said coupling, said tube being flexible; 44. A blood collection device according to claim 43, and wherein bloo d being conducted by said tube is generally transparent so as to be visible to medical personn el.

(46) drawing a first blood portion from the patient to fill the blood collection device while evac uating the air trapped in the blood collection device so that the anaerobic sample is not conta minated with air trapped in the blood collection means; An anaerobic sample is taken from th e patient after generally evacuating the trapped air from the blood collection device.A method of drawing

an anaerobic blood sample from a patient comprising the step of drawing a sample of blood fr om a patient.

(47) temporarily storing the first blood portion after drawing the first blood portion and

returning the first blood portion to the patient after drawing the anaerobic blood sample
; The method of claim (46), further comprising:
(48) withdrawing the first blood portion
further comprises coupling a coupling to a syringe, the coupling sealably coupled to a needle assembly; inserting
the
needle assembly into a patient and coupling the inserted needle assembly and the coupling so that blood is directed through the needle assembly and into the coupling with the syringe atta ched
; evacuating trapped air,
connecting a vacutainer needle of a vacutainer to said vented coupling, said vacutainer needle being in communication with said inserted needle assembly, and a cup with said vacutainer at tached
.
48. The method of claim (47), comprising withdrawing said first blood portion from a ring into said syringe .
(49) wherein withdrawing the anaerobic blood sample comprises establishing blood flow betw een the needle assembly and the vacutainer after the first blood portion has been withdrawn; The method described in .
(50) The method of claim (48), wherein withdrawing the first blood portion into the syringe co mprises allowing blood to flow freely under the pressure of the patient's heart.

detailed description open —

Description:
INDUSTRIAL APPLICABILITY
The present invention is directed to apparatus for taking a blood sample from a patient, and i n particular to apparatus for obtaining a blood sample from a patient in which the partial pres sure of gas within the sample is such that the blood pressure in the patient's body is An impro ved blood collection device is directed to receiving a blood sample so as to approximately equ al the gas partial pressure therein.
(PRIOR ART)
In the medical field, it is necessary to determine the in vivo gaseous equilibrium in the blood of a patient.
A medical worker will typically be concerned with the partial pressures of oxygen and carbon d ioxide. They may also be concerned with ionic species whose activity is related to the gas bala

nce in the blood, such as hydrogen ions and calcium ions.

In order for a blood sample to be valid for gas-in-blood analysis, the sample must be under a naerobic conditions, i.e., to prevent fluctuations in the partial pressure of the gas to be tested (when the blood is outside the patient's body). Must be collected to avoid exposure to gas.The major commercially available blood collection devices that must be present are largely unsatis factory in ensuring the integrity of anaerobic blood collection. An example of a conventional d evice uses a syringe and a vented plunger, where the syringe is removed from the patient unti l the correct blood volume is obtained from the patient by pulling on the vented plunger from no void in the barrel. Slowly withdraw the blood into the barrel of the However, these devices allow some exposure of the blood sample to the atmosphere. Some amount of ambient air will be contained within the barrel before the plunger moves. Thus, the initial portion of blood is e xposed to these gases, thereby changing the partial pressure of the gases contained in this ini tial sample. No means are provided for discarding the first portion of the drawn blood, so the entire sample would be contaminated.

Further, no means are provided to protect the medical personnel of the device against acciden tal bursting or exposure to contaminated blood during the course of the procedure when using the aforementioned device.

Other devices, such as the Becton and Dickenson Vacutainer and vacutainer attachments, hav e shown improved properties to protect medical personnel from exposure to drawn blood. Ho wever, these devices also. It allows some exposure of the first part of the blood sample to the atmosphere.

In addition to the shortcomings of the prior art described above, blood collection devices that provide means for flushing, i.e., injecting, for example, nutrients, medications, etc., into the b lood stream while permitting the collection of an anaerobic blood sample are currently lackin g. not known where.

Accordingly, it is desirable to provide a device for drawing an anaerobic blood sample from a p atient, and it is further desirable to provide a device for drawing a blood sample that can also inject a liquid into the patient's blood stream, i.e., a puncture. It is further desirable to provid e such a device that allows repeated blood sampling without the need for additional needle pl acement, and during scheduled interval sampling, i.e., between other subsequent blood sampl ings. It would be desirable to provide a device for drawing blood samples that can be left in th e patient.

OBJECTS OF THE INVENTION

It is therefore an object of the present invention to provide a blood collection device for drawi ng an anaerobic blood sample from a patient.

It is also an object of the present invention to provide a blood collection device that can withd raw an initial contaminated blood sample portion and maintain complete anaerobicity in the re maining sample.

It is a further object of the present invention to provide a blood collection device that can inje

ct an external liquid into the patient's blood stream.

It is a further object of the present invention to provide a blood sampling device that allows re peated blood sampling without the need for additional puncture or needle placement.

Yet another object of the present invention is to provide a blood collection device that can be l eft on the patient between scheduled intervals of collection, ie, other subsequent blood collect ions.

These and other objects of the present invention are met by providing a coupling for use by m edical personnel when drawing blood from a patient and storing it, which coupling draws the b lood sample. The coupling is particularly adapted for use with a needle assembly for injecting a needle into a patient. A coupling fixedly

connects the elongated hollow shaft and the needle assembly to the shaft for withdrawal by th e needle. a connecting member attached to the first end of the shaft that delivers blood to the shaft, and a coupling attached to the second end of the shaft that connects the shaft to variou s blood storage means. The adapter sleeve further comprises an opening coupled to the shaft intermediate the adapter sleeve and the connecting member, the opening being in communica tion with the opening such that blood received in the shaft communicates with the opening. In another embodiment

of the present invention, a device is provided for blocking blood flow and venting air trapped i n the shaft, particularly flow control means, such as microporous A hydrophobic plug is locate d in the shaft intermediate the opening and the adapter sleeve to restrict blood flow from the shaft to the adapter sleeve while allowing air flow from the shaft to the adapter sleeve. 6 In a nother embodiment of the invention, a valve is provided intermediate the shaft and the openi ng to allow selective communication between the shaft and the opening.

Other embodiments of the invention are particularly pointed out and distinctly claimed in the c laims. The invention, however, as to organization and method of implementation, will best be understood from the following detailed description when read with the accompanying drawing s in which: FIG.

DETAILED DESCRIPTION OF THE INVENTION

A cross-sectional view showing the improved blood collection device of the present invention i s provided in FIG. The blood sampling device comprises an elongated needle 100 having an in sertion end 102 adapted for insertion into a patient's blood stream (artery or vein). Needle 10 0 further has an attachment end 104 attached to first connecting member 106 via cylindrical seal 108 . As is well known in the art, meter 100- has a coaxial passageway extending from in sertion end 102 to attachment end 104 that conducts blood withdrawn from the patient to firs t connecting member 106. As shown in FIG.

Cylindrical seal 10B has a central opening 110 in which mounting end 104 of needle 100 is fix edly mounted. Additionally, the cylindrical seal 108 isIt is fixedly attached to needle receiving end 112 of member 106 . The second connecting member 114 has a mating end 116 adapted to mate with the mating end 118 of the first connecting member 106 so that it is received by

the first connecting member. rice field. Blood from leaflet 100 is directed to second connecting member 114 via mating joints 116,118.

First end 120 of tube 122 is sealingly attached to attachment end 124 of second connecting m ember 114 . A tube 122 is provided for carrying blood withdrawn from the patient through tub e 100 to coupling 126 . Tubing 122 allows the needle to be easily inserted into the patient's bl oodstream and, after insertion, the coupling 126 can be disengaged by medical personnel wit hout undue movement of the total 100 and causing discomfort to the patient. Preferably, the t ube 122 is flexible so as to be operable, and preferably transparent so that the medical perso nnel can visually observe the blood drawn from the patient.

The combination of needle 100, first connecting member 106, second connecting member 11 4, and tube 122 constitutes a needle assembly, readily available from needles, connecting me mbers, and tubes well known in the art. Can be assembled. - By way of example, the first and second connecting members 106 and 114 consist of male and female Luer connectors, as is w ell known in the art.

A coupling 126 is provided for connecting the second end 128 of the tube with each of the firs t and second blood storage means 130 and 132 . To this end, coupling 126 has a connecting member 134 with a central opening that receives second end 128 of tube 122 . Connecting m ember 134 is integrally connected to elongated hollow shaft 136 such that blood delivered to coupling 126 by tube 122 is received within shaft 136 . Adapter sleeve 138 is integrally conne cted to shaft 136 at the end opposite to the end to which connecting member 134 is connecte d. Adapter sleeve 138 is in communication with shaft 136 and is provided for receiving second blood storage means 132, as will be described more fully below.

Coupling 126 further includes an opening 140 integrally connected to shaft 136 intermediate a dapter sleeve 138 and connecting member 134 .

An opening 140 is provided for connecting first blood storage means 130 to shaft 136 of coupl ing 126 . A passageway 162 is provided in shaft 136 proximate opening 140 such that openin g 140 communicates with connecting member 134 . Accordingly, blood delivered to coupling 1 26 by tube 122 is conveyed via adapter sleeve 138 and opening 140 to first and second blood storage means 130 and 132 for storage.

Coupling 126 also has a plug 142 disposed within the shaft between adapter sleeve 138 and o pening 140 . Plug 142 is a fluid flow, e.g., porous plug, venting air trapped within connecting members 106, 114, tube 122, shaft 136, and opening 140 during the early stages of a blood c ollection procedure. It consists of control means. The plug 142 is thus adapted to restrict bloo d flow from the shaft 136 to the adapter sleeve 138 and allow air flow from the shaft to the a dapter sleeve. 142 consists of a microporous, hydrophobic plug, well known in the art. Howev er, those skilled in the art will appreciate that other liquid flow control means may be used in place of the preferred microporous hydrophobic plug 142 .

As previously mentioned, opening 140 is adapted to receive first blood storage means 130 .

A cap 144 is engageable with opening 140 to seal the opening from inadvertent blood loss, w

hich often occurs when first blood storage means 130 is not connected to coupling 126 . Howe ver, in normal operation, cap 144 is removed from opening 140 and connects first blood stora ge means 130 thereto.

In a preferred embodiment of the present invention, the first blood storage means 130 compri ses a syringe of the type having a blood storage chamber 146 and a plunger 148 positioned w ithin the blood storage chamber 146 .

As is well known, in operation, plunger 148 is slowly withdrawn from blood storage chamber 1 46 so that blood enters the chamber. Blood storage means 130 further comprises connection means 150 for connecting blood storage means 130 to opening 140 . In a preferred embodim ent of the invention, opening 140 and connecting member 150 each comprise male and femal e luer connectors. However, it will be apparent to those skilled in the art that other connector members may be provided to sealingly connect first blood storage means 130 to coupling 126 .

In operation, the cap 144 is removed from the opening 140 and the blood reservoir means 13 0 is connected thereto.The blood is then withdrawn, or preferably allowed to flow freely under the pressure of the patient's heart. Meter 100 is inserted into the patient's blood stream so as to be able and delivered to shaft 136 via connecting members 106 , 114 and tubing 122 . Air trapped within connecting members 106, 114, tube 122, shaft 136 and opening 140 is displac ed by the patient's blood entering the flow passageway and vented through porous plug 142, as previously described. .

A first portion of the blood that is withdrawn or flows under cardiac pressure from the patient is exposed to trapped air before being ventilated.As it is exposed, it is generally contaminated and therefore not suitable for anaerobic blood sampling.

This first blood portion is thus withdrawn from the coupling 126 into the blood storage means 130 for temporary storage, while the anaerobic blood sample passes through the second bloo d storage means 132. to be received. After the anaerobic blood sample is received, the blood temporarily stored in blood storage means 130 is discarded or returned to the patient via tube 122 and meter 100 .

A second blood storage means 132 is connected to the coupling 126 via an adapter sleeve 13 8 for withdrawing an anaerobic blood sample. The second blood storage means 132 may com prise a Becton Dickenson vacutainer well known in the art. Blood storage means 132 has a blo od storage chamber 152 for receiving an anaerobic blood sample drawn from the patient. are doing. Needle 154 is sealingly connected to needle hub 156 and their assembly is connected t o blood storage chamber 152 via a compatible coupling 158 (commonly referred to as a vacut ainer adapter). Hermetically connected. Needle 154 has a seal to prevent communication with blood storage chamber 152, as is well known in the art. Additionally, as is well known in the a rt, blood storage chamber 152 is evacuated so as not to contain air that contaminates blood d rawn from the patient.

A compatible coupling 158 provides means for removing the seal from needle 154 in order to

place needle 154 in communication with blood storage chamber 152 .

Adapter sleeve 138 has an internal adapter chamber 160 sized to snugly receive needle hub 1 56 . The length of adapter sleeve 138 and the position of plug 142 within shaft 136 is such th at blood reservoir 132 is fully inserted into adapter sleeve 138 and needle 154 passes through passageway 162 and second end 128 of tube 122 through plug 142 . is selected to lie betwee n A needle guide 164 is positioned within coupling 126 between adapter sleeve 138 and plug 142 to allow a needle to be inserted into coupling 126 coaxially with shaft 136 . Needle guide 164 receives needle 154 during insertion of blood reservoir 132 into coupling 126 and guides t he needle prior to needle insertion into plug 142 so that the needle is coaxial with shaft 136 . provided for positioning.

In operation, blood reservoir means 130 is connected to coupling 126 via opening 140 as prev iously described for collecting an anaerobic blood sample. The meter 100 is inserted into the p atient's bloodstream and air trapped inside the meter 100, connectors 106, 114, tubing 122 a nd coupling 126 is evacuated through plug 142 as previously described.Total 154 of blood stor age means 132 is then inserted through plug 142 and into coupling 126 so that it lies beyond passageway 162 near tube 122 . The contaminated air of the blood sample is removed so that any fraction of contaminated air that accumulates within needle 154 is exhausted through plu g 142, i.e., removed from coupling 126 prior to receiving the anaerobic blood sample. It is des irable to insert gauge 154 into coupling 126 prior to storing the portion in storage means 130 .

After the soot 154 is properly inserted into the coupling 126, the first portion of contaminated blood is drawn from the coupling 126 into the blood storage means 130 for temporary storag e. At this time, the seal on needle 154 is removed by compatible coupling 158, as is well kno wn in the art, so that the anaerobic blood sample is directed to blood reservoir 152. FIG.

To ensure that substantially all of the blood directed to blood storage chamber 152 is blood re ceived from tube 122 and not blood received from blood storage chamber 146 of blood storag e means 130, total 154 is connected to passageway 162. and tube 122 and near second end 128 of tube 122 in coupling 126 in shaft 136 .

In an alternative embodiment of the present invention, when receiving an anaerobic blood sa mple, a valve capable of substantially isolating a contaminated blood sample stored in blood s torage means 130 from shaft 136 during operation; Alternatively, it may be desirable to provi de other selective coupling means.

In addition to the cap 144, a plurality of caps or other sealing means may be provided for posi tioning the total 100 to seal the chamber 160 of the adapter sleeve 138, as is common in the medical industry.

Although only some of the preferred embodiments of the novel blood collection device have b een described in detail herein, many modifications and variations will become readily apparent to those skilled in the art without the true scope and spirit of the invention. It is the intent of t he appended claims to cover all such improvements and modifications that fall within the scop

e of the claims.

Brief description of the drawing open —

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 shows a cross-sectional view of one of the improved blood collection devices of the pre sent invention.

100 Needle

106 First connecting member

114 Second connecting member

122 Tube

126 Coupling

130.132 Blood reservoir Means

134 ... Connection member

136 ... Shaft

138 ·

140 ·

142,

144,

146.

148

154

Adapter sleeve

opening

plug

cam

blood storage chamber plunger

needle



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(P0200)

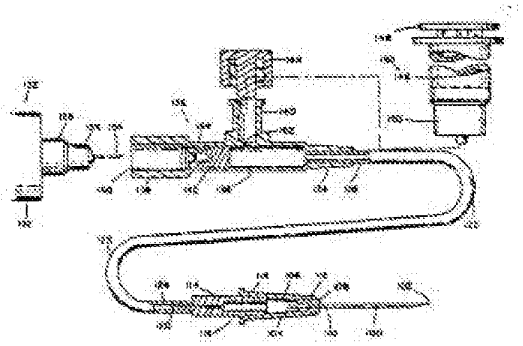
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IMPROVED BLOOD SAMPLER

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Abstract of JPH02224742 (A)



PURPOSE: To keep completely anaerobic of the residual a blood sample, with the first sampled portion of contaminated blood removed, by fixedly coupling a slender hollow shaft and a needle assembly together, with a joint member mounted to the first end of a shaft and an adapter sleeve to the second end. CONSTITUTION: Coupling 126 has joint member 134 which receives the second end 128 of tube 122. Adapter sleeve 138 is connected integrally to shaft 136 at an opposite end of the end to which the joint member 134 is connected. The adapter sleeve 138 communicates with the shaft 136 and receives second blood storage means 132. The coupling 126 has further opening 140 which is joined integrally to the shaft 136 between the adapter sleeve 138 and joint member 134. The blood delivered to the coupling 126 through tube 122 is transferred to the first and second blood storage means 130, 132 respectively for storage therein via the adapter sleeve 138 and opening 140.

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⑤④発明の名称　改良された血液採取装置

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明　細　書

1.発明の名称　改良された血液採取装置

2.特許請求の範囲

(1) 患者から血液を抜き取って貯蔵する際に医療作業員によって使用され、血液サンプルを抜き取るために針組立体の針を患者に挿入する、カップリングにおいて、

第1及び第2の端部を有する細長い中空シャフトと、

前記針組立体を前記シャフトに固定して連結し、それによって、前記針によって引き抜かれた血液を前記シャフトに送ることができる、前記シャフトの第1の端部に取り付けられた接続部材と、

前記シャフトを血液貯蔵手段に接続する、前記シャフトの第2の端部に取り付けられたアダプタースリーブと、

前記シャフトによって受け入れられた血液を連通させるため、前記アダプタースリーブと前記接続部材との間の前記シャフトに連結されて前記接続部材に連通している開口部と、から成るカップリング。

(2) 血液の流れを遮断して、前記シャフト内にたまった空気を排気する手段をさらに備える請求項(1)に記載のカップリング。

(3) 前記空気を排気する手段が、前記シャフトから前記アダプタースリーブへの空気の流れを可能にしつつ、シャフトからアダプタースリーブへの血液の流れを制限する、前記開口部と前記アダプタースリーブとの中間の前記シャフト内に位置している流れ制御手段から成る請求項(2)に記載のカップリング。

(4) 前記流れ制御手段が、微孔質疎水性プラグから成る請求項(3)に記載のカップリング。

(5) 血液貯蔵手段に結合している針を前記プラグを通して案内し、前記針を前記シャフトと同軸にする針案内手段をさらに備える請求項(4)に記載のカップリング。

(6) 患者から抜き取った血液の一部を一時的に貯蔵する血液貯蔵手段をさらに備え、前記血液貯蔵手段は、前記開口部に密封して連結可能である請求項(2)に記載のカップリング。

(7) 前記血液貯蔵手段が、注射器から成る請求項(6)に記載のカップリング。

(8) 前記シャフトと前記開口部との間の選択的な連通を可能にする、前記開口部と前記シャフトの中間に固定して配置されているバルブ手段をさらに備える請求項(2)に記載のカップリング。

(9) 前記開口部を密封する手段をさらに備える請求項(2)に記載のカップリング。

(10)患者から血液サンプルを抜き取って貯蔵するために医療作業員によって使用される血液採取装置において、

血液サンプルを抜き取るために、患者に挿入されるように適合している針手段と、

前記針手段を血液貯蔵手段に連結させるカップリング手段とを備え、

前記カップリング手段は、第1及び第2の開口部を有しており、前記針手段からの血液を前記第1及び第2の開口部に導くようになっている血液採取装置。

(11)血液の流れを遮断して、前記カップリング手段内にたまった空気を排気する手段をさらに備える請求項(10)に記載のカップリング。

(12)前記空気を排気する手段が、前記針手段から前記第1の開口部への空気の流れを可能にしつつ、前記針手段から前記第1の開口部への血液の流れを制限する、前記第1及び第2の開口部の間の前記カップリング手段内に位置している流れ制御手段から成る請求項(11)に記載の血液採取装置。

(13)前記流れ制御手段が、微孔質疎水性プラグから成る請求項(12)に記載の血液採取装置。

(14)血液貯蔵手段に結合している針を前記プラグを通して案内し、前記カップリング手段と同軸になる針案内手段をさらに備える請求項(13)に記載の血液採取装置。

(15)患者から抜き取った血液の一部を一時的に貯蔵する血液貯蔵手段をさらに備え、前記血液貯蔵手段は、前記第2の開口部に密封して連結可能である請求項(14)に記載の血液採取装置。

(16)前記血液貯蔵手段が、注射器から成る請求項(12)に記載の血液採取装置。

(17)前記第2の開口部を密封する手段をさらに備える請求項(12)に記載の血液採取装置。

(18)前記針手段と前記第2の開口部との間の選択的な連通を可能にする、前記針手段と前記第2の開口部の中間に配置されているバルブ手段をさらに備える請求項(12)に記載の血液採取装置。

(19)前記針手段が、患者に挿入する針と、前記針から前記カップリング手段へ導く、細長いチューブと、から成り、前記チューブは、医療作業員が導かれている血液を前記チューブを通して見ることができるように、概ね透明である請求項(12)に記載の血液採取装置。

(20)患者から血液サンプルを抜き取って集める際に医療作業員が使用する血液採取装置において、

患者から血液を抜き取る針手段と、

前記針手段に血液貯蔵手段を選択的に連結するカップリング手段と、を備え、

前記カップリング手段は前記針手段に固定されており、前記カップリング手段は、血液貯蔵手段を受け入れる第1の開口部と、前記第1の開口部と前記針手段との間にある中空のシャフトとを有しており、前記カップリング手段は、血液貯蔵手段を受け入れる第2の開口部をさらに備えており、前記第2の開口部は、前記第1の開口部と前記針手段の間の前記シャフトに取り付けられており、

前記血液採取装置は、前記シャフトから前記第1の開口部への血液の流れを制限するが、前記シャフトから前記第1の開口部への気体の流れを可能にする、前記第1及び第2の開口部の中間の前記シャフト内部に位置している流れ制御装置をさらに備える血液採取装置。

(21)血液の一部を一時的に貯蔵する血液貯蔵手段をさらに備え、前記血液貯蔵手段は、前記針手段から前記シャフトへ送られた血液を受け入れる、前記第2の開口部へ密封して連結されるようになっている請求項(20)に記載の血液採取装置。

(22)前記血液貯蔵手段が、血液貯蔵チャンバーと前記血液貯蔵チャンバー内に位置しているプラ

ンジャーとを有する注射器から成り、前記注射器は、前記血液貯蔵チャンバーを前記第２の開口部へ密封して連結する手段をさらに有している請求項(21)に記載の血液採取装置。

(23)前記流れ制御手段が、微孔質疎水性プラグから成る請求項(20)に記載の血液採取装置。

(24)血液サンプルを貯蔵する血液貯蔵手段をさらに有しており、前記血液貯蔵手段は、前記第１の開口部に密封して取り付け自在であって、前記プラグを通して挿入し、それによって、前記シャフトから前記血液貯蔵手段へ血液を導くようになっている針を有している請求項(23)に記載の血液採取装置。

(25)前記プラグを通して前記血液貯蔵手段の前記針を案内し、前記針を前記シャフトと同軸にする、前記プラグと前記第１の開口部との間の前記シャフト内に位置している案内手段をさらに備えている請求項(24)に記載の血液採取装置。

(26)前記流れ制御手段を通して前記血液貯蔵手段に結合している針を案内し、前記針を前記シャフトと同軸にする、前記流れ制御手段と前記第１の開口部との間の前記シャフト内に位置している案内手段をさらに備えている請求項(20)に記載の血液採取装置。

(27)前記シャフトと前記第２の開口部との間を選択的に連通できるように、バルブ手段をさらに備える請求項(20)に記載の血液採取装置。

(28)前記針手段が、血液サンプルを抜き取るために患者に挿入する針と、患者から抜き取られた血液を前記カップリング手段へ導く細長いチューブとを有し、前記チューブは可撓性を有し、かつ、前記チューブによって導かれている血液が医療作業員に見えるように概ね透明である請求項(20)に記載の血液採取装置。

(29)血液貯蔵チャンバーと該血液貯蔵チャンバー内に位置しているプランジャーとを有する注射器をさらに備え、前記注射器は、前記血液貯蔵チャンバーを前記第２の開口部へ密封して連結する手段をさらに備えている請求項(28)に記載の血液採取装置。

(30)前記第２の開口部を密封するキャップ手段をさらに備える請求項(11)に記載の血液採取装置。

(31)患者から血液サンプルを抜き取って集める際に医療作業員が使用する血液採取装置において、

挿入端部と取り付け端部を有する第１の細長い針部材を備え、前記挿入端部が患者に挿入するようになっており、前記第１の針部材が患者から抜き取られた血液を前記挿入端部から前記取付端部へ運ぶ同軸通路を有しており、

針受け入れ端部と、嵌合端部と、前記針受け入れ端部から前記嵌合端部へ延びる同軸通路と、を有する第１の雌コネクターと、

患者から抜き取られた血液が前記第１の針部材によって前記第１の雌コネクターに運ばれるように、前記第１の針部材の前記取り付け端部を前記第１の雌コネクターの受け入れ端部に固定してかつ密封自在に連結する手段と、

嵌合端部と、取り付け端部と、前記嵌合端部から前記取り付け端部へ延びる同軸通路を有する第１の雄コネクターをさらに備え、前記第１の雄コネクターの前記嵌合端部は、前記第１の雌コネクターへ運ばれた血液が前記第１の雄コネクターによって受け入れられるように、前記第１の雄コネクターの前記嵌合端部に密封自在に嵌合されており、

第１及び第２の端部と、前記第１の端部から前記第２の端部へ延びている通路とを有する細長いチューブをさらに備え、前記チューブの前記第１の端部は、前記第１の雄コネクターによって受け入れられた血液が前記チューブによって送られるように、前記第１の雄コネクターの前記取り付け端部に密封自在に取り付けられており、前記チューブは、可撓性を有し、かつ、前記チューブによって受け入れられた血液が医療作業員に見えるように概ね透明であり、

細長い中空のシャフトと、前記シャフトの第１の端部に取り付けられている接続部材とを有するカップリングをさらに備え、前記カップリングは、前記チューブの第２の端部を前記カップリングに固定して密封自在に連結し、それによって、前記チューブによって受け入れられた

血液を前記カップリングに送り、前記カップリングは、前記シャフトを血液貯蔵手段に接続する、前記シャフトの第２の端部に取り付けられたアダプタースリーブをさらに有し、前記カップリングは、前記アダプタースリーブと前記接続部材との間の前記シャフトに固定して取り付けられて、前記カップリングによって受け入れられた血液が前記第２の雌コネクターと連通するように、前記接続部材と連通している第２の雌コネクターをさらに有し、

前記第２の雌コネクターと前記アダプタースリーブとの間の前記カップリングの前記シャフト内に位置しているプラグをさらに備え、前記プラグは、気体を前記シャフトから逃がして前記シャフトから前記アダプタースリーブへ血液流れを有効に遮断するようになっている血液採取装置。

(32)挿入端部と、連結端部と、前記挿入端部から前記連結端部へ延びる同軸通路とを有する第２の針部材と、

患者から抜き取られた血液を貯蔵するバキュティナー手段とをさらに備え、前記バキュティナー手段は、前記第２の針部材に固定して取り付けられ、前記アダプタースリーブは、前記バキュティナー手段が前記アダプタースリーブの中へ圧入されるように、かつ、前記第２の針部材が前記プラグを通して挿入され、それによって前記カップリングの前記シャフトによって受け入れられた血液を前記バキュティナー手段へ運ぶように、形成されている請求項(31)に記載の血液採取装置。

(33)前記第２の針部材を案内して前記第２の針部材を前記カップリングと同軸の前記プラグへ挿入する、前記プラグと前記アダプタースリーブとの間の前記カップリング内に位置している針案内手段をさらに備えている請求項(32)に記載の血液採取装置。

(34)血液貯蔵手段に結合している針を案内して前記針を前記カップリングへ同軸に挿入する、前記プラグと前記アダプタースリーブとの間の前記カップリング内に位置している針案内手段をさらに備えている請求項(31)に記載の血液採取装置。

(35)前記第２の雌コネクターに係合しそれによって前記第２の雌コネクターから血液が流出するのを防止すべく前記第２の雌コネクターを密封するようになっているキャップ手段をさらに備える請求項(31)に記載の血液採取装置。

(36)一時的に血液を貯蔵する注射器をさらに備え、前記注射器は、血液貯蔵チャンバーと該血液貯蔵チャンバー内に位置するプランジャーとを有し、前記注射器は、前記血液貯蔵手段と連通していて、前記カップリングによって受け入れられた血液が前記注射器内に貯蔵されるように、前記第２の雌コネクターと嵌合するようになっている請求項(31)に記載の血液採取装置。

(37)前記第２の針部材を案内して前記第２の針部材を前記カップリングと同軸の前記プラグへ挿入する、前記プラグと前記アダプタースリーブとの間の前記カップリング内に位置している針案内手段をさらに備えている請求項(36)に記載の血液採取装置。

(38)挿入端部と、連結端部と、前記挿入端部から前記連結端部へ延びる同軸通路とを有する第２の針部材と、

患者から抜き取られた血液を貯蔵するバキュティナー手段とをさらに備え、前記バキュティナー手段は、前記第２の針部材に固定して取り付けられ、前記アダプタースリーブは、前記バキュティナー手段が前記アダプタースリーブの中へ圧入されるように、かつ、前記第２の針部材が前記プラグを通して挿入され、それによって前記カップリングの前記シャフトによって受け入れられた血液を前記バキュティナー手段へ運ぶように、形成されている請求項(37)に記載の血液採取装置。

(39)前記第１の針手段、前記第２の雌コネクター、及び前記アダプタースリーブを各々密封する、第１、第２及び第３のキャップ手段をさらに備える請求項(37)に記載の血液採取装置。

(40)前記第２の雌コネクターと前記シャフトとの間を選択的に連通する、前記第２の雌コネクターに連結されたバルブ手段をさらに備える請求項(31)に記載の血液採取装置。

(41)患者から血液サンプルを抜き取って貯蔵するために、医療作業員が使用する血液採取装置において、

患者から血液を抜き取る針手段と、

患者から抜き取った第1の血液部分を一時的に貯蔵する注射器手段と、

前記針手段を前記注射器手段へ密封自在に連結するカップリング手段とを備え、前記カップリング手段は、前記針手段と前記カップリング手段内にたまった空気を排気する流れ制御手段を有しており、前記カップリング手段は、血液貯蔵手段を受け入れて前記カップリング手段へ貯蔵のために血液を導くようになっているアダプター手段をさらに有しており、前記注射器手段と前記カップリング手段は、前記第1の血液部分を患者に戻すようにさらになっている血液採取装置。

(42)前記カップリング手段が、細長い中空シャフトを有するカップリングを備え、前記カップリング手段が、前記カップリングへ前記針手段を固定して連結する、前記シャフトの第1の端部に取り付けた接続部材をさらに有し、前記アダプター手段は、前記シャフトの第2の端部に取り付けられており、前記カップリングは、前記注射器手段を受け入れる、前記アダプター手段と前記接続部材との間の前記シャフトに固定して取り付けた接続部材をさらに有している請求項(41)に記載の血液採取装置。

(43)前記流れ制御手段が、前記接続部材と前記アダプター手段との間の前記カップリングの前記シャフト内に位置しているプラグから成る請求項(42)に記載の血液採取装置。

(44)前記プラグが微孔質疎水性プラグから成る請求項(43)に記載の血液採取装置。

(45)前記針手段が、血液サンプルを抜き取るために患者に挿入する針と、患者から抜き取られた血液を前記カップリングへ導く、細長いチューブとを有し、前記チューブは可撓性を有し、かつ、前記チューブによって導かれている血液が医療作業員に見えるように概ね透明である請求項(43)に記載の血液採取装置。

(46)前記血液採取装置にたまった空気を排気しながら患者から第1の血液部分を抜き取って前記血液採取装置を満たし、嫌気性サンプルが前記血液採取手段にたまった空気に汚染されないように、前記血液採取装置にたまった空気を概ね排気した後、患者から嫌気性サンプルを抜き取る、

ステップから成る患者から嫌気性血液サンプルを抜き取る方法。

(47)前記第1の血液部分を抜き取った後に、前記第1の血液部分を一時的に貯蔵し、

前記嫌気性血液サンプルを抜き取った後に、前記第1の血液部分を患者に戻す、

ステップをさらに含む請求項(46)に記載の方法。

(48)前記第1の血液部分を抜き取るステップが、

注射器にカップリングを連結するステップをさらに含み、前記カップリングは針組立体に密封自在に連結されており、

さらに、前記第1の血液部分を抜き取るステップが、

血液が前記針組立体を介して前記注射器を取り付けたカップリングの中に導かれるように、患者に前記針組立体を挿入し、

前記挿入された針組立体とカップリング内にたまった空気を排気し、

バキュティナーのバキュティナー針を前記通気されたカップリングに接続して、前記バキュティナー針を前記挿入された針組立体と連通させ、

前記バキュティナーを取り付けたカップリングから前記第1の血液部分を前記注射器の中に抜き取る、

ステップを含んでいる請求項(47)に記載の方法。

(49)前記嫌気性血液サンプルを抜き取るステップが、前記第1の血液部分が抜き取られた後で前記針組立体と前記バキュティナーとの間に血液の流れをつくるステップから成る請求項(48)に記載の方法。

(50)前記第1の血液部分を前記注射器へ抜き取るステップが、患者の心臓の圧力下で自由に血液

を流すステップから成る請求項(48)に記載の方法。

3.発明の詳細な説明

(産業上の利用分野)

本発明は、患者から血液サンプルを採取する装置に向けられたものであり、特に、サンプル内の気体分圧が、患者の生体内における血液内の気体分圧とほぼ等しくなるように、血液サンプルを受け取ることができる、改良された血液採取装置に向けられたものである。

(従来技術)

医療分野では、患者の血液内の、生体内における気体の平衡状態を決定することが必要である。医療作業員は、代表的には、酸素と二酸化炭素の分圧を気にかけるであろう。彼らは、また、例えば水素イオンやカルシウムイオンのような、活性が血液中の気体平衡に関連してくるイオンの種を気にかけるであろう。

血液サンプルを血液中の気体分析のために有効なものにするには、サンプルは、嫌気条件で、すなわち、検査すべき気体の分圧に変動が生ずるのを防止すべく血液が患者の体外の気体にさらされないように、採取されなければならない。現在市販されて利用できる主要な血液採取装置は、嫌気血液採取の完全性を保証しているという点では、概ね妥当であるとはいえない。従来装置の例としては、注射器及びベント式プランジャーが使用されており、バレル内の空隙がない状態からベント式プランジャーを引っ張ることによって、患者から正確な血液体積が得られるまで、患者から注射器のバレルの中に血液をゆっくりと抜き取る。しかしながら、これらの装置は、血液サンプルが外気にさらされるのをある程度許している。プランジャーが移動する前に、ある程度の外気量はバレル内に含有されるであろう。従って、血液の最初の部分はこれらの気体にさらされ、それによって、この最初のサンプルに含有している気体の分圧が変化する。抜き取られた血液のうち最初の部分を捨てる手段は提供されておらず、そのため、全サンプルが汚染されるであろう。

さらに、前述した装置を用いる際に、装置の医療作業員を、作業の途中で汚染された血液の偶発的な破裂や暴露に対して保護する手段も提供されていない。

ベクトンディケンソン(Becton and Dickenson)のバキュテイナー(Vacutainer)及びバキュテイナー付属装置のような他の装置は、抜き取られた血液に対する暴露から医療作業員を保護する、改良された特性を示している。しかしながら、これらの装置もまた、外気に対する血液サンプルの最初の部分の暴露を、ある程度許容してしまう。

前述した従来技術の欠点に加えて、嫌気性血液サンプルの採取を可能にしつつ、流し込み、すなわち血液の流れの中へ、例えば栄養剤や薬等を注入する手段を備える血液採取装置は、現在のところ知られていない。

従って、患者から嫌気性血液サンプルを抜き取る装置を提供することが望ましい。さらに、液体を患者の血液の流れに注入することもできる、血液サンプルを抜き取る装置を提供することがさらに望ましい。穿刺、すなわち針の配置を追加して行う必要のない、繰り返して血液を採取できる、前記装置を提供することがさらに望ましい。また、予定された区間の採取、すなわち他の引き続いて行なわれる血液の採取の間、患者に残してお

くことができる、血液サンプルを抜き取る装置を提供することが望ましい。

(発明の目的)

それゆえ、本発明の目的は、患者から嫌気性血液サンプルを抜き取る血液採取装置を提供することである。

また、本発明の目的は、最初の汚染された血液のサンプル部分を抜き取って、残りのサンプルにおける完全な嫌気性を維持できる、血液採取装置を提供することである。

さらに、本発明の目的は、外部の液体を患者の血液の流れの中に注入できる血液採取装置を提供することである。

さらに、本発明の目的は、穿刺、すなわち針の配置を追加して行なう必要のない、繰り返して血液を採取できる血液採取装置を提供することである。

さらに、本発明の別の目的は、予定された区間の採取、すなわち他の引き続いて行なわれる血液採取の間、患者に残しておくことができる血液採取装置を提供することである。

本発明の、これら及び他の目的は、患者から血液を抜き取ってこれを貯蔵するときに、医療作業員が使用するカップリングを提供することによって、かなえられる。このカップリングは、血液サンプルを引き出すべく、患者に針を注入する針組立体とともに使用するために、特に利用される。カップリングは、細長い中空シャフトと、針組立体を該シャフトに固定的に連結し、針によって引き出された血液をシャフトに送る、シャフトの第1の端部に取り付けられる接続部材と、から成る。カップリングは、シャフトを様々な血液貯蔵手段に接続する、シャフトの第2の端部に取りつけられたアダプタースリーブをさらに備えている。開口部が、アダプタースリーブと接続部材との中間のシャフトに連結されており、シャフトに受け入れられた血液がその開口部と連通するように、その開口部は、接続部材と連通している。

本発明の別の実施例では、血液の流れを遮断してシャフトにたまった空気を通気する装置が提提される。特に、流れ制御手段、例えば、微孔質の疎水性プラグが、シャフトからアダプタースリーブへの空気の流れを可能にしつつ、シャフトからアダプタースリーブへの血液の流れを制限するため、開口部とアダプタースリーブとの中間のシャフト内に位置している。本発明の他の実施例では、シャフトと開口部との選択的な連通を可能にするバルブが、シャフトと開口部との中間に設けられる。

本発明の他の実施例は、特許請求の範囲で特に示され、明瞭に請求される。しかしながら、本発明は、実施の構成や方法に関する限り、添付図面を参照して次の詳細な説明を読むことから最も良く理解できるであろう。

(実施例)

本発明の改良された血液採取装置を示す断面図が第1図に提供されている。血液採取装置は、患者の血液流れ(動脈あるいは静脈)内に挿入するようになった挿入端部102を有する細長い針100を備えている。針100は、さらに、円筒シール108を介して第1の接続部材106に取り付けられている取り付け端部104を有している。当業界で周知のように、針100は、患者から引き出された血液を第1の接続部材106へ導く、挿入端部102から取り付け端部104へ延びる同軸通路を有している。

円筒シール108は、内部に針100の取り付け端部104が固定して取り付けられている中央開口部110を有している。さらに、円筒シール108は、第1の接続部材106の針受け入れ端部112へ固定して取り付けられている。第2の接続部材114は、第1の接続部材106の嵌合端部118と嵌合するようになった嵌合端部116を有しており、その結果、第1の接続部材によって受け入れられた、針100からの血液は、嵌合接合116、118を介して第2の接続部材114に導かれる。

チューブ122の第1の端部120が、第2の接続部材114の取り付け端部124に密封して取り付けられている。チューブ122は、患者から引き出された血液を針100を介してカップリング126へ運ぶために設けられている。チューブ122は、針を患者の血液流れに容易に挿入可能であり、さらに、挿入後、針100に無用な動

きを与えて患者に不快感を生ぜしめることなく、医療作業員がカップリング１２６を操作可能となるように、可撓性であるのが好ましい。さらに、チューブ１２２は、医療作業員が患者から引き出された血液を視覚で観察できるように、透明であるのが好ましい。

針１００と、第１の接続部材１０６と、第２の接続部材１１４と、チューブ１２２との組合わせは、針組立体を構成し、当業界で周知の針、接続部材、及びチューブから容易に組立て可能である。一例として、第１及び第２の接続部材１０６及び１１４は、当業界で周知のように、雄及び雌のルエル(Luer)コネクターから成る。

カップリング１２６は、チューブの第２の端部１２８を、第１及び第２の血液貯蔵手段１３０及び１３２の各々と接続するために設けられている。この目的のために、カップリング１２６は、チューブ１２２の第２の端部１２８を受け入れる中央開口部を有する接続部材１３４を有している。接続部材１３４は、チューブ１２２によってカップリング１２６に送られる血液がシャフト１３６の内部に受け入れられるように、細長い中空シャフト１３６に一体に接続される。アダプタースリーブ１３８は、接続部材１３４が接続されている端部と反対側の端部でシャフト１３６に一体に接続されている。アダプタースリーブ１３８は、シャフト１３６と連通しており、後で完全に説明するように、第２の血液貯蔵手段１３２を受け入れるために設けられる。

カップリング１２６は、さらに、アダプタースリーブ１３８と接続部材１３４との中間のシャフト１３６に一体に接続されている開口部１４０を、さらに有している。開口部１４０は、第１の血液貯蔵手段１３０をカップリング１２６のシャフト１３６へ接続するために設けられる。通路１６２は、開口部１４０が接続部材１３４と連通するように、開口部１４０に近接してシャフト１３６に設けられている。従って、チューブ１２２によってカップリング１２６に送られてきた血液は、貯蔵のため、アダプタースリーブ１３８及び開口部１４０を経由して第１及び第２の血液貯蔵手段１３０及び１３２へ運ばれる。

カップリング１２６は、また、アダプタースリーブ１３８と開口部１４０との間のシャフト内に配置されたプラグ１４２を有している。プラグ１４２は、血液採取作業の初期の段階の間に、接続部材１０６、１１４、チューブ１２２、シャフト１３６、及び開口部１４０内にたまった空気を排気する、例えば、多孔質プラグのような液体流れ制御手段から成る。従って、プラグ１４２は、シャフト１３６からアダプタースリーブ１３８への血液の流れを制限して、シャフトからアダプタースリーブへの空気の流れを可能にするようになっている。本発明の好ましい実施例では、プラグ１４２は、当業界で周知の、微孔質の疎水性プラグから成る。しかしながら、他の液体流れ制御手段が、好ましい微孔質疎水性プラグ１４２の代わりに、用いることができることは、当業者には明らかであろう。

前述したように、開口部１４０は、第１の血液貯蔵手段１３０を受け入れるようになっている。キャップ１４４は、第１の血液貯蔵手段１３０がカップリング１２６に接続されていないときに、しばしばおこる不注意な血液損失から開口部を密封するため、開口部１４０と係合可能である。しかしながら、通常作業では、キャップ１４４は、開口部１４０から取り除かれ、そこに第１の血液貯蔵手段１３０を接続している。

本発明の好ましい実施例では、第１の血液貯蔵手段１３０は、血液貯蔵チャンバー１４６と、その血液貯蔵チャンバー１４６内に配置されたプランジャー１４８を有する形式の注射器から成る。周知のように、操作の際には、プランジャー１４８は、血液がチャンバー内に入るように、血液貯蔵チャンバー１４６からゆっくりと引き出される。血液貯蔵手段１３０は、さらに、血液貯蔵手段１３０を開口部１４０に接続するため、接続手段１５０を備えている。本発明の好ましい実施例では、開口部１４０と接続部材１５０は、各々、雄雌のルエルコネクターから成る。しかしながら、他のコネクター部材が第１の血液貯蔵手段１３０をカップリング１２６に密封して接続するために提供されることは、当業者には明らかであろう。

操作の際は、キャップ１４４は、開口部１４０から取り除かれて、そこに血液貯蔵手段１３０が接続される。次いで、血液が引き出され、あるいは好ましくは患者の心臓の圧力下で自由に流れることができるように、かつ、接続部材１０６、１１４及びチューブ１２２を介して、シャフト１３６に送られるように、患者の血液流れの中に針１００が挿入される。接続部材１０６、１１４、チューブ１２２、シャフト１３６及び開口部１４０内にたまった空気は、前述したように、流れ通路に入った患者の血液によって、置換され、多孔質プラグ１４２を介して通気される。引き出され、あるいは患者からの心臓の圧力下で流れる血液の第１の部分は、通気される前に、たまった空気にさらされるので、概ね汚染されており、それゆえ、嫌気性血液採取に適していない。従って、この第１の血液の部分は、一時的に貯蔵するために、血液貯蔵手段１３０の中へカップリング１２６から引き出され、一方、嫌気性血液サンプルは、第２の血液貯蔵手段１３２を介して受取られる。嫌気性血液サンプルが受取られた後、血液貯蔵手段１３０内に一時的に貯蔵された血液は、捨てられ、あるいは、チューブ１２２及び針１００を介して患者に戻される。

嫌気性血液サンプルを引き出すため、第２の血液貯蔵手段１３２がアダプタースリーブ１３８を介してカップリング１２６に接続されている。第２の血液貯蔵手段１３２は、当業界で周知のベクトン・ディケンソン・バキュティナーから成っていてもよい。血液貯蔵手段１３２は、患者から抜き取られた嫌気性血液サンプルを受け入れる血液貯蔵チャンバー１５２を有している。針１５４は、針ハブ１５６に密封して接続されており、それらの組立体は、適合性を有するカップリング１５８（普通は、バキュテイナーアダプターとして言及されている）を介して血液貯蔵チャンバー１５２に密封して接続されている。当業界で周知のように、針１５４は、血液貯蔵チャンバー１５２と連通することを防止するため、シールを有している。さらに、当業界で周知のように、血液貯蔵チャンバー１５２は、患者から抜き取られた血液を汚染する空気を含まないようにするため、排気されている。適合性を有するカップリング１５８は、針１５４を血液貯蔵チャンバー１５２と連通させて配置するため、針１５４からシールを取り除く手段を備えている。

アダプタースリーブ１３８は、針ハブ１５６をきちんと受け入れるような径でできた内部アダプターチャンバー１６０を有している。アダプタースリーブ１３８の長さとシャフト１３６内のプラグ１４２の位置は、血液貯蔵手段１３２がアダプタースリーブ１３８に完全に挿入され、針１５４がプラグ１４２を通って通路１６２とチューブ１２２の第２の端部１２８との間に位置するように、選択される。針がシャフト１３６と同軸になるようにカップリング１２６内に挿入されることを可能とするため、針ガイド１６４がアダプタースリーブ１３８とプラグ１４２との間のカップリング１２６内に配置されている。針ガイド１６４は、カップリング１２６内への血液貯蔵手段１３２の挿入の間、針１５４を受け入れて、かつ、針がシャフト１３６と同軸となるように、プラグ１４２への針の挿入前に針を位置決めするために、設けられている。

操作の際は、嫌気性血液サンプルを集めるために、血液貯蔵手段１３０が、前述した開口部１４０を介してカップリング１２６に連結される。針１００が患者の血液流れの中に挿入され、針１００、コネクター１０６、１１４、チューブ１２２及びカップリング１２６の内部にたまった空気が前述したようにプラグ１４２を介して排気される。次いで、血液貯蔵手段１３２の針１５４が、チューブ１２２の近傍の通路１６２を越えて位置するように、プラグ１４２を通してカップリング１２６内に挿入される。針１５４内にたまった汚染空気のどんなにわずかの部分でもプラグ１４２を介して排気されるように、すなわち、嫌気性血液サンプルを受け入れる前にカップリング１２６から取り除かれるように、血液サンプルの汚染された部分を貯蔵手段１３０内に貯蔵する前に、針１５４をカップリング１２６へ挿入することが望ましい。

針１５４がカップリング１２６内に適当に挿入された後、汚染された血液の第１の部分はカップ

リング１２６から一時貯蔵のため血液貯蔵手段１３０へ引き出される。このとき、針１５４のシールは、嫌気性血液サンプルが血液貯蔵１５２へ導かれるように、当業界で周知のように、適合性カップリング１５８によって除去される。血液貯蔵チャンバー１５２へ導かれた血液のほぼ全部がチューブ１２２から受け取った血液であって、血液貯蔵手段１３０の血液貯蔵チャンバー１４６から受け取った血液ではないようにするために、針１５４は、通路１６２とチューブ１２２との中間でかつ、チューブ１２２の第２の端部１２８の近傍の、シャフト１３６内のカップリング１２６内に位置していることが好ましい。

本発明の代わりの実施例では、嫌気性血液サンプルを受け取っているとき、血液貯蔵手段１３０内に貯蔵された汚染された血液サンプルを、操作中に、シャフト１３６からほぼ隔離することができるバルブ、あるいは他の選択性カップリング手段を備えることが望ましい。

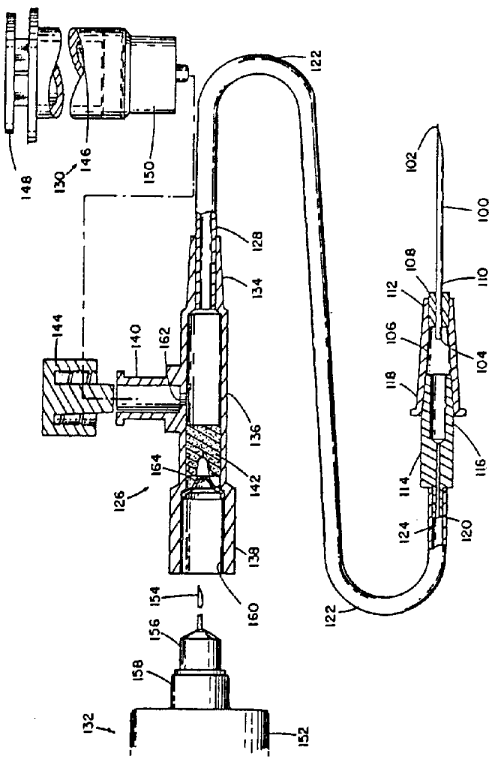
医療業界では普通となっているように、キャップ１４４に加えて、複数のキャップあるいは他のシール手段が、針１００に配置してアダプタースリーブ１３８のチャンバー１６０を密封するために設けられてもよい。

新規な血液採取装置の好ましい実施例のいくつかのみをここで詳細に説明したが、当業者には、多くの改良や変更が容易に明らかとなるであろう。本発明の真の範囲及び精神に入るこのようなすべての改良や変更を包含することが、特許請求の範囲の趣旨である。

4.図面の簡単な説明

第１図は、本発明の改良された血液採取装置の断面図を示す。

１００・・・・・針
１０６・・・・・第１の接続部材
１１４・・・・・第２の接続部材
１２２・・・・・チューブ
１２６・・・・・カップリング
１３０、１３２・血液貯蔵手段
１３４・・・・・接続部材
１３６・・・・・シャフト
１３８・・・・・アダプタースリーブ
１４０・・・・・開口部
１４２・・・・・プラグ
１４４・・・・・キャップ
１４６、１５２・血液貯蔵チャンバー
１４８・・・・・プランジャー
１５４・・・・・針



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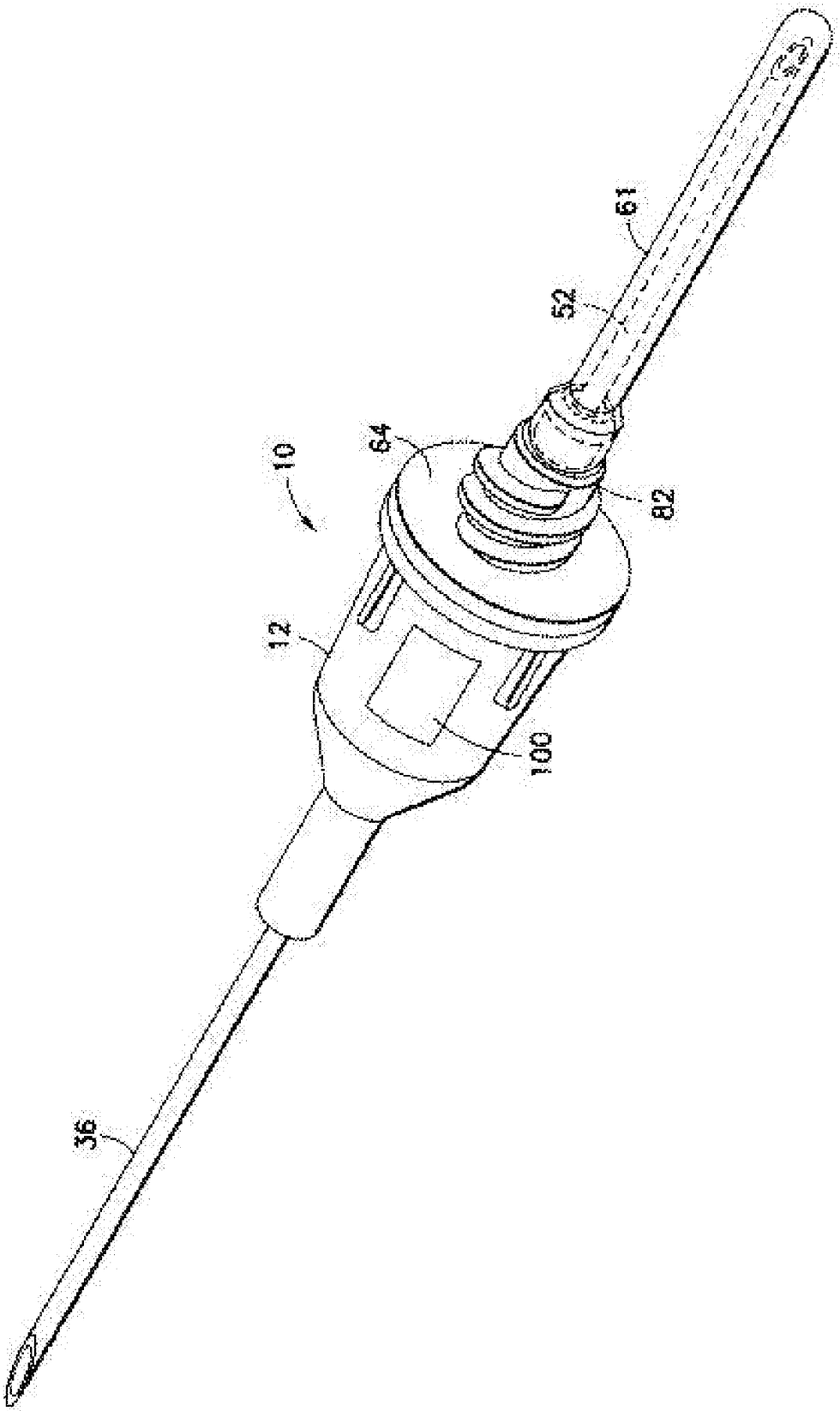
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[Theme code (reference)]
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4C066DD06
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wrap up close —

(57) [Summary] (Modified)
[Problem] To easily confirm that puncturing has been performed reliably when collecting bloo d, and to prevent outflow of fluid such as blood.
A self-venting blood collection needle assembly for extracting at least one fluid sample into a vacuum container for clinical testing, the blood collection needle assembly allowing a flow of b lood to allow a user to successfully perform a venipuncture. To provide a transparent or semi-transparent flashback chamber in which cracking can be visually confirmed. The self-venting mechanism is designed to allow the release of air and prevent the escape of fluids, such as bl ood, during use. Thus, air under venous pressure can be expelled from the blood collection ne edle assembly by the time the blood reaches the venting mechanism.
[Selection drawing] Fig. 1


61
52
64
10
82
12
100
36

The scope of the claims

open —

1. A hub having an inlet end, an
outlet end and a chamber formed therebetween; an
inlet cannula, a distal end external to said hub; an inlet cannula extending through the cann ula and having a lumen attached to the hub in communication with the chamber; an outlet ca nnula having a proximal end outside the hub
; an exit cannula extending through and attached to the hub so as to communicate with the chamber; and multiple specimens mounted over
portions of the exit cannula outside the hub. a multiple sample sleeve, wherein the lumen of the inlet cannula, the chamber, the lumen of the outlet cannula, and an inner surface of the m ultiple sample sleeve form a fluid passage; the fluid passage and the external atmosphere
; a venting mechanism in communication with the needle assembly for permitting the outflo w of air from the needle assembly through the venting mechanism to an external atmosphere and substantially inhibiting the outflow of liquid from the needle assembly through the venting mechanism to the external atmosphere; and a venting mechanism,
wherein said inlet and outlet cannulas are separate or a single cannula having an opening co mmunicating with said chamber.
2.
The needle assembly as recited in claim 1, wherein said venting mechanism extends through said hub.
3.
The needle assembly as recited in claim 2, wherein said venting mechanism comprises a ven ting medium.
[Claim 4]
3. The needle assembly of claim 2, wherein said venting mechanism includes at least one op ening through said hub, said opening including a vent plug.
5. The
needle assembly as recited in claim 4, wherein said venting mechanism further comprises a check valve.
6.
The vent mechanism includes at least one opening through the hub and a vent ring surround ing the inlet cannula, the vent ring being positioned through the hub in the chamber proximat e to the opening. 2. The needle assembly of claim 1, wherein the needle assembly comprises:
7.
The needle assembly of claim 1, wherein said venting mechanism is disposed in said passag

e beyond the proximal end of said exit cannula.

8.

The needle assembly as recited in claim 7, wherein said venting mechanism comprises a ven ting medium.

9.

The needle assembly of claim 1, wherein said hub further comprises a non-patient locking pr ojection, said vent mechanism extending through said non-patient locking projection. .

10.

The needle assembly as recited in claim 9, wherein said venting mechanism comprises a ven ting medium.

11.

The needle assembly of claim 9, wherein said venting mechanism comprises a passageway t hrough said non-patient stop projection and a vent plug disposed in said passageway.

[Claim 12]

10. The needle assembly of claim 9, wherein said venting mechanism comprises a notch ext ending through said non-patient locking projection and a venting disc.

13. The method of claim

9, wherein said venting mechanism comprises at least one opening extending through said n on-patient side locking projection and a vent plug arranged in said opening. needle assembly.

14.

The needle assembly of claim 1, wherein said hub further comprises a non-patient locking pr ojection, at least a portion of said non-patient locking projection comprising said venting mec hanism. .

15. The

needle assembly as recited in claim 14, wherein said venting mechanism comprises a ventin g medium.

16.

At least part of said non-patient side locking projection is made of a porous hydrophobic mat erial, or at least part of said non-patient side locking projection is made of a porous material h aving a hydrophobic surface. 15. The needle assembly of claim 14, wherein the needle assem bly is made of material.

17.

A needle assembly as in claim 14, wherein said venting mechanism comprises a porous mat erial impregnated with a hydrophilic material.

18.

The hub further comprises a non-patient side locking projection to which the multiple sample sleeves are securely attached, and wherein the venting mechanism is disposed between the n on-patient side locking projection and the multiple sample sleeves. 2. The needle assembly of claim 1, wherein the needle assembly is .

19. The
needle assembly as recited in claim 18, wherein said venting mechanism comprises a ventin g sleeve.

[Claim 20]

20. The needle assembly of claim 19, wherein said vent sleeve comprises a porous hydropho bic material or said vent sleeve comprises a porous material with a hydrophobic surface.

21.
The needle assembly of claim 18, wherein said venting mechanism comprises a ventable ven t cord.

22.
The needle assembly of claim 18, wherein said venting mechanism comprises a textile surfac e.

23.
The needle assembly of claim 1, wherein said multiple sample sleeve includes said venting m echanism.

24. The
needle assembly as recited in claim 23, wherein said venting mechanism comprises a ventin g medium.

25. Said
multiple sample sleeve is formed of a porous hydrophobic material or said multiple sample sl eeve comprises a porous material having a hydrophobic surface. A needle assembly as describ ed in .

26.
The needle assembly of claim 1, wherein at least a portion of said hub is formed by a ventin g medium such that said hub constitutes said venting mechanism.

27.
At least a portion of said hub is made of a porous material such that said hub constitutes sai d ventilation mechanism.

2. The needle assembly of claim 1, wherein the needle assembly is formed by:

28.
The needle assembly of claim 1, wherein said hub further comprises a non-patient thread as sembly and a hub insert assembled together to form a reservoir.

29.
The venting mechanism includes a first passage through the non-patient thread assembly to the reservoir, a second passage from the reservoir to the outside atmosphere, and a vent loca ted in the reservoir. 29. The needle assembly of Claim 28, comprising:

30.
Further comprising a non-patient thread assembly, at least a portion of said non-patient thre ad assembly being defined by a vent medium such that said non-patient thread assembly con

stitutes said vent assembly. 2. The needle assembly of claim 1, wherein the needle assembly comprises:

31.

Further comprising a non-patient thread assembly, at least a portion of the non-patient thre ad assembly formed of a porous material such that the non-patient thread assembly constitut es the vent assembly. 2. The needle assembly of claim 1, wherein the needle assembly is .

32.

The needle assembly of claim 1, wherein said venting mechanism comprises a venting mediu m.

33.

The needle assembly of claim 1, further comprising a shield selectively covering said first ca nnula.

34.

a hub having an inlet end, an outlet end and a chamber formed therebetween;

a cannula having a distal end mounted to the hub so as to be external to the hub, a proxima l end and a lumen extending therebetween; and a proximal end of the cannula external to the hub

. Multiple sample sleeves mounted over a portion, wherein the lumen, the inner surface of th e multiple sample sleeve and the chamber form a fluid passageway, and the fluid passageway communicates with an external atmosphere

. a venting mechanism that allows air to escape from the needle assembly through the venti ng mechanism to the external atmosphere and substantially prevents fluid from exiting the ne edle assembly through the venting mechanism to the external atmosphere. A needle assembl y,

comprising: a venting mechanism.

35.

The needle assembly as recited in claim 34, wherein said venting mechanism is disposed in s aid passageway beyond said proximal end of said exit cannula.

36.

The needle assembly of claim 35, wherein said venting mechanism comprises a venting medi um.

37.

The needle assembly of claim 34, wherein the hub further comprises a non-patient locking p rojection, and wherein the vent mechanism extends through the non-patient locking projectio n. .

38. The

needle assembly as recited in claim 37, wherein said venting mechanism comprises a ventin g medium.

39. The needle assembly of claim 37,

wherein said venting mechanism comprises a passageway through said non-patient stop pro jection and a vent plug disposed in said passageway.

[Claim 40]

The vent mechanism includes a notch extending through the non-patient side locking project ion and a vent disc.

38. The needle assembly of claim 37, characterized by:

41. The needle of claim 37,

wherein said venting mechanism comprises at least one opening extending through said non -patient stop projection and a vent plug disposed in said opening. assembly.

42.

The needle assembly of claim 34, further comprising a non-patient locking projection, at leas t a portion of said non-patient locking projection comprising said venting mechanism.

43. The

needle assembly as recited in claim 42, wherein said venting mechanism comprises a ventin g medium.

44.

At least part of said non-patient side locking projection is formed of a porous hydrophobic m aterial, or at least part of said non-patient side locking projection is made of porous material having a hydrophobic surface. 43. The needle assembly according to Claim 42, comprising a material.

45. A

needle assembly as in claim 32, wherein said venting mechanism comprises a porous materi al impregnated with a hydrophilic material.

detailed description open —

Description: BACKGROUND OF THE INVENTION 1.

Field of the Invention The present invention relates to a device for performing a vascular pun cture on a patient to obtain a blood sample. More particularly, the present invention is useful f or collecting multiple blood samples when collecting blood samples from a patient into a vacu um blood collection tube, where the self-venting feature allows the phlebotomist to know if th e vessel has been punctured. of the needle assembly. BACKGROUND OF THE INVENTION Vas cular puncture is the primary method used to obtain blood samples for clinical examination . P erforming a vascular puncture requires the phlebotomist to perform multiple steps simultaneo usly. This step includes evaluating the patient's overall physical and psychological condition to appropriately select the vascular puncture site and technique. The phlebotomist also needs to

select the proper instrumentation, perform techniques to control bleeding, and properly collec t and identify fluid samples for clinical examination. All of these concurrent factors must be id entified by the phlebotomist, as these factors adversely affect vessel dilatation and the length of the vascular puncture procedure. [0003] Various vascular puncture devices have been dev eloped to address the aforementioned problems. These devices include a needle assembly hav ing a hub defining a chamber therein with a single pointed cannula secured to the hub. The va scular end of the cannula is configured to be inserted into a patient's blood vessel and the non -patient end of the cannula has a sealable sleeve and pierces a pierceable stopper disposed wi thin the reduced pressure vessel. is configured as DISCLOSURE OF THE INVENTION [Problem to be Solved by the Invention]

When the vessel end of the cannula is inserted into the vessel, blood flows through the cann ula into the sealable sleeve and into the hub's chamber, which is transparent or translucent fo r visualization ("flashback"). When air is evacuated from the hub chamber, the blood therein is pressurized each time the sealable sleeve is pushed toward the hub chamber by the action of the vacuum reservoir. Due to the time lag between vessel insertion and flashback, the phleb otomist did not obtain a satisfactory vessel puncture because the transparent chamber did not immediately indicate that a vessel puncture had occurred

.

You may mistakenly believe that you were not. The phlebotomist then uses the vacuum cham ber and/or

Unnecessarily repeated vascular punctures requiring replacement of the needle assembly itsel f. Repetition of such procedures prolongs the physical and emotional discomfort experienced b y the patient.

[0006]

If no flashback occurs, the air in the injection cannula and flashback chamber is compressed there, so that the air in the needle hub is pressurized to venous pressure. This pressurized air needs to be expelled somewhere, so when the needle is withdrawn from the patient after the blood draw is complete, this pressurized air pushes the blood towards the tip of the needle. p ush out to

[0007]

Accordingly, to provide a rapid, accurate and cost-effective solution to conventional blood sa mpling methods in which phlebotomists consistently rely on flashback to achieve satisfactory venous punctures. is desired. In addition, a blood collection needle assembly is provided that allows blood to flow directly into the flashback chamber through a relatively short needle and to expel pressurized air from the interior of the needle assembly, thereby providing a vein. It would be particularly desirable to have a direct indication of successful puncture of the assem bly and no leakage of blood from the assembly. As used herein, ventilation media refers to ele ments that actually allow air to pass, such as plugs, coatings, surface treatments, and the lik e. Means

for Solving the Problems

SUMMARY OF THE INVENTION The present invention is a self-venting blood collection needle assembly for extracting at least one fluid sample into a vacuum vessel for clinical testing, the blood collection needle assembly providing visual confirmation of a successful venipuncture by the user. Provide a transparent or translucent flashback chamber for viewing by This self-venti ng mechanism allows the release of air during use, but prevents the escape of liquids such as blood. Venting mechanism, as used herein, refers to one or more devices or elements that all ow air to escape but prevent the passage of liquids. Thus, air under venous pressure can be e xpelled from the blood collection needle assembly by the time it reaches the venting mechanis m. The venting mechanism then blocks or prevents the flow of blood around or through it, all owing blood to be collected into a vacuum collection tube or other suitable blood collection co ntainer. The present invention provides good instant visualization within the flashback chambe r without adversely affecting the blood collection process. There are a variety of suitable vent mechanisms, vent media or vent locations, as described below.

[0009]

A self-venting blood collection needle assembly is provided for drawing at least one fluid sam ple from a patient and subsequently expelling it into at least one vacuum vessel. The self vent ed blood collection needle assembly of the present invention includes a hub having a fluid inle t defined by a cylindrical outer wall. The wall defines a flashback chamber for retaining the blo od sample within the hub and at least a portion of the wall being transparent or translucent so that the jet is visible from the outside. The hub further has a fluid outlet end communicating with the fluid inlet end. A first inlet cannula in fluid communication with the blood inlet end ex tends outwardly therefrom. The first cannula has an inner proximal end located at the proxim al end of the chamber and an opposite outer distal end adapted to puncture a patient's vein. Similarly, a second non-patient exit cannula is disposed in fluid communication with the fluid e xit end and extends outwardly therefrom. The second non-patient cannula has an inner distal end positioned proximal to the first inner end and further includes an outer proximal end oppo site the second inner end. The second non-patient outer proximal end is configured to pass th

rough a pierceable stopper of a vacuum vessel. The second patient cannula further includes a sealable multiple sample sleeve. However, a single cannula containing a notch could be used i nstead of two cannulas. Another alternative cannula configuration is to use a single cannula wi thout a notch to pass through the proximal end of the non-patient cannula, around multiple s ample sleeves and through a vent before flashback occurs. there is The outer portion of the h ub near the proximal end is formed with a single external thread, or other mounting structur e, for receiving blood.

A collection needle assembly can be attached to a collection tube holder or other medical devi ce. Alternatively, the holder can be pre-attached to the needle assembly.

[0010]

In one embodiment, the venting mechanism is located in the flashback chamber of the hub. The use of the double cannula type construction or the notched single cannula is suitable for t his configuration. The vent mechanism thereby communicates the fluid passageway with the o utside atmosphere via the hub.

In another embodiment, a venting mechanism is placed over the proximal end of the non-pati ent cannula which

allows air to pass through the proximal end of the non-patient cannula from which blood is a spirated and then through the vent. means to pass. A single cannula without a notch is suitabl e in this case, but any cannula construction can be used. Specifically, air flows through the sp ace between the outside of the needle and the multiple sample sleeve and exits the fluid pass ageway out the proximal end of the non-patient cannula. The air is then directed to the non-p atient locking lug, non-patient hub threads, non-patient hub body, multiple specimen sleeves, or other location beyond the proximal end of the non-patient cannula. or through vents in any combination of these locations. A collection tube attached to the proximal end of the non-pati ent cannula draws blood only from the fluid passageway and not from the vented space. This embodiment thus allows blood to flow through the entire collection passageway. This also pre vents contact of the blood sample with the vent, which could potentially lead to platelet activa tion or contamination or other undesirable consequences. This also prevents air from being dr awn back into the fluid passageway when a vacuum tube is installed. It should also be noted t hat this embodiment requires a smaller ejection chamber than the previous embodiment in w hich the vent is located in the hub.

[0012]

Another embodiment of the invention has a venting mechanism comprising an integral hub a t least partially formed of a porous material such as sintered plastic, ceramic or metal. This po rous material either before air enters the non-patient cannula or after air exits the proximal e nd and flows through the non-patient cannula into the space between the cannula and the mu ltiple sample sleeve. can be arranged so that the evacuation takes place at the same time. Th e porous material allows air to pass through but prevents blood from leaking. In typical embo diments, this porous material is hydrophobic. Porous materials further include materials that s

well when wet. Other venting methods are possible. The walls of the internal passageway may be coated with a sealant to prevent contamination of the blood sample with porous material. This embodiment allows blood to flow over the entire collection path. If desired, the hub can b e permanently joined to the tube holder to eliminate the need and inconvenience of a threade d connection. Bonding to this holder can be accomplished by solvent, welding, heat, pressure or other suitable means, or a combination thereof. A device integrated in this way can be man ufactured efficiently, and the holder can be discarded together with the needle, thereby increa sing the safety of medical procedures.

[0013]

In yet another embodiment, the vent mechanism vents air out through a side opening locate d in the hub, the opening being shaped to be mechanically retained in or against the opening. covered by a breathable material having This venting material is preferably hydrophobic and t he surface tension is also such that it prevents leakage. The vent media material of this embo diment preferably has a resilient nature and shape so that the energy of the spring holds the vent material against the device. For example, a C-shaped vent medium can be used where t wisting of the shape requires the vent medium to extend over the receiving structure on the h ub. When the vent media is placed on the support structure, it releases and uses its own elast icity to hold it in place without any bonding material such as epoxy that could be absorbed by the vent media and adversely affect it. be done. The venting mechanism of this embodiment may first compress the venting material, place the material in the opening, and then release t he venting material to expand within the opening. BEST

MODE FOR CARRYING OUT THE INVENTION

SUMMARY OF THE INVENTION The present invention is a self-venting blood collection needle assembly with a self-venting mechanism that prevents the escape of fluids such as blood and aids in the release of air, which draws blood or other fluids from a patient through one or mor e vacuum tubes. An assembly is provided that provides a visual indication of vascular insertio n ("flashback") as it is drawn into a blood collection tube. The aeration medium may be a se parate physical element, such as a plug or insert, or an integral part of the device, treated, su ch as by laser drilling, or made wholly or partially of a porous material, or impregnated, for ex ample

.

Note that it may be a film, layer, etc., formed by depositing the material on the device by, coa ting, spraying, or the like.

A blood collection needle assembly according to

one embodiment of the present invention is shown in FIG. The needle assembly 10 includes a hub 12 that carries a fluid entry needle (first cannula) 36 on one side and a fluid exit needle (second cannula) 52 on the opposite side. Fluid withdrawn from the first cannula passes throu gh the hub 12 and is immediately visible in the flashback chamber through the translucent wi

ndow 100, and with the aid of the venting mechanism, at the appropriate time that a proper v essel puncture has occurred. give proper instructions.

[0017]

Figures 2-28 illustrate various embodiments of the present invention including various config urations of venting mechanisms in blood collection needle assemblies. In particular, Figures 2, 3, 4A, 4B and 4C show embodiments in which the venting mechanism is located on the hub p ortion. Figures 5-12 show embodiments in which the venting mechanism is located beyond th e proximal end 60 of the non-patient cannula. Figures 13 and 14 show an embodiment in whic h a portion of the hub of the needle acts as the vent medium. FIG. 15 shows an embodiment i n which the venting mechanism is a unified hub 132 . Figures 16-26 show embodiments in wh ich the ventilation mechanism is a breathable cord. Figures 27A and 27B show an embodimen t in which the vent mechanism is a check valve. Figure 28 shows an embodiment with a single notched cannula. Note that in each of the two cannula embodiments below, a single notched c annula can be used as well.

FIGS.

2, 3, 4A, 4B and 4C illustrate a venting mechanism in which a venting ring 300 is placed aro und the proximal end 301 of first cannula 36. FIG. This vent ring forms an interference fit with the inner wall of flashback chamber 302 . Therefore, air can escape from the ventilation openi ngs 303 to the outside atmosphere through this ventilation ring. These openings can be locate d anywhere on the distal end of the hub. 2 and 3, these openings are located at the distal end of hub 304. FIG. 4A, 4B and 4C show another embodiment in which the vent openings are lon gitudinal vent windows 305 that abut the distal side of the vent ring 300. FIG.

[0019]

Some embodiments include a venting mechanism located beyond the proximal end 60 of the non-patient cannula. This venting mechanism uses a smaller flashback chamber 22a and redu ces the amount of air exhausted from the hub assembly 12 compared to the previous embodi ments such as FIGS. 2, 3, 4A, 4B, 4C. It is advantageous for The next embodiment uses a lar ger annular flange 68a to create a smaller flashback chamber 22a, although other designs are possible. Examples of these designs are a window of translucent/transparent material near th e surface of the hub and/or part of the flashback chamber for better visibility of the flash. Not e that a flashback chamber or window can be placed in the air/blood passageway, especially f or embodiments using a single cannula without a notch. In the embodiment of FIG. 5, air flo ws from the fluid passageway 306 to the proximal end 60 of the non-patient cannula and thro ugh the space 307 between the outside 308 of the needle and the inside of the multiple sampl e sleeve 61 to the non-patient cannula

.

It reaches the position of a vent hole 309 consisting of a locking projection 310 on the patient side and a vent plug 311 that allows air to escape but prevents blood or other fluids from esca ping to the outside atmosphere.

6, 7, 8A, 8B, 9A, 9B, 10A and 10B illustrate embodiments in which the venting mechanism is located beyond the proximal end 60 of the non-patient cannula . is shown. The embodiment o f Figures 6 and 7 shows a vent plug 312 that also functions as at least part of the non-patient side locking projection. As shown in these figures, in both embodiments, at least a portion of t he vent is close to the exterior through which air is exhausted. 8A and 8B show an embodime nt in which the notch 313 in the non-patient locking projection 314 is configured to allow air t o escape to the vent disc 315. FIG. 9A and 9B show another embodiment in which the notch 3 16 in the non-patient locking projection 314 contains a vent plug 317. FIG. 10A and 10B show a non-patient locking projection 318 configuration in which the ventilation sleeve 319 is modifi ed to allow air to escape. In each embodiment, the venting mechanism (and similar elements described herein) allows air to escape, but prevents blood or other fluids from escaping to the outside atmosphere.

FIG.

11 shows another embodiment of a venting mechanism located beyond the proximal end 60 of the non-patient cannula. According to this embodiment, air is vented through the material of the multiple sample sleeve 320 itself which prevents fluid from exiting the non-patient cann ula 52 . The multiple sample sleeve 320 maintains its normal function of being pierced by the sharpened proximal end 60 of the non-patient cannula 52 in response to the force created by the vacuum tube stopper. A multiple sample sleeve 320 can be made that also functions as a vent by forming the sleeve from a porous, hydrophobic material such as those previously desc ribed.

[0023]

12 shows that air passes through narrow passage 353 between the outside of non-patient ne edle 52 and non-patient locking projection 354 and then between base 64 and annular flange 68 to contain vent medium 357. Another embodiment is shown in which it enters the reservoi r 355 of the hub 356 and is discharged to the outside atmosphere via a passageway 358 at th e interface 80 between the hub 356 and the base 64 of the non-patient hub. A hub insert 359 forms a reservoir 355 .

FIGS.

13 and 14 illustrate a venting mechanism in which hub 321 or non-patient threaded assembl y 322 is made of a porous material and thus acts as a venting medium. FIG. 13 shows hub 32 1 as a venting medium for venting air through ramp 28 of hub 321 and out of annular groove 26 into the surrounding atmosphere. FIG. 14 shows a non-patient threaded assembly 322 as a venting medium. This embodiment allows air to pass through the wall of the flashback cham ber 22a and then out through the non-patient side locking projection 324 .

FIG .

15 is made of a porous material venting medium that allows air to escape through the wall o f the annular groove 26 and the flashback chamber 22a and through the fluid passageway 30

6 and out the proximal end 60 of the non-patient cannula. The venting mechanism is shown t o be an integral one-piece hub 325 with the air further passing through the space 307 betwee n the outside of the needle 308 and the inside of the multiple specimen sleeve 61 and then th rough the non-patient locking projections 326 . through and into the surrounding atmosphere. Due to the integral nature of the hub 325, this holder is not threaded and can be pre-attached to the hub 325 by bonding. However, threads may be provided if desired, as shown. Solvents, welding, heat, pressure, other conventional means or combinations thereof are used to bond t he tube holder to the integral non-patient hub 325 .

FIG.

16 illustrates the venting mechanism of a breathable ventable cord 326 located between the inside of the sealing surface of multiple sample sleeve 61 and the non-patient locking projecti on 327 . Due to the cord being placed on the sealing surface, air is evacuated from the space 307 between the outside of the needle 308 and the outside of the multiple sample sleeve 61, but only through the nature of the material of the cord and/or the passageway formed by the cord. The very small dimensions of the prevent fluid leakage

. Venting using this mechanism is accomplished by positioning a venting medium (eg, placem ent, coating, treatment, etc.) between any one or more of the sealing surfaces along the fluid path 306 . Figures 17-26 show cross-sections of cords with suitable breathability. Other shape s and combinations of these shapes are also available. The cord is made by extruding, spinnin g or the like and is advantageously coated with a hydrophobic coating such as wax.

[0027]

In other embodiments, the venting mechanism uses a check valve located anywhere along t he fluid passageway. This valve allows air to pass through but closes when a vacuum is applie d, so when a vacuum collection tube is attached to the tip of the needle, this tube will draw bl ood from the fluid passageway, but not air. Figures 27A and 27B show an example of a check valve. The venting mechanism may be located at any point or points along fluid passageway 3 06 , but is preferably located at hub 328 . The valve 349 itself may be a thin flap such as a pl astic film 350 covering the vent, a seal such as a deformable rubber, or a plastic duckbill type valve, a deformable wrap over the vent, or any other means. or a combination thereof. This v alve 349 is located either proximally or distally to the vent. In the embodiment shown in FIG. 27B, a thin plastic film valve 349 is attached to hub 328 along one sealed edge of film 351 an d is pulled out of fluid passageway 306 by venous pressure during an initial venipuncture. Air i s pushed through the porous vent plug 352 and out under the free edge of the plastic film 34 9 . However, when a vacuum is applied to the fluid passageway 306 (via the blood collection t ube attachment), the thin plastic film 349 sucks tightly against the porous vent plug 352, seal ing the vent to keep air out. Prevents re-entry into the fluid passageway. Thus, this embodime nt serves the primary or backup function of preventing air from re-entering the system after e vacuation has taken place.

[0028]

FIG. 28 shows a blood collection needle assembly with a single cannula 360 and a vent plug 361 that serves as a non-patient locking projection. This cannula 360 is positioned in bore 34 such that bore 365 of cannula 360 is provided at the location of annular groove 26 and remai ns in fluid communication therewith. When cannula 360 is properly positioned, it frictionally e ngages hole 34 or is secured thereto, such as by adhesive. During venipuncture, air flows fro m fluid passageway 306, exits proximal end 362 of cannula, and flows into space 307 betwee n the outside of needle 363 and the inside of multiple sample sleeve 61 to vent plug 361. .
As will be appreciated by those skilled in the art, it

is possible to combine more than one vent mechanism in one device, and to attach the same vent mechanism to one location in one device. Additionally, any of a variety of venting media may be used in the venting mechanism of the present invention. Moreover, the venting mecha nisms described herein are applicable to various devices other than blood collection needle as semblies. Venting media, as used herein, include, for example : a generally hydrophobic sub strate or carrier coated, impregnated, or containing a hydrophilic material that swells on conta ct with water-soluble or water-containing substances
; A porous plug formed of a material whose swellable properties provide a sealing function to the vent when in contact with blood; Matte finish, micro-sized passages, laser drilled holes, to rtuous passages ; vent holes provided by a porous material or holes, gaps or passages large e nough to allow air to pass but small enough to prevent blood leakage, e.g. provided between sealing surfaces in the cord;

A porous plug that closes when in contact with blood, using biological phenomena such as coa gulation and/or cell agglutination to block the vent, or a super plug that seals the vent by swe lling on contact with aqueous fluids
. Absorbent material; or
Check valves: thin flaps such as plastic films covering vents, deformable seals such as rubber or duckbill type valves, or deformable wraps covering vents.
or combinations thereof. Preferably, the porous plug is coated with, impregnated with, or con taining a hydrophilic material such as carboxymethylcellulose (CMC) or polyacrylate, or a hydr ophobic material such as high density polyethylene (HDPE)
.
formed by Alternative hydrophobic materials include, but are not limited to, polytetrafluoroeth ylene (PTFE), ultra high molecular weight polyethylene (UHMPE), nylon 6, polypropylene (PP), polyvinylidene fluoride, or polyethersulfone. (PES). As will be described in further detail belo w, the venting media of the present invention are suitable for venting mechanisms and device s, including one or more micro-dimensioned matte-finished passages, laser-drilled holes, vent able Cords, superabsorbent check valves, or other means, or any combination thereof, may al

ternatively be used. Thus, although any particular venting medium, such as, for example, a pl ug, is referred to herein, it is intended to be non-limiting and to include other suitable membe rs of venting media.

[0032]

One embodiment of the venting media consists of micro-sized holes formed in the outer wal l. These holes are large enough to allow air to pass, but small enough to prevent blood leakag e. The vent can be any number, including one, but multiple holes are preferred for reliable fun ction. These holes are laser drilled, ie they are burned through the wall using one or more las er beams. The substrate can be any common material, but a thin plastic film is preferred. The venting mechanism can include a check valve as previously described. This venting mechanis m may be located at any convenient space along the fluid passageway within the syringe or p atient cannula, hub, or additional component, but to produce a flush along the entire length of the tube, , is preferably provided at the proximal end.

[0033]

Porous plugs that are sealed by biological phenomena when in contact with blood use porous materials such as sintered plastics, ceramics, or metals, or use breathable cords, or have sma ll pores between parts. or by placing a biological agent in the space. The vent may be of any c onventional shape. Venting may occur at any location(s) in the fluid passageway, but preferab ly at the proximal end, such as the hub, close to the collection device. The vent is made of an d includes a stimulant that interacts with blood to promote clotting and/or cell clumping such t hat clotted and/or congealed cells inhibit flow through the vent. , preferably adjacent to or co operating with. Examples of clotting stimulants are silica, crushed glass, or glass fibers. One e xample of a glue is a lectin. Examples of platelet activators are collagen or thrombin. Neutraliz ing agents for anticoagulants such as protomin sulfate may be included. The biological stimula nt can be applied as a powder, solution, suspension, slurry, or other form using any convenien t process. It may be dried or vacuum freeze dried. Various other changes and modifications can be made by those skilled in the art without departing from the scope or spirit of this inven tion, all of which are intended to be within the scope of the invention

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is intended as

BRIEF DESCRIPTION OF THE DRAWINGS

[0035]

FIG. 1 is a perspective view of a blood collection needle assembly;

2 is a cross-sectional view of another embodiment of the blood collection needle assembly of t he present invention; FIG.

3 is a side sectional view similar to FIG. 2, but showing another embodiment of the invention; FIG.

4A is a side cross-sectional view similar to FIG. 2, but showing another embodiment of the pr esent invention; FIG.

4B is a side view of FIG. 4B; FIG.

4C is a front view of FIG. 4BA looking in the direction of RR; FIG.

5 is a cross-sectional view of one embodiment of a blood collection needle assembly; FIG.

FIG. 6 is a cross-sectional view similar to FIG. 5, but showing another embodiment of the inve ntion;

FIG. 7 is a cross-sectional view similar to FIG. 5, but showing another embodiment of the inve ntion;

8A is a cross-sectional view similar to FIG. 5, but showing another embodiment of the inventi on; FIG.

8B is a front view of FIG. 8A looking in the direction XX; FIG.

9A is a cross-sectional view similar to FIG. 5, but showing another embodiment of the inventi on; FIG.

9B is a front view of FIG. 9A looking in the direction YY; FIG.

10A is a cross-sectional view similar to FIG. 5, but showing another embodiment of the invent ion; FIG.

10B is an enlarged view of FIG. 10A viewed from area Z; FIG.

FIG. 11 is a cross-sectional view of one embodiment of a blood collection needle assembly;

FIG. 12 is a cross-sectional view of one embodiment of a blood collection needle assembly;

FIG. 13 is a cross-sectional view of one embodiment of a blood collection needle assembly;

FIG. 14 is a cross-sectional view of one embodiment of a blood collection needle assembly;

15 is a cross-sectional view of one embodiment of a blood collection needle assembly; FIG.

FIG. 16 is a cross-sectional view of one embodiment of a blood collection needle assembly;

FIG. 17 is a cross-sectional view of one embodiment of a ventable cord;

FIG. 18 is a cross-sectional view similar to FIG. 17 but showing another embodiment of the in vention;

Figure 19 is a cross-sectional view similar to Figure 17 but showing another embodiment of th e invention;

Figure 20 is a cross-sectional view similar to Figure 17 but showing another embodiment of th e invention;

Figure 21 is a cross-sectional view similar to Figure 17 but showing another embodiment of th e invention;

Figure 22 is a cross-sectional view similar to Figure 17 but showing another embodiment of th e invention;

Figure 23 is a cross-sectional view similar to Figure 17 but showing another embodiment of th e invention;

FIG. 24 is a cross-sectional view similar to FIG. 17 but showing another embodiment of the in vention;

Figure 25 is a cross-sectional view similar to Figure 17 but showing another embodiment of th e invention;

Figure 26 is a cross-sectional view similar to Figure 17 but showing another embodiment of th e invention;

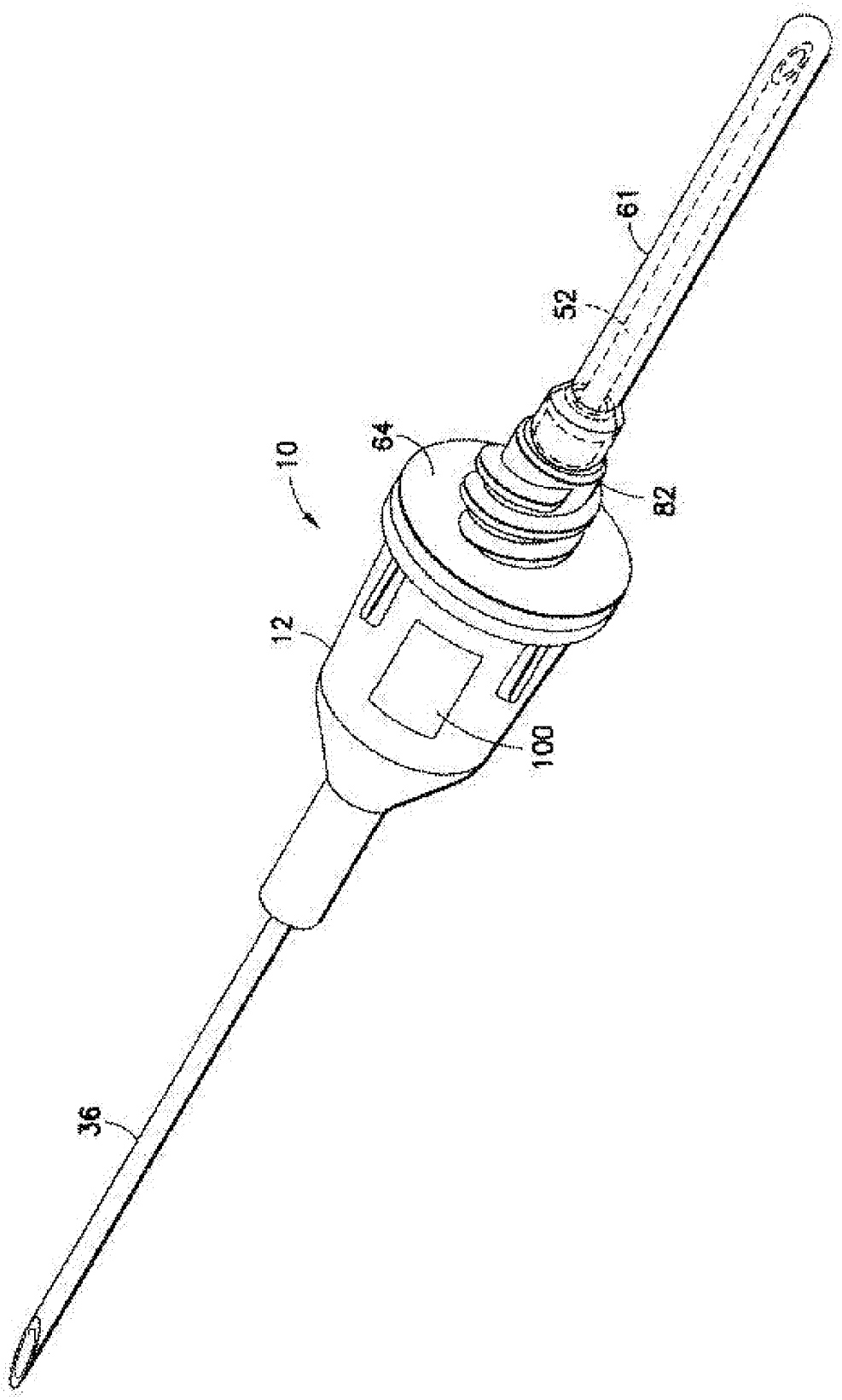
Figure 27A is a cross-sectional view of one embodiment of a blood collection needle assembly;

27B is an enlarged view of FIG. 27A viewed from region R; FIG.

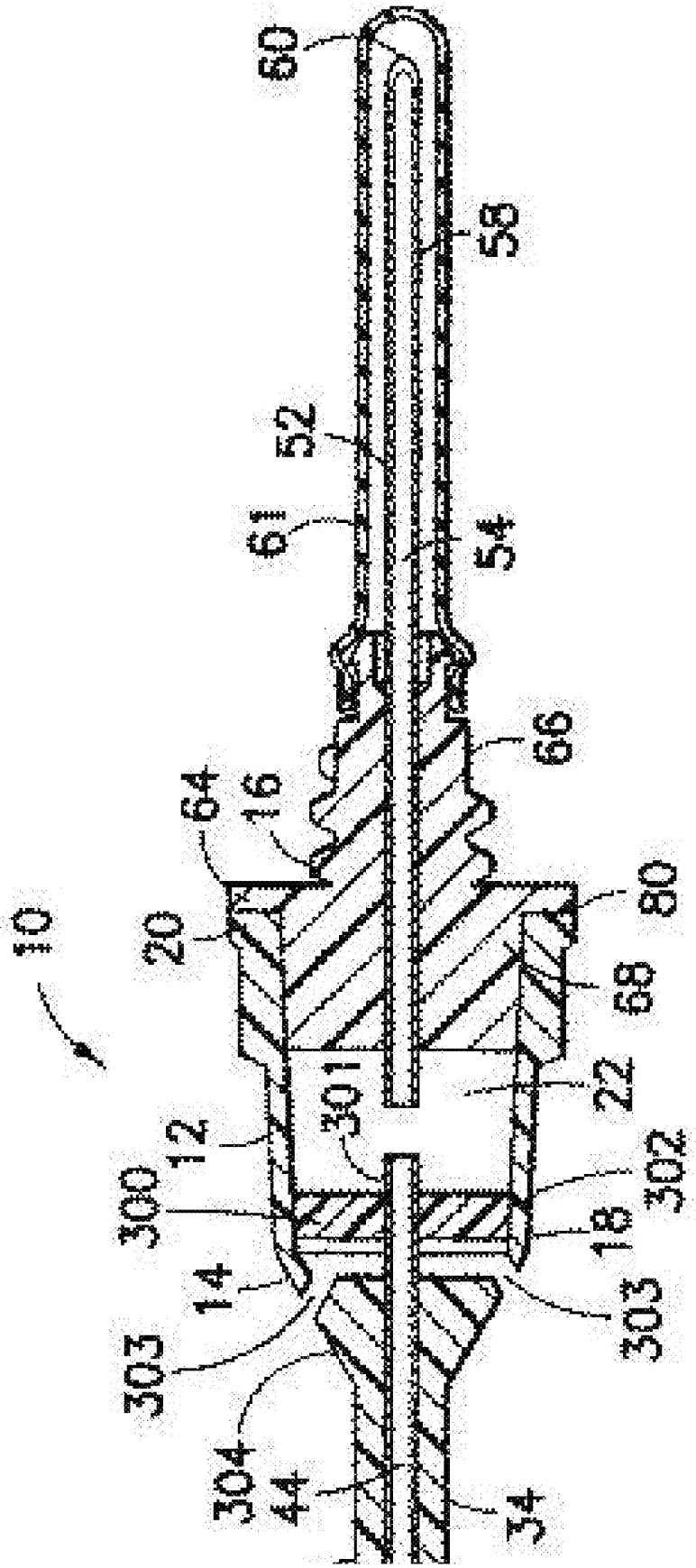
Figure 28 is a cross-sectional view of one embodiment of a blood collection needle assembly;

drawing	open ----

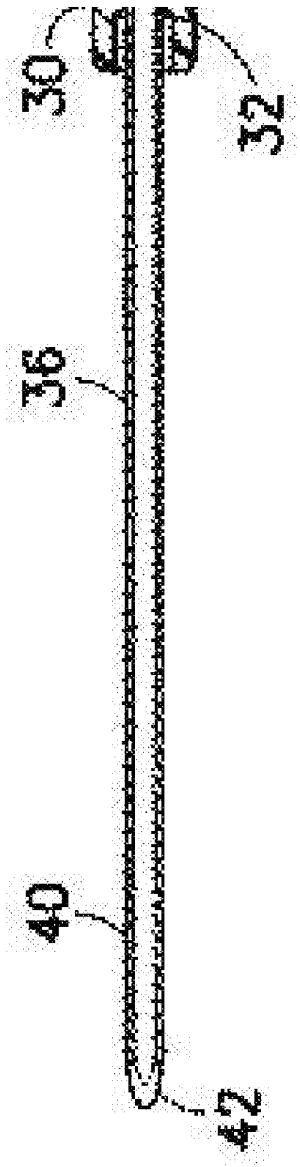
[Fig. 1]

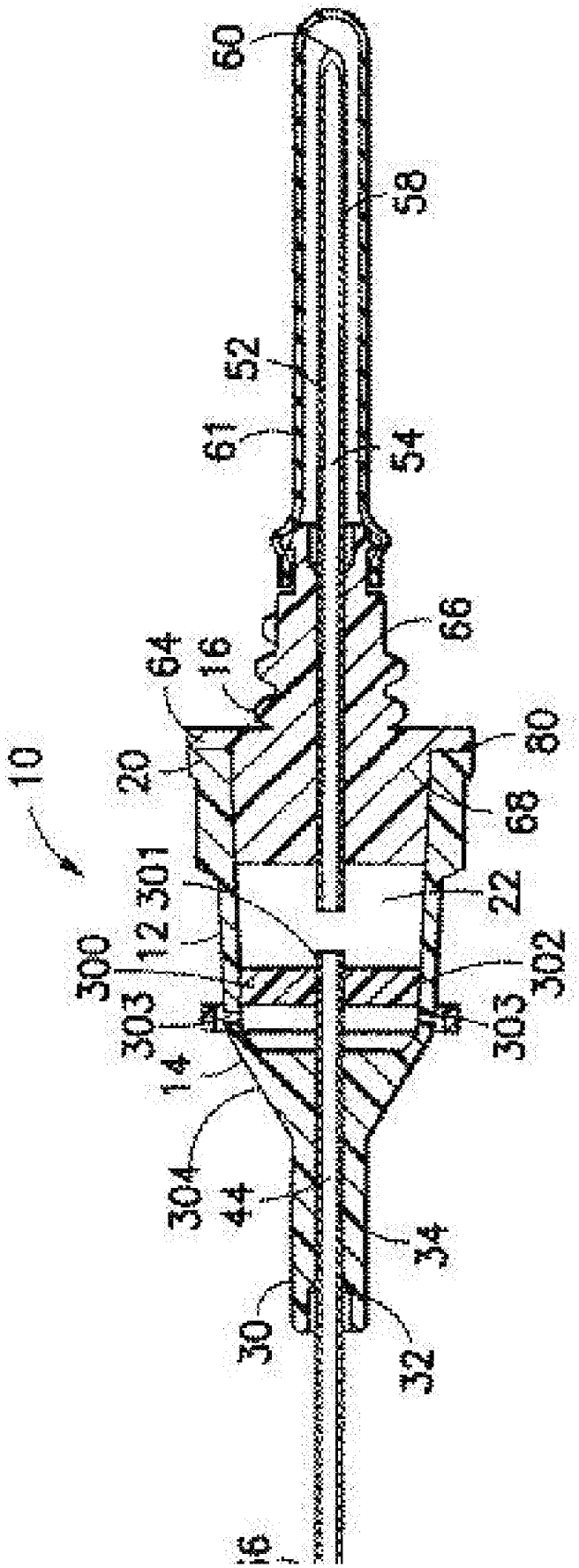


[Figure 2]

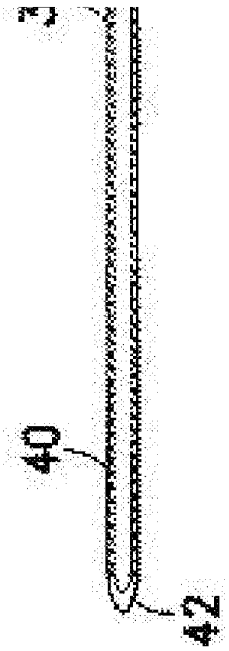

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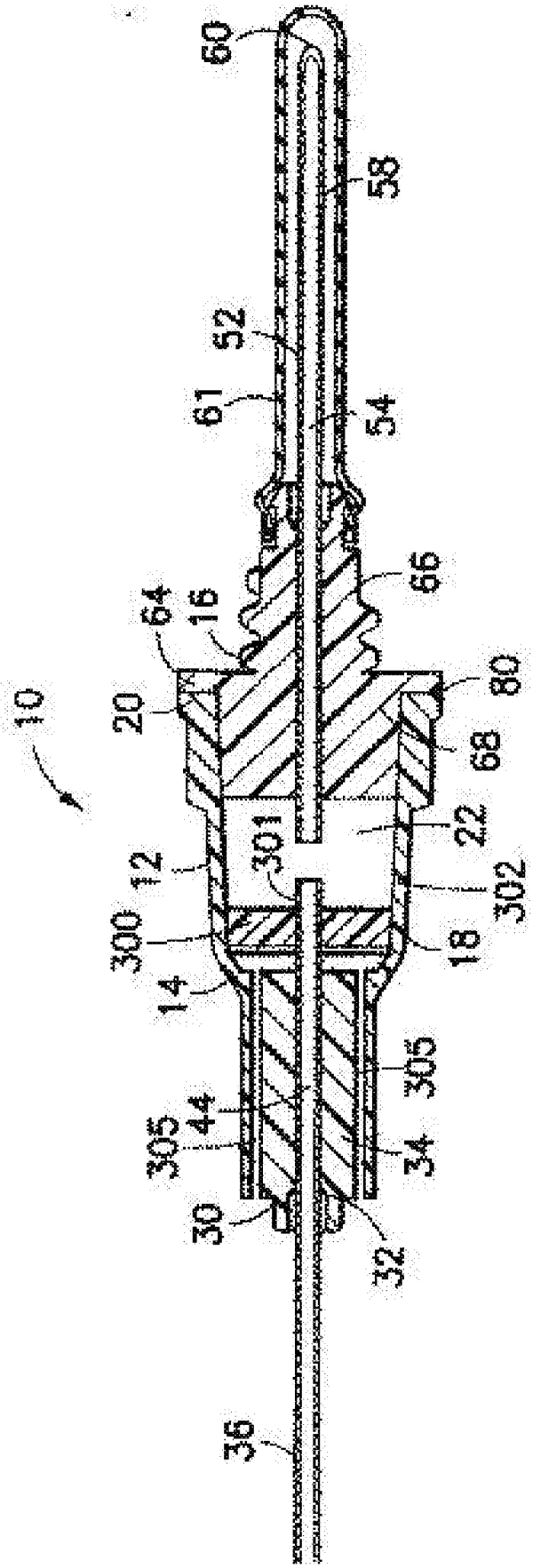
[Figure 3]



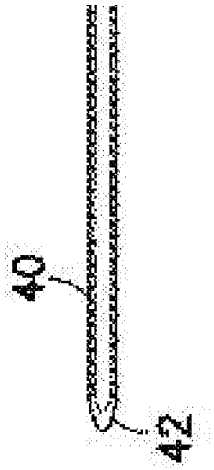

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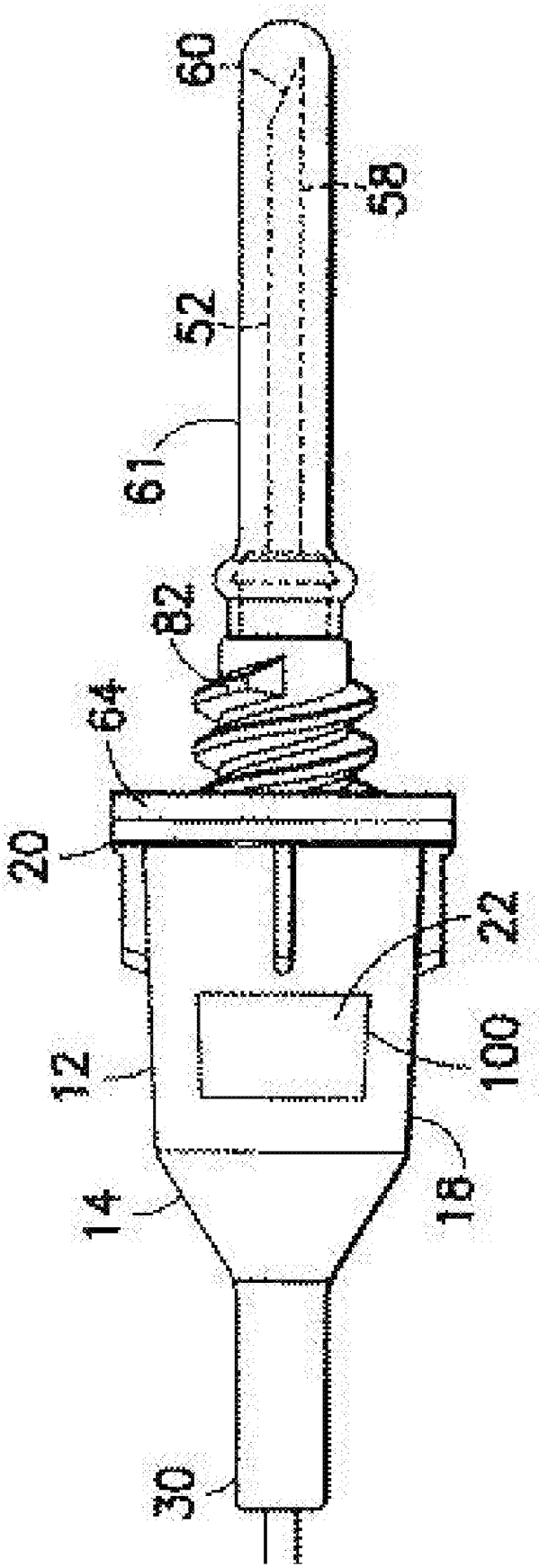
[Fig. 4A]



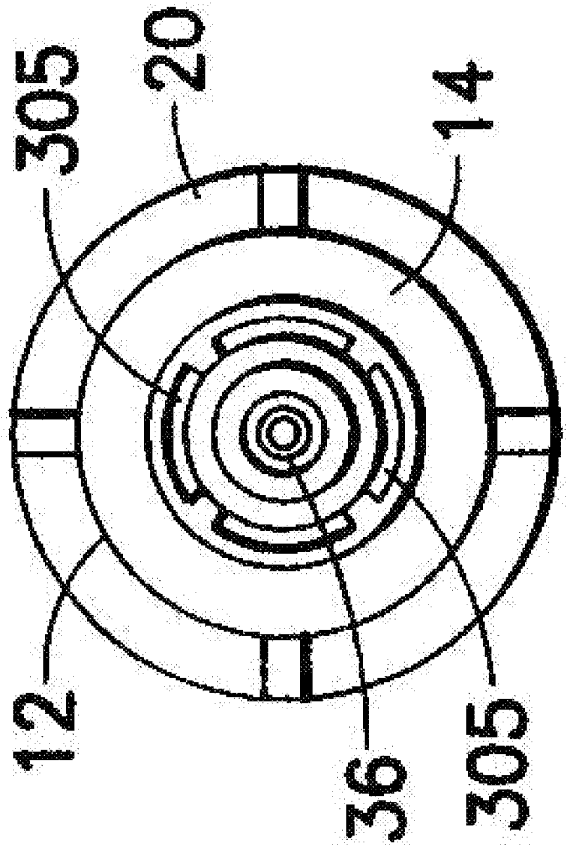

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[Fig. 4B]

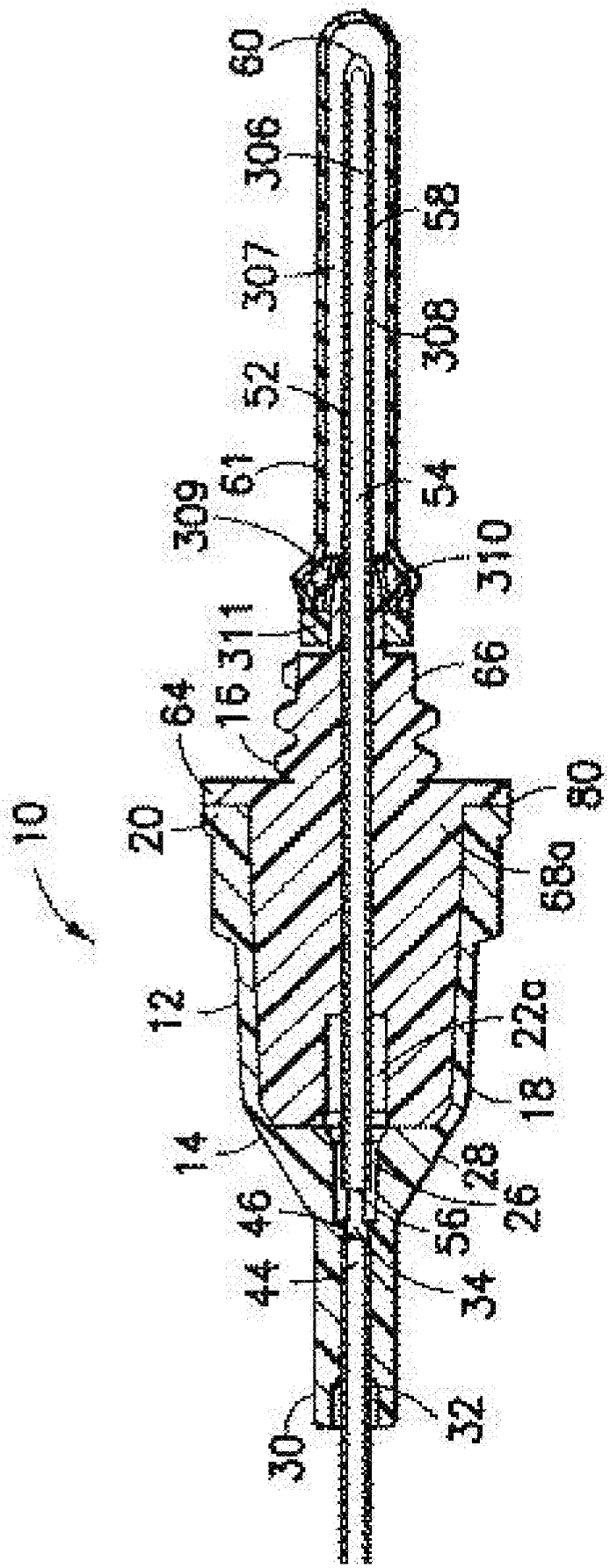



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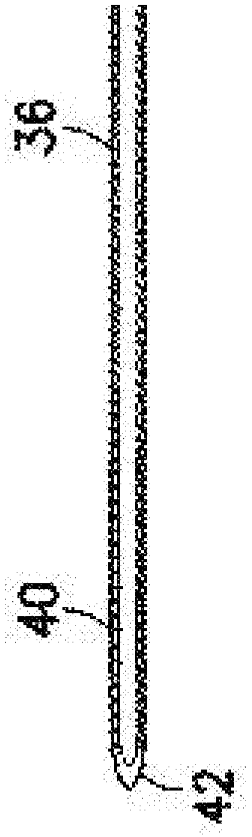
[Fig. 4C]

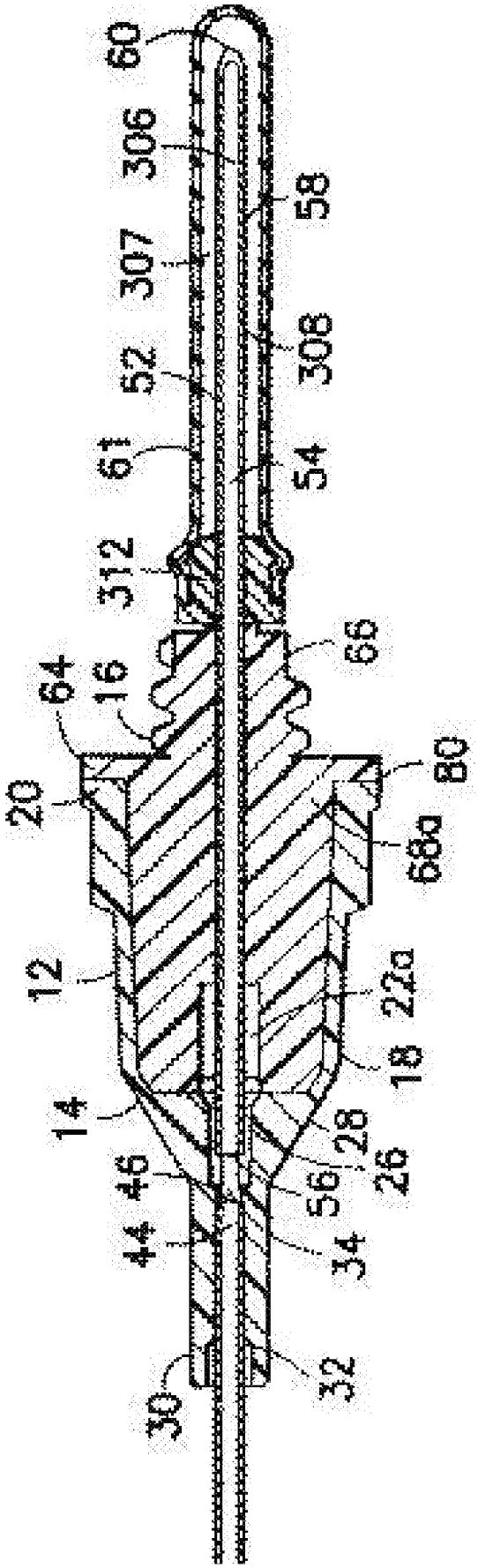


[Figure 5]

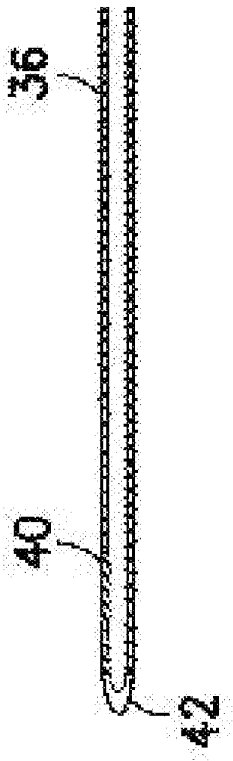

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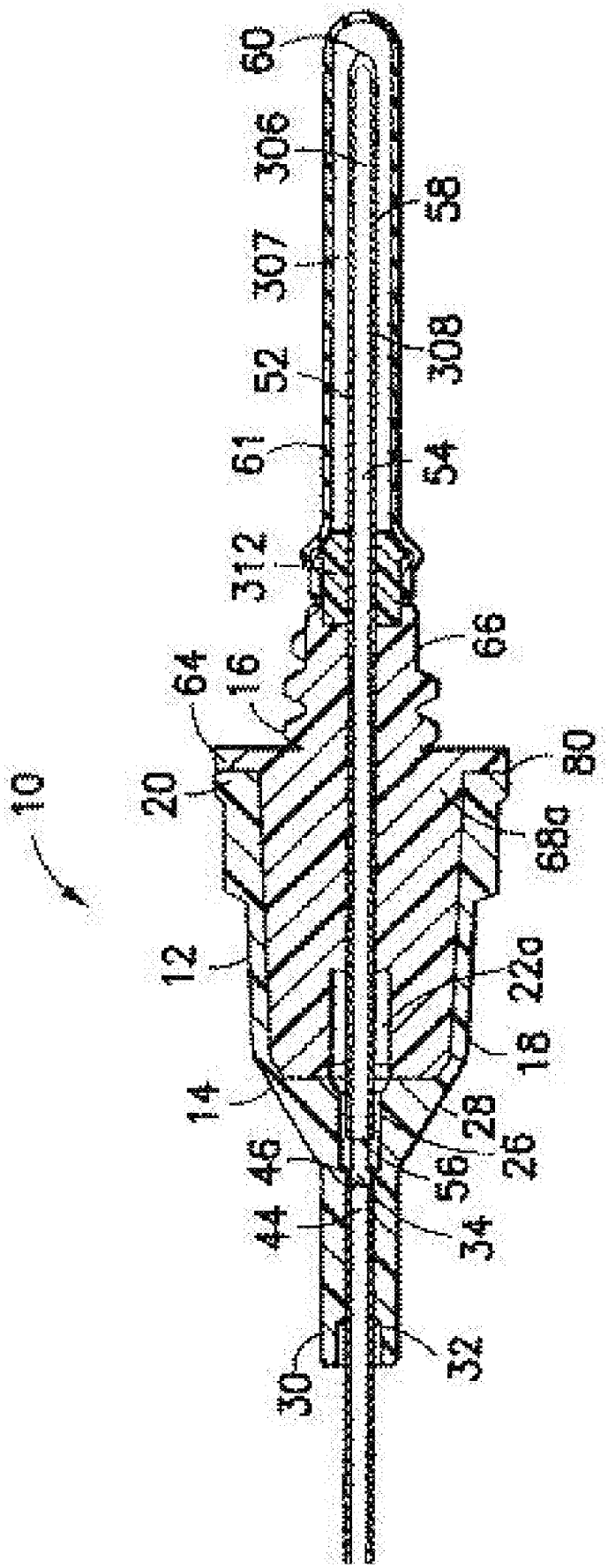
[Fig. 6]



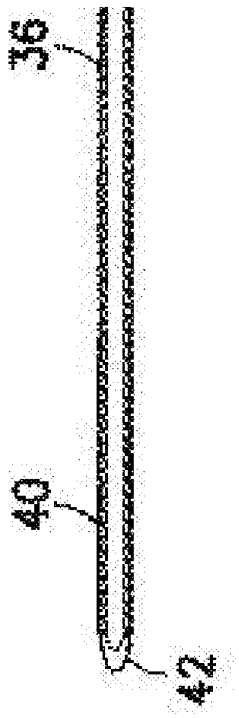

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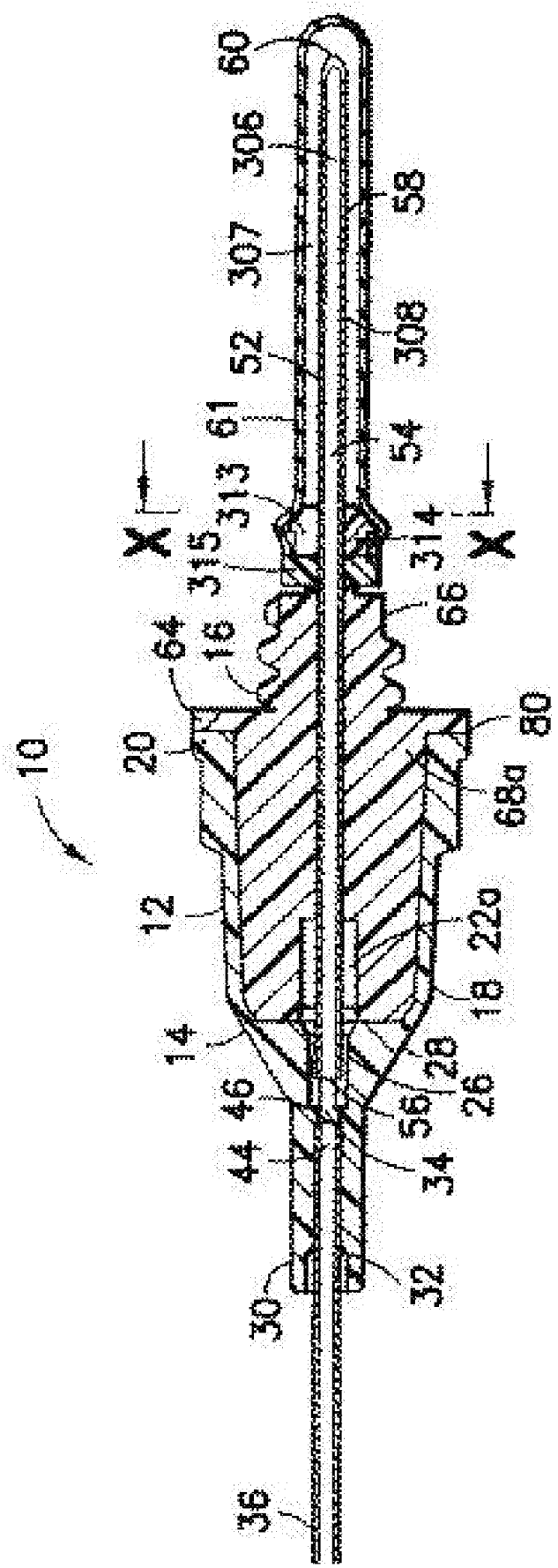
[Fig. 7]



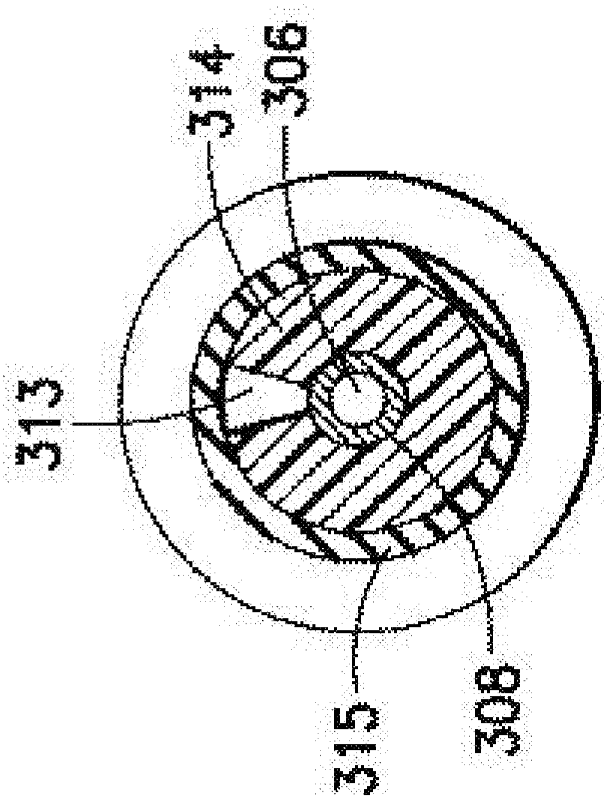

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[Fig. 8A]

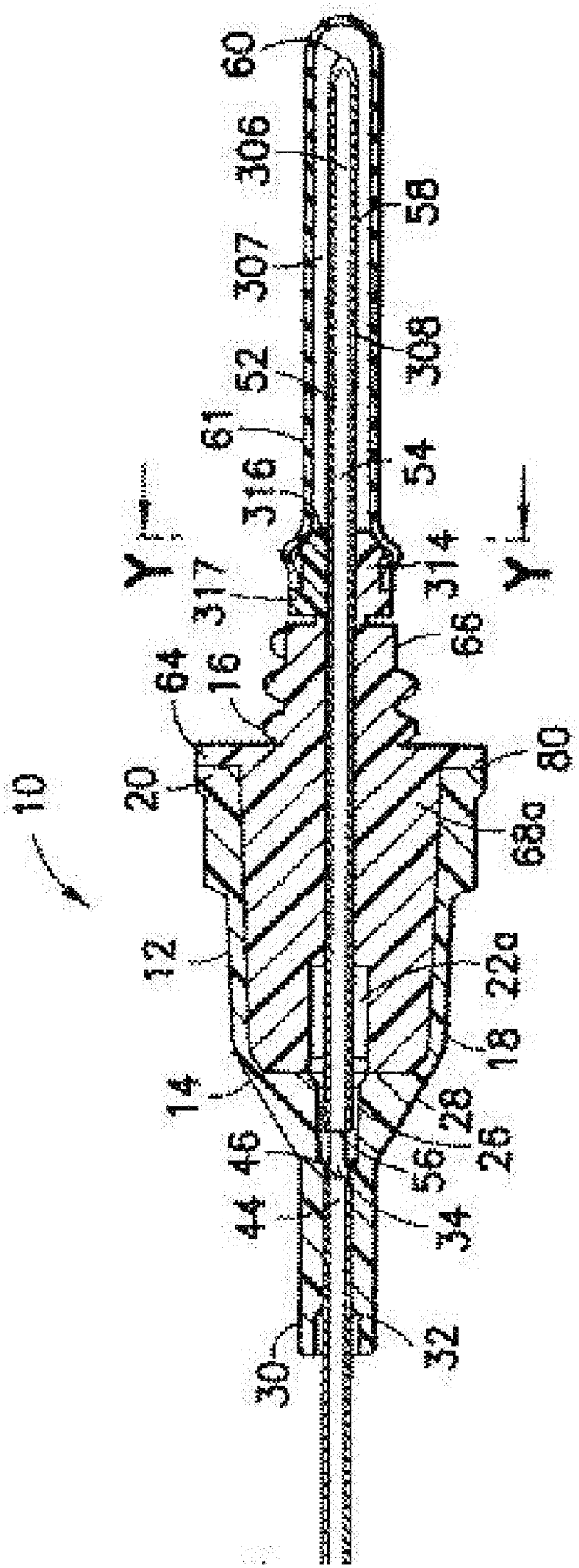



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[Fig. 8B]

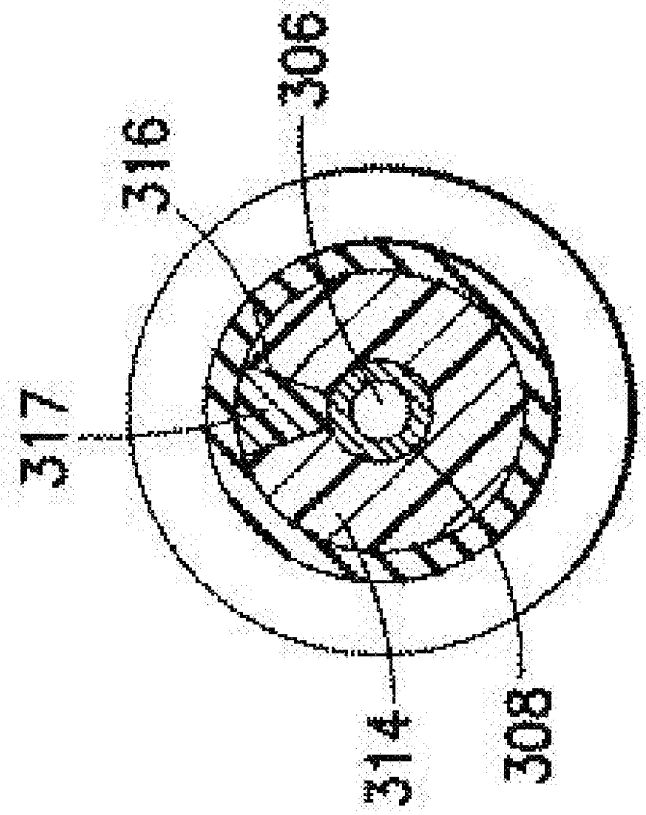


[Fig. 9A]

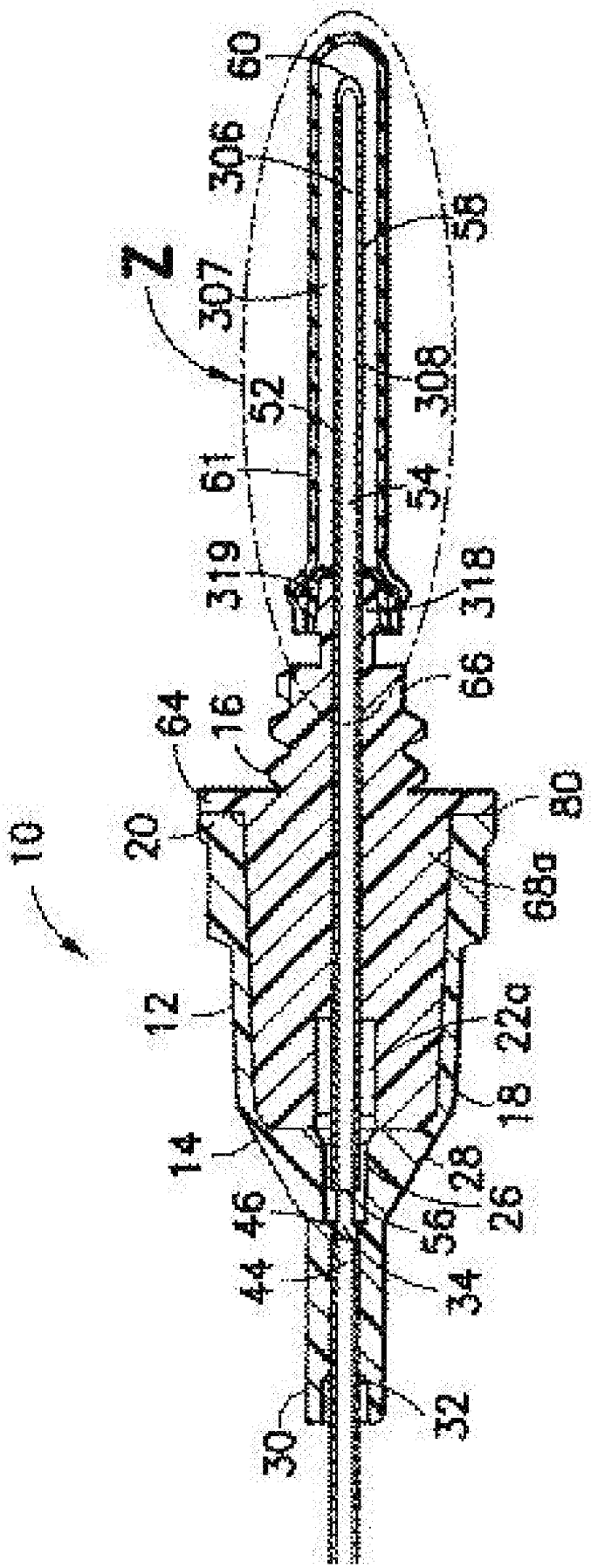

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[Fig. 9B]

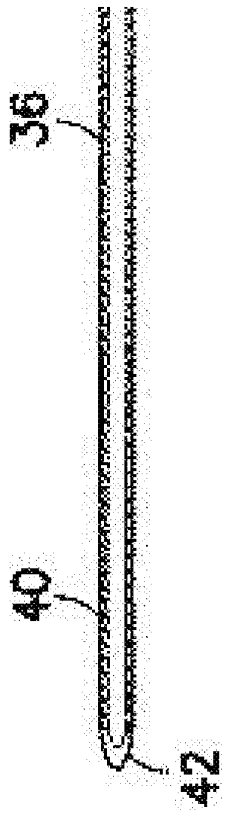


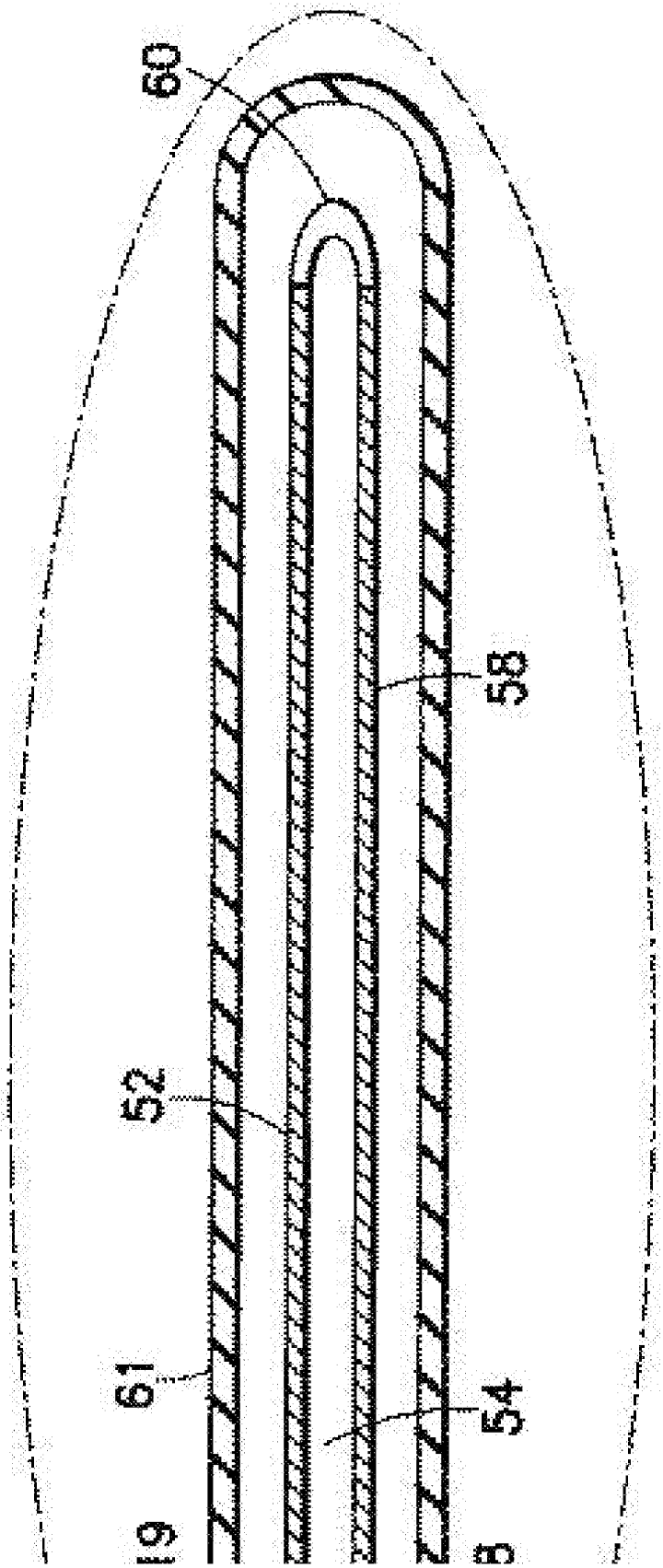


[Fig. 10A]

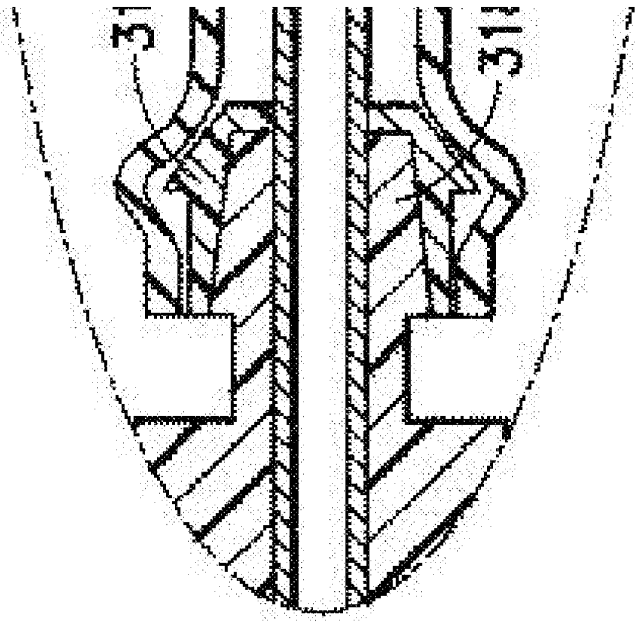

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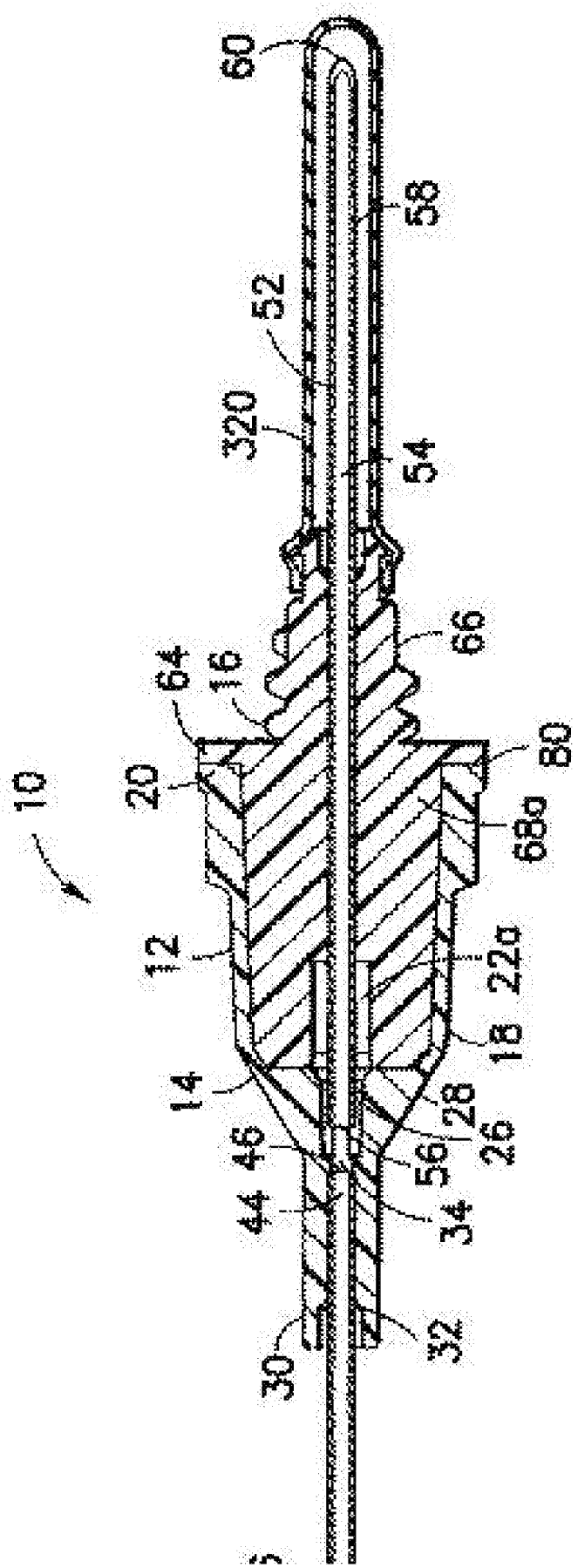
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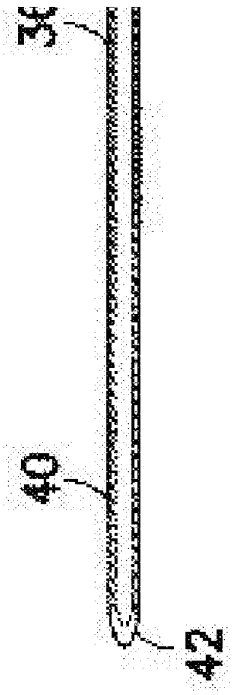

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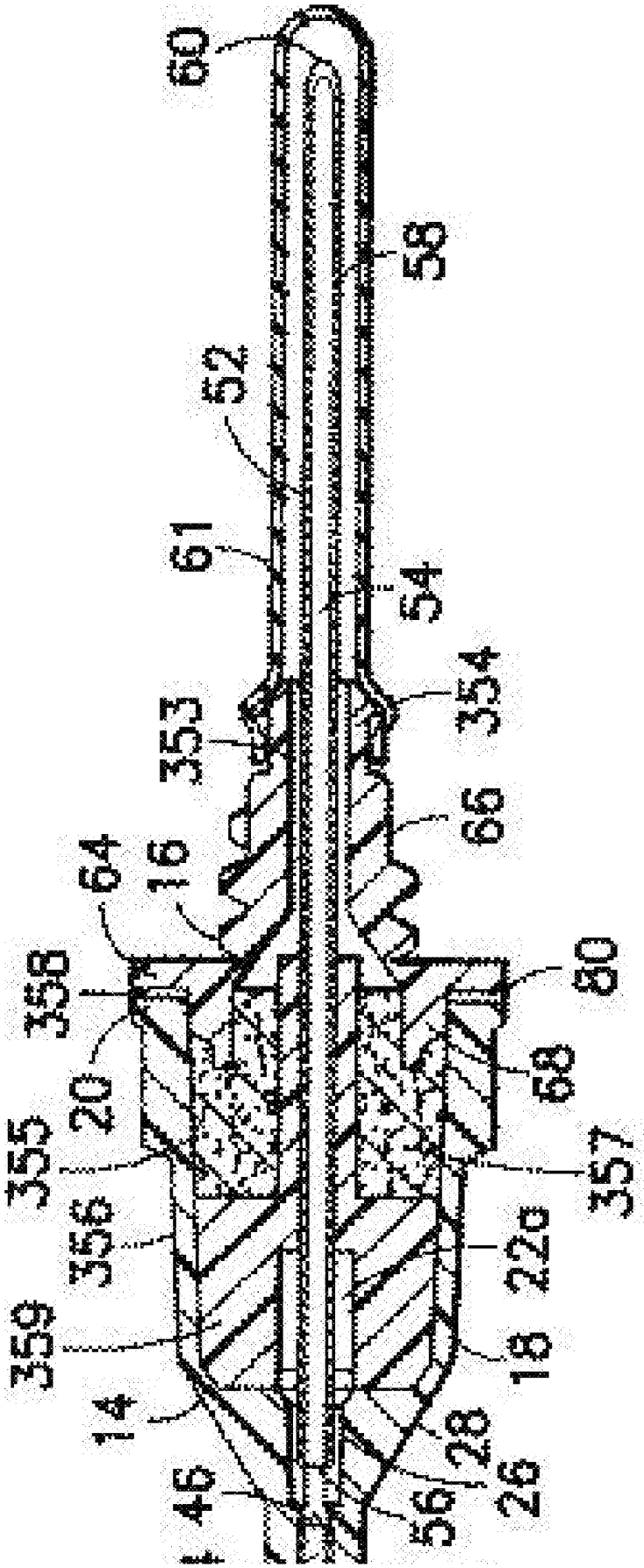
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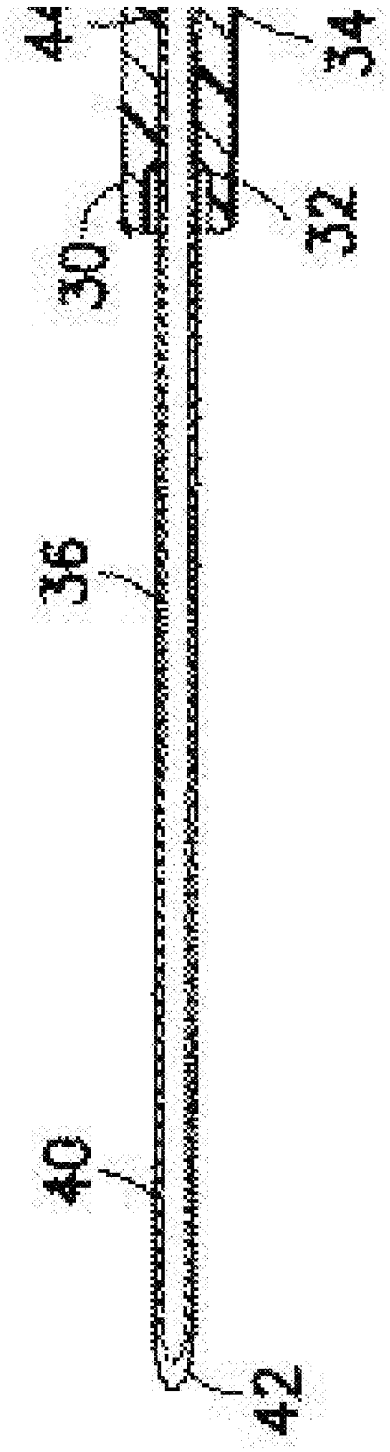

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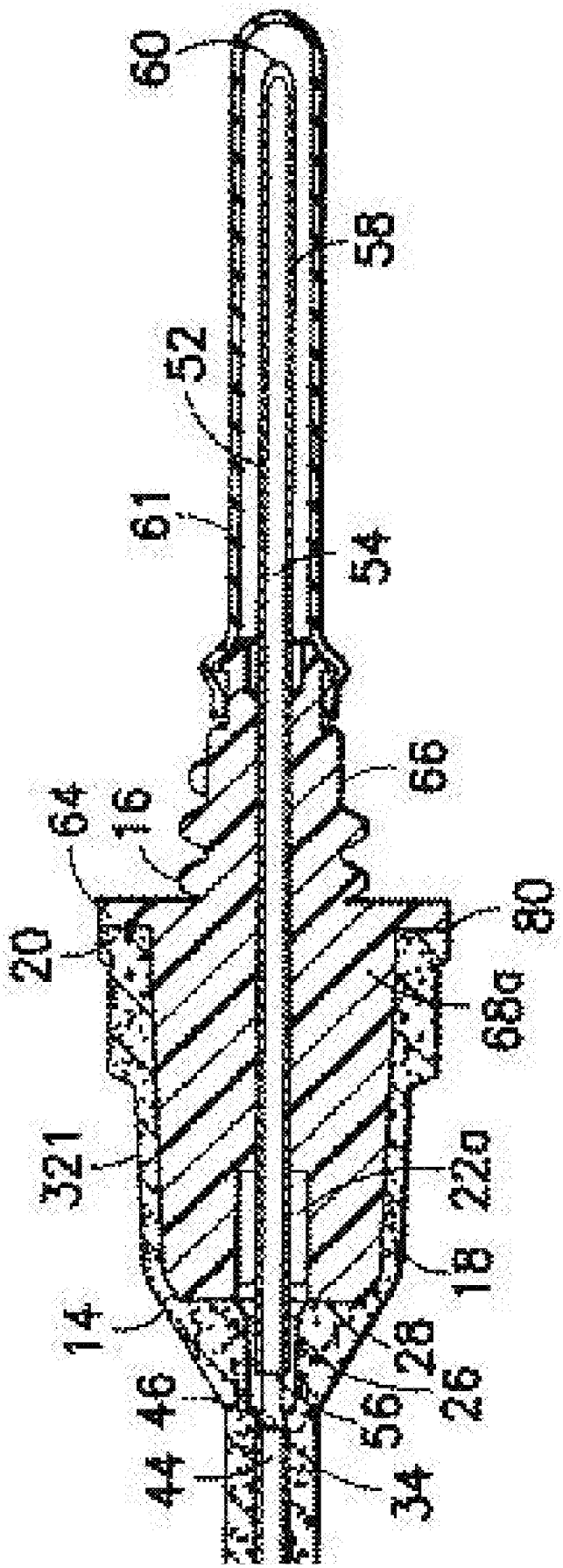
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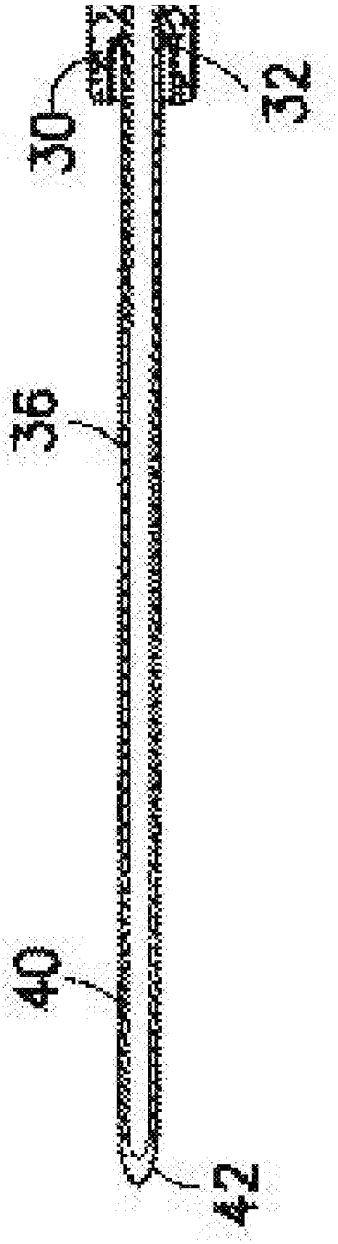

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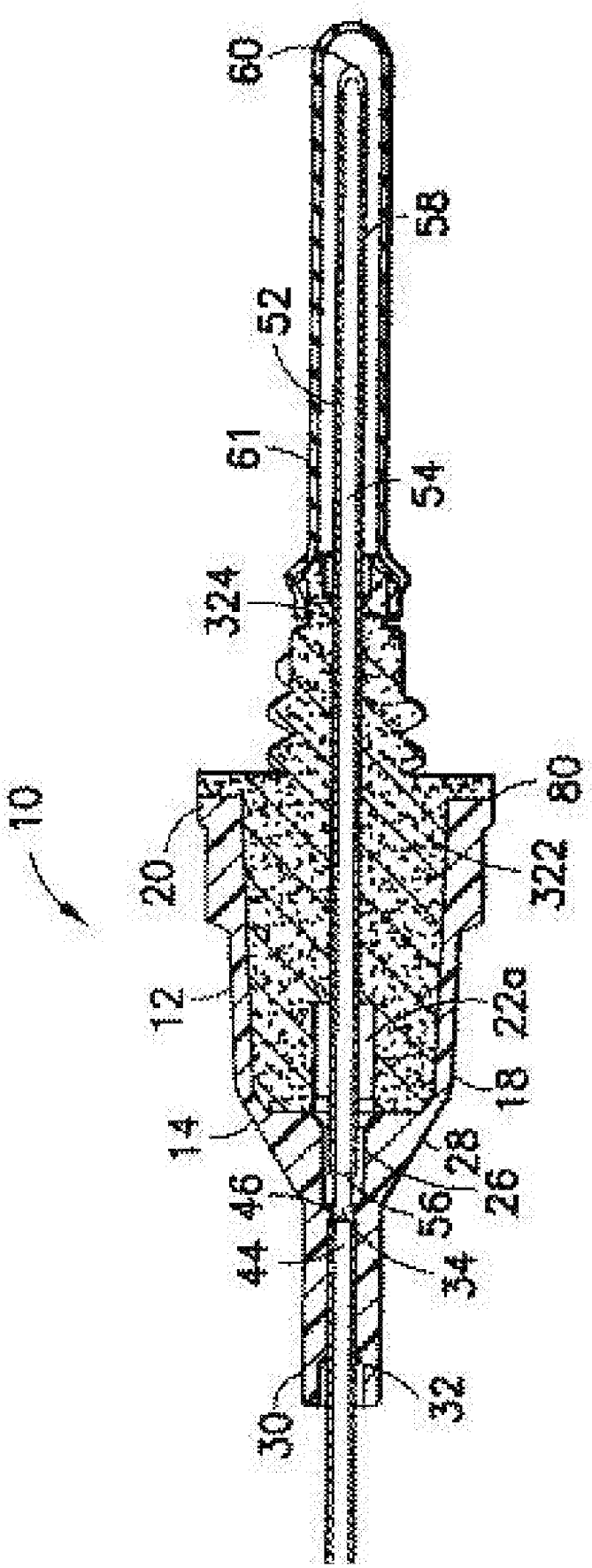
[Fig. 13]



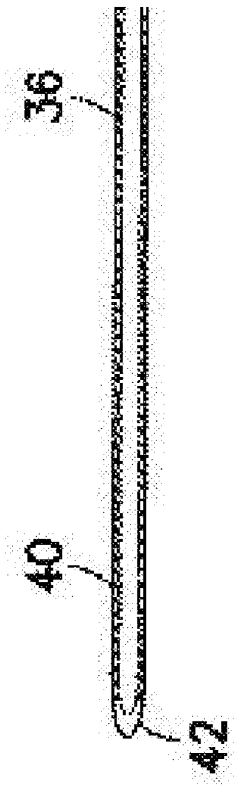

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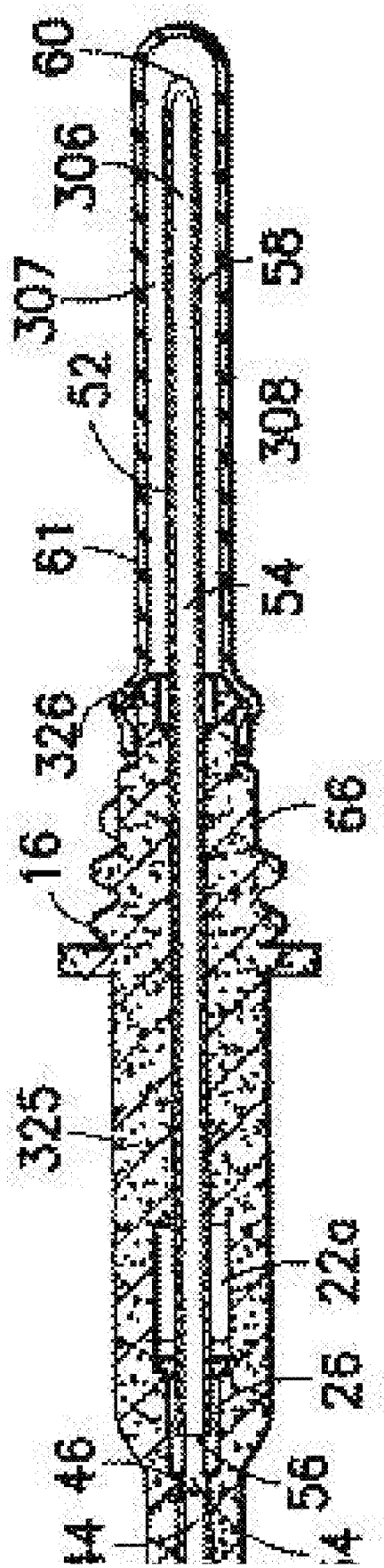
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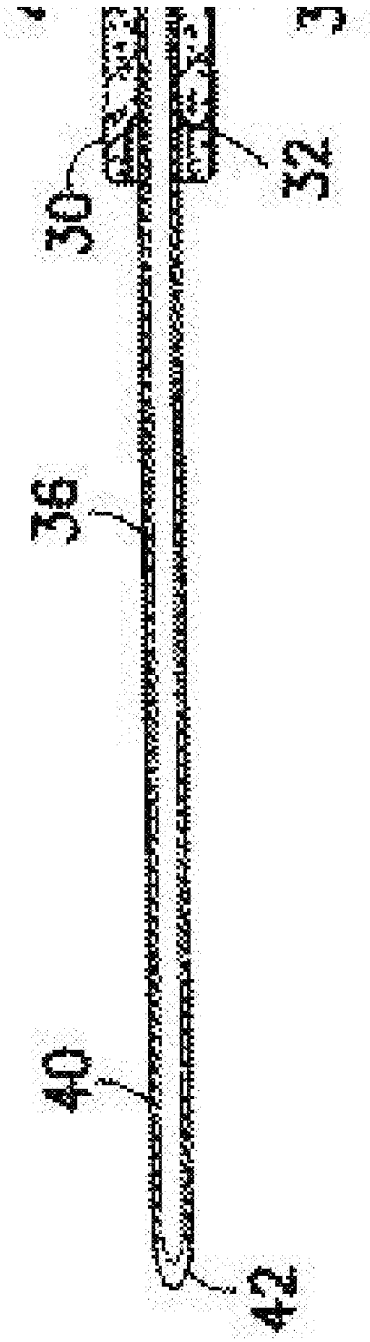

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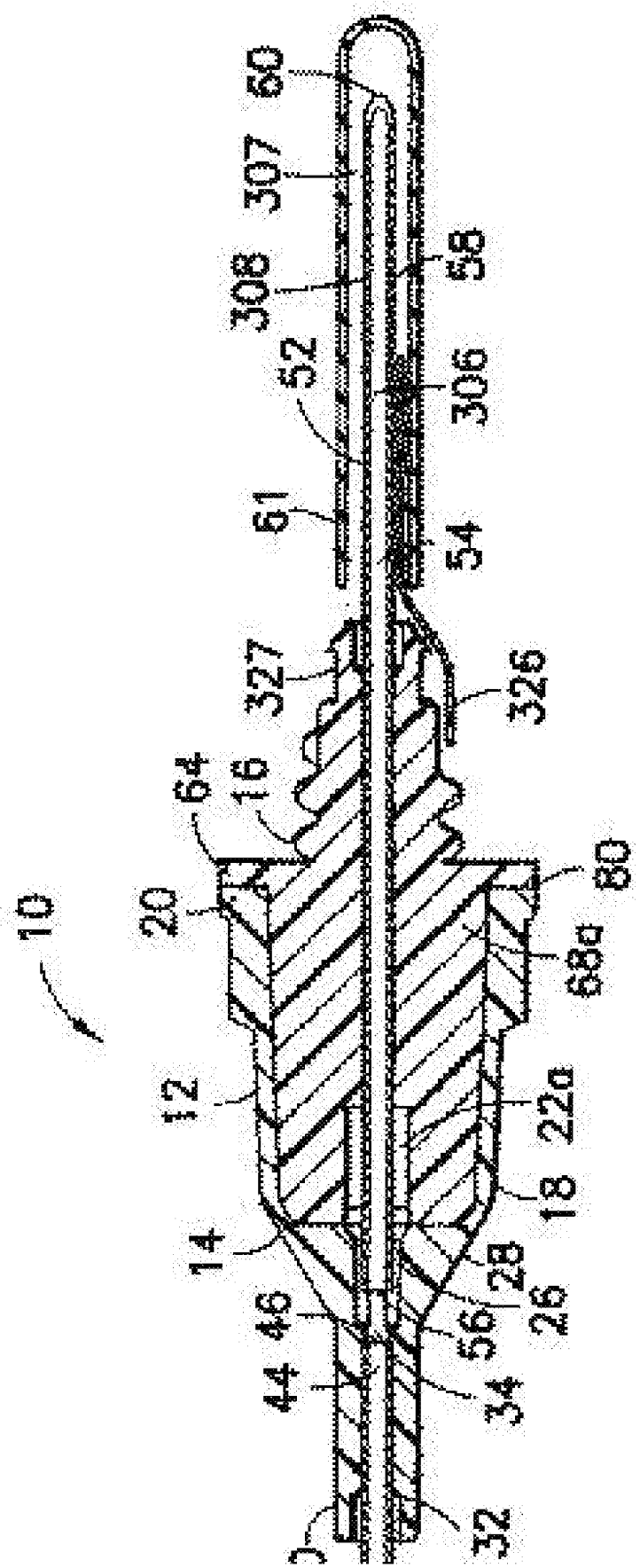
[Fig. 15]



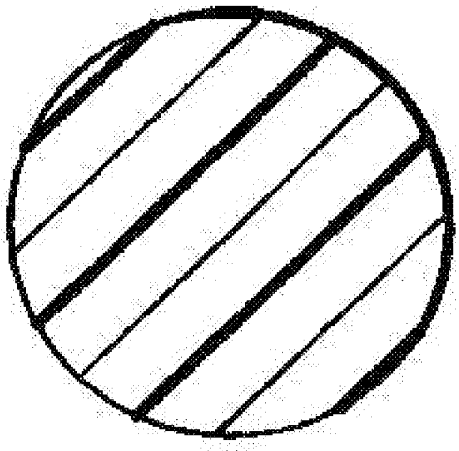

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[Fig. 16]

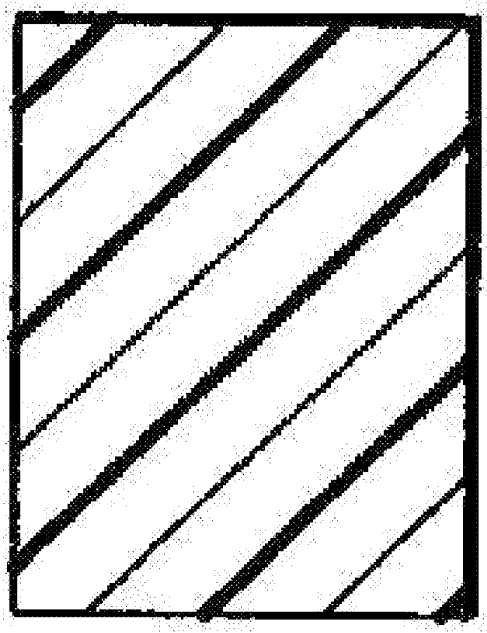



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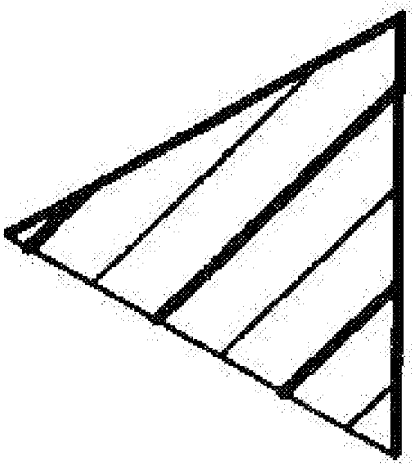
[Fig. 17]



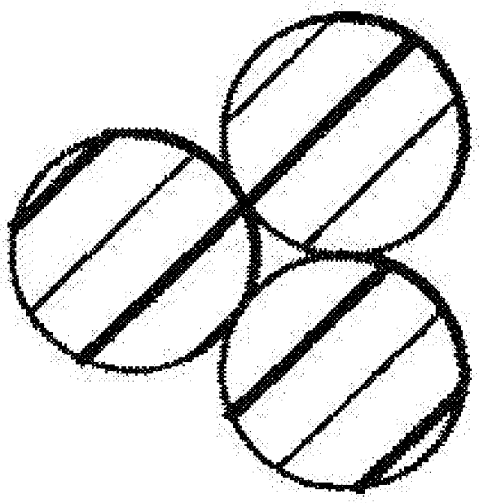
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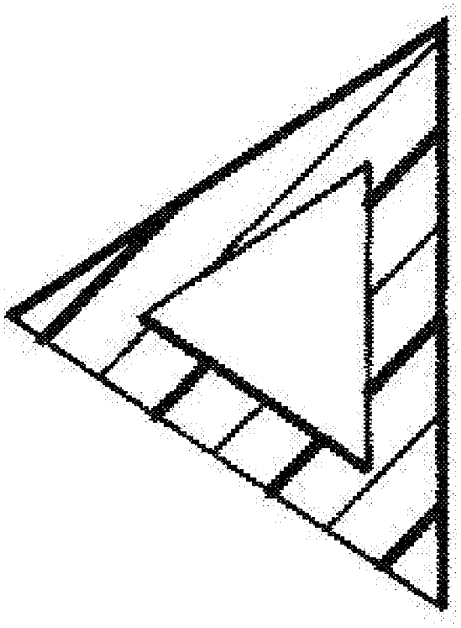
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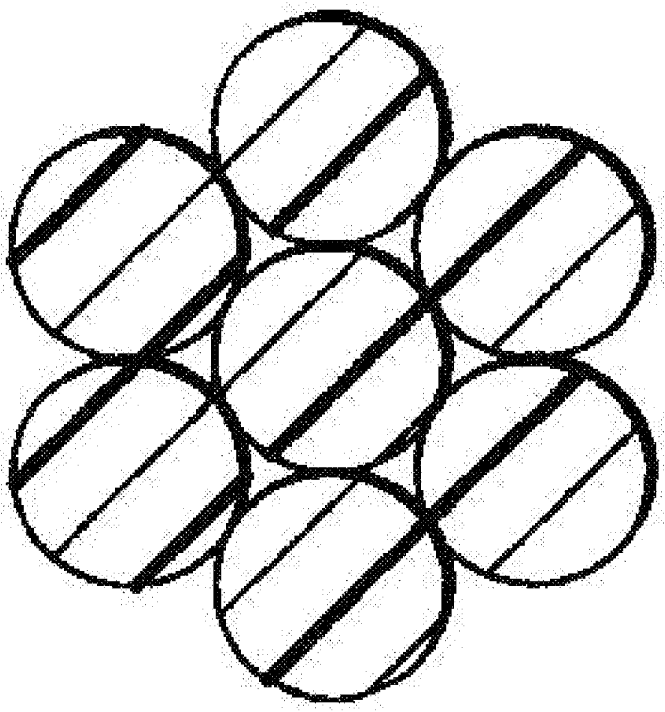
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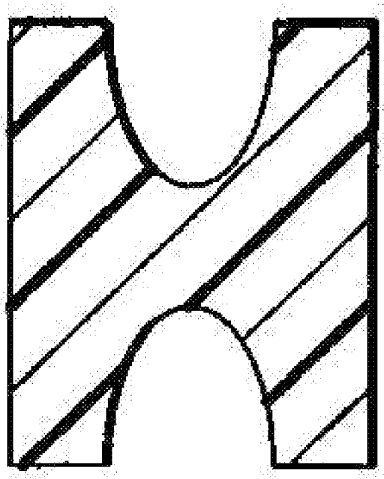
[Fig. 21]



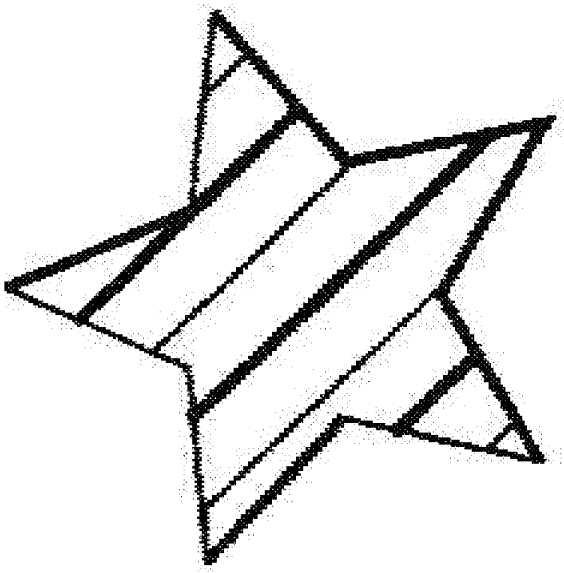
[Fig. 22]



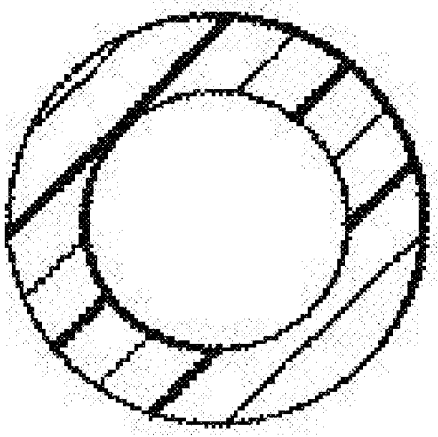
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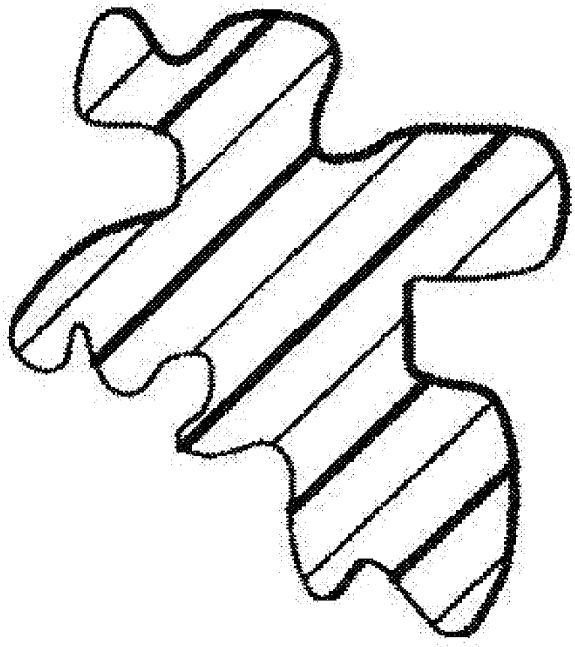
[Fig.24]



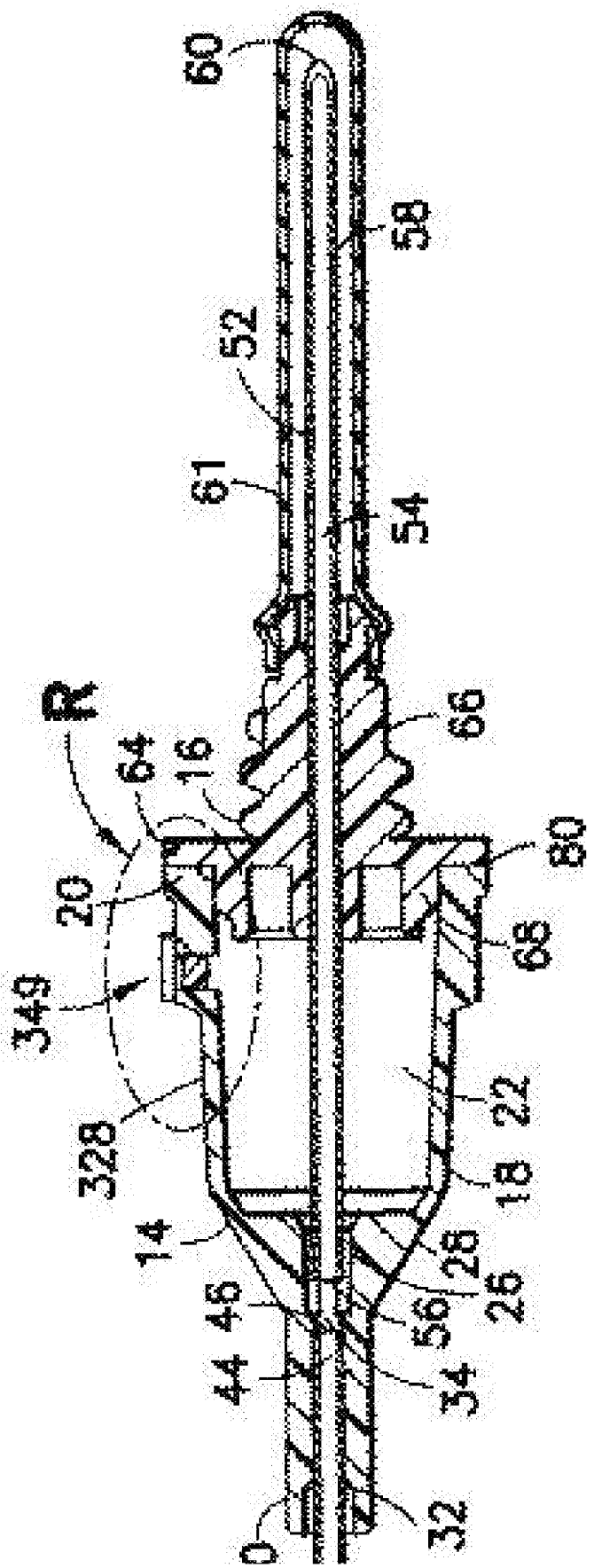
[Fig.25]



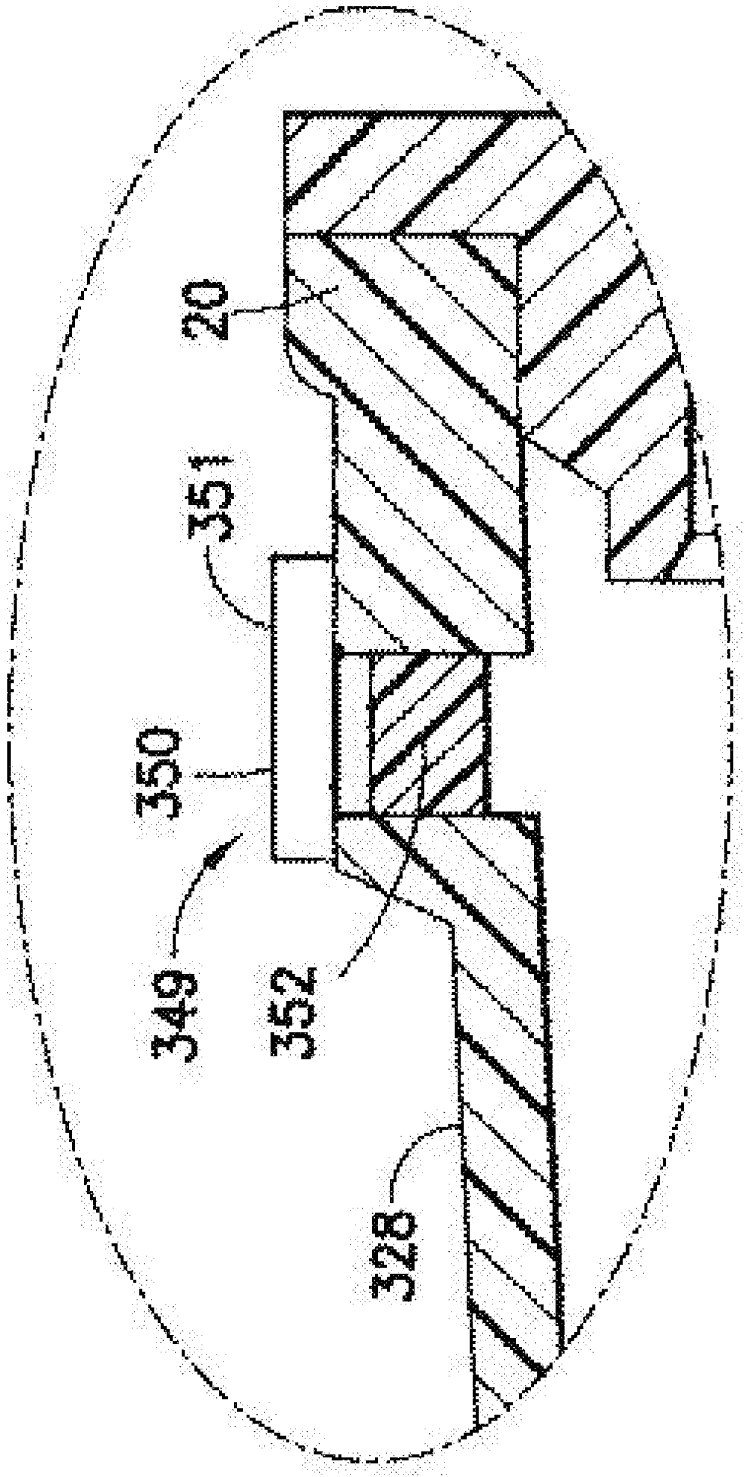
[Fig.26]



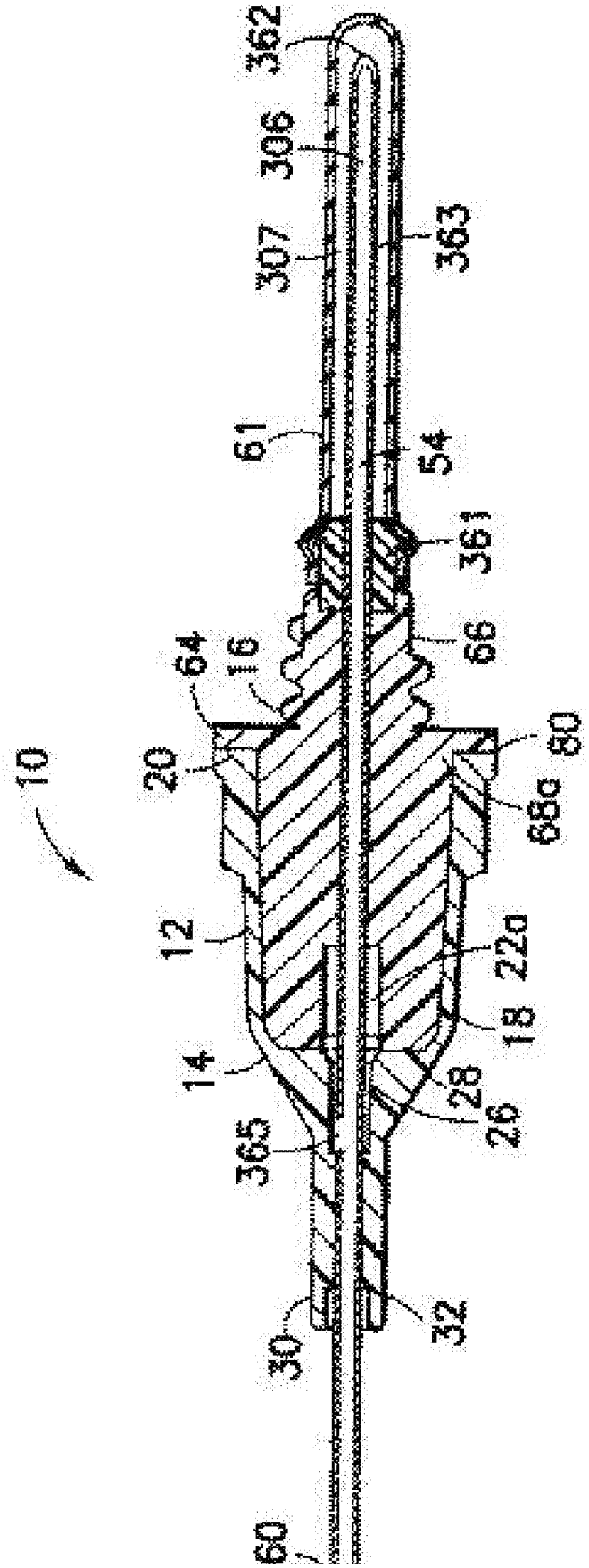
[Fig. 27A]


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[Fig. 27B]



[Fig.28]


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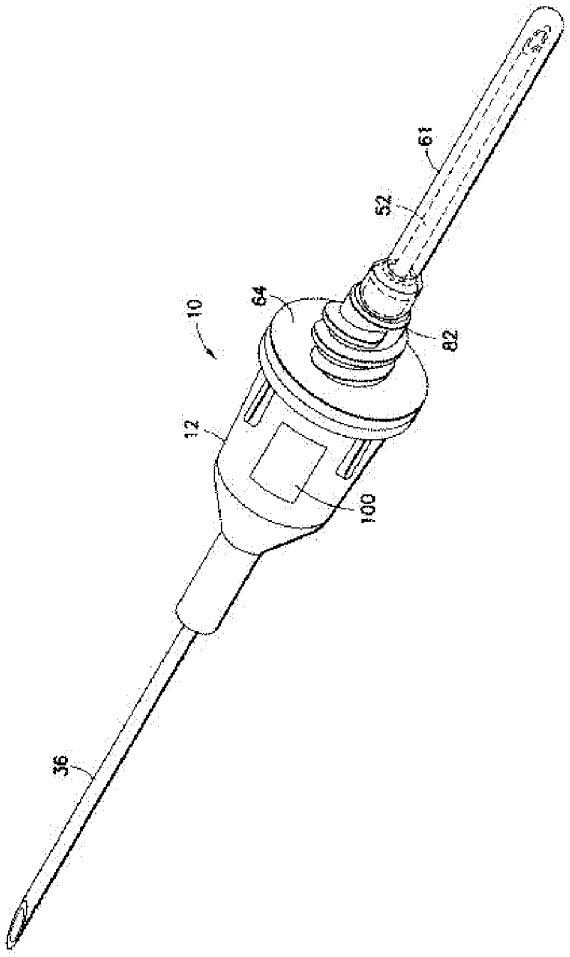
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FLASHBACK BLOOD COLLECTION NEEDLE

Inventor(s): NAIR HAREESH; SWENSON KIRK D; CONWAY HUGH T; NEWBY C MARK; BLOCH CURTIS; LEVY RICHARD; WILKINSON BRADLEY; SCHNEIDER JAMES C; TOWNS BRYAN; ISKRA MICHAEL; ELLIS ROBERT; BENNETT MICHAEL; MARSDEN STEWART ± (NAIR HAREESH, ; SWENSON KIRK D, ; CONWAY HUGH T, ; NEWBY C MARK, ; BLOCH CURTIS, ; LEVY RICHARD, ; WILKINSON BRADLEY, ; SCHNEIDER JAMES C, ; TOWNS BRYAN, ; ISKRA MICHAEL, ; ELLIS ROBERT, ; BENNETT MICHAEL, ; MARSDEN STEWART)

Applicant(s): BECTON DICKINSON CO ± (BECTON DICKINSON & CO)

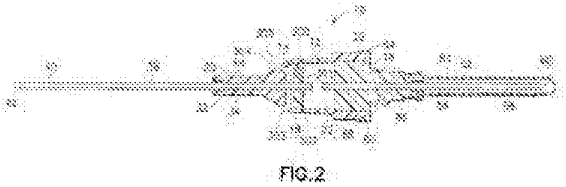
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- cooperative: **A61B5/15003 (EP, US); A61B5/150213 (EP, US); A61B5/150389 (EP, US); A61B5/150488 (EP, US); A61B5/150496 (EP, US); A61B5/150572 (EP, US); A61B5/150732 (EP, US); A61B5/1545 (EP, US)**

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Abstract of JP2005349196 (A)


FIG.2

PROBLEM TO BE SOLVED: To easily confirm that puncture is surely performed at the time of blood collection and to prevent an outflow of fluid such as blood. ;SOLUTION: The application refers to a self-venting blood collection needle assembly for the extraction of at least one fluid sample into an evacuated container for laboratory testing. This blood collection needle assembly provides a clear or translucent flashback chamber for the blood to flow into, for visualization by a user to confirm successful vein puncture. The self-venting mechanism permits escape of air during use, and which, typically, also prevents an outflow of fluid, such as blood. Thus, air under venous pressure will be allowed to escape from the blood collection needle assembly until the blood reaches the venting mechanism. ;COPYRIGHT: (C)2006,JPO&NCIPI

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(P2005-349196A)
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A61M	5/158	A61M	5/32		4C066
A61M	5/32	A61M	5/14	369F	
		A61M	5/14	369H	

審査請求 未請求　請求項の数 45　OL　外国語出願　（全 22 頁）

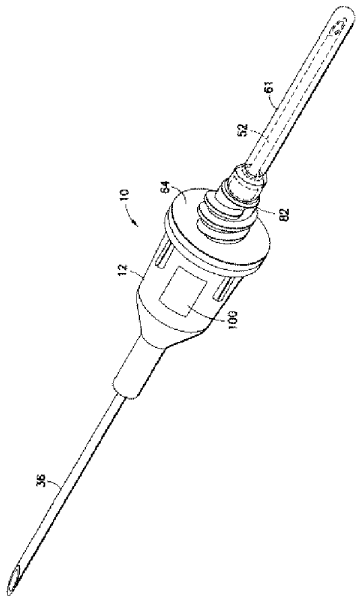
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(33)優先権主張国　米国 (US)

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最終頁に続く

(54)【発明の名称】フラッシュバック式血液採取針

(57)【要約】　（修正有）
【課題】血液採取時に穿刺が確実に行なわれていることを容易に確認でき、且つ血液などの流体の流出を防止する。
【解決手段】臨床検査のために減圧容器に少なくとも１つの流体試料を抽出する自己通気型血液採取針アセンブリであり、この血液採取針アセンブリは、血液を流入させて使用者が静脈穿刺がうまく行われたことを目視によって確認できる透明または半透明のフラッシュバックチャンバを提供する。この自己通気機構は使用の際に空気の放出を可能にし、且つ血液などの流体の流出を防止するように構成されている。こうして、静脈圧力下の空気は、血液が通気機構に到達するまでにこの血液採取針アセンブリから放出することができる。
【選択図】図１



【特許請求の範囲】
【請求項1】
入口端と、出口端と、これら両端の間に形成されたチャンバを有するハブと、
入口カニューレであって、前記ハブの外側にある末端と、この入口カニューレを貫通して延在し、前記チャンバと連通するように前記ハブに装着される内腔とを有する入口カニューレと、
出口カニューレであって、前記ハブの外側にある基端と、この出口カニューレを貫通して延在し、前記チャンバに連通するように前記ハブに装着される内腔とを有する出口カニューレと、
前記ハブの外側に位置する前記出口カニューレの部分を覆って装着されるマルチプル試料スリーブであって、前記入口カニューレの内腔と、前記チャンバと、前記出口カニューレの内腔と、このマルチプル試料スリーブの内面とが流体通路を形成するマルチプル試料スリーブと、
前記流体通路と外部雰囲気とを連通させる通気機構であって、針アセンブリからこの通気機構を介して外部雰囲気への空気の流出を可能にすると共に前記針アセンブリから前記通気機構を介して前記外部雰囲気への液体の流出を実質的に阻止する通気機構と、
を具え、前記入口および出口カニューレが別個のものであるか、または前記チャンバに連通する開口を持った１本のカニューレであることを特徴とする針アセンブリ。
【請求項2】
前記通気機構が前記ハブを介して延在していることを特徴とする請求項１に記載の針アセンブリ。
【請求項3】
前記通気機構が通気媒体を具えていることを特徴とする請求項２に記載の針アセンブリ。
【請求項4】
前記通気機構が前記ハブを貫通する少なくとも１つの開口を具え、該開口は通気栓を具えていることを特徴とする請求項２に記載の針アセンブリ。
【請求項5】
前記通気機構が逆止め弁をさらに具えていることを特徴とする請求項４に記載の針アセンブリ。
【請求項6】
前記通気機構が前記ハブを貫通する少なくとも１つの開口と、前記入口カニューレを取り囲む通気リングとを具え、該通気リングは前記チャンバ内の前記ハブを介して前記開口の近傍に位置していることを特徴とする請求項１に記載の針アセンブリ。
【請求項7】
前記通気機構が前記出口カニューレの基端を越えて前記通路に配されていることを特徴とする請求項１に記載の針アセンブリ。
【請求項8】
前記通気機構が通気媒体を具えていることを特徴とする請求項７に記載の針アセンブリ。
【請求項9】
前記ハブが非患者側係止突起をさらに具え、前記通気機構がこの非患者側係止突起を介して延在していることを特徴とする請求項１に記載の針アセンブリ。
【請求項10】
前記通気機構が通気媒体を具えていることを特徴とする請求項９に記載の針アセンブリ。
【請求項11】
前記通気機構が前記非患者側係止突起を貫通する通路と、この通路に配された通気栓とを具えていることを特徴とする請求項９に記載の針アセンブリ。

【請求項12】
前記通気機構が前記非患者側係止突起を貫通する切欠きと、通気円板とを具えていることを特徴とする請求項９に記載の針アセンブリ。
【請求項13】
前記通気機構が、前記非患者側係止突起を貫通する少なくとも１つの開口と、この開口に配された通気栓とを具えていることを特徴とする請求項９に記載の針アセンブリ。
【請求項14】
前記ハブが非患者側係止突起をさらに具え、この非患者側係止突起の少なくとも一部が前記通気機構を具えていることを特徴とする請求項１に記載の針アセンブリ。
【請求項15】
前記通気機構が通気媒体を具えていることを特徴とする請求項１４に記載の針アセンブリ。
【請求項16】
前記非患者側係止突起の少なくとも一部が多孔質疎水性材料で形成されているか、または前記非患者側係止突起の少なくとも一部が疎水性の表面を持った多孔質材料で形成されていることを特徴とする請求項１４に記載の針アセンブリ。
【請求項17】
前記通気機構が親水性材料を含浸させた多孔質材料を具えていることを特徴とする請求項１４に記載の針アセンブリ。
【請求項18】
前記ハブは、前記マルチプル試料スリーブがしっかりと装着される非患者側係止突起をさらに具え、前記通気機構が前記非患者側係止突起と前記マルチプル試料スリーブとの間に配されていることを特徴とする請求項１に記載の針アセンブリ。
【請求項19】
前記通気機構が通気スリーブを具えていることを特徴とする請求項１８に記載の針アセンブリ。
【請求項20】
前記通気スリーブが多孔質の疎水性材料を具えるか、または前記通気スリーブが疎水性表面を持った多孔質材料を具えていることを特徴とする請求項１９に記載の針アセンブリ。
【請求項21】
前記通気機構が通気可能な通気コードを具えていることを特徴とする請求項１８に記載の針アセンブリ。
【請求項22】
前記通気機構が織物面を具えていることを特徴とする請求項１８に記載の針アセンブリ。
【請求項23】
前記マルチプル試料スリーブが前記通気機構を具えていることを特徴とする請求項１に記載の針アセンブリ。
【請求項24】
前記通気機構が通気媒体を具えていることを特徴とする請求項２３に記載の針アセンブリ。
【請求項25】
前記マルチプル試料スリーブが多孔質の疎水性材料にて形成されるか、または前記マルチプル試料スリーブが疎水性表面を持った多孔質材料を具えていることを特徴とする請求項２３に記載の針アセンブリ。
【請求項26】
前記ハブが前記通気機構を構成するように、前記ハブの少なくとも一部が通気媒体によって形成されていることを特徴とする請求項１に記載の針アセンブリ。
【請求項27】

前記ハブが前記通気機構を構成するように、前記ハブの少なくとも一部が多孔質材料によって形成されていることを特徴とする請求項１に記載の針アセンブリ。
【請求項28】
前記ハブが非患者側ねじ山アセンブリとハブインサートとをさらに具え、これらを組み立ててリザーバを形成することを特徴とする請求項１に記載の針アセンブリ。
【請求項29】
前記通気機構が、前記非患者側ねじ山アセンブリを通って前記リザーバに達する第１通路と、前記リザーバから外部雰囲気に至る第２通路と、前記リザーバに配された通気栓とを具えていることを特徴とする請求項２８に記載の針アセンブリ。
【請求項30】
非患者側ねじ山アセンブリをさらに具え、この非患者側ねじ山アセンブリの少なくとも一部は、当該非患者側ねじ山アセンブリが前記通気アセンブリを構成するように、通気媒体によって形成されていることを特徴とする請求項１に記載の針アセンブリ。
【請求項31】
非患者側ねじ山アセンブリをさらに具え、この非患者側ねじ山アセンブリの少なくとも一部は、当該非患者側ねじ山アセンブリが前記通気アセンブリを構成するように、多孔質材料によって形成されていることを特徴とする請求項１に記載の針アセンブリ。
【請求項32】
前記通気機構が通気媒体を具えていることを特徴とする請求項１に記載の針アセンブリ。
【請求項33】
前記第１カニューレを選択的に被覆するシールドをさらに具えていることを特徴とする請求項１に記載の針アセンブリ。
【請求項34】
入口端と、出口端と、これら両端の間に形成されたチャンバとを有するハブと、
このハブの外側にあるように前記ハブに装着される末端と、基端と、これら両端の間に延在する内腔とを有するカニューレと、
前記ハブの外側に位置する前記カニューレの基端の部分を覆って装着されるマルチプル試料スリーブであって、前記内腔と、このマルチプル試料スリーブの内面と、前記チャンバとで流体通路を形成するマルチプル試料スリーブと、
前記流体通路と外部雰囲気とを連通する通気機構であって、針アセンブリからこの通気機構を通って外部雰囲気への空気の流出を可能にすると共に針アセンブリから当該通気機構を介して外部雰囲気への液体の流出を実質的に阻止する通気機構と
を具えたことを特徴とする針アセンブリ。
【請求項35】
前記通気機構が前記出口カニューレの前記基端を越えて前記通路に配されていることを特徴とする請求項３４に記載の針アセンブリ。
【請求項36】
前記通気機構が通気媒体を具えていることを特徴とする請求項３５に記載の針アセンブリ。
【請求項37】
前記ハブが非患者側係止突起をさらに具え、前記通気機構がこの非患者側係止突起を通って延在していることを特徴とする請求項３４に記載の針アセンブリ。
【請求項38】
前記通気機構が通気媒体を具えていることを特徴とする請求項３７に記載の針アセンブリ。
【請求項39】
前記通気機構が前記非患者側係止突起を貫通する通路と、この通路に配された通気栓とを具えていることを特徴とする請求項３７に記載の針アセンブリ。
【請求項40】

前記通気機構が前記非患者側係止突起を貫通する切欠きと、通気円板とを具えていることを特徴とする請求項３７に記載の針アセンブリ。
【請求項41】
前記通気機構が前記非患者側係止突起を貫通する少なくとも１つの開口と、この開口に配された通気栓とを具えていることを特徴とする請求項３７に記載の針アセンブリ。
【請求項42】
非患者側係止突起をさらに具え、この非患者側係止突起の少なくとも一部が前記通気機構を具えていることを特徴とする請求項３４に記載の針アセンブリ。
【請求項43】
前記通気機構が通気媒体を具えていることを特徴とする請求項４２に記載の針アセンブリ。
【請求項44】
前記非患者側係止突起の少なくとも一部が多孔質の疎水性材料にて形成されるか、または前記非患者側係止突起の少なくとも一部が疎水性表面を持った多孔質材料を具えていることを特徴とする請求項４２に記載の針アセンブリ。
【請求項45】
前記通気機構が親水性材料を含浸した多孔質材料を具えていることを特徴とする請求項３２に記載の針アセンブリ。
【発明の詳細な説明】
【技術分野】
【0001】
本発明は、患者に血管穿刺を行って血液試料を採取する装置に関する。さらに詳しくは、本発明は、患者から血液試料を減圧血液採取管に採取する場合、自己通気特性によって瀉血士が血管への穿刺ができたか否かを知ることができるマルチプル血液試料を採取するための針アセンブリに関する。
【背景技術】
【0002】
血管穿刺は臨床検査用の血液試料を得るのに用いられる主たる方法である。血管穿刺を行う場合、瀉血士は複数のステップを同時に行う必要がある。このステップとしては、患者の全体的な身体的および心理的状態を評価して、血管穿刺箇所と技術を適正に選択することを含む。瀉血士は、適正な対応器具を選び、出血を制御する技術を実行し、そして臨床検査用の流体試料を適正に採取し且つ特定することも必要である。これらの要因は血管の膨張と血管穿刺処置の長さに悪影響を与えるので、瀉血士はこれらの同時に起こる要因のすべてを確認しなければならない。
【0003】
前述の問題に対応するため、種々の血管穿刺装置が開発されている。これらの装置は、内部にチャンバを画成したハブを有する針アセンブリを含んでおり、両端が尖った１本のカニューレがこのハブに固定されている。このカニューレの血管側の端は患者の血管に挿入されるように構成され、このカニューレの非患者側の端は密閉可能なスリーブを有し、減圧容器内に配された突き刺し可能なストッパを突き刺すように構成されている。
【発明の開示】
【発明が解決しようとする課題】
【0004】
カニューレの血管側の端を血管に挿入すると、血液はカニューレを通って密閉可能なスリーブと、可視化（「フラッシュバック」）のために透明または半透明であるハブのチャンバとに流入する。ハブのチャンバから空気が排出されると、その中の血液は減圧容器の作用によって密閉可能なスリーブがハブのチャンバの方に押される度に加圧される。
【0005】
血管挿入とフラッシュバックとの間の時間差に起因して、血管穿刺が行われたことが即時に透明チャンバに示されなかったことによって、瀉血士は満足すべき血管への穿刺が得られなかったと誤って信じるかもしれない。そして、瀉血士は、減圧容器および／または

針アセンブリ自体の交換を必要とする血管穿刺を不必要に繰り返しことになる。このような処置の繰り返しは患者の受ける身体的、情緒的不快感を長引かせる。

【0006】

フラッシュバックが生じなかった場合、注射カニューレおよびフラッシュバックチャンバの空気がそこで圧縮されるので、針のハブ内の空気は静脈圧力まで加圧される。この加圧された空気は、何れかに排出されることが必要であり、そこで、血液採取が終了した後に注射針が患者から引き抜かれる時、この加圧空気は血液を注射針の先端の方に押し出す。

【0007】

従って、瀉血士が一貫してフラッシュバックを頼りにしている従来の血液採取方法に対し、迅速、正確且つコスト効果の高い解決策を提供し、満足すべき静脈への穿刺を行うことが望まれている。さらに、血液を比較的短い針を介してフラッシュバックチャンバに直接流すことができ、そして針アセンブリの内部から加圧された空気を排出することができる血液採取針アセンブリを提供し、それによって静脈への穿刺が成功し、このアセンブリからの血液の漏洩が無いことを直接的に示すことが、特に望まれている。ここで用いられるように、通気媒体は空気を実際に通す要素、例えば栓，被覆，表面処理などを示している。

【課題を解決するための手段】

【0008】

本発明は、少なくとも１つの流体試料を臨床検査用に減圧容器に抽出する自己通気型の血液採取針アセンブリであり、この血液採取針アセンブリは、静脈穿刺がうまく行われたことを使用者が目視によって確認するための、透明または半透明のフラッシュバックチャンバを提供する。この自己通気型機構は、使用の際に空気の放出を可能にするが、血液などの液体の流出は阻止する。ここで使用されている通気機構とは、空気を排出させるが、液体の通過を阻止する１つ以上の装置または要素のことを称する。従って、静脈圧力下の空気を、通気機構に到達するまでに血液採取針アセンブリから排出することができる。そしてこの通気機構は、これを迂回または通って血液が流れることを遮断または防止し、血液が減圧採取管その他の適宜な血液採取容器に採取されることを可能にする。本発明は、血液採取プロセスに悪影響を与えることなく、フラッシュバックチャンバ内における良好な瞬時可視化を提供する。以下に述べるように、好適な種々の通気機構，通気媒体または通気位置が存在する。

【0009】

少なくとも１つの流体試料を患者から採取して少なくとも１つの減圧容器内に引き続いて排出するため、自己通気型血液採取針アセンブリが提供される。本発明の自己通気型血液採取針アセンブリは、円筒状外壁によって画成された流体入口を有するハブを具えている。この壁は、ハブ内に血液試料を保持するためのフラッシュバックチャンバと、外から噴出が目視できるように透明または半透明の壁の少なくとも一部とを画成している。このハブは、流体入口端に連通する流体出口端をさらに具えている。この血液入口端に流体連通する第１の入口側カニューレがそこから外向きに延在している。この第の１カニューレはチャンバの基端に位置する内側基端と、これと反対側で患者の静脈を穿刺するように構成された外側末端とを有する。同様に、流体出口端に流体連通する第２の非患者側出口カニューレが配され、そこから外向きに延在している。この第２の非患者側カニューレは、前記第１の内側端の基端側に位置決めされた内側末端を有し、前記第２の内側端の反対側の外側基端をさらに具えている。この第２の非患者側外側基端は、減圧容器の突き刺し可能なストッパを貫通するように構成されている。第２の患者側カニューレは、さらに密閉可能なマルチプル試料スリーブを具えている。しかしながら、２本のカニューレの代わりに切欠きを含む１本のカニューレを使用することもできる。他の別なカニューレの構成は、非患者側カニューレの基端を通り、マルチプル試料スリーブを巡って通気孔を通った後、フラッシュバックが起こるように、切欠きの無い１本のカニューレを用いている。基端近傍のハブの外側部分は、一条の外側ねじ山、またはその他の装着構造で形成され、血液

採取針アセンブリを採取管ホルダその他の医療装置に装着することができる。あるいは、このホルダを針アセンブリに予め取り付けておくことができる。

【0010】

一実施形態において、通気機構はハブのフラッシュバックチャンバに配されている。前記２本カニューレ型構造または切欠き付き１本カニューレの使用は、この構成に適している。これによって、通気機構は、ハブを介して流体通路と外部雰囲気とを連通させる。

【0011】

他の実施形態において、通気機構が非患者側カニューレの基端を越えて配され、これは空気が、血液が吸引される非患者側カニューレの基端を通過し、次いで通気孔を通過することを意味する。この場合、切欠きを持たない１本カニューレが適しているが、あらゆるカニューレ構造が使用可能である。詳しくは、空気は針の外側とマルチプル試料スリーブとの間の空間を流れ、流体通路から非患者側カニューレの基端の外に排出される。次に、空気は、非患者側係止突起か、非患者側ハブのねじ山か、非患者側のハブ本体か、マルチプル試料スリーブか、またはその他の非患者側カニューレの基端を越えた位置やこれらの位置を組合せた位置にある通気機構を介して流れる。非患者側カニューレの基端に装着される採取管は、流体通路のみから血液を吸引し、通気空間からは吸引しない。従って、この実施形態は、採取通路全体を通して血液を流すことができる。これは、潜在的に血小板の活性化か、汚染またはその他の望ましくない結果をもたらす血液試料の通気孔への接触も防ぐ。これは、減圧管が装着された場合、空気が流体通路に逆に吸い込まれることも防止する。この実施形態は、通気孔がハブに配された前述の実施形態に比べて、小さな噴出チャンバしか必要でないことにも注目すべきである。

【0012】

本発明の別の実施形態は、少なくとも一部が焼結プラスチック，セラミックまたは金属などの多孔質材料で形成された一体化されたハブからなる通気機構を有している。この多孔質材料は、空気が非患者側カニューレに入る前か、または空気が基端を出てカニューレとマルチプル試料スリーブとの間の空間へと非患者側カニューレを通って流れた後の何れかに、排気が行われるように配置することができる。多孔質材料は空気の通気は行うが、血液の漏洩は阻止する。典型的な実施形態において、この多孔質材料は疎水性である。多孔質材料は、濡れると膨潤する材料をさらに含んでいる。他の通気方法も可能である。内部通路の壁面は、多孔質材料による血液試料の汚染を防ぐシーラントによってコーティングされてもよい。この実施形態は、全採取経路に亙って血液を流すことができる。ねじ山による接続の必要性や不便さを排除するため、必要に応じてハブは恒久的に管ホルダに接合することができる。このホルダへの接合は、溶剤，溶着，加熱，加圧または他の適当な手段、あるいはこれらの組み合せによって行うことができる。このようにして一体化された装置は効率よく製造され、ホルダが針と一緒に廃棄されることによって、医療行為の安全性を高めることができる。

【0013】

さらに別の実施形態において、通気機構はハブに配された側面開口を介して空気を外に排出するが、この開口は、当該開口内にまたは開口に接して機械的に保持されるような形状を有する通気材料によって覆われている。この通気材料は疎水性であることが好ましく、表面張力もまた漏洩を防止するようになっている。この実施形態の通気媒体材料は、ばねのエネルギーが通気材料をこの装置に対して保持するように、弾性的な性質および形状を有していることが好ましい。例えば、形状が捻じれるには通気媒体がハブ上の受け入れ構造の全体に亙って伸びることが必要なＣ字型形状の通気媒体を使用することができる。通気媒体が支持構造体に設置されると、通気媒体に吸収されて悪影響を与えることのあるエポキシなどの接合材料が無くても、それは解放されてそれ自体の弾性を用いて所定の位置に保持される。この実施形態の通気機構は、最初に通気用材料を圧縮し、この材料を開口に置き、そして通気用材料を解放して開口内で拡張させるようにしてもよい。

【発明を実施するための最良の形態】

【0014】

本発明は、血液などの流体の流出を防止すると共に空気の放出を助ける自己通気機構を具えた自己通気型血液採取用針アセンブリであって、患者から血液やその他の流体を１本以上の減圧血液採取管に採取する際、血管への挿入の可視的指示（「フラッシュバック」）を与えるアセンブリを提供するものである。

【0015】

通気媒体は、例えば栓やインサートなどの別の物理的要素か、レーザー穿孔などによって処理されたり全体的または部分的に多孔質材料にて形成される装置の一体部品か、あるいは例えば含浸，被覆，スプレーなどにより装置に対して材料を配することによって形成される膜や層などであってよいことに留意されたい。

【0016】

本発明の一実施形態にかかる血液採取針アセンブリを図１に示す。針アセンブリ１０は、一方の側に流体入口針（第１カニューレ）３６を、反対側に非患者側の流体出口針（第２カニューレ）５２を支えるハブ１２を具えている。第１カニューレから採取された流体はハブ１２を通り、半透明の窓１００を介してフラッシュバックチャンバ内で直ちにに見ることができ、通気機構の助けによる適正な血管穿刺が行われたことの適時な指示を与える。

【0017】

図２～図２８は、血液採取針アセンブリにおける通気機構の種々の構成を含む本発明の種々の実施形態を示す。特に、図２，図３，図４Ａ，図４Ｂおよび図４Ｃは、通気機構がハブの部分に配された実施形態を示している。図５～図１２は、通気機構が非患者側カニューレの基端６０を越えた所に配された実施形態を示している。図１３および図１４は、針のハブの一部が通気媒体として作動する実施形態を示している。図１５は、通気機構が単一化されたハブ１３２である実施形態を示している。図１６～図２６は、通気機構が通気性を有するコードである実施形態を示している。図２７Ａおよび図２７Ｂは、通気機構が逆止め弁である実施形態を示している。図２８は、１つの切欠き付きカニューレを具えた実施形態を示している。２本のカニューレがある以下の各実施形態において、１本の切欠き付きカニューレが同様に使用可能であることに留意されたい。

【0018】

図２，図３，図４Ａ，図４Ｂおよび図４Ｃは、第１カニューレ３６の基端３０１の周囲に通気リング３００を配した通気機構を示している。この通気リングは、フラッシュバックチャンバ３０２の内壁と締まり嵌めを形成する。従って、空気はこの通気リングを介して通気開口３０３から外部雰囲気へ放出できる。これらの開口をハブの末端のどこにでも配することができる。図２および図３において、これらの開口はハブ３０４の末端に配されている。図４Ａ，図４Ｂおよび図４Ｃには、通気開口が通気リング３００の末端側に当接する長手方向の通気窓３０５である別の実施形態が示されている。

【0019】

幾つかの実施形態は、非患者側カニューレの基端６０を越えた所に配した通気機構を具えている。この通気機構は、より小さなフラッシュバックチャンバ２２ａを用い、図２，図３，図４Ａ，図４Ｂ，図４Ｃなどの前述の実施形態に比べて、ハブアセンブリ１２から排気される空気の量を減らすのに有利である。次の実施形態は、より大きな環状フランジ６８ａを用い、より小さなフラッシュバックチャンバ２２ａを作っているが、別な設計でもよい。これらの設計の例は、フラッシュを見やすくするためのハブの表面に近い半透明／透明材料の窓および／またはフラッシュバックチャンバの一部である。特に切欠きの無い１本のカニューレを使用する実施形態の場合、フラッシュバックチャンバまたは窓を空気／血液通路に配することができることに留意されたい。

【0020】

図５の実施形態において、空気は流体通路３０６から非患者側カニューレの基端６０まで流れ、さらに針の外側３０８とマルチプル試料スリーブ６１の内側との間の空間３０７を通って、非患者側の係止突起３１０と空気の流出は許すが血液その他の流体は外部雰囲気へ流出させない通気栓３１１とで構成されている通気孔３０９の位置まで達する。

【0021】
図６，図７，図８Ａ，図８Ｂ，図９Ａ，図９Ｂ，図１０Ａおよび図１０Ｂは、通気機構が非患者側カニューレの基端６０の越えた所に設けられている実施形態を示している。図６および図７の実施形態は、非患者側の係止突起の少なくとも一部としても機能する通気栓３１２を示す。これらの図に示されているように、両方の実施形態では、通気孔の少なくとも一部が外部に接近しており、これを介して空気を排気する。図８Ａおよび図８Ｂは、非患者側の係止突起３１４における切欠き３１３が空気を通気用円板３１５に逃がすように構成された実施形態を示している。図９Ａおよび図９Ｂは、非患者側の係止突起３１４における切欠き３１６が通気栓３１７を含んでいる別の実施形態を示している。図１０Ａおよび図１０Ｂは、通気スリーブ３１９が空気を逃がすように改変された非患者側の係止突起３１８の構成を示している。各実施形態においては、通気機構（およびここに述べられた類似のエレメント）が空気を流出させるが、血液その他の流体が外部雰囲気に流出することは防止している。

【0022】
図１１は、非患者側のカニューレの基端６０を越えた所に設けられた通気機構の別の実施形態を示す。この実施形態によれば、空気は、非患者側のカニューレ５２からの流体の流出を防ぐマルチプル試料スリーブ３２０自体の材料を通って排気される。このマルチプル試料スリーブ３２０は、減圧採取管のストッパによって生じる力に応じて、非患者側カニューレ５２の尖った基端６０によって突き破られるその正常な機能を維持している。スリーブを前述のような多孔質の疎水性材料で形成することにより、通気孔としても機能するマルチプル試料スリーブ３２０を作ることができる。

【0023】
図１２は、空気が非患者側針５２の外側と非患者側係止突起３５４との間の狭い通路３５３を通り、次にベース６４と環状フランジ６８との間を通って通気媒体３５７を収容するハブ３５６のリザーバ３５５内に入り、ハブ３５６と非患者側ハブのベース６４との間の境界８０に設けた通路３５８を介して外部雰囲気に排出される別の実施形態を示している。ハブのインサート３５９がリザーバ３５５を形成している。

【0024】
図１３および図１４は、ハブ３２１または非患者側のねじ山付きアセンブリ３２２が多孔質材料で作られ、従って通気媒体として作用する通気機構を示している。図１３は、空気をハブ３２１の傾斜部２８を通って環状溝２６から周囲の大気中に排出する通気媒体としてのハブ３２１を示している。図１４は、通気媒体としての非患者側のねじ山付きアセンブリ３２２を示している。この実施形態は、空気をフラッシュバックチャンバ２２ａの壁に通し、次に非患者側の係止突起３２４を通して放出させることができる。

【0025】
図１５は、環状溝２６とフラッシュバックチャンバ２２ａの壁を通じ、且つ流体通路３０６を介して空気を逃し、非患者側のカニューレの基端６０から排出する多孔質材料の通気媒体で作られた一体化されたワンピース型のハブ３２５である通気機構を示し、空気はさらに針３０８の外側とマルチプル試料スリーブ６１の内側との間の空間３０７を通り、次いで非患者側係止突起３２６を通って周囲の大気中に流出する。一体化されたハブ３２５の性質によって、このホルダはねじ山を設けず、接合によって予めハブ３２５に装着可能である。しかし、図示のように必要に応じてねじ山を設けてもよい。管ホルダをこの一体型の非患者側のハブ３２５に接合するには、溶剤，溶着，加熱，圧力その他、従来からある手段やそれらの組合せが用いられる。

【0026】
図１６は、マルチプル試料スリーブ６１の密閉表面の内側と非患者側の係止突起３２７との間に設けられた通気性を有する通気可能なコード３２６の通気機構を示している。密閉表面にコードが設けられているので、空気は針３０８の外側とマルチプル試料スリーブ６１の外側との間の空間３０７から排出されるが、コードの材料の性質および／またはコードによって形成される通路の寸法が非常に小さいことによって流体の漏洩が防止される

。この機構を使用した通気は、通気媒体（例えば設置，被覆，処理などの）を流体通路３０６に沿って任意の１つまたは複数の密閉表面の間に位置させることにより行われる。図１７～図２６は、好適な通気性を有するコードの断面を示す。その他の形状やこれらの形状の組み合せも利用可能である。コードは押し出しや紡織などで作られ、そしてワックスなどの疎水性のコーティングを施すことが有利である。

【0027】

他の実施形態において、通気機構は流体通路に沿った何れかに配される逆止め弁を使用している。この弁は、空気を通過させるが真空がもたらされると閉じ、従って減圧採取管が針の先端に取り付けられると、この管は流体通路から血液を吸引するが、空気を吸い込まない。図２７Ａおよび図２７Ｂは、逆止め弁の一例を示す。この通気機構を流体通路３０６に沿った任意の箇所（単数または複数）に設けることができるが、好ましくはハブ３２８に設けられる。この弁３４９自体は、通気孔を被覆するプラスチックフィルム３５０などの薄いフラップ，変形可能なゴムなどのシール，またはプラスチック製ダックビル型の弁，通気孔を覆う変形可能なラップ，他の任意の手段，またはこれらの組み合せであってよい。この弁３４９は、通気孔に対して基端側または末端側に位置している。図２７Ｂに示した実施形態では、薄いプラスチックフィルムの弁３４９が、フィルム３５１の一方の密閉された縁に沿ってハブ３２８に取り付けられ、最初の静脈穿刺の際に、静脈圧力によって流体通路３０６から多孔質通気栓３５２を介して空気が押し出され、プラスチックフィルム３４９の固定されていない縁の下から出て行く。しかし、流体通路３０６に（血液採取管の取り付け部を介して）真空がもたらされると、薄いプラスチックフィルム３４９が多孔質通気栓３５２に対してぴったりと吸い付けられ、通気孔を密閉して空気が流体通路に再び入ることを防止する。こうして、この実施形態は、排気が行われた後でシステム内に空気が再侵入することを防ぐ、主たるまたはバックアップの機能を発揮する。

【0028】

図２８は、１本のカニューレ３６０と非患者側の係止突起として機能する通気栓３６１とを具えた血液採取針アセンブリを示している。このカニューレ３６０は、カニューレ３６０の孔３６５が環状溝２６の位置に設けられ、これとの流体連通を保つように、孔３４に位置している。カニューレ３６０が適正に位置決めされると、カニューレは孔３４と摩擦係合し、または接着剤などによってこれに固定される。静脈穿刺の際には、空気は流体通路３０６から流れ、カニューレの基端３６２から排出され、さらに針３６３の外側とマルチプル試料スリーブ６１の内側との間の空間３０７に流れ、通気栓３６１に達する。

【0029】

当業者ならば理解できるように、１つの装置に１つ以上の通気機構を組み合わせたり、同じ通気機構を１つの装置の１つの箇所に取り付けることが可能である。さらに、本発明の通気機構に種々の通気媒体の任意のものを使用することも可能である。さらに、ここに述べられた通気機構は、血液採取針アセンブリ以外の種々の装置にも適用可能である。

【0030】

ここで使用される通気媒体は、例えば

・水溶性または水を含む物質に接触すると膨潤する親水性材料がコーティングされ，含浸され，またはこれを含む一般的に疎水性の基材またはキャリア材料にて形成され、この膨潤可能な性質によって、血液に接触すると通気孔に密閉機能が与えられる多孔質栓か、

・艶消し仕上げ，微小寸法の通路，レーザー穿設孔，曲りくねった通路、多孔質材料によって設けられるか、または穴，間隙または通路が空気を通すには充分に大きいが、血液の漏洩を防ぐためには充分に小さい、例えばコードにおけるシール面の間に設けられる通気孔か、

・例えば通気孔を塞ぐ凝固および／または細胞の膠着による生物学的現象を利用し、血液と接触すると塞がる多孔質栓か、

・水性流体と接触して膨潤することにより、通気孔を密閉する超吸収性材料か、または

・逆止め弁：例えば通気孔を覆うプラスチックフィルムなどの薄いフラップ，ゴムまたはダックビル型弁の如き変形可能なシール，または通気孔を覆う変形可能なラップ

の何れかまたはこれらの組み合せを含むことができる。

【0031】

好ましくは、多孔質栓は、カルボキシメチルセルロース（ＣＭＣ）またはポリアクリレートなどの親水性材料によって被覆されるか、含浸させられるか、またはこれを含む高密度ポリエチレン（ＨＤＰＥ）などの疎水性材料にて形成される。代わりの疎水性材料として、これに限定されるものではないが、ポリテトラフルオロエチレン（ＰＴＦＥ），超高分子量ポリエチレン（ＵＨＭＰＥ），ナイロン６，ポリプロピレン（ＰＰ），ポリビニリデンフルオライド，またはポリエーテルスルホン（ＰＥＳ）が挙げられる。次にさらに詳細に説明されるように、本発明の通気媒体は、通気機構および装置に好適なものとして、艶消し仕上げされた１つ以上の微小寸法の通路，レーザー穿設孔，通気可能なコード，超吸収性逆止め弁，または他の手段、あるいはこれらの任意の組み合せを代わりに用いることができる。このように、例えば栓などの任意の特定な通気媒体についてここで述べているが、これらに限定するものではなく、他の通気媒体の適当な部材も含むことを意図している。

【0032】

通気媒体の一実施形態は、外壁に形成された微小寸法の孔からなる。これらの孔は空気を通すには充分に大きいが、血液の漏洩を阻止するには充分に小さい。この通気孔は、１つの孔を含む任意の数でよいが、信頼性のある機能のためには複数の孔が好ましい。これらの孔は、レーザーにて穿孔され、即ちこれらは１本以上のレーザービームを用いて壁を焼き切って貫通形成される。基板は普通の材料でよいが、薄いプラスチックフィルムが好ましい。通気機構は前述のように逆止め弁を含むことができる。この通気機構は注射器側または患者側カニューレ，ハブ，または付加された構成部品内の流体通路に沿った都合のよい任意の空間に設けられるが、管の全長に亙ってフラッシュを発生させるには、基端に設けられるのが好ましい。

【0033】

血液と接触すると生物学的現象によって密閉される多孔質栓は、例えば焼結プラスチック，セラミック，または金属の如き多孔質材料を用いるか、あるいは通気可能なコードを用いるか、または部品間の小さな孔や空間に生物学的薬剤を配置することによって用いることができる。この通気孔は従来からある任意の形状であってよい。通気は流体通路の任意の位置（単数および複数）で行われるが、採取装置に近いハブなどの基端が好ましい。通気孔は、凝固しおよび／または固まった細胞が通気孔を通過する流れを阻止するように、血液と相互作用して凝血および／または細胞の膠着を促進する刺激剤で作られ、これを含み、これと隣接し、またはこれと協同することが好ましい。凝血刺激剤の一例は、シリカ，破砕ガラス，またはガラス繊維である。膠着剤の一例はレクチンである。血小板賦活剤の一例はコラーゲンまたはトロンビンである。プロトミンスルフェートなどの抗凝固剤のための中和剤が含まれていてもよい。生物学的刺激剤は、粉末，溶液，懸濁液，スラリー，または他の形状として、都合の良い任意のプロセスを用いて付与することができる。これは乾燥、または真空凍結乾燥したものであってよい。

【0034】

当業者であれば本発明の範囲や精神から逸脱することなく、種々の他の変更や修正を行うことが可能であり、これらの変更や修正は、すべて本発明の範囲に入るものとして意図されるものである。

【図面の簡単な説明】

【0035】

【図1】血液採取針アセンブリの斜視図である。

【図2】本発明の血液採取針アセンブリの別の実施形態の断面図である。

【図3】図２と同様な側断面図であるが、本発明の別の実施形態を示している。

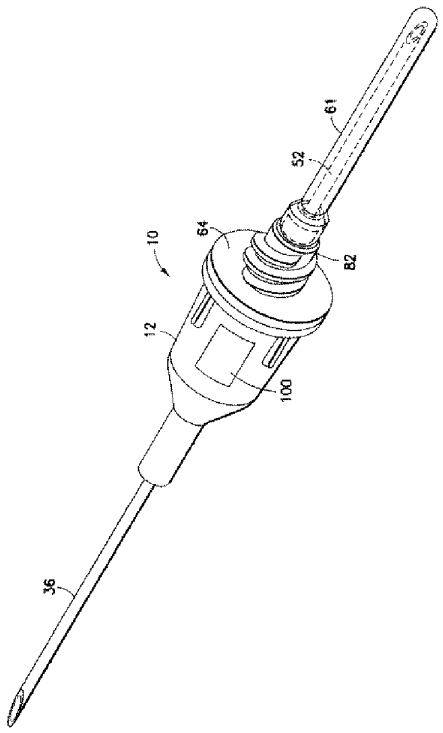
【図4A】図２と同様な側断面図であるが、本発明の別の実施形態を示している。

【図4B】図４Ｂの側面図である。

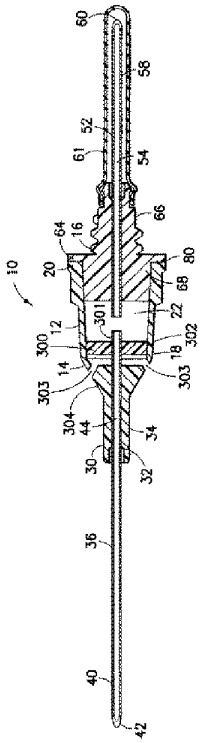
【図4C】Ｒ－Ｒの方向から見た図４ＢＡの正面図である。

【図5】血液採取針アセンブリの一実施形態の断面図である。
【図6】図５と同様な断面図であるが、本発明の別の実施形態を示している。
【図7】図５と同様な断面図であるが、本発明の別の実施形態を示している。
【図8A】図５と同様な断面図であるが、本発明の別の実施形態を示している。
【図8B】Ｘ－Ｘの方向から見た図８Ａの正面図である。
【図9A】図５と同様な断面図であるが、本発明の別の実施形態を示している。
【図9B】Ｙ－Ｙの方向から見た図９Ａの正面図である。
【図10A】図５と同様な断面図であるが、本発明の別の実施形態を示している。
【図10B】領域Ｚから見た図１０Ａの拡大図である。
【図11】血液採取針アセンブリの一実施形態の断面図である。
【図12】血液採取針アセンブリの一実施形態の断面図である。
【図13】血液採取針アセンブリの一実施形態の断面図である。
【図14】血液採取針アセンブリの一実施形態の断面図である。
【図15】血液採取針アセンブリの一実施形態の断面図である。
【図16】血液採取針アセンブリの一実施形態の断面図である。
【図17】通気可能なコードの一実施形態の断面図である。
【図18】図１７と同様な断面図であるが、本発明の別の実施形態を示している。
【図19】図１７と同様な断面図であるが、本発明の別の実施形態を示している。
【図20】図１７と同様な断面図であるが、本発明の別の実施形態を示している。
【図21】図１７と同様な断面図であるが、本発明の別の実施形態を示している。
【図22】図１７と同様な断面図であるが、本発明の別の実施形態を示している。
【図23】図１７と同様な断面図であるが、本発明の別の実施形態を示している。
【図24】図１７と同様な断面図であるが、本発明の別の実施形態を示している。
【図25】図１７と同様な断面図であるが、本発明の別の実施形態を示している。
【図26】図１７と同様な断面図であるが、本発明の別の実施形態を示している。
【図27A】血液採取針アセンブリの一実施形態の断面図である。
【図27B】領域Ｒから見た図２７Ａの拡大図である。
【図28】血液採取針アセンブリの一実施形態の断面図である。

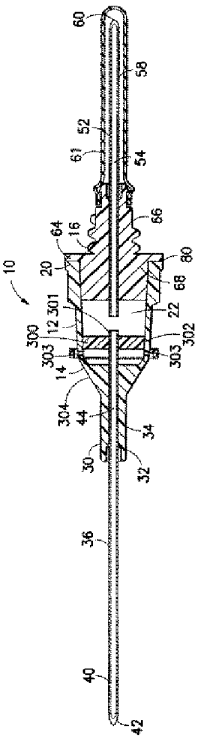
【図1】


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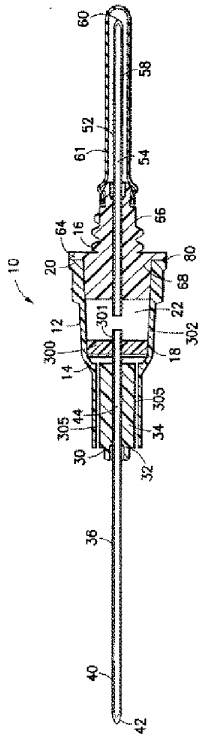
【図2】


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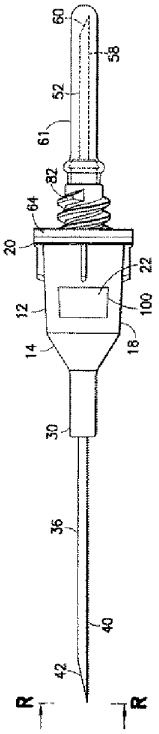
【図3】


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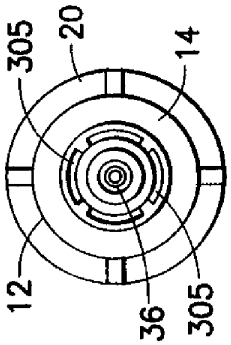
【図4A】


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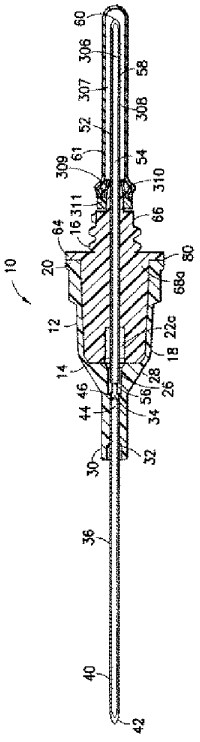
【図4B】


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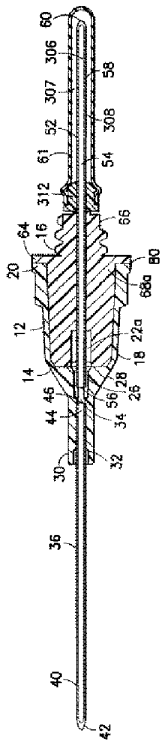
【図4C】


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305

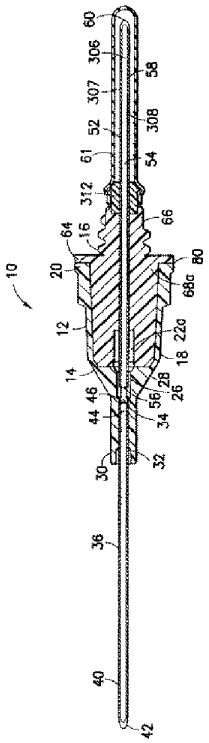
【図5】


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311
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68a
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22c
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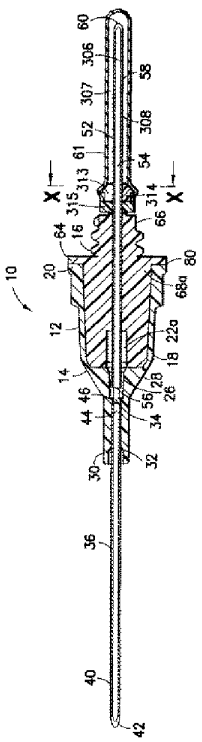
【図6】


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22a
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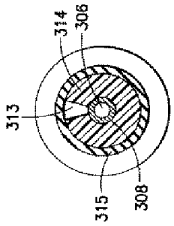
【図7】



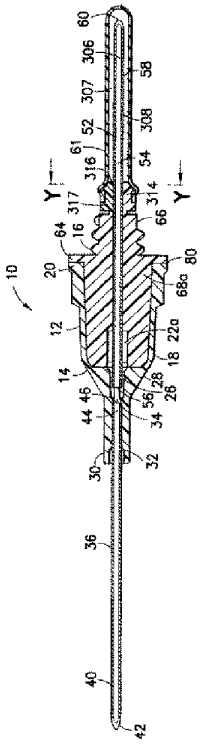
【図8A】



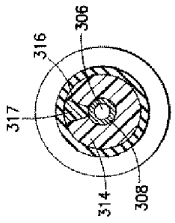
【図8B】



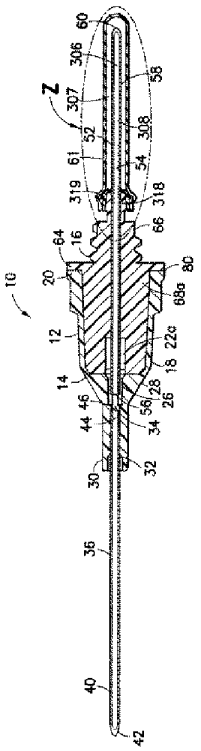
【図9A】



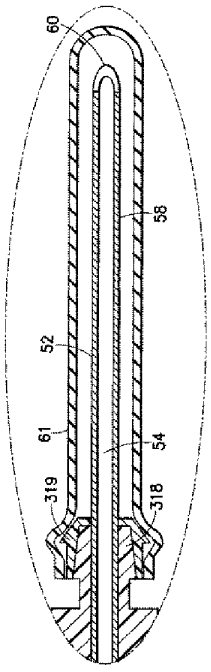
【図9B】



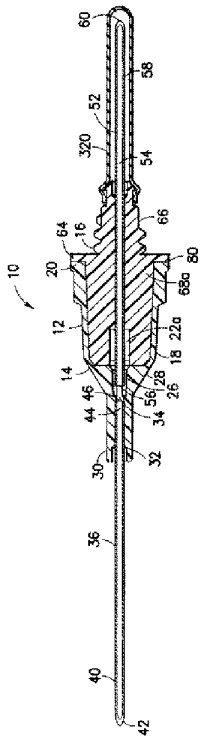
【図10A】



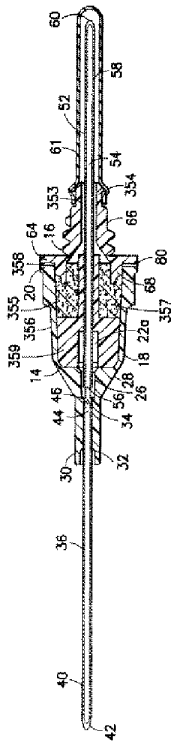
【図10B】



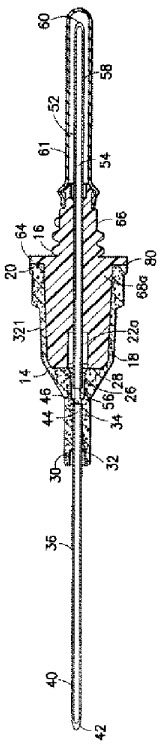
【図11】



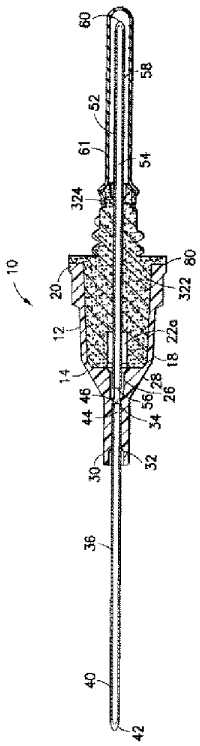
【図12】



【図13】



【図14】



【図15】

